Sobrevida libre de rechazo o falla en pacientes sometidos a queratoplastia penetrante

Nombres y apellidos:

José Enrique Carpio Cordero
Código estudiantil: 2022217145897

Juan David Sánchez Barahona
Código estudiantil: 2022217146247

Trabajo de Investigación presentado como requisito para optar el título de:
Especialista en Oftalmología

Tutores:

Natina Ester Pinto Osorio
Md | Spc Oftalmología

Henry J González Torres
Bio | Spc App Stat | Msc Bio (GENPOP) | PhD (C) Biomed

RESUMEN

La queratoplastia penetrante (QP) es una técnica quirúrgica ampliamente empleada para tratar enfermedades corneales que afectan la transparencia y funcionalidad visual. A pesar de los avances, el rechazo inmunológico y la falla del injerto siguen siendo desafíos relevantes para su sobrevida a largo plazo.

Objetivo: Evaluar la sobrevida libre de rechazo o falla del injerto en pacientes sometidos a queratoplastia penetrante en una institución de referencia en Barranquilla entre 2018 y 2023.

Métodos: Se realizó un estudio retrospectivo y analítico. Se incluyeron 299 pacientes mayores de 18 años con seguimiento postoperatorio ≥6 meses. Se recolectaron variables clínicas, quirúrgicas y del donante. Se aplicaron análisis descriptivos, pruebas de asociación (Chi-cuadrado, Wilcoxon) y curvas de Kaplan-Meier para estimar la sobrevida según sexo, medio de preservación y tiempo de isquemia. Se utilizó R (v4.3.3) para el análisis.

Resultados: La sobrevida libre de rechazo o falla a los 12 meses fue del 91% (IC 95%: 87.6–94.5%). No se encontraron diferencias significativas por sexo ni por tiempo de isquemia. La tasa de rechazo fue mayor en injertos preservados con Optisol (22%) comparado con Eusol (7.3%, $p<0.001$), aunque la sobrevida general fue similar. El queratocono fue más frecuente en hombres jóvenes, mientras que leucomas y rechazos previos predominaron en mujeres mayores.

Conclusión: La QP muestra una alta efectividad a corto plazo. El medio de preservación y la patología de base podrían influir en el riesgo de rechazo, lo que resalta la necesidad de estrategias individualizadas.

Palabras clave: Queratoplastia penetrante; Rechazo del injerto; Medio de preservación; Sobrevida; Córnea.

ABSTRACT

Penetrating keratoplasty (PK) is a widely used surgical technique for treating corneal diseases that impair transparency and visual function. Despite technical advances, graft rejection and failure remain significant challenges for long-term survival.

Objective: To evaluate rejection-free or graft failure-free survival in patients undergoing penetrating keratoplasty at a referral institution in Barranquilla between 2018 and 2023.

Methods: A retrospective, analytical study was conducted. A total of 299 patients aged >18 years with ≥6 months of postoperative follow-up were included. Clinical, surgical, and donor variables were collected. Descriptive statistics, chi-square and Wilcoxon tests were used, and Kaplan-Meier survival curves estimated graft survival by sex, preservation medium, and ischemia time. R software (v4.3.3) was used for analysis.

Results: Graft survival free of rejection/failure at 12 months was 91% (95% CI: 87.6–94.5%). No significant differences were observed by sex or ischemia time. Rejection was more frequent with grafts preserved in Optisol (22%) compared to Eusol (7.3%, $p<0.001$), although overall survival was similar. Keratoconus was more prevalent in younger males, whereas leucomas and prior rejections were more common in older females.

Conclusion: PK demonstrates high short-term effectiveness. Preservation medium and underlying pathology may influence rejection risk, highlighting the importance of individualized strategies.

Keywords: Penetrating keratoplasty; Graft rejection; Preservation medium; Survival; Cornea.

REFERENCIAS BIBLIOGRÁFICAS

1. Gurnani B, Kaur K. Penetrating Keratoplasty. StatPearls. 2025.
2. Yang Y, Zeng H, Gong L, Lin T. Risk Factors for Graft Failure After Penetrating Keratoplasty in Eastern China from 2018 to 2021. Ann Transplant. 2024 Oct;29:e945388.
3. Pedersen IB, Ivarsen A, Hjortdal J. Graft rejection and failure following endothelial keratoplasty (DSAEK) and penetrating keratoplasty for secondary endothelial failure. Acta Ophthalmol. 2015 Mar;93(2):172–7.
4. Hawa-Montiel H. Trasplante de córnea. Criterio clínico quirúrgico. Rev Investig Clin. 2005;57(2):358–67.
5. Nova MAS, Murillo YRA. Informe anual 2020 de la Red de Donación y Trasplantes en Colombia del Instituto Nacional de Salud. Inst Nac SALUD. 2020;10.
6. Vidaurrazaga-Sosa GM, Bravo-Ramírez KD, Ornelas-Aguirre JM. Factors associated with corneal transplant failure. Rev Mex Oftalmol (English Ed. 2022 Feb;96(1).
7. Goel MK, Khanna P, Kishore J. Understanding survival analysis: Kaplan-Meier estimate. Int J Ayurveda Res. 2010 Oct;1(4):274–8.
8. Leyva E, Pérez Parra Z, Pérez A, Ochoa M, Hernández S. Perfil epidemiológico del donante y del receptor en trasplante de córnea en el Instituto Cubano de Oftalmología “Ramón Pando Ferrer.” Rev Cuba Oftalmol. 2014;27:558–68.
9. Asimellis G, Kaufman EJ. Keratoconus. StatPearls. 2025.
10. Barraquer RI, Pareja-Aricò L, Gómez-Benlloch A, Michael R. Risk factors for graft failure after penetrating keratoplasty. Medicine (Baltimore). 2019 Apr;98(17):e15274.
11. Song A, Deshmukh R, Lin H, Ang M, Mehta JS, Chodosh J, et al. Post-keratoplasty Infectious Keratitis: Epidemiology, Risk Factors, Management, and Outcomes. Front Med. 2021;8:707242.
12. Ittah-Cohen I, Knoeri MJ, Bourcier T, Merabet L, Bouheraoua N, Borderie VM. Infectious keratitis following corneal transplantation: A long-term cohort study. Clin Experiment Ophthalmol. 2024 May;52(4):402–15.
13. Rahman I, Carley F, Hillarby C, Brahma A, Tullo AB. Penetrating keratoplasty: indications, outcomes, and complications. Eye (Lond). 2009 Jun;23(6):1288–94.
14. Szaflik JP, Major J, Izdebska J, Lao M, Szaflik J. Systemic immunosuppression with mycophenolate mofetil to prevent corneal graft rejection after high-risk penetrating keratoplasty: a 2-year follow-up study. Graefes Arch Clin Exp Ophthalmol. 2016 Feb;254(2):307–14.
15. Reinhard T, Reis A, Böhringer D, Malinowski M, Voiculescu A, Heering P, et al. Systemic mycophenolate mofetil in comparison with systemic cyclosporin A in high-risk keratoplasty patients: 3 years’ results of a randomized prospective clinical trial. Graefes Arch Clin Exp Ophthalmol. 2001 Jun;239(5):367–72.

16. Hernández-Da Mota SE, Paniagua Jacobo M, Gómez Revuelta G, Páez Martínez RM. [Corneal transplant in a second level hospital. A survival analysis]. Gac Med Mex. 2013;149(4):425–30.
17. Maghsoudlou P, Sood G, Gurnani B, Akhondi H. Cornea Transplantation. StatPearls. 2025.
18. Gain P, Jullienne R, He Z, Aldossary M, Acquart S, Cognasse F, et al. Global Survey of Corneal Transplantation and Eye Banking. JAMA Ophthalmol [Internet]. 2016 Feb;134(2):167–73. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26633035
19. Bahar I, Kaiserman I, Lange AP, Levinger E, Sansanayudh W, Singal N, et al. Femtosecond laser versus manual dissection for top hat penetrating keratoplasty. Br J Ophthalmol. 2009 Jan;93(1):73–8.
20. Matthaei M, Sandhaeger H, Hermel M, Adler W, Jun AS, Cursiefen C, et al. Changing Indications in Penetrating Keratoplasty: A Systematic Review of 34 Years of Global Reporting. Transplantation. 2017 Jun;101(6):1387–99.
21. Mamalis N, Craig MT, Coulter VL, Lundergan MK, Olson RJ. Penetrating keratoplasty 1981 – 1988: Clinical indications and pathologic findings. J Cataract Refract Surg. 1991 Mar;17(2):163–7.
22. Keane M, Coster D, Ziaei M, Williams K. Deep anterior lamellar keratoplasty versus penetrating keratoplasty for treating keratoconus. Cochrane Database Syst Rev. 2014 Jul;2014(7).
23. Klintworth GK. Corneal dystrophies. Orphanet J Rare Dis. 2009 Feb;4:7.
24. Crawford AZ, Patel D V, McGhee CN. A brief history of corneal transplantation: From ancient to modern. Oman J Ophthalmol. 2013 Sep;6(Suppl 1):S12-7.
25. Armitage WJ, Tullo AB, Larkin DFP. The first successful full-thickness corneal transplant: a commentary on Eduard Zirm's landmark paper of 1906. Br J Ophthalmol. 2006 Oct;90(10):1222–3.
26. Landau D, Siganos CS, Mechoulam H, Solomon A, Frucht-Pery J. Astigmatism After Mersilene and Nylon Suture Use for Penetrating Keratoplasty. Cornea. 2006 Jul;25(6):691–4.
27. Van Meter WS, Gussler JR, Soloman KD, Wood TO. Postkeratoplasty astigmatism control. Single continuous suture adjustment versus selective interrupted suture removal. Ophthalmology. 1991 Feb;98(2):177–83.
28. Tran TM, Farid M. Update on Femtosecond Laser-Enabled Keratoplasty. Cornea. 2023 Apr;42(4):395–403.
29. Levinger E, Trivizki O, Levinger S, Kremer I. Outcome of "mushroom" pattern femtosecond laser-assisted keratoplasty versus conventional penetrating keratoplasty in patients with keratoconus. Cornea. 2014 May;33(5):481–5.
30. Gupta PK, Berdahl JP, Chan CC, Rocha KM, Yeu E, Ayres B, et al. The corneal endothelium: clinical review of endothelial cell health and function. J Cataract Refract Surg. 2021 Sep;47(9):1218–26.
31. Hos D, Matthaei M, Bock F, Maruyama K, Notara M, Clahsen T, et al. Immune reactions after modern lamellar (DALK, DSAEK, DMEK) versus conventional penetrating corneal transplantation. Prog Retin Eye Res. 2019 Nov;73:100768.

32. Singh NP, Said DG, Dua HS. Lamellar keratoplasty techniques. Indian J Ophthalmol. 2018 Sep;66(9):1239–50.
33. Watson SL, Tuft SJ, Dart JKG. Patterns of rejection after deep lamellar keratoplasty. Ophthalmology. 2006 Apr;113(4):556–60.
34. Gurnani B, Czyz CN, Mahabadi N, Havens SJ. Corneal Graft Rejection. StatPearls. 2025.
35. Al-Mezaine H, Wagoner MD, King Khaled Eye Specialist Hospital Cornea Transplant Study Group. Repeat penetrating keratoplasty: indications, graft survival, and visual outcome. Br J Ophthalmol. 2006 Mar;90(3):324–7.
36. Gurnani B, Somani AN, Moshirfar M, Patel BC. Fuchs Endothelial Dystrophy. StatPearls. 2025.
37. Castano G, Elnahry AG, Mada PK. Fungal Keratitis. StatPearls. 2025.
38. Nguyen NX, Seitz B, Langenbucher A, Wenkel H, Cursiefen C. [Clinical aspects and treatment of immune reactions following penetrating normal-risk keratoplasty]. Klin Monbl Augenheilkd. 2004 Jun;221(6):467–72.
39. Qi X, Wang L, Zhang X, Liu M, Gao H. Topical administration of tacrolimus and corticosteroids in tapering doses is effective in preventing immune rejection in high-risk keratoplasty: a 5-year follow-up study. BMC Ophthalmol. 2022 Dec;22(1):101.
40. Nguyen P, Barte F, Shinada S, Yiu SC. Management of Corneal Graft Rejection - A Case Series Report and Review of the Literature. J Clin Exp Ophthalmol. 2010 Sep;1(103).
41. Reis A, Reinhard T, Voiculescu A, Kutkuhn B, Godehardt E, Spelsberg H, et al. Mycophenolate mofetil versus cyclosporin A in high risk keratoplasty patients: a prospectively randomised clinical trial. Br J Ophthalmol. 1999 Nov;83(11):1268–71.
42. Birnbaum F, Mayweg S, Reis A, Böhringer D, Seitz B, Engelmann K, et al. Mycophenolate mofetil (MMF) following penetrating high-risk keratoplasty: long-term results of a prospective, randomised, multicentre study. Eye. 2009 Nov;23(11):2063–70.
43. Writing Committee for the Cornea Donor Study Research Group, Mannis MJ, Holland EJ, Gal RL, Dontchev M, Kollman C, et al. The effect of donor age on penetrating keratoplasty for endothelial disease: graft survival after 10 years in the Cornea Donor Study. Ophthalmology. 2013 Dec;120(12):2419–27.
44. Kozioł M, Nowak MS, Udziela M, Szaflik JP. The Association between Diabetes Mellitus and Keratoplasty in Poland in the Years 2013-2017. Int J Environ Res Public Health. 2021 Sep;18(18).
45. Pramanik S, Musch DC, Sutphin JE, Farjo AA. Extended long-term outcomes of penetrating keratoplasty for keratoconus. Ophthalmology. 2006 Sep;113(9):1633–8.
46. Vieira-Potter VJ, Karamichos D, Lee DJ. Ocular Complications of Diabetes and Therapeutic Approaches. Biomed Res Int. 2016;2016:3801570.
47. Dziedziak J, Zaleska-Żmijewska A, Szaflik JP, Cudnoch-Jędrzejewska A. Impact of Arterial Hypertension on the Eye: A Review of the Pathogenesis, Diagnostic Methods, and Treatment of Hypertensive Retinopathy. Med Sci

Monit. 2022 Jan;28:e935135.
48. V??lker-Dieben HJ, Claas FHJ, Schreuder GMT, Schipper RF, Pels E, Persijn GG, et al. BENEFICIAL EFFECT OF HLA-DR MATCHING ON THE SURVIVAL OF CORNEAL ALLOGRAFTS1. Transplantation. 2000 Aug;70(4):640–8.
49. Hu K, Patel J, Swiston C, Patel BC. Ophthalmic Manifestations of Coronavirus (COVID-19). StatPearls. 2025.
50. Greenlee EC, Kwon YH. Graft failure: III. Glaucoma escalation after penetrating keratoplasty. Int Ophthalmol. 2008 Jun;28(3):191–207.
51. Zang YX, Peng RM, Qu Y, Liu XZ, Hong J. [Risk factors of cytomegalovirus infection in patients with failed corneal grafts]. Zhonghua Yan Ke Za Zhi. 2024 Feb;60(2):137–46.
52. Cornea Donor Study Investigator Group, Lass JH, Gal RL, Dontchev M, Beck RW, Kollman C, et al. Donor age and corneal endothelial cell loss 5 years after successful corneal transplantation. Specular microscopy ancillary study results. Ophthalmology. 2008 Apr;115(4):627-632.e8.
53. Sousa SJ de F e. Eye bank procedures : donor selection criteria Procedimentos em banco de olhos : critério de seleção do doador. 2018;81(1):6–8.
54. Lass JH, Benetz BA, Gal RL, Kollman C, Raghinaru D, Dontchev M, et al. Donor Age and Factors Related to Endothelial Cell Loss 10 Years after Penetrating Keratoplasty. Ophthalmology. 2013 Dec;120(12):2428–35.
55. Kaur K, Gurnani B. Specular Microscopy. StatPearls. 2025.
56. Agbato D, Rickford K, Laroche D. Central Corneal Thickness and Glaucoma Risk: The Importance of Corneal Pachymetry in Screening Adults Over 50 and Glaucoma Suspects. Clin Ophthalmol. 2025;19:563–70.
57. O'Donnell C, Wolffsohn JS. Grading of corneal transparency. Contact Lens Anterior Eye. 2004 Dec;27(4):161–70.
58. Martin R. Cornea and anterior eye assessment with slit lamp biomicroscopy, specular microscopy, confocal microscopy, and ultrasound biomicroscopy. Indian J Ophthalmol. 2018 Feb;66(2):195–201.
59. Lindstrom RL, Kaufman HE, Skelnik DL, Laing RA, Lass JH, Musch DC, et al. Optisol Corneal Storage Medium. Am J Ophthalmol. 1992 Sep;114(3):345–56.
60. Mena-Linares EE, Vázquez-Maya L, García-Carmona K, Martínez-Mijares MA, Baldivieso-Hurtado R. Endothelial cell viability comparing Eusol-C vs Optisol-GS as corneal preservation medium. Rev M□dica del Hosp Gen M□xico [Internet]. 2023 Oct 3;86(4). Available from: https://www.hospitalgeneral.mx/frame_eng.php?id=177
61. Nelson JD, Lange DB, Lindstrom RL, Doughman DJ, Hatchell DL. McCarey-Kaufman (MK) Organ Culture and MK Medium-Shifted Corneas. Arch Ophthalmol. 1984 Feb;102(2):308–11.
62. Qureshi S, Dohlman TH. Penetrating Keratoplasty: Indications and Graft Survival by Geographic Region. Semin Ophthalmol. 2023 Jan;38(1):31–43.
63. Feizi S. Corneal endothelial cell dysfunction: etiologies and management.

Ther Adv Ophthalmol. 2018;10:2515841418815802.
64. Oliver-Gutierrez D, Pares-Alfonso C, Anglada-Masferrer N, Bisbe L. Khodadoust Line Indicating Graft Rejection in Descemet's Stripping Automated Endothelial Keratoplasty: A Unique Case Report. J Curr Ophthalmol. 2024;36(1):96–8.
65. Price FW, Whitson WE, Marks RG. Progression of Visual Acuity after Penetrating Keratoplasty. Ophthalmology. 1991 Aug;98(8):1177–85.
66. Ang M, Mehta JS, Lim F, Bose S, Htoon HM, Tan D. Endothelial Cell Loss and Graft Survival after Descemet's Stripping Automated Endothelial Keratoplasty and Penetrating Keratoplasty. Ophthalmology. 2012 Nov;119(11):2239–44.
67. Saikumar Doradla L, Lal H, Kaul A, Bhaduaria D, Jain M, Prasad N, et al. Clinical profile and outcomes of De novo posttransplant thrombotic microangiopathy. Saudi J Kidney Dis Transplant. 2020;31(1):160.
68. Means TL, Geroski DH, Hadley A, Lynn MJ, Edelhauser HF. Viability of human corneal endothelium following Optisol-GS storage. Arch Ophthalmol (Chicago, Ill 1960) [Internet]. 1995 Jun;113(6):805–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/7786224
69. Abd ElHafeez S, D'Arrigo G, Leonardis D, Fusaro M, Tripepi G, Roumeliotis S. Methods to Analyze Time-to-Event Data: The Cox Regression Analysis. Oxid Med Cell Longev. 2021;2021:1302811.
70. Shin KY, Lim DH, Han K, Chung TY. Higher incidence of penetrating keratoplasty having effects on repeated keratoplasty in South Korea: A nationwide population-based study. PLoS One. 2020;15(7):e0235233.
71. Tan DT, Dart JK, Holland EJ, Kinoshita S. Corneal transplantation. Lancet [Internet]. 2012 May;379(9827):1749–61. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0140673612604371
72. Castellanos-González JA, Orozco-Vega R, González Ojeda A, Martínez Ruiz AM, Fuentes-Orozco C. Evaluation of the quality of life related to vision after penetrating keratoplasty. Arch la Soc Española Oftalmol (English Ed. 2021 Feb;96(2):69–73.
73. Aneeq Ansari MS, Zulfiqar N, Nafees K, Shaheen M. Improvement In Visual Acuity Six Months After Penetrating Keratoplasty In Patients Of Keratoconus. J Ayub Med Coll Abbottabad. 2021;33(2):289–92.
74. Chan CM, Wong TY, Yeong SM, Lim TH, Tan DT. Penetrating keratoplasty in the Singapore National Eye Centre and donor cornea acquisition in the Singapore Eye Bank. Ann Acad Med Singapore. 1997 Jul;26(4):395–400.
75. Yu AL, Kaiser M, Schaumberger M, Messmer E, Kook D, Welge-Lussen U. Perioperative and postoperative risk factors for corneal graft failure. Clin Ophthalmol. 2014;8:1641–7.
76. Böhringer D, Reinhard T. [Prognosis in repeat keratoplasty: per indication analysis in a large monocentric cohort]. Klin Monbl Augenheilkd. 2008 Jan;225(1):50–6.
77. Chung IK, Kim BS, Han KD, Yoo YS, Kim H, Jeong C. Ten-year incidence of keratoconus in relation to sex, age, and thyroid gland dysfunction: a nationwide population-based cohort study (2009–2018). Ann Transl Med.

2024;12(3):45–45.
78. Fink BA, Wagner H, Steger-May K, Rosenstiel C, Roediger T, McMahon TT, et al. Differences in keratoconus as a function of gender. Am J Ophthalmol. 2005 Sep;140(3):459–68.
79. Chuckpaiwong V, Jongkhajornpong P, Rajsirisongsri P, Sontichai V, Nijvipakul S, Lekhanont K. Impact of gender mismatch on corneal graft rejection and rejection-related graft failure in repeat penetrating keratoplasty. PLoS One. 2022;17(10):e0276043.
80. Zhai LY, Zhang XR, Liu H, Ma Y, Xu HC. Observation of topical tacrolimus on high-risk penetrating keratoplasty patients: a randomized clinical trial study. Eye (Lond). 2020 Sep;34(9):1600–7.
81. Hopkinson CL, Romano V, Kaye RA, Steger B, Stewart RMK, Tsagkataki M, et al. The Influence of Donor and Recipient Gender Incompatibility on Corneal Transplant Rejection and Failure. Am J Transplant. 2017 Jan;17(1):210–7.
82. Figueiredo GS, Kolli SSP, Ahmad S, Gales K, Figueiredo FC. Urrets-Zavalia syndrome following penetrating keratoplasty for keratoconus. Graefes Arch Clin Exp Ophthalmol. 2013 Mar;251(3):809–15.
83. Kostelná H, Rosocha J, Paulíková E, Kozák I, Antalová M, Mahel M, et al. Pathological findings in cornea tissue of patients with penetrating keratoplasty. Folia Histochem Cytobiol. 2010 Jan;48(2):267–72.
84. Mayer K, Reinhard T, Reis A, Niehues T, Claas FH, Sundmacher R. Differential contribution of natural killer cells to corneal graft rejection in 3-week-old versus mature rats. Transplantation. 2003 Aug;76(3):578–82.
85. Bal S, Ciolino JB. Penetrating keratoplasty using collagen crosslinked donor tissue: A case report. Am J Ophthalmol case reports. 2021 Jun;22:101039.
86. Abudou M, Wu T, Evans JR, Chen X. Immunosuppressants for the prophylaxis of corneal graft rejection after penetrating keratoplasty. Cochrane database Syst Rev. 2015 Aug;2015(8):CD007603.
87. Barraquer J. Immunosuppressive Agents in Penetrating Keratoplasty. Am J Ophthalmol. 1985 Jul;100(1):61–4.
88. Basu PK. A review of methods for storage of corneas for keratoplasty. Indian J Ophthalmol. 1995;
89. Jones NR, Hobbs FR, Taylor CJ. Prognosis following a diagnosis of heart failure and the role of primary care: a review of the literature. BJGP open [Internet]. 2017 Oct 4;1(3):bjgpopen17X101013. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30564675