Keratoconus: Breaking paradigms and contradictions of a new subspecialty

Ceratocone: Quebra de paradigmas e contradições de uma nova subespecialidade

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The first valid publication on keratoconus in the medical literature came from England in 1854, under the authorship of Dr. John Nottingham, entitled "CONICAL CORNEA". This publication covered several aspects of the disease that is still relatively relevant and current, despite the inexorable limitations of the scientific knowledge in the nineteenth century.[1] Keratoconus and ectatic diseases of the cornea remained among the topics of major interest in Cornea and External Diseases because these diseases have been among the most important indications for corneal transplant, and also one for fitting special contact lenses accordingly to the prospective reviews of Rabinowitz and McGuee.[2,3] However, with the emergence of Refractive Surgery as a subspecialty, a rapid and accelerated development began.[3-6] In fact, elective surgeries to treat refractive errors with the aim of reducing the need for visual correction has determined the need for greater scientific knowledge to increase the safety and efficacy levels of these procedures that are performed in typically normal corneas. All this scientific evolution was benefitial for the management of several diseases, especially keratoconus and ectatic corneal diseases.[5]

Two different factors can be emphasized among the relations between refractive surgery and ectatic corneal diseases: I. The development of refractive surgery technologies to manage these diseases[4,7] and II. The need to identify subclinical cases with high risk of developing progressive iatrogenic ectasia.[8-11] Among the surgical techniques we emphasize the crosslinking described by Wollensak et al. and Paz et al.[12,13] in order to stabilize the progression of ectasia. Crosslinking created a new possibility of surgical management of keratoconus, because until then surgery would be reccomended exclusively for visual rehabilitation in patients with severe forms. In addition to crosslinking, we highlight the implant of intraestromal ring segments, independently described for the management of keratoconus by Ferrara et al.[14] and Colin et al.,[15,16] with the aim of regularizing the cornea. The surface photoablation techniques with excimer laser can also be indicated in cases of keratoconus in isolation,[17-19] or in association with crosslinking as in the Athens protocol (top-guided therapeutic PRK and crosslinking) described by Kanellopoulos, [20] and the Cretan protocol (PTK for debriding epithelium and crosslinking) described by Kymionis et al., [21] among others. The surface ablation can also be carried out after ring segment implantation, as described by Ertan et al. and Coskunseven et al.[22,23] In addition, phakic lenses may be indicated in cases of keratoconus.[24-26]

Still regarding the advances of Refractive Surgery applied to the management of keratoconus, we can mention the improvements in the excimer laser to make customized plans based on topography exams or corneal tomography or ocular aberrometry, and the revolutionary femtosecond laser with different applications in surgeries for keratoconus.[27] For the ring segment implant, the creation

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of the laser tunnel means greater predictability in the depth of the implant and consequent greater predictability and also a significant reduction, in complications such as extrusion.[28-30] It can also be used to create pockets[31] or tunnels[32] for riboflavin injection in alternative crosslinking techniques without removing the epithelium, also femtosecond laser can be used for deep[33] or penetrating lamellar keratoplasty techniques.[34]

In fact, this development determined that several paradigms were broken, but also that controversies and paradoxes were established.[35] For example, penetrating corneal keratoplasty or transplant was only for advanced cases with intolerance to contact lens adaptation, and would be the only effective surgery for keratoconus. Penetrating transplant evolved to lamellar transplant,[36] which could present similar visual results with the techniques for deep dissection with lower chances of rejection.[36,37] On the other hand, different procedures may be indicated prior to keratoplasty,[38] but the indication of when, why and which procedure to be performed deserves individualized considerations for each case.

However, there is no consensus among experts on some aspects of the indication of surgery in all cases of keratoconus.[6] Many times we can observe the same patient with an eye having indication for surgery, what should be done as soon as possible, and the other eye with no indication for being to be operated, but followed carefully.[4,35,38] In general, these alternative procedures to corneal transplant have a better chance of success in cases when the disease is not very advanced. On the other hand, the very early indication is not justified considering the cost-risk versus benefit.[35] For example, while Koller et al. indicated that preoperative corrected visual acuity better than 20/25 is associated with an increased risk of complications, maximum keratometry exceeding 58D was considered a significant risk factor for treatment failure.[39] In other words, we can understand that if the indication is very early, there is a very high risk, but if the indication is too late, surgery has less chances of success. However, other ways of promoting crosslinking such as using riboflavin in oral supplementation or even with crosslinking without removing the epithelium may be considered,[40] an individualized approach shall be established. This should be according to the clinical condition of each patient and the therapeutic possibilities and availability of each center proposing to treat keratoconus.

In this context, it should be noted that elective refractive procedures should be differentiated from therapeutic procedures.[7] The objective of elective refractive visual correction is to reduce dependance on glasses or contact lenses, with residual ametropia and uncorrected visual acuity being the most important metrics for success, along with patient satisfaction.[41] On the other hand, therapeutic procedures should not primarily target uncorrected vision. These results are desirable, but the reestablishment of functional vision corrected by glasses or even contact lenses is what should be considered success. Thus, a result considered successful for a therapeutic procedure may represent a poor outcome or even a real disaster in a patient who was originally presented for elective refractive surgery.

In a simple way, surgery is indicated primarily for cases of keratoconus considering the therapeutic purposes to avoid the worsening of ectasia and visual rehabilitation. Therefore, it is recommended for cases with documented worsening of ectasia. It is also justified when identifying a high risk for progression, which requires detailed documentation of the case. In addition, the classic indication of improving the visual performance of the patient should be established when the vision is not satisfactory despite the correction methods typically glasses and contact lenses. While dissatisfaction with vision can be quite variable among patients, the orientation of patients and their relatives is especially relevant. With proper education, informed decision-making is possible, with greater adherence to treatment (compliance), and expectations become more realistic. In addition, suffering with illness can be minimized, which goes according to the most basic principles of the physician's work. In fact, patient orientation is challenging as patients may have difficulty understanding medical terms and issues, as well as being emotionally shaken. Considering these aspects, a patient awareness campaign was launched in Brazil in 2018 and quickly became international - THE VIOLET JUNE. This was established to promote awareness of the disease, but also to educate and spread the message about the risks associated with scratching, rubbing or even pressuring the eyes (Figure 1). It is important to mention that one of the few 100% total agreement points in the consensus was that scratching the eyes can cause or worsen corneal ectasia. [6] This campaign corroborates other initiatives such as November 10 as World Ceratoconus Awareness Day sponsored by the US National Keratoconus Foundation (NKCF - https://www.nkcf.org/world-kc-day-2017).

Figure 1: . Keratoconus awareness campaign "Violet June"Scratching or rubbing the eyes impairs vision! Poor information damages more than the disease.

Clinical management of keratoconus includes, patient education about the disease and control of allergy and inflammation of the ocular surface. The prescription of glasses shall be at least tried as the first line for visual rehabilitation.[6] A retrospective study has shown that ocular aberrometry can facilitate manifest refraction, allowing improvement of visual acuity in up to 60% of cases of keratoconus.[42] New refractive approaches based on aberrometry with lenses made with accuracy less than 0.05D can bring clinical benefit, such as the ZEISS iScription lens and the digital system VISION R-800 of ESSILOR. However, it should be noted that contact lens adaptation is the most efficient way for visual rehabilitation, and should be considered for cases in which the glasses were not satisfactory. On the other hand, it was agreed that the use of contact lenses does not offer the benefit of stabilizing ectasia, and that lenses for aesthetic reasons should be used with caution if the patient has adequate vision with glasses.[6] However, such compliance does not mean, for example, that patients with mild to moderate forms of keratoconus can not benefit from the adequate adaptation of gelatin lenses or other types of lenses providing good visual correction. The patients deserve to understand the disease and especially that they can not scratch the eyes, as well as understand the need of follow-up with imaging exams allowing to identify progression in a sensible way before a marked worsening occurs.[35]

One of the most controversial points is the possible indication of refractive surgery in cases of mild keratoconus. Typically, these cases present satisfactory insight with the sphero-cylindrical correction of low-order aberrations. In these cases, the approach with intraocular lens implant may be more adequate.[43] But especially in cases with low ametropia we can consider surface ablation techniques according to the clinical characteristics.[17-19] Regarding indication, anisotropy and other aspects related to visual quality are important. Again, adequate clinical documentation[11] and patient guidance are essential, especially when the approach is refractive rather than therapeutic.[7] Patients should understand that they can not scratch the eyes, they need follow-up, and they possibly need crosslinking. On the other hand, the indication of crosslinking associated with the prophylactic refractive procedure is still controversial, and should not be considered as a "green light" to indicate refractive surgery in cases of keratoconus.

Another factor worth mentioning is the high and possibly increasing number of patients with keratoconus. Both the incidence (new cases) and the prevalence (total cases) of the disease have increased, which is certainly related to the greater diagnostic sensitivity resulting from advances in corneal imaging exams,[11] but may also be related to others environmental and/or genetic factors.[35,44] The classic Kennedy study from 1935 to 1982 in Minnesota showed an incidence of 2 cases per 100,000 inhabitants per year, and a prevalence of 54.5 per 100,000 inhabitants.[45] It is critical to recognize that this study had limited diagnostic testing techniques, such as scissors retinoscopy and irregular keratometry reflexes, which are only positive at more advanced stages of disease. This explains why 41% of the cases presented as "unilateral" in the initial diagnosis.[45] It was established that keratoconus is a bilateral disease with asymmetric presentation, but there is a possibility of unilateral ectasia occurring due to mechanical causes.[6] It is emphasized that the characterization of unilateral ectasia requires advanced diagnostic tests in longitudinal studies with more than one year of follow-up.[46-48] In fact, the prevalence of the disease can vary significantly according to the diagnostic criterion. For example, a study carried out in India showed a reduction of 2.3% to 0.6% by simply changing the keratometric criterion from 48D to 49D.[49] However, with well-established criteria and more than one examiner to evaluate the results of the tomography with rotational Scheimpflug (Pentacam HR, Oculus, Wetzlar, Germany), Torres- Netto et al. found a prevalence of 4.79% of keratoconus in a prospective study involving 522 pediatric patients (average age of 16.8 +/- 4.2, ranging from 6 to 21 years) in Riyadh, Saudi Arabia. Although there is no data in Brazil on the incidence or prevalence of keratoconus, this information may be very relevant. However, it is necessary and definitely possible to carry out studies in Brazil to know the epidemiology of the disease in our country. Such knowledge may determine strategies for public health programs aimed at reducing visual impairment and consequently the impact caused by keratoconus.

All these factors corroborate the idea that we are facing a new subspecialty when we deal with keratoconus and ectasic diseases of the cornea.[50] In 2013, an international journal, the International Journal of Keratoconus and Ectatic Corneal Diseases (IJKECD; http://www.ijkecd.com) was created with the aim of concentrating publications in this area. The IJKECD reflects the exponential increase in the number of publications on the subject. For example, a review in Pubmed on the articles published with the term "keratoconus" showed 5,588 publications in December 2016 which increased to 6,301 in July 2018 and to 6,572 in February 2019. It is relevant to note that the number of publications indexed only in the year 2018 exceeds all papers published until 1980, and is also higher than the total number of publications throughout the 1990s.[35] In fact, this profusion of publications clearly reflects the relevance of keratoconus in our setting, and it is possible to predict its continuous and accelerated progression. We empohasize the advances in diagnosis based on artificial intelligence to integrate imaging techniques,[10,11,51-53] as well as the applications of genetics and other techniques of molecular biology as described by Shetty et al.[54-58] Such advances increase accuracy for diagnosis as well as provide prognostic information and custom treatment planning, such as new progressive-thickness ring implants (Keraring AS, Mediphacos) and personalized tomography--based crosslinking.[59,60] All of this progress definitely increases more and more our ability to help patients with keratoconus and ectatic corneal diseases.

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