

Update on Management of Astigmatism after Penetrating Keratoplasty

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ABSTRACT

There are several therapeutic options in the management of astigmatism after Penetrating Keratoplasty (PK). New publications continue to present improvements to established approaches as well as the development of new therapeutic possibilities and new technologies. This study reviews the most recent publications on astigmatism management after PK to guide a more updated management.

INTRODUCTION

Due to the immunological privileges of the cornea, corneal transplantation is the most common type of allograft in the world [1]. Keratoplasty is indicated in pathologies that affect corneal transparency or drastically reduce its refractive functionality, such as in advanced keratoconus. Even though surgery is successfully performed in most cases, making the transplanted cornea reasonably regular with an useful residual refraction may be more difficult than leaving it transparent. Corneal astigmatism is still the main cause of decreased visual acuity after PK [2]. When significant astigmatism is present, it compromises the resulting visual acuity. Even with a mastered surgical technique, this undesirable complication can occur.

Some surgical and non-surgical procedures are available to manage unsatisfactory results and ensure visual improvement. Approximately 10% of patients that undergo PK require further surgical intervention [3]. Newer surgical techniques, such as anterior lamellar transplants, may minimize intraoperative and postoperative complications but do not overcome other problems, such as residual astigmatism. Much has been published to minimize this and this review focuses on the current available management of post-keratoplasty corneal astigmatism. We present the main treatment options, ranging from suture removal to newer surgical techniques.

CAUSES OF ASTIGMATISM IN PENETRATING CORNEAL TRANSPLANTS

There are numerous causes of astigmatism following corneal transplant. These include oval or oblique trephination, retained donor or recipient Descemet's membrane, disparity in size or thickness between the donor and recipient, vascularization or diseases in the periphery of the recipient cornea, irregular healing and unbalanced tension of the sutures [4]. It is worth mentioning that the main indication for PK globally is still keratoconus. Therefore, the cornea to be trephined may have peripheral deformation. These localized abnormal areas may cause premature suture loosening, with induction of asymmetric and irregular astigmatism [5].

Additionally, in some cases, there may be scar formation that extend to the periphery, generating tissue retraction and deformity of the trephination contour, inducing postoperative astigmatism [6]. The peripheral vascularization of the corneal graft generates a greater migration of fibroblasts and, as a result, more intense fibrosis, causing imbalance of healing and induction of delayed irregular astigmatism [5,6].

MANAGEMENT OF CORNEAL TRANSPLANT ASTIGMATISM

Intraoperative

Surgical technique: Intraoperative adjustments are recommended to achieve better visual rehabilitation and refractive outcomes. The type of trephination is crucial for surgical success. Horizontal alignment of the limbal plane is mandatory, as well as the selection of the graft size to be transplanted.

Vacuum trephines help to minimize the chance of edge irregularities, eccentric trephination of the corneal tissue, as well as, assist in the congruence between donor/recipient. Some studies have shown that one way to reduce the myopic spherical equivalent of keratoplasty candidates is by performing trephinations of the same diameter (donor and recipient) [7,8]. This difference was demonstrated as a factor that influences the degree of astigmatism after suture removal. However, there is still debate about this and Satitpitakul [9] et al showed that there was no change in astigmatism related to this parameter.

Mechanical trephination can lead to torsions induced by radial and tangential forces, which can create irregular edges in the corneal tissue, generating discrepancies between the recipient and donor cornea. Olson [10] reported that 0.1 mm of tissue disparity at the graft-host junction can induce up to 4 D of astigmatism. Van Rii [11] concluded that the trephination of the recipient cornea results in a larger size than the diameter of the trephine used. In addition, this diameter is larger at the level of the Descemet membrane, resulting in divergent cutting angles, which may interfere with postoperative astigmatism. This is explained as a result of the ballooning effect of the cornea caused by increased pressure during the act of trephination. This mechanism is one of the main disadvantages of a mechanical trephine [12].

Punching of the donor cornea should be performed preferably through the epithelial side, with the use of an artificial anterior

chamber. This way, the incision matches the direction on the recipient [12]. Regular, circular and central trephination is crucial to achieve post-operative refractive success. To help achieve this, the use of femtosecond or excimer lasers may improve surgical micromanipulations producing more precise incisions and bringing more reproducibility and regularity in trephination of corneal tissues [13-15].

Seitz B et al [16] demonstrate that excimer laser has better results in visual acuity, less myopia and astigmatism after suture removal, compared to the mechanical trepanation technique. The benefit of the use of femtosecond laser exceeds the improvement in trephination precision. This laser allows custom cut architectures (zigzag, mushroom, top hat, Christmas tree) that may improve surgical outcomes [17]. Li et al [18] have shown lower keratometry values in the postoperative period when the femtosecond laser was used. Other studies [19-21] comparing M-DALK (manual DALK) to F-DALK (femtosecond laser-assisted DALK) report that there was no significant difference in residual astigmatism at 12 or 24 months after surgery.

The correct positioning of the first 4 cardinal sutures has a significant impact in the residual astigmatism. They help the coaptation of the graft tissue and the stabilization of the anterior chamber to allow the correct positioning of the remaining sutures with proper tension.

Corneal sutures work as vectors. Thus, it is desired that, at the end of surgery, the sum of the forces induced by all stitches is close to zero. The ideal depth should be 90% of the corneal stroma in both the recipient and the donor, thus helping to avoid the formation of steps or asymmetry [22]. The type of suture in corneal transplants also has a great influence on the refractive results. Continuous suture presents some advantages such as faster execution, less inflammatory reaction and less astigmatic induction, however it cannot be removed until full healing is completed. For this reason, when there is significant astigmatism postoperatively, its control is harder when compared to interrupted sutures [23]. Nevertheless, continuous suture allows for readjustment of the thread tension by relaxing the sutures on the steeper meridian and tightening them over the flatter axis [22].

Postoperative

Spectacles and contact lenses: The most used and conservative methods of controlling postoperative corneal astigmatism are spectacles and Contact Lenses (CLs). We know that spectacles offer insufficient correction for larger and/or irregular astigmatism. It is worth noting that in the presence of significant anisometropia, its use is further limited [24]. Another option is the use of Rigid Gas Permeable (RGP) CLs to achieve a better visual acuity and obtain binocularity. However, their fitting may be challenging due to the irregular corneal graft profile, which is usually flat centrally and steep in the periphery. In addition, large variations in corneal curvature and asymmetry can lead to CLs decentration and intolerance. Newer variations and adjustments in the design of RGPs have increased the success of CL fitting. The introduction of multicurved lenses and the possibility of increasing their diameter are innovations that have facilitated their use. It is worth mentioning that the use of hydrogel lenses is ineffective in correcting irregular or highly astigmatic corneas [25]. Additionally, with these lenses there is a higher risk of reducing oxygen supply to the graft, which would cause ischemia and a greater risk of transplant rejection [25,26].

In some cases, the use of scleral lenses can substantially improve visual quality. Scleral lens designs have recently regained popularity and have opened new perspectives for RGP fitting over irregular corneas. Fitting can be done based on the types of scleral lenses: spherical lens, lens with toric anterior surface, lens with toric periphery, and lens with toric periphery and toric anterior surface simultaneously. These CLs have greatly facilitated the visual correction of irregular astigmatism and improve patient satisfaction [27].

Selective suture removal: The cornea has elastic and viscoelastic biomechanical properties that represent the ability of corneal tissue to deform reversibly under tension [28]. These properties can be altered when placing corneal sutures or removing them. Selective suture removal is one of the crucial steps to control post-operative corneal astigmatism. However, the effect of this removal is unpredictable, ranging from a significant decrease to an unexpected increase in astigmatism. The selective removal of corneal sutures should be performed in the steepest meridian aiming to flatten it. The keratometry value prior to suture removal is the most important factor in

achieving a reduction in postoperative astigmatism. Other factors can influence the astigmatic change such as time interval from surgery, difference in donor-receptor trephination size and corneal transplant indications [29].

Satitpitakul et al [9] showed that there is a 1.05 D reduction in astigmatism for each suture removed. These findings help to predict the amount of astigmatic change in the cornea after suture removal and avoid unnecessary suture removal, which can lead to complications such as worsening vision, graft rejection, retained suture material, infection and wound dehiscence [30,31]. Removing only one suture at a time can bring better results when compared to removing multiple simultaneous sutures [32,33]. In addition, there is no correlation between astigmatic alteration and suture removal time (6 to 95 months) [9]. This finding is consistent with various studies [29,34] using vector analysis to calculate optical changes after suture removal. Therefore, when astigmatism is reduced to an acceptable level and with satisfactory visual acuity, as long as they remain intact, the remaining sutures should be left in situ for at least 95 months. This avoids undesirable astigmatic changes [9].

There are controversies as to the ideal time that sutures should be removed. Most authors agree that after 6 months of surgery there is already good healing, to remove the first sutures [35,36]. Sarhan et al [36] showed that there was no significant astigmatic difference between 30-40 min after suture removal and after 4-6 weeks without removing additional sutures (mean 4.37 D and 4.24 D respectively). Hence, it is suggested that removing a second set of sutures in the same follow-up visit would speed up visual rehabilitation, besides reducing the number of visits during the post-operative period. Topical antibiotic and steroids should be used after every episode of suture removal to avoid infection and/or graft rejection [37]. After initial removal, non-adjacent sutures can be removed every 4-6 weeks, as needed [38,39]. Another important point is to avoid pulling the suture knot through the Graft-Host Junction (GHJ), especially when done in the early postoperative period. This could lead to dehiscence of the GHJ. In general, the purpose of selective suture removal is to make astigmatism a little more regular to allow satisfactory visual acuity, either with glasses or CLs.

Astigmatic keratotomy: Astigmatic keratotomy aims to flatten the steep corneal meridian through one or two relaxing peripheral incisions. These incisions can be transverse or, more often, arcuate. Simultaneously with the flattening caused by the incision in the steep axis, there is a steepening of the axis located at 90° through the so-called coupling effect [40]. This steepening can be increased by the use of traction sutures in the flatter meridian, which usually aims an overcorrection in order to control the astigmatism by selective removal of the sutures later. The relaxing incisions can be made in the donor, GHJ or in the host cornea, but the latter is not recommended because it is believed that the GHJ works as a new limbus and decreases the effect of the incision in the corneal center [41]. Not only the location, the depth and the extent of the incisions may vary the treatment effect, the age and gender of the patient are factors that can influence the resulting astigmatic change [42,43]. The incisions can be performed manually, with a diamond knife, with a Hanna arcutome or with a femtosecond laser.

The incisions made with femtosecond laser are more precise and reproducible than those made with the manual technique. Previous studies comparing astigmatic keratotomy between patients using the manual technique and the femtosecond lasers showed better visual results with the latter, although with no statistical significance [44-46].

A problem associated with astigmatic keratotomy is the unpredictable results, which can be explained by the multiple variables related to the incisions. In addition to those already mentioned, the effect is also associated with the amount of preoperative astigmatism [40].

St. Clair et al. have published a nomogram for planning femtosecond arcuate keratotomy after PK and Deep Anterior Lamellar Keratoplasty (DALK) cases. They showed that 67% of the variation in the surgically induced astigmatism correction can be attributed to the amount of preoperative astigmatism, arch length, depth and incision diameter, while 33% of this variation would be associated with unknown factors or inherent variability. Based on this, the authors elaborated a nomogram correlating the preoperative astigmatism with the magnitude of the incision. In this nomogram the depth of the incision varies between 85 and 90% of corneal thickness, the arch length

between 60 and 90° and the optical zone between 6.2 and 7.0mm [47].

Wedge resection: Wedge resection is a method of controlling corneal irregularity usually reserved for cases with high levels of residual astigmatism, generally greater than 10.0D. In this procedure, a crescent of corneal tissue is removed from the donor or the host cornea in the flatter meridian, which can be done manually or with a femtosecond laser. Then, tight sutures are performed in the excised location aiming for initial overcorrection. For each 0.1mm of resected tissue, there is a steepening of 1 to 2 D in the treated meridian [48]. The difficulty in excising the wedges with precision is associated with the low predictability of this technique [49].

A recently published series of 39 cases showed a reduction in the initial average keratometric astigmatism from 7.99 to 2.45D with good stability even after 1 year, along with an improvement in the best spectacle-corrected visual acuity. The manual technique with a diamond knife was used adopting Barraquer's nomogram, and a 90 degree arch from the donor cornea was removed, 0.1mm per diopter of subjective astigmatism up to 6D and from there on 0.05mm per each additional diopter [50]. Although implementing this procedure with a femtosecond laser has proven to be a safe and effective alternative, with greater precision in excising the corneal tissue [51], to date, there are no case series or specific nomograms for this method. Wound revision may be necessary when the graft overrides the recipient bed or when small dehiscences occur and, in these cases, keratometry values can be used during resuturing to help reducing the astigmatism.

Intracorneal ring segments (ICRS): The intracorneal rings represent an alternative to corneal transplantation in many cases of keratoconus with transparent corneas [52]. It has also been proved to be useful as an alternative in reducing penetrating and lamellar post-transplant astigmatism. A series of 59 eyes that had undergone intracorneal ring implantation following PK using the manual technique showed a reduction from $-6.34 \pm 3.4D$ to $-2.66 \pm 2.52D$ and an improvement of at least 1 line of Corrected Distance Visual Acuity (CDVA) in 73% of the patients. In this study, implantation was performed at least 2 years after surgery and at least 3 months after complete removal of the sutures for the procedure. Ferrara's ring was implanted at 80% of the corneal thickness. The

authors also suggest that the ring segments should be implanted in an optical zone of 5mm to keep a safe distance from the GHJ and avoid complications associated with neovascularization and wound dehiscence, which still occurred in 5% of cases [53].

Another study evaluating the effectiveness of the ICRS after DALK in 25 eyes showed positive results by reducing topographic astigmatism and spherical equivalent, as well as improving the CDVA [54]. The use of the femtosecond laser to create the corneal tunnel for ICRS implantation has been shown to be safer than the manual technique by reducing complications such as ring extrusion and perforation. Lisa et al. proposed a nomogram using femtosecond laser-assisted ICRS implantation in which the apical diameter (5.0mm or 6.0mm) of the ICRS and the length of the arch are chosen based on the amount of refractive astigmatism and the implantation axis coinciding with the flatter axis in the topography. In the study they evaluated the results in 32 eyes based on this nomogram and reported that mean UDVA improved from 0.16 ± 0.15 preoperatively to 0.43 ± 0.28 postoperatively ($P < .0001$) and mean CDVA from 0.67 ± 0.22 to 0.80 ± 0.19 ($P < .0001$) [55].

Refractive laser surgery: Laser vision correction has the advantage that, in addition to being able to treat corneal astigmatism, it can also address the spherical refractive error. The use of mitomycin-C has considerably reduced postoperative haze in cases of Photorefractive Keratectomy (PRK), which possibly tends to occur more often after PK, making this procedure an option for these cases [56]. A comparative study showed no difference in refractive and visual outcomes between Laser in situ keratomileusis (LASIK) and PRK after PK in series of few cases [57]. Maximum amount of astigmatism that can be treated is a limiting factor, usually around 6D in both techniques. Some authors suggest performing LASIK in two steps. The idea is to create the flap first and after 8 to 12 weeks perform the photo ablative treatment, because in these very irregular corneas the creation of the flap can induce changes in astigmatism [58].

Traditional ablative procedures are limited to treat only low-order aberrations. This is a problem in post-transplant cases because these patients may also present with significant irregular astigmatism and higher-order aberrations. Wave front-guided and topography-guided treatments have arisen in

an attempt to reduce higher-order aberrations and improve visual quality. Most devices that use wave front analysis to guide cornea ablation have limited capacity to correctly measure through highly aberrant corneas [59]. This way, topography-guided ablations may be preferable. A small retrospective study of topography-guided treatment, showed good visual and refractive results, but comparative studies are lacking to consider superiority to traditional treatments [60].

Toric intraocular lens: Another therapeutic option is toric Intraocular Lens (IOL) implantation. This can be done using either phakic IOLs or conventional pseudophakic lenses used after cataract surgery or refractive lens exchange. This type of treatment is limited to treat lower order aberrations. It is able to correct large spherical errors and astigmatism up to 15 D with customized toric IOLs [61]. An advantage is the minimal manipulation of the cornea, maintaining the corneal structural integrity and allowing better predictability of the results. However, an important limitation of toric IOLs is the inability to fully correct irregular astigmatism with non-orthogonal axis. Therefore, the main indication is for patients with minimally irregular astigmatism, in other words those who usually achieve adequate astigmatism spectacle correction.

However, a recent retrospective cohort study evaluated implanting toric IOLs in 88 eyes with irregular astigmatism and observed a refractive astigmatism reduction from $2.31 \pm 1.78D$ to $0.87 \pm 1.10D$ [62]. Toric IOLs in these cases are still controversial, and further studies are needed to assess the real benefit in irregular astigmatism. The possibility of having another corneal transplant should also be considered when deciding to treat astigmatism with toric IOLs. There is also the option of implanting sulcus-supported IOL to correct residual refractive error in phakic patients, but these lenses may rotate postoperatively compromising the result [63].

Phakic IOLs are also an option for these patients especially the younger ones with clear lenses. These implants may correct astigmatism up to 7.5D. Significant reduction in spherical equivalent and refractive astigmatism have already been shown in patients after PK and DALK treated with phakic lenses, however higher endothelial cells loss may be a problem in these patients [64,65].

Small aperture optics: A new approach in the treatment of irregular astigmatism is the use of small aperture implants such

as the Xtra Focus (Morcher Ghmb, Germany). This device resembles an IOL, however it is opaque to visible light and has a 1.3mm central hole that acts as a diaphragm. It uses the pinhole principle that blocks peripheral rays and increases depth of focus. The Xtra Focus pinhole is made of foldable hydrophobic acrylic material and can be inserted through a 2.2mm incision, it was proposed to be implanted as a piggy back lens in pseudophakic eyes [66]. Trindade et al. published a series of prospective cases where the device was implanted in 24 eyes with irregular astigmatism, 7 of them after PK. It was shown an improvement in uncorrected distance visual acuity from 20/200 to 20/50 with statistical significance ($P < 0.01$), and also CDVA, near uncorrected and corrected visual acuities. A high level of satisfaction was also obtained in a subjective questionnaire. Despite limiting indirect binocular ophthalmoscopy and retinal treatments, such as laser photocoagulation, the Xtra Focus is transparent to infrared and allows evaluation with IR-based imaging tests, such as OCT and scanning laser ophthalmoscopes [66].

In another study of the same group with 60 cases, the Xtra Focus pinhole was implanted in the capsular bag together with the primary IOL, in order to achieve better device stability and less decentralization. Again, they obtained a significant improvement in visual acuity and a low rate of complications, with good stability in the 4-year follow-up [67]. Another option is the IC-8 IOL (Acu Focus, USA). This is a hydrophobic IOL with a pinhole mask embedded in its center. The inner aperture is 1.36mm and the outer diameter is 3.23mm. Shajariet al implanted IC-8 IOL in the capsular bag during standard cataract surgery in 17 eyes with severe corneal irregularities due to keratoconus, PK, post-radial keratotomy or scarring after ocular trauma. CDVA improved from 0.37 ± 0.09 to 0.19 ± 0.06 Log MAR 3 months postoperatively and they also showed significant improvement in uncorrected distance, intermediate and near visual acuity [68]. An important limitation for irregular corneas is the current dioptric power range of this IOL (15.5 D–27.5 D).

Repeat keratoplasty: When other measures fail to treat astigmatism after keratoplasty, a new corneal transplant can be done. However this option should be avoided mainly because of the increased risk of rejection after a second transplant. A small series of cases of retransplantation to

correct high or irregular astigmatism, mostly composed of primary indications for keratoconus, showed that although there may be improvement in BCVA, there was only a statistical reduction in topographic / keratometric astigmatism in the first year after surgery. In addition, after second suture removal, the average keratometric values increase, losing the statistical difference that had been found until then [69].

CONCLUSION

Despite advances in available technologies, the incidence of high and irregular astigmatism secondary to penetrating and lamellar transplants is still a frequent complication and source of frustration for patients and corneal surgeons. An adequate surgical technique, combined with the correct management of sutures in the postoperative period, allow acceptable results to be achieved in most cases. As this is not always the case, corneal surgeons must learn and master the well-established surgical techniques, as well as newer approaches available, and, this way, try to match their patients' visual expectations.

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