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Research Article

Histopathological Findings in Donated and Transplanted Human Corneas: A Descriptive Study

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Abstract

Corneal transplantation is one of the most frequently performed tissue procedures worldwide. Histopathological evaluation of donated and transplanted corneas allows for the identification of structural alterations that may impact graft viability, optimize tissue selection criteria, and strengthen the quality of the procurement and allocation process.

This paper describes the histopathological findings observed in donated corneas and harvested corneas from donor and recipient patients during transplant procedures performed over a period of one year at a tertiary care hospital.

A descriptive, retrospective, and observational study was conducted in which histological slides from 390 corneas processed by the institutional service of Pathological Anatomy were reviewed, corresponding to 256 donors selected by Donors Coordination and 134 recipients selected by Corneal Transplant Service. Structural alterations in the different corneal layers were evaluated, as well as the presence of inflammation, vascularization, or calcification. The findings were systematized and classified according to the type of tissue (donated or explanted) and the compromised structure.

In the donated corneas, 57.81% showed some histological alteration, the most common being elastosis (18.04%), mainly in the tectonic corneal subgroup; absence of epithelium (28.9%) and endothelium (28.91%) was also documented in this group. In the explanted corneas of recipient patients, 18.7% showed alterations, most notably inflammation (11.2%), fibrosis, ulceration, and calcification according to the keratopathy previously diagnosed clinically. The epithelium and endothelium were the most affected layers in both groups.

These findings reveal a high frequency of histological alterations in donated tissues, many of them subclinical. Systematic evaluation of these changes can improve selection criteria in Donors' Coordination to optimize surgical outcomes.

Kew Words: cornea; histopathology; corneal transplantation; tissue donation; keratopathy; elastosis

1. Introduction

The cornea is an avascular, transparent, and highly specialized tissue that constitutes the main refractive surface of the eye, providing more than 70% of the total dioptric power.[1] Its architecture is composed of five histological layers: epithelium, Bowman's membrane, stroma, Descemet's membrane, and endothelium; whose integrity is essential to preserve transparency and its multiple functions.[2] When this is compromised by trauma, infection, dystrophy, degeneration, or other diseases, a corneal transplant may be necessary to preserve eye function and integrity.[3.4]

Advances in penetrating and lamellar keratoplasty techniques have improved visual success rates and graft survival. However, transplant success depends not only on the surgical technique but also on the quality of the donated tissue.[5] Currently, corneal tissue selection criteria in eye banks are based on clinical and serological parameters, complemented by specular microscopy evaluation. However, there is growing evidence that these criteria may not be sufficient to detect relevant structural alterations that compromise graft function.[6]

In this context, histopathological examination of corneal tissue, although not part of routine protocols for candidate selection, has been proposed as a valuable complementary tool to retrospectively optimize tissue selection and allocation. [3,7]

The literature in Mexico is limited regarding the structural characterization of donated and explanted corneas. [8,9] A histopathological analysis of corneal tissues processed by a national reference center identified subclinical alterations that go undetected in conventional evaluation. Furthermore, this type of analysis provides

valuable information on the most common damage patterns in our donor and recipient population, which could contribute to optimizing tissue allocation, reducing rejection rates, and improving long-term visual outcomes. [10,11] This information may also be useful for promoting public eye health policies and strengthening eye bank protocols in the country.[12]

This study documented the presence of relevant histopathological findings in donated and explanted corneas including inflammation, elastosis, epithelial or endothelial loss, fibrosis, ulceration, and calcification. These alterations may reflect degenerative, infectious, immune-mediated, or postmortem processes and have direct implications for graft viability, transparency, and survival. [13,14]

2. Materials and methods.

2.1. Corneas

Corneas donated to the Corneal Transplant Service of the Specialties Hospital of the Century XXI National Medical Center, Mexican Institute of Social Security (IMSS) that were not transplanted due to lack of a suitable recipient were used and the leftover bedding from the corneas transplanted, as well as corneal tissue removed from recipient patients during corneal transplants. The study was conducted from January to December 2024 and was retrospective, observational, cross-sectional, and descriptive. The study was approved by the local research committee with institutional record number R-2025-3601-079. The following inclusion and exclusion criteria were considered.

Inclusion criteria: 1. Corneal tissue from adult patients of either gender during 2024, whose histopathological study was performed by the Anatomy Pathology Service of the same hospital. 2. Corneal tissue removed in corneal transplants from adult patients of either gender during 2024, whose histopathological study was also performed.

Exclusion criteria: 1. Corneas without a histopathological examination. 2. Corneas with a histopathological examination that could not be assessed due to poor quality.

The corneas were classified into two groups based on origin and histopathological analysis as follows: 1. Donated corneas, which in turn include the residual rim of transplanted corneas, as well as non-transplanted corneas with tectonic function. 2. Corneas removed from corneal transplant recipients.

2.2. Data collection.

The information search was conducted retrospectively in the patients' medical records, as well as in the records of the donors included in the study period. Histopathological samples submitted to the Department of Pathology during 2024 at the National Medical Center "Siglo XXI" Specialty Hospital were reviewed in accordance with the national regulatory protocol for organ donation. All evaluations were performed by certified pathologists and subjected to blinded peer review.

2.3. Ethical Aspects.

There was no research risk, as a retrospective study it was conducted on tissue from deceased donors, so the integrity and health of patients who meet the inclusion criteria for the study were not jeopardized. While, tissues extracted from recipient patients to perform the corneal transplant were sent for histopathological study as in any other medical-surgical procedure where tissue is extracted, so this information was collected retrospectively.

2.4. Statistical Analysis.

Since the main objective of the study is to describe the characteristics and distribution of variables without establishing causal relationships between them, statistical analysis focused on summarizing and organizing the information to provide a clear view of the patterns and frequencies in the collected data. The following were performed: 1. Frequency and distribution analysis of qualitative variables. 2. Measures of central tendency and dispersion for quantitative variables. For the analysis of variables, averages were used as measures of central tendency and standard deviation as measures of dispersion if the distribution was like normal. Otherwise, the variables were summarized using medians and interquartile ranges. 3. Descriptive analysis of ordinal variables. For ordinal qualitative variables (such as the severity of the histopathological alteration, corneal vascularization, etc.), descriptive statistics were used to observe the frequency of each category within the ordinal scales.

3. Results

The sample consisted of a total of 256 donors and 134 recipients.

3.1. Donors

The characteristics of the donors included in the analysis are presented in Table 1. The average donor age was 44.57 ± 12.47 years, with a proportion of men of 63.7% and women of 36.3%. Regarding the lateral distribution of the donated eyeball, an almost uniform distribution was recorded, with 126 corneas from the right eye (49.2%) and 130 from the left eye (50.8%).

Age	44.57 ± 12.47 Years (Mean ± S. D.)	
	Donors (n = 256)	
Male = 163 (63.7)		Female = 93 (36.3)
	Laterality	
Right Eye = 126 (49.2)		Left Eye = 130 (50.8)
Diagnosis of death		
Cardiovascular diseases	121 (47.3)	
Respiratory diseases	39 (15.2)	
Trauma	22 (8.6)	
Infectious diseases	2 (0.8)	
Neurological diseases	11 (4.3)	
Cerebrovascular diseases	30 (11.7)	
Metabolic diseases	18 (7.0)	
Renal diseases	8 (3.1)	
Abdominal diseases	2 (0.8)	
Others	3 (1.2)	
	Serology	
Positive 0 (0)		Negative 256 (100)
	Destiny	
Optics 137 (53.5)		Tectonics 119 (46.5)

Table 1: Characteristics of the donors included in the study. ( ) = %

Of the total sample, serology was negative in 100% of cases. Regarding the use of corneal tissue, it was determined that 137 corneas (53.5%) were assigned for optical purposes, i.e., for vision restoration, while 119 (46.5%) were used for tectonic purposes, primarily to preserve the structural integrity of the eyeball.

3.2. Histopathological characteristics of donated corneas

The presence of histopathological abnormalities and their frequency were investigated in donated corneas. Of the 256 corneas, 148 (57.81%) presented some type of histopathological abnormality, while 42.19% (n=108) showed no classified abnormalities (Figure 1).

Regarding abnormalities, elastosis was the most prevalent, identified in 46 cases (18.04%), followed by isolated inflammation in 17 cases (6.67%). Combined lesions were also recorded, with two cases of elastosis with inflammation (0.78%) and one case of ulceration with inflammation (0.39%) documented, while 189 corneas (74.12%) showed no classified abnormalities. Related to the severity of the alterations, 51 cases (19.9%) were attributed to mild lesions, while moderate and severe lesions each only accounted for 3.1% of the tissues examined. In the remaining 189 corneal tissues (73.8%), this classification was not implemented due to the absence of alterations.

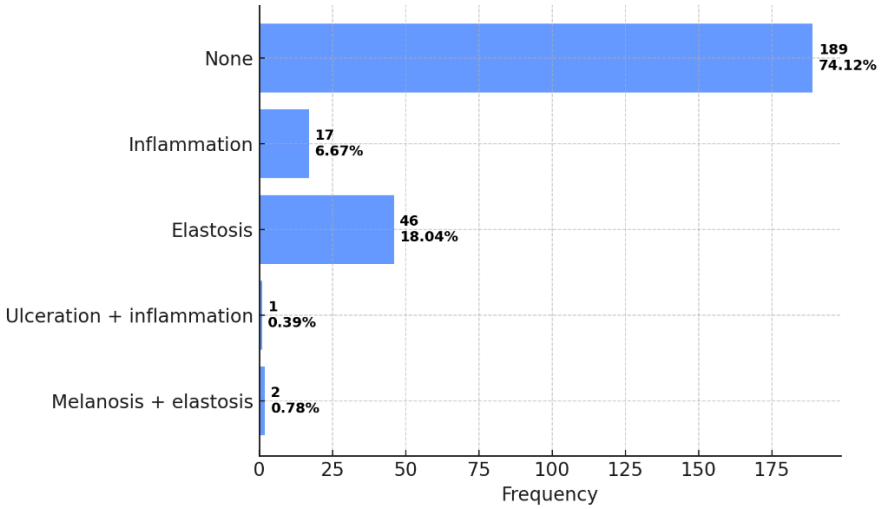

Figure 1: Frequency of histopathological abnormalities found in donated corneas.

During the structural evaluation, the epithelium stood out as one of the most affected layers. 175 tissues (68.4%) exhibited preserved epithelium, while the remaining 74 (28.9%) showed epithelial absence. A small proportion of tissues exhibited detachment (2.3%) or folding (0.4%) of epithelium. Bowman's membrane exhibited no abnormalities in any instance (100% normal), a situation that contrasts with the stroma, where detachments were detected in five tissues (2.0%) and thickening in three (1.2%). The majority (96.9%) reported a normal state. Descemet's membrane was detached in two cases (0.8%) and folded in one (0.4%). The percentage of normality was significantly high (98.8%). Finally, the morphology of the endothelium showed similarities to that of the epithelium, as only 175 tissues (68.36%) exhibited normal morphology. Endothelial absence was recorded in 74 individuals (28.91%), detachment in 6 individuals (2.34%), and folding in 1 individual (0.39%).

In the perilimbar conjunctiva, pathological abnormalities were detected in 46 tissues, representing 17.9% of the cases. These included elastosis (9.38%), inflammation (4.69%), melanosis (2.34%), calcification (0.39%), and complications of these alterations, such as melanosis with elastosis (0.78%) or inflammation with thickening (0.39%). The most of tissues, specifically 82.03%, did not exhibit alterations in this region.

Only 5 tissues (2.0%) presented calcifications, while vascularization was a rare alteration, observed in only 1 case (0.4%). Chronic inflammation material was detected in 14 cases (5.5%), and acute inflammation infiltrate in 6 tissues (2.3%).

3.3. Recipient patients

The characteristics of the recipient patients included in the analysis are presented in Table 2. A total of 134 recipient patients were included in the analysis: 53.73% were male and 46.27% were female, with a mean age of 57.65 ± 19.32 years. In 55.97% of cases, the right eye was transplanted, while in 44.03% it was the left.

Age	57.65 ± 19.32 Years (Mean ± S. D.)
Recipients (n = 134)	
Male = 72 (53.73)	Female = 62 (46.27)
Laterality	
Right Eye = 75 (55.97)	Left Eye = 59 (44.03)
Clinical Diagnosis	
Bullous Keratopathy	49 (36.57)
Keratoconus	25 (18.66)
Corneal rejection	17 (12.69)
Corneal ulcer	12 (8.96)
Sequelae of herpetic keratitis	11 (8.21)
Sequelae of bacterial keratitis	6 (4.48)
Sequelae of ocular trauma	5 (3.73)
Fuchs' dystrophy	4 (2.99)
Sequelae of Acanthamoeba keratitis	2 (1.49)

Descematocele	2 (1.49)
Sequela of lagophthalmos	1 (0.75)

Table 2. Characteristics of the recipients included in the study. ( ) = %

The characteristics and histopathological findings of the recipient corneal tissues were also analyzed.

According to the clinical diagnosis, bullous keratopathy was the most frequent indication, representing 36.57% of cases, followed by keratoconus (18.66%) and corneal graft rejection (12.69%). To a lesser extent, cases of corneal ulcer were identified in 8.96%, sequelae of herpetic keratitis in 8.21%, bacterial keratitis in 4.48%, and sequelae of ocular trauma in 3.73%. Other less frequent causes included Fuchs' dystrophy (2.99%), sequela of Acanthamoeba keratitis (1.49%), descematocele (1.49%), and sequela of lagophthalmos (0.75%)

In the analysis of the 134 tissues, the majority (n = 109, 81.3%) did not exhibit classified histopathological alterations but presented isolated anomalies. However, in 25 cases (18.7%), various types of lesions were detected. Inflammation was identified as the most prevalent alteration, occurring in 15 corneal tissues (11.2%), followed by ulceration (2.2%), calcification (1.5%), and other less frequent conditions such as fibrosis, necrosis, or infection, each with a frequency of 0.7%. Complications of lesions in certain tissues were also identified, such as inflammation with necrosis and ulceration accompanied by inflammation and necrosis. Regarding the severity of the alterations, they were identified as mild in 9.7% of the tissues, moderate in 3.0%, and severe in 6.0%.

Classifying the anomalies observed by layers in the removed tissues. In the epithelium, only 40 corneas, representing 29.85%, preserved a normal morphology. The most frequently observed anomalies included epithelial absence in 41.04%, bulla formation in 5.33%, subepithelial fibrosis in 4.48%, dyskeratosis in 3.73%, and acanthosis in 2.91%. Additionally, 9.7% of the tissues exhibited two or more epithelial abnormalities simultaneously; cases with simultaneous presence of bullae and subepithelial fibrosis were documented in three cases (2.2%), as well as bullae accompanied by dyskeratosis in two cases (1.5%), and bullae with fibrosis and acanthosis in two other tissues (1.5%). Less commonly, combinations such as epithelial detachment with bullae, bullae with calcification, subepithelial fibrosis associated with acanthosis, dyskeratosis with acanthosis, and the coexistence of epithelial absence, bullae, and fibrosis in the same tissue were identified; each of these combinations was present in one case (0.7%), (Figure 2).

Bowman's membrane was preserved in its original state in most cases (89.6%), however, alterations such as folding (2.99%), calcification (2.24%), detachment (1.49%), absence (1.49%), thinning (0.75%) were found, as well as the combination of thinning and detachment in one of the cases.

Normal stroma was recorded in 95 tissues (70.9%), however, changes such as thickening (10.4%), disorganization (8.2%), calcification (2.2%), and vascularization (2.2%) were detected, among other alterations. Various alterations were observed in certain tissues, such as disorganization in conjunction with calcification and cyst formation (0.7%).

In 85.8% of cases, Descemet's membrane was normal. While the most common abnormalities including folding (11.9%), and to a lesser extent, sloughing (0.7%), or combinations such as thickening and folding (1.5%).

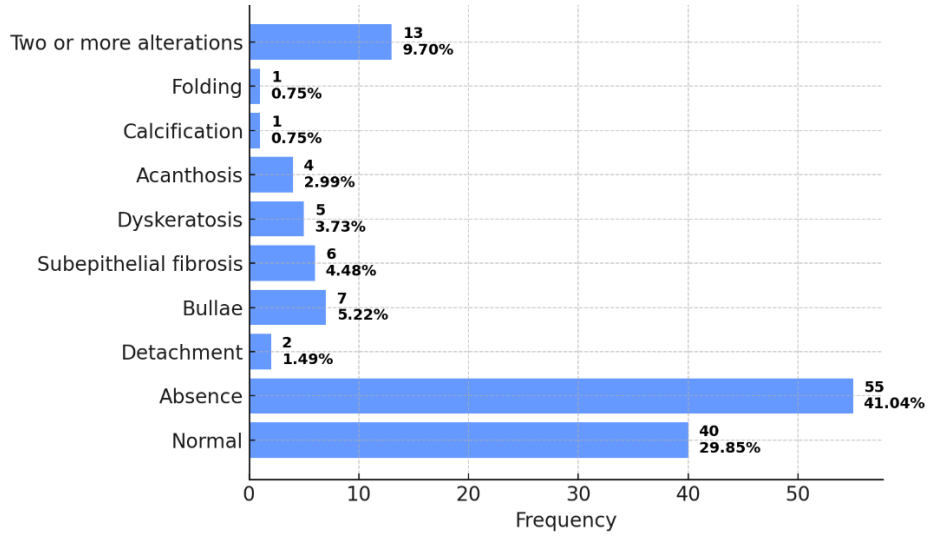

Figure 2: Frequency of histopathological abnormalities found in corneal epithelium of recipients.

Regarding the endothelium, only 54 tissues (40.3%) presented a normal structure, while endothelial absence was recorded in 75 tissues (56.0%), and to a lesser extent, detachment (0.7%) and folding (3.0%).

Calcifications were recorded in five tissues (3.7%), while vascularization was also observed in four cases (3.0%). Ultimately, the manifestation of inflammation was negligible: only one tissue (0.75%) showed acute inflammation, while 99.25% (n=133) did not show inflammatory infiltration.

4. Discussion

This study describes in detail the histopathological findings in 390 corneas processed by the institutional service of Pathological Anatomy were reviewed, corresponding to 256 donors selected by Donors Coordination and 134 recipients selected by Corneal Transplant Service. This analysis represents a significant contribution to national knowledge about the structural quality of corneal tissues used in keratoplasty procedures, the subclinical alterations present in non-transplanted tectonic corneas, and the characteristic histopathological patterns of explanted tissues, frequently associated with advanced pathologies.

4.1. Findings in the donated corneal group

In the group of donated corneas, which included both the residual rims of transplanted tissue and tectonic corneas not used in the transplant procedure, 57.81% presented at least one histopathological alteration. The most frequent alteration was elastosis (18.04%), identified as a

histological pattern characterized by the abnormal reorganization of limbal stromal fibers: tortuous, fragmented, and increased in number, partially replacing normal corneal collagen (Figure 3). This finding is typical of chronic actinic damage associated with prolonged exposure to ultraviolet radiation and has been widely documented in tissues such as the skin.[15]

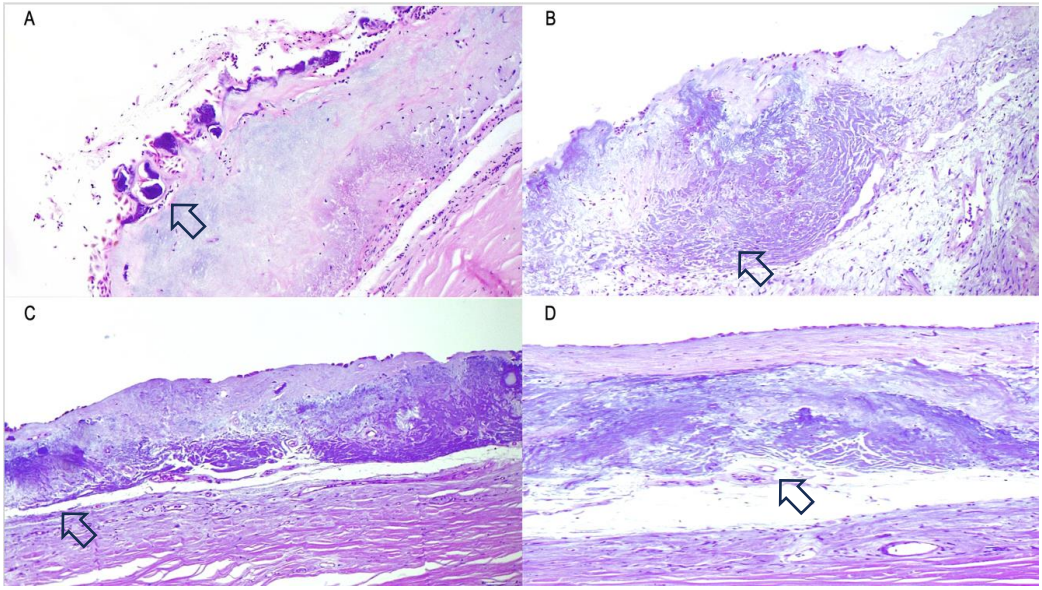

Figure 3: Histopathological section photograph with hematoxylin and eosin staining x10. A) Elastosis with calcification. B) Nodular elastosis. C and D) Plaque elastosis.

The observed corneal elastosis do not shares characteristics with the alterations associated with sun damage as pterygium and pinguecula; in this case it presents as acellular, avascular tissue with minimal inflammation, which differentiates it from clinically active entities such as pterygium, in which main histologic findings include invading pterygium epithelial cells with proliferative features, squamous metaplasia, hyperplasia of goblet cells, underlying disrupted Bowman's layer, stromal fibroblasts and vessels, altered extracellular matrix with accumulation of collagen and elastin fibers, and inflammatory infiltration.[16] Its presence in donated tissue, particularly in the sclero-corneal limbus region, suggests a prolonged history of sun exposure, especially in elderly patients. Although it is not an absolute contraindication for transplantation, it can affect the optical quality of the graft and should be considered during the preoperative evaluation.

Other common alterations included loss or damage to the corneal epithelium (28.9%) and endothelium (28.91%), which may be related to the postmortem time, handling during procurement, or tissue preservation conditions. Histologically, epithelial denudation can be observed as the loss of the superficial layer with exposure of the basement membrane or Bowman's membrane, while endothelial absence manifests as the disappearance of the posterior monolayer, often accompanied by undulations or folds in Descemet's membrane. These observations reinforce the need to standardize tissue procurement and preservation protocols, as the endothelium is essential for maintaining corneal transparency and graft function. [10,13] Perilimbal conjunctival alterations have also been identified, such as melanosis, elastosis, and inflammation, which reflect chronic degenerative processes or prolonged environmental exposure.

4.2. Findings in the explanted corneal group

In the group of explanted corneas from recipients, 18.7% were found to have classified structural histological alterations, with inflammation being the predominant finding (11.2%), followed by fibrosis, ulceration, and calcification.[17] Acute inflammation is characterized by a neutrophilic infiltrate, while chronic inflammation presents lymphocytes, plasma cells, and occasionally macrophages. These responses may be related to infectious keratitis, immune-mediated diseases, or rejection of previous grafts. Fibrosis was identified as a pattern of disorganized collagen in the stroma, representing a chronic reparative response that alters the lamellar architecture. Corneal ulceration, evidenced by loss of epithelium and surface stroma, is a common consequence of pathologies such as infectious or autoimmune keratitis. Calcification, observed as intensely stained basophilic deposits in the stroma or Bowman's membrane, may be associated with chronic inflammatory processes or local metabolic alterations. Despite these findings, it is noteworthy that more than 80% of the explanted grafts did not present major histological alterations, which opens the possibility of implementing lamellar techniques, such as Deep Anterior Lamellar Keratoplasty (DALK) or Descemet Stripping Automated Endothelial Keratoplasty (DSAEK), in patients with localized corneal diseases where the deep stromal structure remains functional. However, the present study did not include individual clinical correlation for each case, which represents a limitation that should be considered for future research.

4.3. Comparison between affected corneal layers

Layer-by-layer analysis showed that the epithelium and endothelium were the most affected in both groups. Endothelial absence was more frequent in explanted corneas (56%) than in donor corneas (28.91%), which could reflect irreversible damage secondary to advanced corneal disease or previous surgical procedures. This finding is consistent with that reported by who documented progressive endothelial loss in chronic keratopathies and after penetrating keratoplasty [14]. Cases of corneal vascularization (0.4% in donors, 3.0% in recipients) and calcification (2.9% and 3.7%, respectively) were also identified. Both findings, although less frequent, are clinically relevant due to their association with an increased risk of immunological rejection, persistent chronic inflammation, and decreased graft survival.[7,13]

4.4. Clinical value of histological analysis and perspectives

Even when histological examination prior to transplantation is not performed; however, the results obtained in this study show that postoperative microscopic evaluation can provide relevant information on the viability and quality of the transplanted tissue, as well as on alterations not clinically detected at the time of procurement.

We consider that although this study is limited by its retrospective, single-center design, and the lack of individualized clinical correlation, it represents a pioneering effort in the structural characterization of corneas in a highly specialized center in Mexico. The findings support the need for internal classification protocols, encourage the rational use of available tissue, and promote future multicenter research that correlates histopathological findings, clinical variables, and long-term visual outcomes.

5. Conclusions

These results underscore the usefulness of histopathological analysis as a tool for monitoring and continuously improving corneal tissue traceability. Its post-transplant application contributes to optimizing obtaining, preservation, allocation, and disposal processes, in addition to providing evidence for the design of more rigorous strategies for evaluating ocular tissue.

It is recommended that multicenter research be continued to correlate these findings with the clinical and functional outcomes of the grafts, thus strengthening the safety and efficacy of corneal transplantation in public health institutions.

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