Titolo rivista/libro: Ophthalmology

Titolo articolo/sezione: Follow-up Extension Up to 43 Years of Modified Osteo-Odonto-Keratoprosthesis

Autore/i: Colliardo P , Taloni A , Taloni M , Falcinelli G , Petitti L , Lucisano A , Busin M , Scorcia V , Giannaccare G

ISSN: 0161-6420

DOI: 10.1016/j.ophtha.2023.05.010

Anno: 2023

Volume: 130

Fascicolo: 9

Editore:

Pag. iniziale: 995

Pag. finale: 997

Armin Handzic, MD[1,*]
Marko Tien, BSc[2,*]
Roisin Maire O'Cearbhaill, MD[3]
Jim Shenchu Xie, BHSc[4]
Kirill Zaslavsky, MD, PhD[1]
Jonathan Micieli, MD[1,5,6]
Edward Margolin, MD[1,5]

[1]*Department of Ophthalmology and Vision Sciences, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada;* [2]*Faculty of Medicine, University of British Columbia, Vancouver, British Columbia, Canada;* [3]*Division of Neuroradiology, Department of Radiology, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada;* [4]*Michael G. DeGroote School of Medicine, McMaster University, Hamilton, Ontario, Canada;* [5]*Division of Neurology, Department of Medicine, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada;* [6]*Kensington Vision and Research Center, Toronto, Ontario, Canada*
[*]*Both authors contributed equally as first authors.*

Disclosure(s):
All authors have completed and submitted the ICMJE disclosures form. The author(s) have no proprietary or commercial interest in any materials discussed in this article.

HUMAN SUBJECTS: Human subjects were included in this study. The research protocol was approved by the University of Toronto Research Ethics Board and adhered to the tenets of the Declaration of Helsinki. The requirement for informed consent was waived because of the retrospective nature of the study.

No animal subjects were included in this study.

Author Contributions:
Conception and design: Handzic, Tien, Margolin
Analysis and interpretation: Handzic, Tien, Xie, Zaslavsky, Micieli, Margolin
Data collection: Handzic, Tien, Cearbhaill, Xie, Margolin
Obtained funding: N/A; Study was performed as part of regular employment duties at their institutions. No additional funding was provided.
Overall responsibility: Handzic, Tien, Cearbhaill, Xie, Zaslavsky, Micieli, Margolin

Keywords:
MOG, MOG-optic neuritis, Myelin oligodendrocyte glycoprotein, Poor visual outcome MOG, Predictor of visual outcome MOG.

Correspondence:
Edward Margolin, MD, Department of Ophthalmology and Visual Sciences, Department of Medicine, Division of Neurology, University of Toronto, 801 Eglinton Avenue West, Suite 301, Toronto, ON M5N 1E3, Canada. E-mail: Edward.margolin@uhn.ca.

References

1. Jarius S, Ruprecht K, Kleiter I, et al. MOG-IgG in NMO and related disorders: a multicenter study of 50 patients. Part 2: epidemiology, clinical presentation, radiological and laboratory features, treatment responses, and long-term outcome. *J Neuroinflammation*. 2016;13(1):280.
2. Jurynczyk M, Messina S, Woodhall MR, et al. Clinical presentation and prognosis in MOG-antibody disease: a UK study. *Brain*. 2017;140(12):3128–3138.
3. Morrow SA, Fraser JA, Day C, et al. Effect of treating acute optic neuritis with bioequivalent oral vs intravenous corticosteroids: a randomized clinical trial. *JAMA Neurol*. 2018;75(6):690–696.
4. Deschamps R, Philibert M, Lamirel C, et al. Visual field loss and structure-function relationships in optic neuritis associated with myelin oligodendrocyte glycoprotein antibody. *Mult Scler*. 2021;27(6):855–863.
5. Chen JJ, Flanagan EP, Jitprapaikulsan J, et al. Myelin oligodendrocyte glycoprotein antibody–positive optic neuritis: clinical characteristics, radiologic clues, and outcome. *Am J Ophthalmol*. 2018;195:8–15.
6. Stiebel-Kalish H, Hellmann MA, Mimouni M, et al. Does time equal vision in the acute treatment of a cohort of AQP4 and MOG optic neuritis? *Neurol Neuroimmunol Neuroinflamm*. 2019;6(4).
7. Chen JJ, Flanagan EP, Bhatti MT, et al. Details and outcomes of a large cohort of MOG-IgG associated optic neuritis. *Mult Scler Relat Disord*. 2022;68:104237.

Follow-up Extension Up to 43 Years of Modified Osteo-Odonto-Keratoprosthesis

The osteo-odonto-keratoprosthesis is a biological corneal prosthesis (KPro), introduced by Strampelli in 1964. It uses an osteodental lamina as a biological haptic derived from an autologous mono-radicular tooth. An acrylic optical cylinder at the center of the lamina replaces the cornea, and the resulting osteo-dental-acrylic lamina is preferably covered by autologous buccal mucosa or, if not available, by skin (Fig S1, available at www.aaojournal.org).[1] In 2005, Falcinelli et al[2] proposed several advances to the original surgical technique, the so-called modified osteo-odonto-keratoprosthesis (MOOKP), reporting favorable results in a large cohort of patients who underwent surgery between 1973 and 1999 and followed up to 25 years.[2]

This study aimed at extending the follow-up of the same cohort of patients, providing further evidence about long-term anatomic and functional outcomes of the MOOKP technique. The study adhered to the tenets of the Declaration of Helsinki. Institutional Review Board approval was obtained from San Camillo Hospital, Rome, Italy. Detailed informed consent was obtained from all patients.

Inclusion criteria were untreatable corneal disease and preoperative best-corrected visual acuity (BCVA) $\geq$ 0.52 logarithm of the minimum angle of resolution (logMAR) in both eyes or in the eye eligible for surgery, with BCVA $\geq$ 1.00 logMAR in the fellow noneligible eye. Pediatric patients (< 17 years), eyes with no light perception, and eyes affected by sight-threatening conditions of the posterior pole or uncontrolled glaucoma were excluded. Details about the surgical technique and the preoperative/postoperative evaluation have been reported in previous articles by Falcinelli et al.[2,3]

This study included 229 eyes of 205 patients (122 men, 83 women; age 54.1 $\pm$ 15.2 years). The most common indications for MOOKP included bilateral blindness or low vision caused by chemical burns or physical trauma (n = 84), end-stage dry eye due to ocular mucous membrane pemphigoid (n = 54), trachoma (n = 11), Sjögren's syndrome (n = 11), Steven-Johnson syndrome (n = 7), and Lyell syndrome (n = 8).

Autologous buccal mucosa was used in 206 eyes, skin was used in 22 eyes, and vaginal mucosa was used in 1 eye. Unlike the previous case series by Falcinelli et al[2] that analyzed

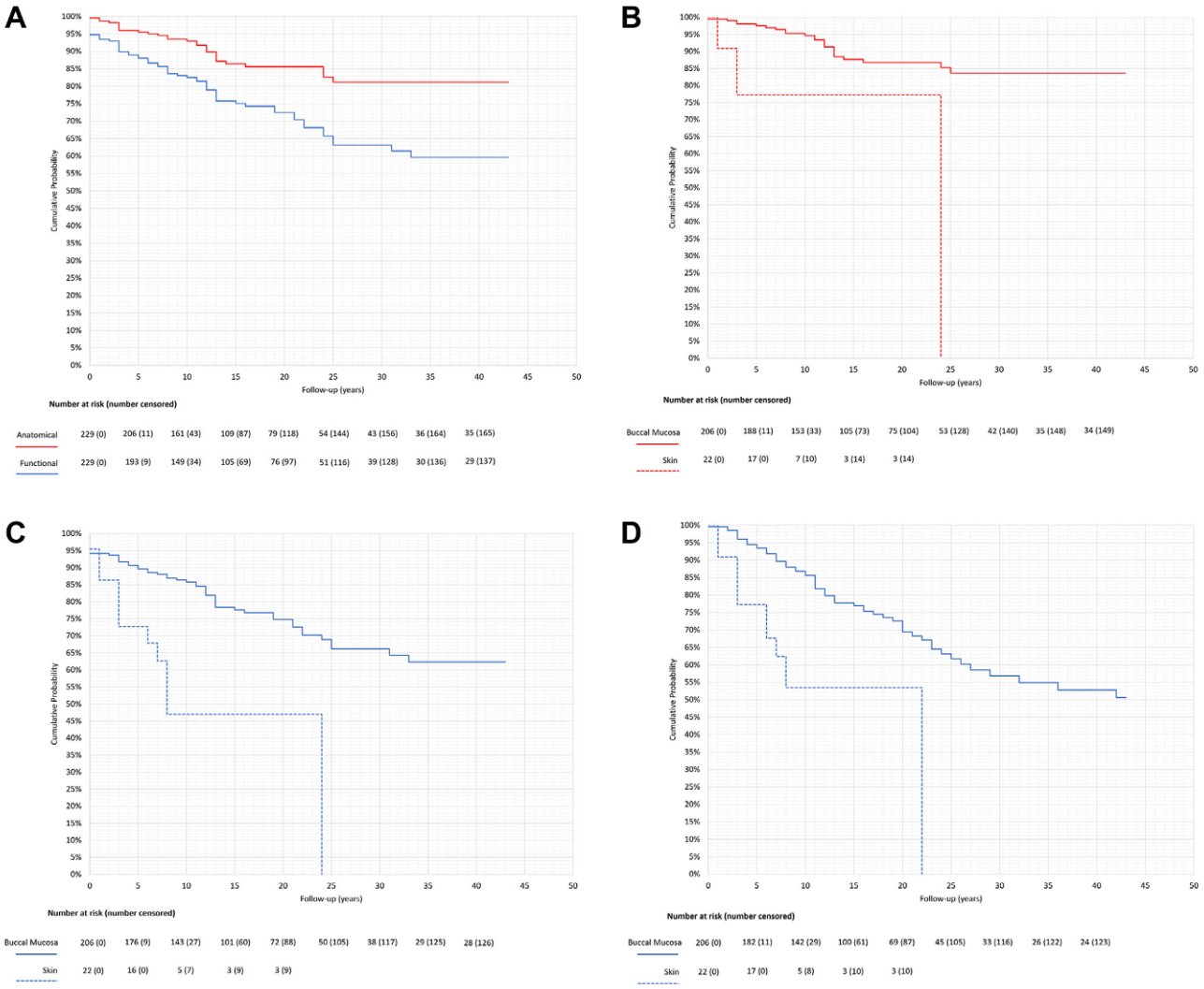

Figure 2. Kaplan–Meier analysis estimating overall anatomic (red continue line) and functional survival cumulative probability (**blue continue line**) **(A)**. Kaplan–Meier analysis estimating anatomic survival cumulative probability **(B)**, functional survival cumulative probability **(C)**, cumulative probability of retaining the best-corrected postoperative visual acuity (BCVA) within 2 lines **(D)**, and for eyes covered by buccal mucosa (**continue lines**) and by skin (**dashed lines**).

results of only eyes covered by buccal mucosa, eyes covered by both buccal mucosa and skin were evaluated and compared in this study.

Mean preoperative BCVA was 2.44 ± 0.42 logMAR (95% confidence interval [CI], 2.39–2.50), with no significant difference between eyes covered by buccal mucosa and eyes covered by skin ($P > 0.2$). Mean postoperative BCVA at 3 months was 0.23 ± 0.49 logMAR (95% CI, 0.17–0.30), significantly improved compared with baseline ($P < 0.001$). Overall, BCVA was 0.00 logMAR in 136 eyes (59.4%), > 0.00 and ≤ 0.40 logMAR in 55 eyes (24.0%), > 0.40 and ≤ 1.00 logMAR in 26 eyes (11.4%), and > 1.00 logMAR in 12 eyes (5.2%).

The mean follow-up period was 16.0 ± 9.5 years (95% CI, 14.7–17.2), ranging from 6 months to 43 years. Anatomic and functional survival rates of the MOOKP implant were drawn in Kaplan–Meier curves. Anatomic failure was defined as any injury or disease that requires the removal of the osteo-odonto-keratoprosthesis implant, whereas functional failure was defined as BCVA > 1.0 logMAR. The number censored included losses to follow-up and deaths. Kaplan–Meier curves were compared by log-rank test.

According to the Kaplan–Meier analysis (Fig 2A), anatomic survival cumulative probabilities were 96.0% at 5 years (number at risk [nr] = 206), 93.5% at 10 years (nr = 161), 85.6% at 20 years (nr = 79), 81.1% both at 30 years (nr = 43) and at 40 years (nr = 35), and functional success rates were 89.0% at 5 years (nr = 193), 83.1% at 10 years (nr = 149), 72.4% at 20 years (nr = 76), 63.2% at 30 years (nr = 39), and 59.6% at 40 years (nr = 29).

Anatomic and functional Kaplan–Meier curves for eyes covered by buccal mucosa and skin are shown in Figure 2B and C. Concerning eyes covered by buccal mucosa, most anatomic failures occurred within the first 25 years (n = 22), whereas 1 was reported afterward. Likewise, most functional failures occurred within the first 25 years (n = 48), with only 4 cases reported after the 25-year threshold. Eyes covered by skin showed significantly lower anatomic (chi-square = 11.324; $P < 0.001$) and functional chi-square = 26.428; $P < 0.001$) survival probability, with a maximum follow-up of 24 years.

Mean postoperative BCVA during follow-up is reported in Table S1 (available at www.aaojournal.org). Postoperative BCVA $\leq$ 1.0 logMAR remained unchanged in 146 of 217 eyes (67.3%) for the entire duration of the follow-up. The cumulative probability for an individual patient of maintaining the postoperative BCVA within 2 lines, according to Kaplan−Meier analysis, is shown in Figure 2D. Eyes covered by skin had a significantly lower probability to maintain postoperative BCVA (chi-square = 12.340; $P < 0.001$). Overall, mean postoperative BCVA at the last follow-up visit was 0.78 ± 1.06 logMAR (95% CI, 0.64−0.91).

Intraoperative and postoperative complications are reported in Table S2 (available at www.aaojournal.org). In line with data previously reported,[4] the most threatening complications were endophthalmitis (n = 18), retinal detachment (n = 10), instability/expulsion of the optical cylinder (n = 12), and expulsion of the prosthesis (n = 2). After MOOKP, glaucoma developed in 23 of 145 nonglaucomatous eyes (15.9%) and worsened in 35 of 84 eyes with preexisting glaucoma (41.7%). Of these, 56 eyes developed glaucoma within 25 years from surgery.

To the best of our knowledge, this study evaluates the longest follow-up for a cohort of patients who underwent MOOKP surgery (PubMed, keywords osteo-odonto-keratoprosthesis, years 1965−2023). Long-term anatomic and functional survival probabilities at 40 years were approximately 80% and 60%, respectively, with a decreasing rate of failures and complications over time, especially after the 25-year threshold. These positive results may be due to the characteristics of the osteo-dental support, which constitutes a heterotopic autotransplant with fundamental biological properties of immunological defense, repair, and proliferation typical of living tissues Fig S1, www.aaojournal.org.[2,5,6] The lower survivability of eyes covered by skin confirms the essential role of the buccal mucosa overlay, which is in contact with and nourishes both the alveolar bone and dentine, resembling the anatomic structure of the tooth neck inside the oral cavity.[6,7]

Acknowledgments

On the centenary of his birth, in loving memory of late Giancarlo Falcinelli, father of the MOOKP, whose long professional life was dedicated to cure corneal blindness and to perfect a keratoprosthesis technique used for the sake of all patients worldwide.

Paolo Colliardo, MD[1]
Andrea Taloni, MD[2]
Maurizio Taloni, MD[1]
Giovanni Falcinelli, MD[3]
Luigi Petitti, MD[2]
Andrea Lucisano, MD[2]
Massimo Busin, MD[4,5,6]
Vincenzo Scorcia, MD[2]
Giuseppe Giannaccare, MD, PhD[2]

[1]*Osteo-odonto-keratoprosthesis Foundation, Rome, Italy;* [2]*Department of Ophthalmology, University Magna Graecia of Catanzaro, Viale Europa, Catanzaro, Italy;* [3]*Department of Ophthalmology, San Camillo Hospital, Rome, Italy;* [4]*Department of Translational Medicine, University of Ferrara, Forlì, Italy;* [5]*Department of Ophthalmology, Ospedali Privati Forlì "Villa Igea," Forlì, Italy;* [6]*Istituto Internazionale per la Ricerca e Formazione in Oftalmologia (IRFO), Forlì, Italy*

Disclosure(s):
All authors have completed and submitted the ICMJE disclosures form. The author(s) have no proprietary or commercial interest in any materials discussed in this article.
HUMAN SUBJECTS: Human subjects were included in this study. Institutional Review Board approval was obtained from San Camillo Hospital, Rome, Italy. Detailed informed consent was obtained from all patients. The study adhered to the tenets of the Declaration of Helsinki. No animal subjects were used in this study.
Author Contributions:
Conception and design: Colliardo, Taloni, Taloni, Falcinelli, Lucisano, Busin, Scorcia, Giannaccare
Data collection: Colliardo, Taloni, Taloni, Falcinelli, Petitti, Giannaccare
Analysis and interpretation: Colliardo, Taloni, Taloni, Falcinelli, Petitti, Lucisano, Busin, Scorcia, Giannaccare
Obtained funding: N/A; Study was performed as part of regular employment duties at Department of Ophthalmology, San Camillo Hospital, Rome, Italy. No additional funding was provided.
Overall responsibility: Colliardo, Taloni, Taloni, Scorcia, Giannaccare

Correspondence:
Vincenzo Scorcia, MD, University Magna Graecia of Catanzaro, Viale Europa, Catanzaro, 88100, Italy. E-mail: vscorcia@unicz.it.

References

1. Ricci R, Pecorella I, Ciardi A, et al. Strampelli's osteo-odonto-keratoprosthesis. Clinical and histological long-term features of three prostheses. *Br J Ophthalmol*. 1992;76:232−234.
2. Falcinelli G, Falsini B, Taloni M, et al. Modified osteo-odonto-keratoprosthesis for Treatment of corneal blindness: long-term anatomical and functional outcomes in 181 cases. *Arch Ophthalmol*. 2005;123:1319−1329.
3. Hille K, Grabner G, Liu C, et al. Standards for modified osteoodontokeratoprosthesis (OOKP) surgery according to Strampelli and Falcinelli: The Rome-Vienna protocol. *Cornea*. 2005;24:895−908.
4. Rishi P, Rishi E, Agarwal V, et al. Vitreoretinal complications and outcomes in 92 eyes undergoing surgery for modified osteo-odonto-keratoprosthesis: a 10-year review. *Ophthalmology*. 2018;125:832−841.
5. Falcinelli G, Colliardo P, Falcinelli G, Taloni M. Modified osteo-odonto-keratoprosthesis: over 30 years of experience. In: *6th KPro Study Group Meeting*. Florida: University of Miami; May 6, 2006.
6. Pecorella I, Taloni M, Ciardi A, et al. Osteo-odonto-keratoprosthesis: a human model of autotransplant. *Curr Eye Res*. 2006;31:835−843.
7. Falcinelli G, Colliardo P, Falcinelli G, et al. Modified osteo-odonto-keratoprosthesis (MOOKP): indications, contraindications, and surgical technique. In: Cortina M, De La Cruz J, eds. *Keratoprosthesis and Artificial Corneas*. Springer; 2015:191−204.