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Research Article

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Histopathological Findings in Secondary Refractive Surgery Ectasias

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Introduction

Corneal ectasia secondary to refractive surgery or iatrogenic ectasia is a progressive entity consisting of corneal thinning, increased curvature and decreased visual acuity with and without correction. Its prevalence rate ranges from 0.02 to 0.6% according to different series, and in the fewer cases of this complication, corneal transplantation or penetrating keratoplasty (PK) is the only treatment measure to restore vision in these patients. Despite the reports and identification of some risk factors, the mechanisms of ectasia secondary to refractive surgery are not completely clear. In this study we observed histopathological alterations in the corneas studied with clinical diagnosis of iatrogenic ectasia. We support the previously reported in the literature demonstrating alterations in the posterior layers of the cornea, i.e. loss of endothelial cells and decrease in the residual stromal bed. In the current series also found other important alterations in the anterior layers that have only been described in non iatrogenic ectasias of the keratoconus type. These data suggest that there are more risk factors, which have not been previously reported in the development of this complication, which remains one of the most serious and feared after refractive surgery.

Refractive surgery had its beginning in a real manner with the advent of the radial keratotomy (RK), in which there were radial cuts in the cornea and a considerable depth (90% of depth), in order to overcome the resistance of this, and it was the reason that changes its curvature and thus achieve the refractive effect [1,2].

With the advent of the photo-refractive surgery at the beginning of the 90's, was obtained more certainty as to the safety and results in refractive surgery, even the possibility of being able to re-operate to patients not satisfied of RK upon [3,4].

LASIK (Laser assisted in Situ Keratomileusis) technique is currently the most used at the global level, due to its predictability, stability, and its rapid recovery, and also, that does not develop as a complication the appearance of stromal haze that occurs much more frequently in the technique of photorefractive keratectomy (PRK). Another point in favor of the technique of LASIK over PRK, is that you can operate both refractions rates as moderate and high, depending on the corneal pachymetry (higher corneal thickness, higher is the refraction that can be corrected with security) [5].

Regardless of the system used for the measurement of central corneal thickness, must always be the refraction to try and perform the necessary calculations for you after the surgery the stromal bed is >350 microns (μ) enough to prevent the development of a corneal ectasia, especially with <500μ thick prior to surgery. The corneas with thinner pachymetry than normal and abnormally pronounced curves will have a greater probability of generating an ectasia refractive surgery [6].

The ectasia is a rare condition in which the eye becomes progressively more short-sighted, with irregular astigmatism, an increase in the slope, topographical, and corneal thinning, resulting in a loss of visual acuity and without correct [7].

Iatrogenic keratectasia, after refractive surgery, have been described in the NICE systematic review as the most serious of all the complications associated with this procedure, which can lead to severe vision loss [8].

The corneal ectasia is a rare but well described complication of LASIK surgery, which indicates a biomechanical resistance altered, but has rarely been reported after the PRK, except in the cases with features suggestive of ectasia or a family history of keratoconus and the cases of multiple treatments [9-11].

In case of iatrogenic ectasia, the initial treatment is conservatively with visual rehabilitation, which is usually effective, but in some cases they need surgical treatment, which consists in PK. The advances in the knowledge of the risk factors and methods of detection will further reduce the incidence of this complication and improve treatment for patients in which occurs the ectasia [12].

In this study we determined the histopathologic features, quantitative (measures) and qualitative (alterations in each of the corneal layers) and the demographic characteristics of the patients.

We present evidence of the importance of the alteration in the anterior layers of the cornea as complementary risk factors for the development of iatrogenic Keratectasia.

Material and Methods

This was a retrospective, observational, cross-sectional and descriptive study.

Was initiated with the revision of histopathologic reports of patients with a clinical diagnosis of ectasia and history of refractive surgery, for a period of 10 years (March 1, 2004 to February 28, 2014). Were excluded cases with a history of wound and/or corneal infection, as well as partial thickness corneas.

The data of each patient were collected in a database prepared for this purpose. Subsequently, photomicrographs of sections stained with hematoxylin & Eosin, PAS and Masson's trichrome were taken, with 10x and 40x objective lenses. The measurement of the corneal thicknesses was done through the AxioVision microscope version 4.8.2.

The histopathological variables were divided into two groups: qualitative, which were used to describe the alterations found in each of the layers of the cornea, and quantitative, which were subdivided into those general measurements, i.e. those that were performed in all corneas: thickness in the area of greater ectasia and epithelial thickness, and according to the type of refractive surgery.

In the cases of LASIK the following measurements were made: thickness in the zone of greater ectasia, epithelial thickness, thickness of flap and flap stroma (including epithelium), as well as residual stromal bed (Figure 1).

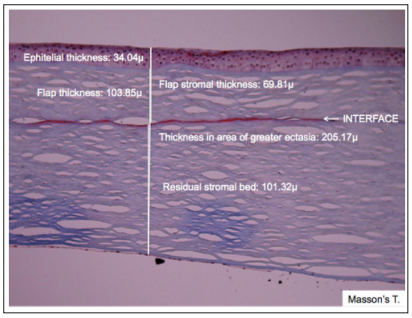


Figure 1: Histopathologic quantitative variables measures in cases of LASIK

In the cases of RK were measured: thickness in the zone of greater ectasia, epithelial thickness in that area and intrastromal thickness of the epithelium in the incision zone; in addition the scope of the incision in the corneal stroma was determined (Figure 2).

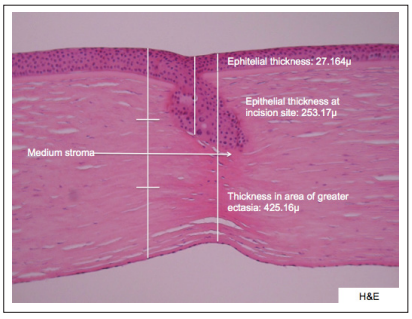


Figure 2: Histopathologic quantitative variables measures in cases of RK

In cases that were not within the categories of LASIK or RK, only the general measurements and the description of alterations in corneal layers.

Results

Fifty corneas of 47 patients were studied, with no gender predominance. The mean age was 37.8 years and the time elapsed between refractive surgery and corneal transplantation was 10.5 years. summarizes the demographic data of the patients.

Table 1: Patient demographic data (n=47)

	Min	Max	Media	SD
Age(years)	16	58	37.8	10.5
Time between refractive surgery and PK (years)	0.58	25	10.5	6.7

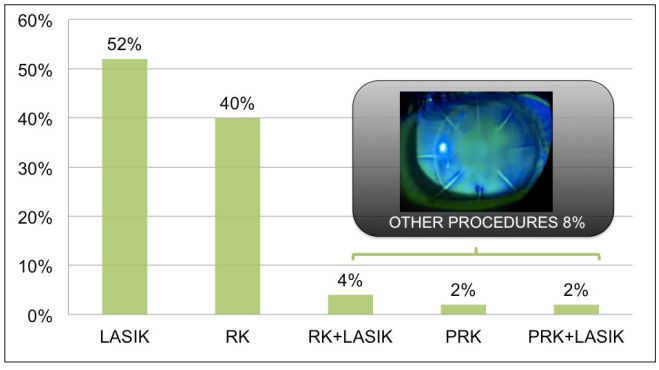
The type of refractive surgery that was most frequently performed was LASIK, followed by RK, the remaining percentage was occupied by other procedures, including two cases of RK + LASIK, one case of PRK and one case of PRK + LASIK (Graph 1).

The range of the general measures is concentrated in Table 2. The mean of the thickness in the zone of greater ectasia with 344.83 µ is emphasized, and the mean of the epithelium measured in that zone with 38.06 µ.

Table 2: Corneal general measures (n=50)

Corneal Thickness	Min	Max	Media	SD
Major zone ectasia (microns)	118.75	569.51	344.83	112.12
Epithelium	5.8	92.91	38.06	23.41

In cases of LASIK, the area with the highest ectasia was found with a minimum measurement of 118.75 µ and a maximum thickness of 569.51 µ. The epithelium presented a range of 5.8 to 92.91 µ. The averages of the upper layers below 200 µ, however the average flap is above 150 µ. The residual stromal bed presented an average of 181.34 µ (Table 3).



Graph 1: Type of refractive surgery

Table 3: Corneal measures in LASIK (n=26)

Corneal thickness (microns)	Min	Max	Media	SD
Greater ectasia zone	118.75	569.51	330.97	117.78
Epithelium	5.8	92.91	40.60	25.61
Flap	64.65	374.91	162.29	76.47
Stromal Flap	32.32	273.85	106.63	55.85
Stromal residual bed	51.68	532.14	181.34	120.58

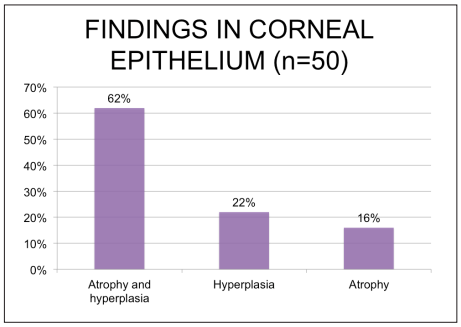
In the cases of RK, the thickness in the zone of greater ectasia fluctuated between 160.37 and 547.08 µ, presenting an average of 344.11 µ. In the epithelial thickness important contrasts were found, with a mean in the zone of greater ectasia of 29.90 µ and 136.04 µ in the incision zone (Table 4).

Table 4: Corneal measures in RK (n=20)

Corneal thickness (microns)	Min	Max	Media	SD
Greater ectasia zone	160.37	547.08	344.11	98.89
Epithelium	6.21	60.17	29.90	17.11
Epithelium at incision site	38.12	279.7	136.04	63.62

In the corneal epithelium the alterations found were: alternation of atrophy with hyperplasia in 31 cases (Figure 3a), followed just by hyperplasia in 11 cases, and just atrophy in 8 of them (Graph 2).

As epithelial findings, intracellular edema was found in 88% of cases (Figure 3b), followed by blisters in 46%, dyskeratocytes in 20% and pannus in 4%.



Graph 2: Histopathological findings in corneal epithelium

In relation to the Bowman layer, partial loss is reported in 21 cases (Figure 4), focal rupture in 15, and normality in 10, in 2 cases rupture and loss, and in 2 more absence of the layer.

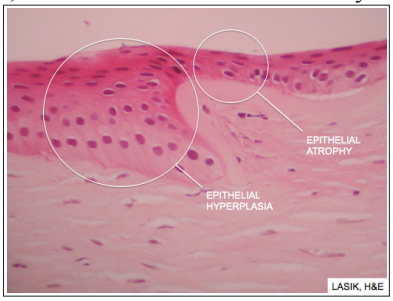


Figure 3a: Alternation of atrophy and epithelial hyperplasia in a case of post-LASIK ectasia

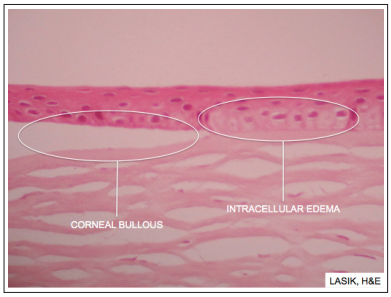


Figure 3b: The presence of intracellular edema and epithelial bullae in a case of LASIK

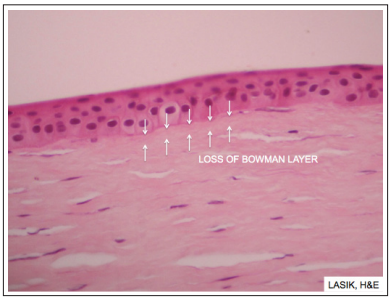


Figure 4: Loss of Bowman's layer in a case of post- LASIK ectasia

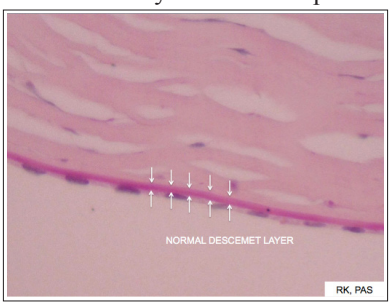


Figure 5: Normal Descemet's membrane in a case of ectasia post-RK

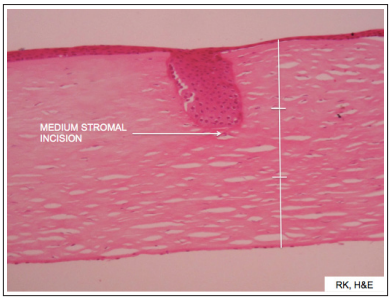


Figure 6: Incision in a case of RK that reaches the intermediate stroma

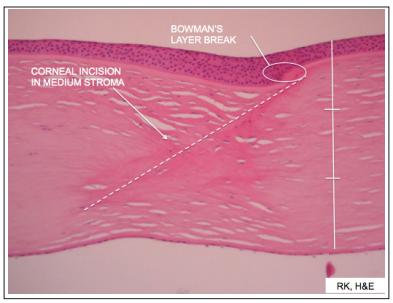
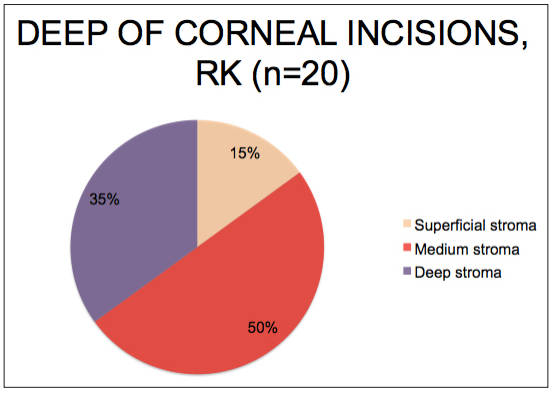


Figure 7: Incision in a case of RK that reaches the deep stroma and Bowman's layer rupture

Of the 20 cases of RK, 50% showed the scope of the midstroma incisions (Figure 6), in 35% the incisions reached the deep stroma (Figure 7) and the superficial stroma in 15% (Graph 3).

Regarding the endothelium, 28 cases presented loss of endothelial cells, in 2 cases they were absent, and in 20 cases there was no alteration (Figures 8a&b and Graph 4).



Graph 3: Deep of corneal incisions in RK cases

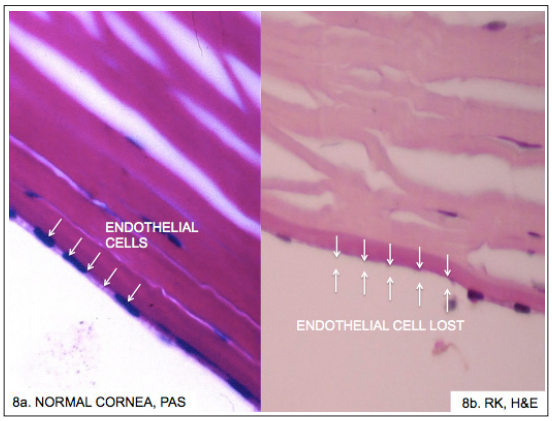
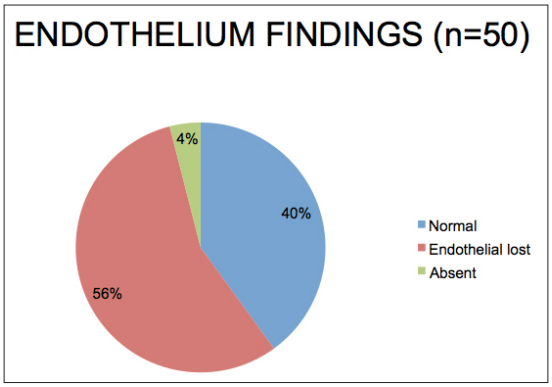


Figure 8a & 8b: Photomicrographs comparative advantages between the endothelium of a normal cornea and a case of RK



Graph 4: Corneal endothelium findings

Discussion

Corneal ectasia following refractive surgery is a rare but potentially devastating complication, which can occur when residual stromal bed is thin, resulting in loss of biomechanical stability of the cornea. It is recommended to leave a residual stromal bed greater than 250 µ, especially in corneas less than 500 µ in total thickness, to minimize the risk of ectasia, however, there are reports of patients with a stromal bed of 250 µ or thicker who have developed ectasia, which leads us to consider that there may be some other factors that contribute to the development of keratectasia after this type of surgical procedure [13].

It is important to keep in mind the contraindications already known for refractive surgery, (diseases of collagen, predisposition to hypertrophic scarring or keloid formation, diabetes, prolonged steroid or immunosuppressive treatments, certain congenital or acquired corneal disorders, irregular astigmatism, uveitis, glaucoma, vitreoretinal alterations that predispose to retinal detachment, among others), in the preoperative evaluation of the patient who wishes to undergo such intervention [6,14,15].

In the present study we found that the mean age of patients was 37.8 years, coinciding with the age ranges reported by Randleman *et al*, although there are other studies, that do not report correlation of the patient's age with the presentation of keratectasia. Gurkan *et al*, report a slight predominance by the male gender, whereas we do not find predominance by gender [16-19].

Of the current studies that have analyzed the characteristics of the corneal tissue in the complications, the ones that we find are LASIK surgery, which is explained by the disuse of the RK; in this study we also find LASIK as the most frequently performed procedure [18,20].

Twa *et al*., report the time of post-LASIK ectasia (between refractive surgery and the diagnosis of ectasia) with an average of 13 months and a range of 6 to 20 months; Gurkan et al., 19 report an average of 36 months and we report a range of 7 months to 25 years, with an average of 10.5 years, but this difference can be explained because in this study we measured the time elapsed between refractive surgery and the final treatment of ectasia with PK [21].

Brenner *et al*., found a mean corneal thickness of 534.18 µ in eyes with LASIK ectasia, while Gurkan et al. [19]. reported a thinner central corneal thickness than most studies, averaging 447.43 µ microns; we reported an average of 344.83 µ [22].

The current series as well as other studies, reported thinning in epithelial thickness [20,23]. In the Bowman layer, we found uptures and other alterations reviously described in the literarture [18,20].

Regarding the stroma, of the findings reported in previous studies, such as thinning collagen lamellae, scars in the stroma, presence of inflammation and an iron ring around the ectasia, we report the presence of incisional stromal scars in cases of RK, however we did not find in the literature published reports related to measurements of corneal RK projections [13,24,25]. In the Descemet's membrane, in the majority of the patients, no alterations were found, coinciding with Meghpara et al [20]. and in the endothelium we reported decrease of cells, as did Moshifar et al., Meghpara et al., report central flap thicknesses of 60 to 136 µ and central residual stromal thicknesses of 129 to 264 µ, while we found a flap with thicknesses ranging from 64.65 to 374.91 µ and residual stromal thicknesses of 51.68 to 532.14 µ [20,26].

Conclusions

Some other published papers in the literature have shown that alterations such as reduction in the thickness of the residual stromal bed, as well as secondary endothelial loss, contribute to changes in corneal ectasia. The current series support the previously described factors, and we add in important ways alterations in the anterior layers.

The anterior findings such as alternation of epithelial atrophy with hyperplasia, partial loss or rupture in Bowman's layer, as well as the thinning in the thickness of the flap involving epithelium and stroma, are factors that contribute significantly to the development of corneal ectasias. These histopathological findings are complications caused by corneal biomechanical instability secondary to refractive surgical procedures.

The previous risk factors mentioned in this study can contribute in avoiding keratectasia as a complication related to this type of refractive surgeries.

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