Corneal Ectasia: prevention and management

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in Lisbon

CORNEAL ectasia is an often-perplexing problem when it arises spontaneously and it is among the most dreaded of potential side effects of corneal refractive surgery. New strategies to deal with both the idiopathic and iatrogenic forms of the condition were the focus of a symposium at the X X III Congress of the ESCRS.

Genetics and corneal ectasia
Francois Malecaze MD commenced the session with an update on current research into the genetics of keratoconus.

Dr Malecaze noted that forme fruste keratoconus is one of the major causes of post-LASIK corneal ectasia and the condition may be due to genetic factors in the majority of cases. Identification of the gene or genes responsible for keratoconus might lead to the development of blood tests that would enable surgeons to identify patients at risk of keratectasia before any clinical signs of keratoconus are evident. Such discoveries might also lead to better treatments of the condition.

“Genetics are an elegant strategy to elucidate the phenomena underlying the corneal deformation and consequently could lead to new therapeutic strategies aimed at slowing down its evolution and avoiding corneal grafting,” he said.

Topography has proved to be a valuable tool in detecting keratoconus suspects, enabling clinicians to identify warning signs such as moderate inferior steepening. However, topography does not enable surgeons to distinguish between early-stage keratoconus and “pseudo-keratoconus”, that is, an irregular cornea that is not undergoing progressive change. A more definitive diagnosis might be afforded by a blood test for keratoconus genes.

“Detecting forme fruste keratoconus is a major problem when screening patients for refractive surgery. Improving the diagnostic criteria will also allow for better topographical characterisation of the condition,” he added.

Research supports genetic basis
As of now, no specific gene has been identified in association with keratoconus. However, the genetic basis for the condition is strongly supported by familial studies. For example, Thalainen et al. were able to demonstrate in a study carried out in 1986 that clinical keratoconus is familial in 10% of cases. More recent research that took subclinical forme fruste keratoconus into account suggested that familial keratoconus represents at least 40% of cases and that the relative risk is 39-fold higher in first degree relatives than in the general population.

In addition, genetic research involving linkage analysis appears to be closing in on the genes responsible for familial keratoconus. Several research groups have localised some chromosomal regions that are potentially implicated in the condition. In addition, an ongoing European Multicentre study has localised a region on chromosome 2 containing a gene responsible for 70% of European familial keratoconus cases.

“It is reasonable to hypothesise that within the next few years, the keratoconus gene will be discovered,” he said.

Dr Malecaze noted that the European Multicentre study into the genetics of keratoconus is supported by INSERM, RETINA France and Toulouse Hospital. He added that anyone who wished to participate should contact him. They are looking for families having at least three keratoconus cases, he said.

Prevention of ectasia
Juan J Pérez-Santonja MD, FEBO told the symposium that there are several steps a refractive surgeon can take pre- and intra-operatively to minimise the risk of corneal ectasia in patients undergoing LASIK procedures.

Ectasia is characterised by a progressive thinning and a progressive central and inferior steepening of the cornea. Studies suggest it occurs in 0.3% of eyes after LASIK. Dr Pérez-Santonja said that in his own series of patients it has happened in two eyes out of 5500 LASIK procedures (0.036%).

Current theories suggest that the two main causes of post-LASIK ectasia are pre-existing corneal pathology (keratoconus or forme fruste keratoconus) and mechanical instability produced by the weakening of the residual stromal bed induced by flap creation and laser ablation. Careful and preoperative assessment of the cornea can greatly reduce the risk of ectasia from either of those causes, Dr Pérez-Santonja said.

Pre-existing corneal pathology accounts for more than 30% of cases of post-LASIK ectasia. He therefore strongly advised against offering corneal ablative procedures to patients with corneal topography suggestive of keratoconus or forme fruste keratoconus. He also recommended testing contact lens-wearing patients after several weeks without using their lenses to eliminate the possibility of lens-induced corneal warpage.

The reduction of the mechanical stability of the cornea results from the thinning of the stromal bed to such a point that it is unable to withstand the eye’s IOP. Eyes with a residual stromal thickness of 250 microns or less account for 56% of cases of post-LASIK ectasia and those with a residual stromal thickness of 300 microns or less account for 77% of cases, he noted.

“W e can’t name a specific figure for what the minimal residual stromal thickness should be, but 300 microns or more keeps us in the safe zone,” he said.

The residual stromal thickness following LASIK procedures depends on flap thickness and ablation depth. As flap thickness is not completely predictable, refractive LASIK can sometimes leave the stromal bed thinner than expected, he added.

“The laser ablation is not a big issue except in very high myopia, where the ablation takes longer and the cornea can dehydrate during the procedure. The main issue is the flap thickness, the thicker the flap the deeper the ablation will be.”

Steps to avoiding ectasia
There are several steps refractive surgeons can take to ensure that the residual stromal bed is within the safety zone of at least 300 microns in thickness following LASIK procedures, Dr Pérez-Santonja said.

Prior to surgery, the surgeon should estimate the residual stromal thickness by subtracting the predicted flap thickness and ablation depth from the preoperative central pachymetry measurements. During surgery, intraoperative pachymetry should be performed immediately after lifting the flap.

The surgeon can then estimate the residual stromal thickness by subtracting this value and the ablation depth from the preoperative central corneal thickness. One month following surgery, and before epithelial hyperplasia occurs, the surgeon should again estimate residual stromal thickness by subtracting the measured flap thickness from the postoperative central corneal thickness. In this way, it is possible to judge whether the residual stromal...
thick will be adequate for subsequent enhancement procedures, he added. “Refuse all cases with abnormal corneal topography until we have new tools to investigate these patients and use intraoperative pachymetry in every single LASIK procedure. If we stick to these principles we will not see many cases of post-LASIK ectasia,” he summarised.

Collagen cross-linking
Dr Seiler told the symposium that progressive keratoconus can be transformed into a more benign, non-progressive forme fruste keratoconus by a technique called collagen cross-linking. Corneas stiffened in this way may then be amenable to customised ablations enabling patients to achieve good vision with spectacle correction.

Collagen cross-linking stiffens collagen by creating new chemical bonds between collagen molecules. It occurs naturally as a consequence of ageing and diabetes. It can be induced by a variety of chemical means, both with and without radiation.

Dr Seiler’s procedure involves scraping of the epithelium from the central 9.0mm of the cornea, applying riboflavin in 20% dextrane and irradiation of the area with 3mW/cm2 of ultraviolet light at a wavelength of 365nm for 30 minutes.

The ultraviolet light causes riboflavin to release oxygen radicals, which in turn create new cross-linking bonds between lamellar fibres and within the collagen molecules. It thereby induces a one-and-a-half-fold increase in the mechanical stability of the stromal tissue, he explained. Animal studies and early clinical results have shown this effect in their current regimen to have the best risk/benefit ratio, he added.

Clinical results so far suggest that in addition to halting the progression of keratoconus it also causes keratoconic corneas to assume a more normal homogenous shape with consequent improvements in visual acuity.

Clinical trial
In a study involving 26 eyes of 25 keratoconus patients who underwent the cross-linking treatment, corneal topography showed progression halted in every case after a follow-up of one to five years (mean 2.4 years). In addition, maximal K-readings decreased by a mean of 1.38 D (p<0.01) and were significantly reduced in 65% of the cases. Furthermore, visual acuity improved by a mean of 1.3 lines (p<0.01).

Epithelial healing was uneventful in all cases and there have been no reports of any side effects, he added. “With collagen cross-linking we can stabilise progressive keratoconus and transfer it into the forme fruste state,” he said.

Cross-linking can also yield very good results in eyes with post-LASIK keratectasia, Dr Seiler said. Dr Seiler noted that in the few cases he has treated in this way, there has been a regression of the keratoconus. The drawback is that the riboflavin can penetrate through the thinned stromal tissues and induce corneal oedema, which can last several months.

Dr Seiler said he envisioned that collagen cross-linking could become a standard technique for forme fruste keratoconus and could be followed by customised ablation once the corneal tissue had stabilised. “It is not emmetropia we would be aiming for in such treatments but good visual acuity with spectacles,” he added.

Intracorneal ring segments
Another alternative for the treatment of keratoconus and post-LASIK ectasia is the implantation of intracorneal ring segments, said Prof Antonio Marinho MD.

“Implantation of intracorneal ring segments adds tissue to the periphery of the cornea. It flattens the central cornea, re-centres the apex, reduces myopia and astigmatism and makes optical correction possible.”

The two types of intracorneal ring segment that are currently available are Intacs® (Addition Technology) and Ferrara Rings (Mediphacos, Brazil). There are also two main types of ectasia. They are classical ectasia - seen most often in keratoconus - where the steepest part of the cornea is displaced downwards, and central ectasia - seen most often in post-LASIK ectasia - where the steepest part of the cornea is central, he said.

Dr Marinho said that his current approach to the treatment of keratectasia is to implant one Intacs segment in cases of classical ectasia and two Ferrara Ring segments in centrally steep cases.

Intacs are ring segments of 150º of arc with an inner diameter of 6.8mm and outer diameter of 8.1mm, he noted. They are hexagonal in cross section and range in thickness from 0.25mm to 0.45mm in 0.05mm increments. To treat classical keratectasia, Dr Marinho implants one 0.45mm Intacs segment upon the cone through a 7.0mm temporal incision at a depth of 70% of the thinnest corneal depth.

“The applanation induced by the rings is very different from case to case, varying from 13.0 D in some cases to almost no applanation in others.”

In a study involving 15 eyes of 12 patients with classic keratoconus who underwent implantation of Intacs, K values dropped from a mean of 57.0 D (range:49-66 D) to 50 D (range:44-57 D) after a follow-up of three months.

“The applanation induced by the rings was extremely variable ranging from 1.0 D to around 6.0 D. However, Dr Marinho stressed that the procedure should not be regarded as a means of refractive correction but as a means of disease stabilisation and optical improvement.

He noted that BCVA improved by a mean of 5.3 lines (range:0-9 lines) and only one eye had no improvement and no eyes got worse. In addition the eyes with little or no improvement in BCVA achieved visual acuities with spectacles that were as good as they had previously achieved with contact lenses.

Furthermore, centration was very good in nine eyes and good in the remaining six
Ferrara rings

Dr. Antonio Marinho said that while he has good results with Intacs ring segment in eyes with asymmetric classical keratoconus, his results using two rings in the more symmetric central cases have been unsatisfactory to date. However, he did have good early results with the Ferrara Ring, which like Intacs have ring segments 150º of arc but have a smaller inner and outer diameter (4.4mm and 5.6mm) and are triangular in cross-section. They range in thickness from 0.2mm to 0.35mm in 0.05mm increments.

He said that he has implanted the ring segments in three eyes of two patients, one with keratoconus and the other with post-LASIK ectasia. In all eyes he implanted two symmetrical rings of the same power. He noted that at three months follow-up both patients had important improvements in B.C.A. They also appeared to have more predictable results than is achieved with Intacs in classical keratectasia.

“Intraconal rings may be used in all cases of corneal ectasia where visual acuity is not good with glasses and the patient is unable or unwilling to use contact lenses. If the ectasia progresses, intraconal rings should be implanted at once,” he added.

Deep anterior lamellar keratoplasty

Mohammed Anwar FRCS informed the delegates at the symposium that in keratoconus patients in whom keratoplasty is indicated, deep anterior lamellar keratoplasty can provide visual outcome equivalent to those of penetrating keratoplasty with negligible risk of rejection. As the endothelium is healthy in almost all eyes with keratoconus, penetrating keratoplasty is unjustified in such cases. Dr. Anwar noted it is the endothelium of the donor cornea which undergoes immune rejection in corneal grafts, he pointed out.

“Deep anterior lamellar keratoplasty is superior to penetrating keratoplasty. There is no risk of immune rejection and there is also reduced endothelial cell loss and better long-term graft survival. There are also minimal steroid related complications and easier follow-up.”

Deep stromal and Big Bubble – current deep lamellar techniques

There are at present two main deep anterior lamellar keratoplasty techniques, Dr. Anwar noted. There is the deep stromal procedure which leaves behind varying amounts of residual stroma (50-100 microns). Then there is his own ‘Big Bubble’ technique which involves generating a big air bubble between the stroma and Descemet’s membrane. Removal of the stroma exposes the smooth Descemet’s membrane, he said.

The drawback of the deep stromal technique is that the stroma-stroma interface can give rise to haze and stromal scarring. In contrast, the Big Bubble technique provides a more natural and standardised interface between the donor and host tissues, he added.

“AT a symposium on ‘Modern Lamellar Surgery’ in Barcelona, ESCRS 2004, there was a consensus that exposing Descemet’s membrane provides better visual results. The Big Bubble technique is the safest and fastest method of Descemet’s membrane exposure and provides a higher quality host/graft interface.”

The Big Bubble technique involves making a pre-cut with a trephine first and then injecting air with a bent needle, with the bevel facing the anterior chamber. The surgeon then forces the plunger so that the air leaks through the residual stroma along the path of least resistance, thus creating a large bubble between the stroma and Descemet’s membrane. The Big Bubble is outlined by a white circular band at the base of the cornea. The Descemet’s membrane is stripped off from the donor button by a smooth tipped forceps, Dr. Anwar explained.

Surgeons should be aware of a learning curve with the technique. He noted that he had a 9% rate of intraoperative perforations in his early cases. However, his perforation rate has dropped to 5% among his last 100 patients.

Dr. Anwar presented a review of the results he had obtained with the bubble technique in a series of 316 eyes of 219 patients with keratoconus. The patients had a mean age of 22 years and their preoperative visual acuity ranged from hand movements to 20/60.

After a follow-up of six months to 16 years, B.C.A. was 20/40 or better in 80%, 20/30 or better in 25% and 20/20 or better in 17%. He also noted that in two series of patients who had undergone penetrating keratoplasty for keratoconus at King Khalid Eye Specialist Hospital, Riyadh, Saudi Arabia, B.C.A. of 20/30 or better was achieved by only 5-7% of the cases.

Penetrating keratoplasty has long track record

Sadeer Hannush MD

Sadeer B. Hannush MD concluded the session by pointing out that of all the keratoplasty procedures, penetrating keratoplasty is the most tried and tested. Furthermore, penetrating keratoplasty for keratoconus is the most successful transplant procedure of any kind. “Compared to other solid organ transplants, corneal transplantation is the most successful. Stratified across various corneal diagnosis groups, corneal transplantation for keratoconus is the most successful of all,” he said.

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Limitations of the procedure include the availability of suitable donor tissue, and intra- and postoperative complications. The eye is exposed to the danger of allograft rejection and wound dehiscence though trauma. There have also been reports of late changes in the corneal toxicity, although it remains unclear whether this results from recurrent ectasia in graft tissue or from inadequate excision of the diseased tissue from the recipient cornea in the first place.

However, in almost every series the results have been very good, he said. He noted that in a series published by Buzard et al (JCRS 1997) of 104 eyes that underwent penetrating keratoplasty for keratoconus, the mean visual acuity was 20/25 after a mean follow-up of 42 months.

Dr. Hannush said that in his own experience he has performed penetrating keratoplasty for keratoconus in 119 eyes. Of those eyes 92 eyes were free of concomitant ocular pathology and had a follow-up of at least one year.

At a mean follow-up of 65.1 months (range: 12 - 202 months) 31 eyes had a mean uncorrected visual acuity of 20/50, which the patients were content to leave uncorrected. Another 19 eyes achieved 20/30 with rigid gas-permeable contact lenses, and 40 eyes achieved 20/40 with spectacles.

Most important of all, there were no cases of graft failure and none of the patients required re-grafts.

“Penetrating keratoplasty is a very effective method for surgical management of moderate to advanced keratoconus. It is relatively easy to perform, is associated with good-to-excellent long term results and has stood the test of time,” he added.

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