Outcomes of Penetrating Keratoplasty and Boston Type 1 Keratoprosthesis in Aniridia-Associated Keratopathy: A Systematic Review and Meta-Analysis

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• BACKGROUND: Congenital aniridia is a rare condition, which may lead to aniridia-associated keratopathy (AAK) and corneal blindness. Our objective was to compare the surgical outcomes of penetrating keratoplasty (PK) and Boston type 1 keratoprosthesis (KPro) implantation in patients with AAK.

• DESIGN: Systematic review and meta-analysis of individual patient data (IPD).

• METHODS: The study was preregistered in the PROSPERO database (registration number: CRD420250650812). A comprehensive search of Embase, MEDLINE (via PubMed), and the Cochrane Central Register of Controlled Trials (CENTRAL) was performed up to February 17, 2025. Eligible studies reported clinical outcomes after PK or KPro in patients with AAK, specifically graft survival, success rates, best spectacle-corrected visual acuity (BSCVA), and postoperative complications. Data extraction and synthesis followed the Cochrane Handbook, and risk of bias was assessed using the Joanna Briggs Institute Critical Appraisal Checklists.

• RESULTS: Of the 1,590 studies screened, 26 case series comprising 325 eyes with AAK were included in the meta-analysis. IPD were available from 14 studies. Anatomical success was significantly higher with KPro (0.82%, 95% CI: 0.65 to 0.92) than graft survival after PK (0.38%, 95% CI: 0.13 to 0.72) ($P = .009$). Cox regression analysis showed a significantly higher hazard of graft failure after PK compared to anatomical failure with KPro (HR = 2.92, 95% CI: 1.24 to 6.84; $P = .014$). No significant difference was observed in BSCVA improvement between PK (-0.73, 95% CI: -1.55 to 0.09) and KPro (-0.51, 95% CI: -0.82 to -0.20) ($P = .48$). Similarly, postoperative complication rates did not differ significantly between the two procedures ($P = .62$).

• CONCLUSIONS: In patients with AAK, KPro shows superior anatomical success compared to graft survival following PK. Postoperative improvements in visual acuity and the incidence of complications do not differ significantly between the two procedures. The main limitations of this analysis are the relatively small sample size across studies, the limited duration of follow-up, and the heterogeneity of study designs. (Am J Ophthalmol 2026;282: 405–415. © 2025 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/))

INTRODUCTION

CONGENITAL ANIRIDIA IS A RARE, PANOCULAR condition that affects 1/64 000 to 1/96 000 people.[1] It generally presents bilaterally and is marked by a spectrum of iris hypoplasia. About two-thirds of cases show a familial pattern, predominantly following an autosomal dominant inheritance, while the remainder occur sporadically.[2] The condition is most often associated with mutations in the PAX6 gene, a key regulator of ocular development.[3] Clinical features may include secondary glaucoma, cataracts, optic nerve and foveal hypoplasia, nystagmus, and aniridia-associated keratopathy (AAK).[4]

AAK is a leading cause of visual impairment in individuals with aniridia, affecting over 90% of patients within the first decade of life.[5,6] The underlying cause of AAK is limbal stem cell deficiency (LSCD), which leads to pannus formation, conjunctivalization, recurrent corneal erosions or ulcers, subepithelial fibrosis, and ultimately progressive corneal opacification and blindness.[7]

Historically, penetrating keratoplasty (PK) was the primary surgical treatment for advanced corneal opacification. However, in cases of AAK, PK alone often fails due to the

underlying LSCD, resulting in high rates of graft rejection and failure.[8] More recently, the Boston Type I keratoprosthesis (KPro) has gained recognition as a safe and effective alternative, particularly in patients with advanced corneal disease and multiple failed grafts, where further PK is unlikely to succeed.[9] There is no clear consensus on the optimal surgical approach for managing severe AAK.

This study aims to perform a systematic review and meta-analysis comparing PK and KPro implantation in patients with AAK. Key outcomes of interest include surgical success rates -graft survival and anatomical success rate- as well as visual acuity, and procedure-related complications. The underlying hypothesis is that meaningful differences may exist in postoperative outcomes between these two surgical modalities. By synthesizing available evidence, this study seeks to provide valuable insights to support clinical decision-making and improve the management of severe AAK.

METHODS

This systematic review and meta-analysis is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 recommendation[10] and the study protocol was preregistered in the PROSPERO database (registration number: CRD420250650812). The methodology followed the recommendations outlined in the Cochrane Handbook for systematic reviews.[11]

• INFORMATION SOURCE AND SEARCH STRATEGY: A systematic literature search was conducted in the electronic databases Embase, MEDLINE (via PubMed), and the Cochrane Central Register of Controlled Trials (CENTRAL) to identify relevant studies published up to February 17, 2025, with no language restrictions. The search strategy included the following keywords: ((aniridia) OR (aniridic) OR (PAX6)) AND ((penetrating keratoplasty) OR (PKP) OR (PK) OR (transplantation) OR (keratoprosthesis) OR (KPro) OR (limbo-keratoplasty) OR (limbokeratoplasty)). No additional search filters were applied.

• ELIGIBILITY CRITERIA: The research question was developed using the Population-Intervention-Comparator-Outcomes (PICO) framework. Eligible studies included patients with congenital aniridia (P) who underwent PK, KPro, or limbo-keratoplasty (I and C). Studies were required to report at least one of the following outcomes (O): graft survival, surgical success rate, pre- and postoperative best-corrected visual acuity (BCVA), or postoperative complications.

Studies were included if they evaluated at least one of the treatment modalities with or without a control for AAK and reported relevant outcome data. Both retrospective and prospective cohort studies, as well as case series, were eligible. Case reports, duplicates, and nonhuman studies were excluded from the analysis.

Due to the insufficient number of studies and limited data available on limbo-keratoplasty, we deviated from the original protocol and excluded this procedure from outcome analysis.

• SELECTION PROCESS: All references were managed using EndNote 20 reference management software (Clarivate Analytics, Philadelphia, PA, USA). After automatic and manual removal of duplicates, titles, abstracts, and full texts were independently screened by three reviewers (Li, Liu, and Tóth). Discrepancies were resolved through discussion with a fourth reviewer (Szentmáry). Full-text articles of potentially eligible studies were then assessed for final inclusion. In cases of overlapping study populations, the study with the larger sample size was included to prevent data duplication.

• DATA COLLECTION PROCESS AND ITEMS: Data from articles meeting the inclusion criteria were extracted into an Excel spreadsheet (Microsoft Office 2016, Microsoft, Redmond, WA, USA). Extracted information included general study details (author, year, study design), patient demographics (age, gender), number of subjects, and follow-up duration. Both baseline (preoperative) and postoperative outcomes were recorded, with data collected at multiple time points when available. Specifically, the following variables were extracted: graft survival following PK; anatomical success rate after KPro; best spectacle-corrected visual acuity (BSCVA; converted to logMAR), and postoperative complications following both procedures. Graft survival was defined as transplanted corneal tissue clear and in place, without irreversible rejection or failure, following PK, at the end of the follow-up period. Regaring KPro, anatomical success was defined as KPro retention during the follow-up period. Additional parameters, such as prior penetrating keratoplasty and previous intraocular procedures, were also collected.

For studies presenting outcomes like graft survival or success rates via Kaplan–Meier (KM) curves, quantitative values were extracted using WebPlotDigitizer (https://automeris.io/WebPlotDigitizer.html, accessed July 10, 2025) to facilitate further analysis. Where available, individual patient data (IPD) were collected directly from study authors. Discrepancies in data extraction were resolved through team consensus.

• QUALITY ASSESSMENT OF INCLUDED STUDIES: The risk of bias was assessed using the Joanna Briggs Institute Critical Appraisal Checklists[12] for observational studies and case series. Any disagreements among reviewers regarding the risk of bias assessment were resolved through discussion. If consensus could not be reached, a third reviewer was consulted to make the final decision.

• STATISTICAL METHODS AND DATA SYNTHESIS: All statistical analyses were conducted in R (R Core Team,

2025; version 4.4.3). Conventional meta-analyses were performed using the meta, nlme, sjPlot, survival and coxme packages, following the recommendations of Harrer et al.[13] A P-value < 0.05 was considered statistically significant for all analyses. Random-effects models were applied throughout.

IPD meta-analyses were conducted using linear mixed-effects regression models, except for survival data, which were analysed with mixed-effects (frailty) Cox proportional hazards models. Covariate effects were assessed by including them as fixed effects in the respective regression models, with study ID specified as a random effect. Linear mixed-effects models were fitted using the lme() function from the nlme package, and model summaries were generated with the tab_model() function from the sjPlot package. Mixed-effect Cox models were fitted using the coxme() function of the coxme package.

Since only a subset of studies reported IPD, study-level meta-analyses were also conducted, combining IPD with studies providing only summary statistics. Classical inverse-variance random-effects meta-analyses were applied using the restricted maximum likelihood (REML) estimator and Hartung-Knapp adjustment to pool means and mean differences. In several cases, the SDs of the pre-and post-treatment outcomes were available or could be estimated, but the SD (SD) of the change was missing. Following the Cochrane Handbook,[11] we imputed several different correlations. In a few studies with available IPD, correlations between pre- and post-treatment values could be calculated directly. Based on these, we imputed correlation coefficients of −0.75, −0.25, 0.13, 0.05, 0.3, and 0.66 into the formula for the SD of the change from baseline. All tested correlations yielded similar results. The published results are based on a correlation of 0.05. It should be emphasized that although the pooled estimates and their CIs (CI) were largely stable accross imputations, the CIs of individual study results naturally depended on the imputed correlation.

Pooled proportions were calculated using the generalized mixed-effect approach of Stijnen et al.[14] Subgroup analyses and subgroup difference P-values were generated using the classical mixed-effects approach implemented in the meta-gen() and metaprop() functions of the meta package.

Forest plots were used to visualize pooled estimates with 95% confidence and prediction intervals. Between-study heterogeneity was assessed using the I^2 statistic (with CIs) and Cochrane's Q-statistic. IPD meta-analysis results were illustrated with scatterplots and modified boxplots, complemented by group means and patient-level observations. KM curves were digitized using the WebPlotDigitizer tool and individual-level survival data were reconstructed from KM curves via inverse estimation methods, as described by Guyot et al.[15]

A leave-one-out sensitivity analysis regarding graft survival after PK and anatomical success after KPro was conducted. Assessment of publication bias was not feasible, as each subgroup included fewer than ten studies.

• ASSESSMENT OF THE GRADE OF EVIDENCE: Due to the limited number of comparative studies available, it was not possible to formally assess the level of evidence for the outcomes analysed.

RESULTS

• SEARCH AND STUDY SELECTION: Our systematic search retrieved 1590 articles. After removal of duplicates, 1196 publications were screened, of which 26 met the criteria for qualitative and quantitative synthesis (Figure 1).

• BASIC CHARACTERISTICS OF INCLUDED STUDIES: Table 1 summarizes the baseline characteristics of the included studies. A total of 26 retrospective case series comprising 325 eyes with AAK were analysed and included in the meta-analysis and systematic review. Additionally, IPD were available from 14 studies.

In cases where cataract was present at the time of surgery, penetrating keratoplasty (PK) was performed concurrently with phacoemulsification and intraocular lens implantation. Limbal stem cell transplantation (LSCT) was performed in only one case (0.8%), concurrently with PK. None of the patients underwent LSCT before or after PK among the analysed cases.

• SUCCESS RATES AND GRAFT SURVIVAL: Original data on graft survival from all included studies on PK and on anatomical success rates from all included studies on KPro in patients with AAK, derived from deconstructed KM curves and available IPD, are presented in Figure 2.

Anatomical success rates were significantly higher following KPro compared to graft survival after PK (P = .009) (Figure 3). The pooled estimates were as follows: graft survival after PK 0.38% [95% CI: 0.13-0.72] and anatomical success rate after KPro 0.82% [95% CI: 0.65-0.92]. Individual Cox regression analysis revealed a significantly higher hazard of graft failure after PK compared with anatomical failure after KPro (HR = 2.92, 95% CI: 1.24-6.84, P = .014).

Cox frailty regression analysis of IPD indicated that neither prior intraocular surgery nor prior PK had a significant impact on anatomical success after KPro, nor on graft survival after PK ($P \geq$ .11) (Table S1). In all sensitivity analyses, the difference between graft survival after PK (range 0.326 to 0.558) and anatomical success following KPro (range 0.788 to 0.841) remained statistically significant (Table S2).

• BEST SPECTACLE-CORRECTED VISUAL ACUITY: There was no significant difference in BSCVA improvement between PK [−0.73 (95% CI: −1.55 to 0.09)] and KPro [−0.51 (95% CI: −0.82 to − 0.20)] (P = .48) (Figure 4).

TABLE 1. Basic Characteristics of the Included Studies ($n = 26$)

First author (year)	Design	Country	Recruitment period	No. of eyes	No. of patients (woman %)	Age (mean ± SD, years)	GR 1	GR 2	Mean follow up (months)	Outcome
Akpek et al[16]	Multicenter RCS	USA	NR	16	15 (40.0)	44.2 ± 14.0	KPro	-	24.1	SR, BSCVA, POC
Au et al[17]	RCS	USA	NR	4	2 (100)	49.0 ± 11.6	PK	-	18.3	SR, BSCVA, POC
Bakhtiari et al[18]	Multicenter RCS	USA	1999-2010	9	9 (66.7)	39.1 ± 26.2	KPro	-	26.1	SR, BSCVA
Batu Oto et al[19]	RCS	Turkey	2000-2020	6	NR (NR)	NR	PK	-	≥ 12.0	SR
Bradley et al[20]	RCS	USA	2004-2008	3	NR (NR)	66.7 ± 6.4	KPro	-	9.0	SR
Ciolino et al[21]	Multicenter PCS	USA	2003-2008	7	NR (NR)	NR	KPro	-	NR	SR
De la Paz et al[8]	RCS	Spain	1956-2007	16	NR (NR)	NR	PK	-	NR	SR, POC
Dyer et al[6]	RCS	Spain	2010-2019	12	10 (70.0)	37.1 ± 21.5	KPro	-	58.7	SR, BSCVA, POC
Farah et al[22]	RCS	Germany	2012-2019	20	10 (62.5)	52 ± 8	PK	-	40.7	SR, BSCVA, POC
Fung et al[23]	Multicenter RCS	Canada	2010-2014	5	NR (NR)	8.2 ± 6.7	KPro	-	20.5	SR, BSCVA, POC
Gomes et al[24]	RCS	USA	NR	5	2 (66.7)	16.8 ± 10.6	PK	-	NR	SR, BSCVA, POC
Greiner et al[25]	RCS	USA	2004-2010	5	5 (NR)	NR	KPro	-	NR	POC
Hassanaly et al[7]	RCS	Canada	2008-2012	26	19 (47.4)	56.0 ± 11.0	KPro	-	28.7	SR, BSCVA, POC
Hovlykke et al[26]	RCS	Denmark	1971-2011	2	NR (NR)	10.5 ± 7.8	PK	-	12.0	SR
Jacobson et al[27]	RCS	USA	2012-2020	37	NR (NR)	NR	PK	KPro	NR	SR, POC
Kremer et al[28]	RCS	USA	1986-1991	11	8 (NR)	NR	PK	-	36	BSCVA, POC
Lee et al[29]	RCS	South Korea	1991-2016	6	6 (50.0)	1.6 ± 1.4	PK	-	26.8	SR, POC
Majander et al[30]	RCS	Finland	1968-2011	2	2 (NR)	NR	PK	-	NR	SR
Mayer et al[31]	RCS	USA	2000-2002	22	15 (NR)	NR	PK	-	NR	SR
Nascimento e Silva et al[32]	RCS	USA	2007-2015	22	22 (63.6)	46.7 ± 13.2	KPro	-	70.7	SR, BSCVA, POC
Park et al[33]	RCS	South Korea	1996-1997	4	4 (NR)	22.0 ± 22.3	PK	-	9.9	BSCVA, POC
Rixen et al[34]	RCS	USA	2009-2011	7	7 (42.9)	52.0 ± 22.5	KPro	-	18.4	SR, BSCVA, POC
Rudnisky et al[35]	Multicenter PCS	USA	2003-2008	7	NR (NR)	NR	KPro	-	NR	BSCVA
Shah et al[5]	RCS	USA	2004-2012	46	34 (NR)	43.5 ± 19.8	KPro	-	54.0	SR, POC
Wróblewska-Czajka et al[36]	Multicenter RCS	Poland	1999-2022	3	NR (NR)	NR	KPro	-	≥ 12.0	POC
Yazdanpanah et al[37]	RCS	USA	2005-2018	22	NR (NR)	41.3	KPro	-	91.1	SR, POC

PCS = prospective case series; RCS = retrospective case series; GR = Group; PK = penetrating keratoplasty; KPro = Boston type 1 keratoprosthesis implantation; SR = success rate/survival rate; NR = not reported; BSCVA = best spectacle-corrected visual acuity; POC = postoperative complications.
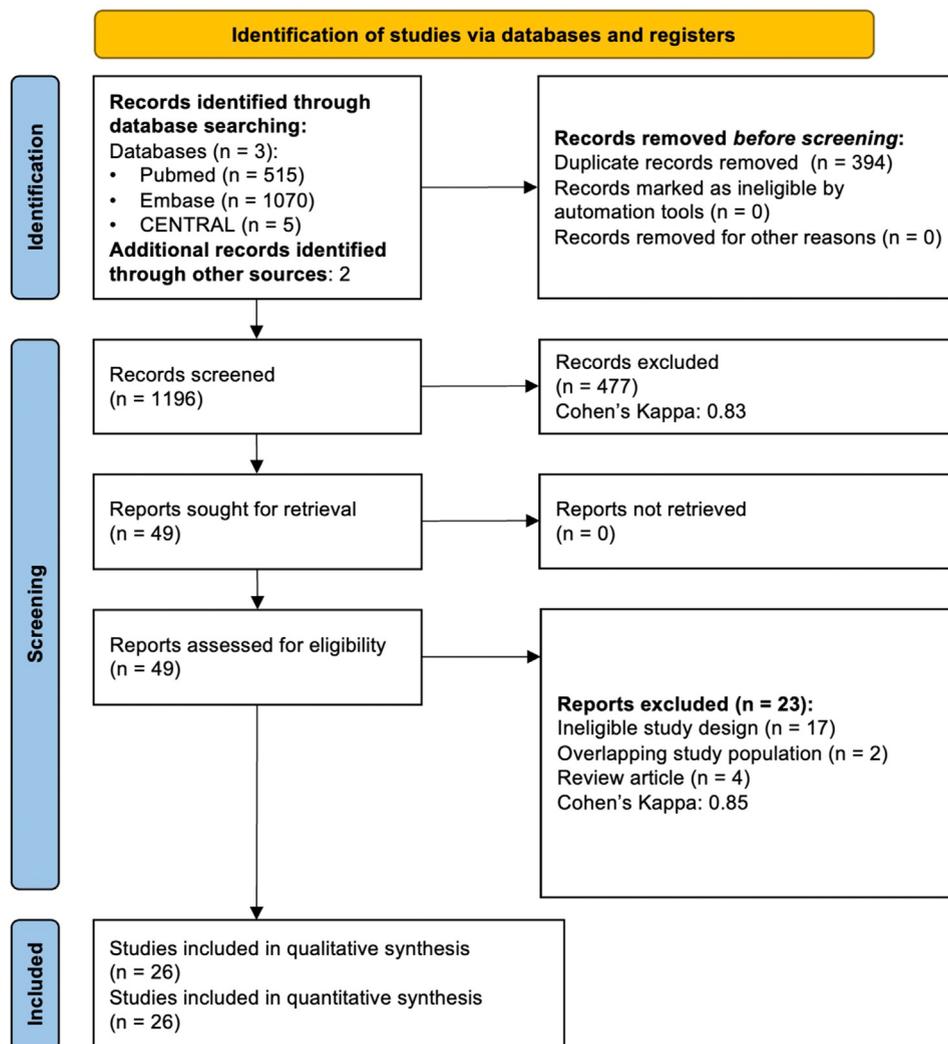
FIGURE 1. Flow chart of study identification.

Overall, 14.8% (n = 4) of patients achieved and maintained 20/100 or better vision after PK, whereas 15.6% (n = 14) did so after KPro (Table S3). Consistent with the outcome of our conventional meta-analysis, regression analyses based on IPD showed no statistically significant difference in BSCVA improvement between PK and KPro, both in the univariate ($P = .511$) and multivariate mixed-effect regression models ($P = .889$) (Table S4 and Figure S1). In contrast, both univariate ($P = .017$) and multivariate ($P = .024$) regression analyses indicated that a history of prior intraocular surgery was associated with significantly less postoperative BSCVA improvement compared with patients without such a history (Table S4 and Figure S1). Previous PK had no significant effect on BSCVA improvement, as shown by the univariate ($P = .548$) and multivariate ($P = .818$) models (Table S4 and Figure S1). Glaucoma onset or progression had no significant effect on BSCVA improvement, as demonstrated by the univariate ($P = .463$)

and multivariate ($P = .120$) models (Table S4 and Figure S1). Finally, there was no significant association between postoperative follow-up time and BSCVA improvement in either the univariate ($P = .296$) or multivariate ($P = .137$) models (Table S4 and Figure S1). Estimated coefficients for all regression analyses, along with their respective 95% CIs, are presented in Table S4.

• POSTOPERATIVE COMPLICATIONS: The most common complications after PK were persistent epithelial defects (n = 21; 21.0%) and graft rejection (n = 15; 15.0%). Following KPro, the most frequent complications included retroprosthetic membrane formation (RPM) (n = 66; 36.2%), glaucoma progression or new-onset glaucoma (n = 32; 17.5%), and corneal melting (n = 29; 15.9%) (Table S5). No significant difference in the overall rate of postoperative complications was found between PK and KPro ($P = .62$) (Figure 5). The rate of glaucoma progression or
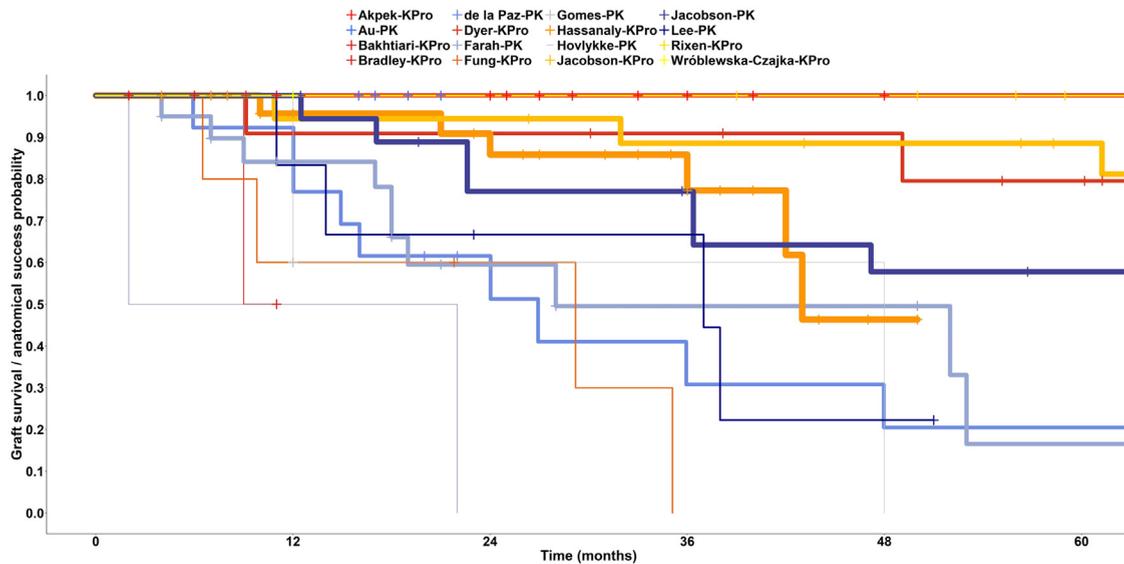
FIGURE 2. Kaplan–Meier curves showing time-to-event data for penetrating keratoplasty (PK) and Boston type 1 keratoprosthesis (KPro) across all included studies, reconstructed from published curves and individual patient data (IPD). Events represent graft failures for PK and anatomical failures for KPro.
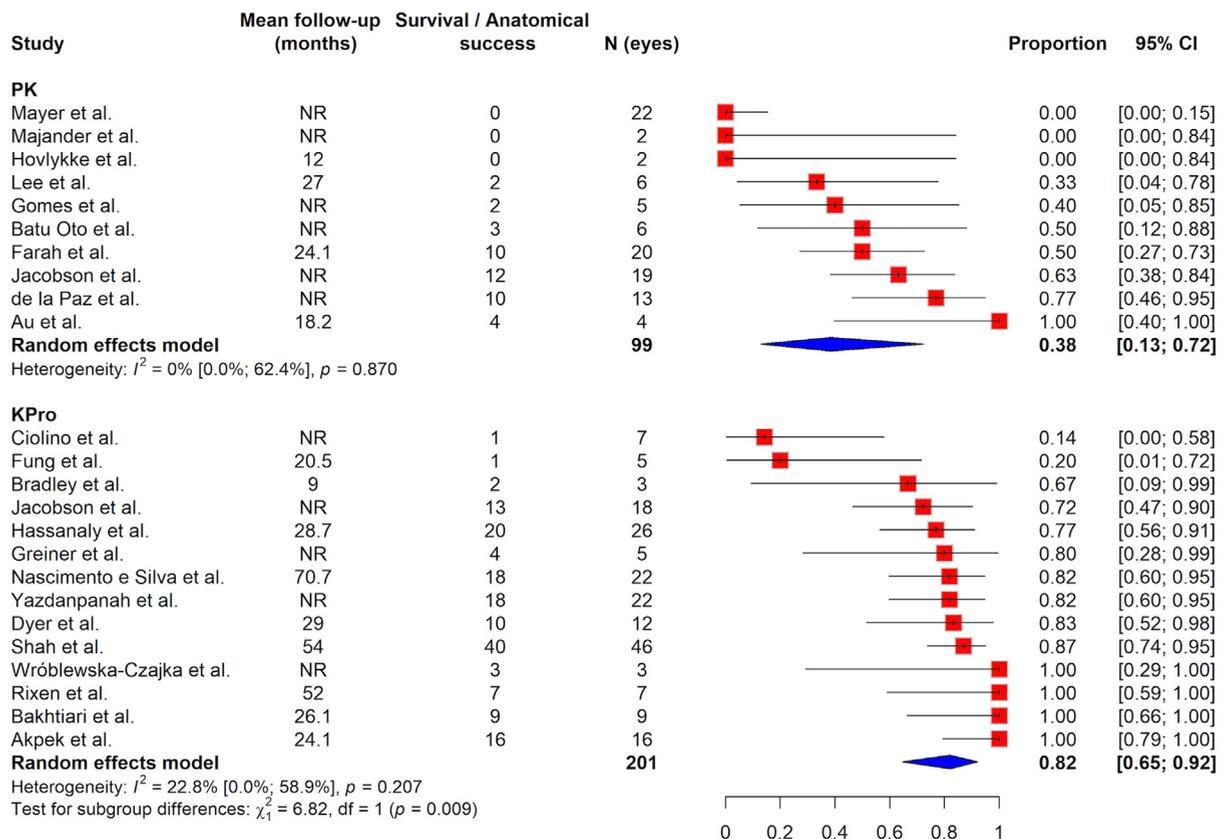

Study	Mean follow-up (months)	Survival / Anatomical success	N (eyes)		Proportion	95% CI
PK						
Mayer et al.	NR	0	22		0.00	[0.00; 0.15]
Majander et al.	NR	0	2		0.00	[0.00; 0.84]
Hovlykke et al.	12	0	2		0.00	[0.00; 0.84]
Lee et al.	27	2	6		0.33	[0.04; 0.78]
Gomes et al.	NR	2	5		0.40	[0.05; 0.85]
Batu Oto et al.	NR	3	6		0.50	[0.12; 0.88]
Farah et al.	24.1	10	20		0.50	[0.27; 0.73]
Jacobson et al.	NR	12	19		0.63	[0.38; 0.84]
de la Paz et al.	NR	10	13		0.77	[0.46; 0.95]
Au et al.	18.2	4	4		1.00	[0.40; 1.00]
Random effects model			**99**		**0.38**	**[0.13; 0.72]**
Heterogeneity: $I^2 = 0\%$ [0.0%; 62.4%], $p = 0.870$						
KPro						
Ciolino et al.	NR	1	7		0.14	[0.00; 0.58]
Fung et al.	20.5	1	5		0.20	[0.01; 0.72]
Bradley et al.	9	2	3		0.67	[0.09; 0.99]
Jacobson et al.	NR	13	18		0.72	[0.47; 0.90]
Hassanaly et al.	28.7	20	26		0.77	[0.56; 0.91]
Greiner et al.	NR	4	5		0.80	[0.28; 0.99]
Nascimento e Silva et al.	70.7	18	22		0.82	[0.60; 0.95]
Yazdanpanah et al.	NR	18	22		0.82	[0.60; 0.95]
Dyer et al.	29	10	12		0.83	[0.52; 0.98]
Shah et al.	54	40	46		0.87	[0.74; 0.95]
Wróblewska-Czajka et al.	NR	3	3		1.00	[0.29; 1.00]
Rixen et al.	52	7	7		1.00	[0.59; 1.00]
Bakhtiari et al.	26.1	9	9		1.00	[0.66; 1.00]
Akpek et al.	24.1	16	16		1.00	[0.79; 1.00]
Random effects model			**201**		**0.82**	**[0.65; 0.92]**
Heterogeneity: $I^2 = 22.8\%$ [0.0%; 58.9%], $p = 0.207$						
Test for subgroup differences: $\chi^2_1 = 6.82$, df = 1 ($p = 0.009$)						

FIGURE 3. Proportion of surviving grafts after penetrating keratoplasty (PK) and anatomical success after Boston type 1 keratoprosthesis (KPro) in patients with aniridia-associated keratopathy. The values represent the number of successful cases during the substantially varying follow-up periods of the included studies.
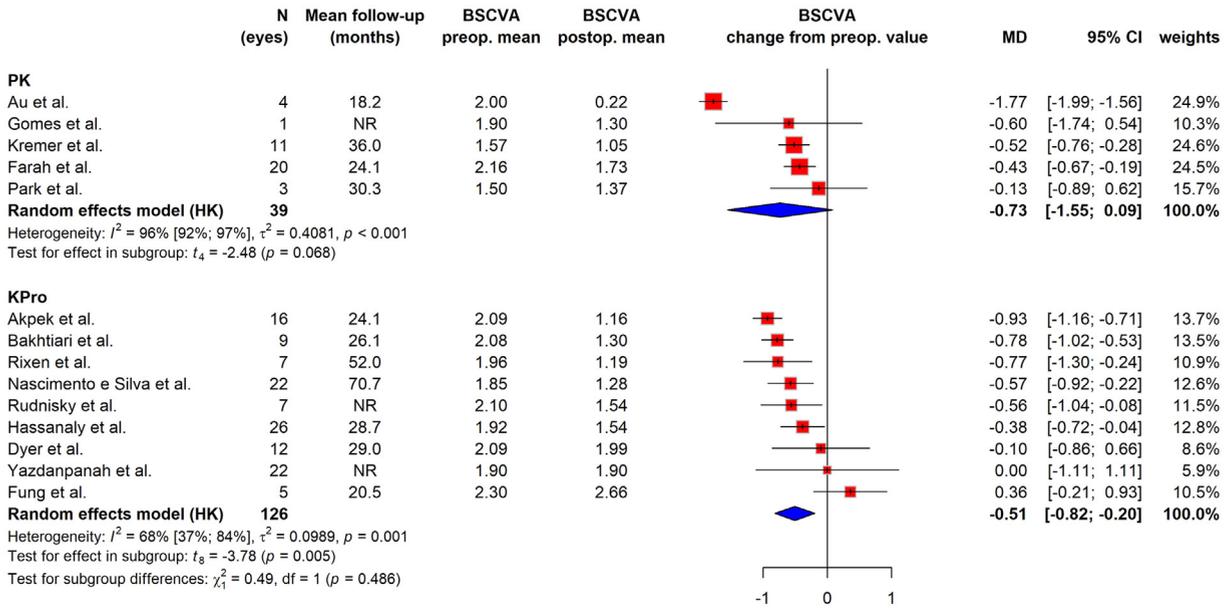
	N (eyes)	Mean follow-up (months)	BSCVA preop. mean	BSCVA postop. mean	BSCVA change from preop. value	MD	95% CI	weights
PK								
Au et al.	4	18.2	2.00	0.22		-1.77	[-1.99; -1.56]	24.9%
Gomes et al.	1	NR	1.90	1.30		-0.60	[-1.74; 0.54]	10.3%
Kremer et al.	11	36.0	1.57	1.05		-0.52	[-0.76; -0.28]	24.6%
Farah et al.	20	24.1	2.16	1.73		-0.43	[-0.67; -0.19]	24.5%
Park et al.	3	30.3	1.50	1.37		-0.13	[-0.89; 0.62]	15.7%
Random effects model (HK)	**39**					**-0.73**	**[-1.55; 0.09]**	**100.0%**

Heterogeneity: I^2 = 96% [92%; 97%], τ^2 = 0.4081, p < 0.001
Test for effect in subgroup: t_4 = -2.48 (p = 0.068)

	N (eyes)	Mean follow-up (months)	BSCVA preop. mean	BSCVA postop. mean	BSCVA change from preop. value	MD	95% CI	weights
KPro								
Akpek et al.	16	24.1	2.09	1.16		-0.93	[-1.16; -0.71]	13.7%
Bakhtiari et al.	9	26.1	2.08	1.30		-0.78	[-1.02; -0.53]	13.5%
Rixen et al.	7	52.0	1.96	1.19		-0.77	[-1.30; -0.24]	10.9%
Nascimento e Silva et al.	22	70.7	1.85	1.28		-0.57	[-0.92; -0.22]	12.6%
Rudnisky et al.	7	NR	2.10	1.54		-0.56	[-1.04; -0.08]	11.5%
Hassanaly et al.	26	28.7	1.92	1.54		-0.38	[-0.72; -0.04]	12.8%
Dyer et al.	12	29.0	2.09	1.99		-0.10	[-0.86; 0.66]	8.6%
Yazdanpanah et al.	22	NR	1.90	1.90		0.00	[-1.11; 1.11]	5.9%
Fung et al.	5	20.5	2.30	2.66		0.36	[-0.21; 0.93]	10.5%
Random effects model (HK)	**126**					**-0.51**	**[-0.82; -0.20]**	**100.0%**

Heterogeneity: I^2 = 68% [37%; 84%], τ^2 = 0.0989, p = 0.001
Test for effect in subgroup: t_8 = -3.78 (p = 0.005)
Test for subgroup differences: χ_1^2 = 0.49, df = 1 (p = 0.486)

FIGURE 4. Best spectacle-corrected visual acuity (BSCVA) improvement following penetrating keratoplasty (PK) and Boston type 1 keratoprosthesis (KPro) in people with aniridia associated keratopathy.
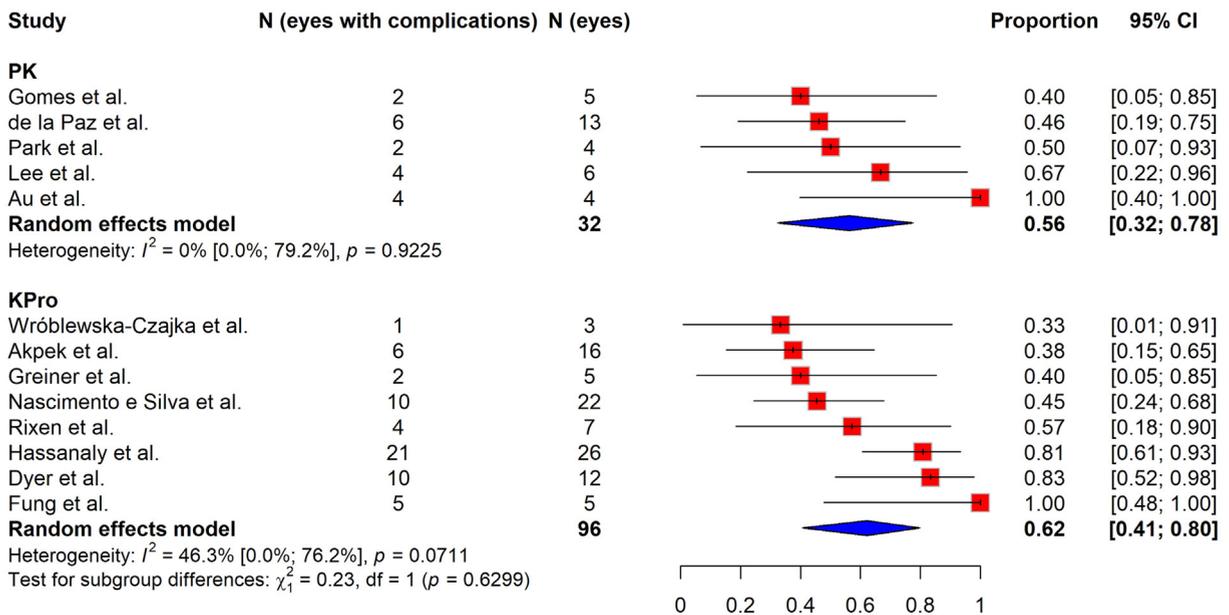
Study	N (eyes with complications)	N (eyes)		Proportion	95% CI
PK					
Gomes et al.	2	5		0.40	[0.05; 0.85]
de la Paz et al.	6	13		0.46	[0.19; 0.75]
Park et al.	2	4		0.50	[0.07; 0.93]
Lee et al.	4	6		0.67	[0.22; 0.96]
Au et al.	4	4		1.00	[0.40; 1.00]
Random effects model		**32**		**0.56**	**[0.32; 0.78]**

Heterogeneity: I^2 = 0% [0.0%; 79.2%], p = 0.9225

Study	N (eyes with complications)	N (eyes)		Proportion	95% CI
KPro					
Wróblewska-Czajka et al.	1	3		0.33	[0.01; 0.91]
Akpek et al.	6	16		0.38	[0.15; 0.65]
Greiner et al.	2	5		0.40	[0.05; 0.85]
Nascimento e Silva et al.	10	22		0.45	[0.24; 0.68]
Rixen et al.	4	7		0.57	[0.18; 0.90]
Hassanaly et al.	21	26		0.81	[0.61; 0.93]
Dyer et al.	10	12		0.83	[0.52; 0.98]
Fung et al.	5	5		1.00	[0.48; 1.00]
Random effects model		**96**		**0.62**	**[0.41; 0.80]**

Heterogeneity: I^2 = 46.3% [0.0%; 76.2%], p = 0.0711
Test for subgroup differences: χ_1^2 = 0.23, df = 1 (p = 0.6299)

FIGURE 5. Postoperative complications after penetrating keratoplasty (PK) and Boston type 1 keratoprosthesis (KPro) in people with aniridia associated keratopathy.

new-onset glaucoma did not differ significantly between PK and KPro (P = .12) (Figure S2). No cases of no light perception (NLP) BSCVA occurred following PK, whereas the proportion of NLP BSCVA after KPro was 0.09 (95% CI: 0.02-0.28) (Figure S3).

• **RISK OF BIAS:** The risk of bias showed some variation across the included studies, as evaluated using the JBI Critical Appraisal Tool (Tables S6).

DISCUSSION

In this meta-analysis, we compared surgical success rates, visual acuity, and postoperative complication rates—following PK and KPro implantation in patients with AAK.

PK has historically been the primary surgical intervention for advanced corneal opacification. However, its

effectiveness in the long-term management of AAK is limited, as it does not address the underlying limbal stem cell deficiency—a key factor in AAK pathogenesis.[8] The introduction of KPro has shifted the treatment paradigm for severe ocular surface disorders associated with limbal stem cell deficiency, such as chemical burns, mucous membrane pemphigoid, Stevens-Johnson syndrome, and AAK. KPro is increasingly considered a more viable option in cases where conventional corneal grafting is likely to fail. Some studies advocate for primary KPro implantation in patients with AAK, suggesting that early intervention yields better long-term visual potential compared to secondary implantation following failed PK.[37,38]

Nevertheless, comparing outcomes between PK and KPro in AAK remains challenging due to small sample sizes and heterogeneity across study populations. Variability in outcome reporting, particularly across different follow-up intervals in retrospective case series, introduces confounding factors. In this context, survival analysis offers a more reliable method for assessing surgical success and visual prognosis.

In a previous meta-analysis involving mixed etiologies of limbal stem cell deficiency, Ahmad et al[39] found significantly higher anatomical success rates following KPro compared to PK (98.9% vs 79% at 1 year; 94% vs 67% at 2 years). Similarly, Priddy et al[40] reported an anatomical success rate of 88% at 2 years following KPro implantation in a heterogeneous patient cohort. In line with these findings, our results demonstrated that KPro is associated with a higher anatomical success rate than PK in the treatment of AAK.

Despite its anatomical benefits, visual outcomes following KPro implantation often remain suboptimal. In a large multicenter study involving a heterogeneous population, Rudnisky et al[35] reported that only 6.0% of patients achieved a final BCVA better than 20/60. Similarly, a meta-analysis by Ahmad et al[39] found that while a visual acuity of 20/200 or better was achieved in 42% of eyes after PK, this outcome was observed in 80% of KPro-treated eyes at 2 years.

Nevertheless, visual prognosis in AAK is frequently limited by coexisting ocular anomalies such as macular and optic nerve hypoplasia.[7,35] Furthermore, preoperative glaucoma is present in up to 100% of individuals with AAK,[6] significantly contributing to poor visual outcomes regardless of surgical intervention. While KPro may initially improve vision in the majority of patients, this benefit often diminishes over time. Shah et al reported that at 4.5 years postoperatively, only 43.5% of patients maintained any visual improvement compared to their preoperative status.[5]

Importantly, there is a lack of robust data on medium- and long-term visual outcomes following both PK and KPro in the AAK population. The limited number of longitudinal studies hampers our ability to draw firm conclusions regarding the sustained efficacy and safety of these interventions.[40] Furthermore, visual deterioration in AAK patients after surgical intervention is likely multifactorial. In addition to structural abnormalities and preexisting glaucoma, progression of optic neuropathy may be driven by chronic low-grade inflammation, cytokine dysregulation, and potential toxic damage to the optic nerve.[7,32]

In terms of safety, both PK and Boston Type I KPro demonstrated similar overall rates of postoperative complications in patients with AAK. Nevertheless, the nature and implications of these complications differ between the two procedures. In the PK group, the most frequently observed complications included persistent epithelial defects, graft rejection, corneal neovascularization, and subepithelial scarring. These complications are closely associated with underlying limbal stem cell deficiency and are often indicative of progressive graft failure. In contrast, in the KPro group, common postoperative complications included RPM formation, progression or new-onset glaucoma, corneal melting, and retinal detachment. Among these, RPM was the most prevalent complication, as consistently reported in the literature.[38-40] Furthermore, aniridia itself appears to predispose patients to RPM development, potentially due to aniridia-associated fibrosis syndrome.[5,7,35,37]

Glaucoma is a well-recognized complication following both PK and KPro and is thought to arise from anterior synechiae formation and prolonged corticosteroid use.[39] Monitoring intraocular pressure (IOP) in KPro-implanted eyes remains a significant clinical challenge due to the lack of a corneal surface, complicating the assessment of glaucoma progression.[35] Therefore, patients with KPro implants require close and regular monitoring for glaucomatous changes.[37]

Corneal melting represents a particularly severe complication after KPro implantation. It can lead to devastating sequelae such as aqueous leakage, endophthalmitis, choroidal or retinal detachment, and even extrusion of the device.[9]

Although the overall complication rates are comparable between PK and KPro, the potential for catastrophic anatomical failure and irreversible vision loss is higher with KPro. This risk is especially concerning in younger patients, in whom the long-term safety profile of KPro is less favorable. In such cases, KPro may not represent the optimal surgical option.[39]

• STRENGTHS AND LIMITATIONS: This meta-analysis presents several important strengths. (1) It is the first meta-analysis to directly cf the surgical outcomes of PK and KPro specifically in patients with AAK. By focusing on this rare and complex condition, the study addresses a critical gap in the literature. (2) The use of IPD for data synthesis significantly enhances the accuracy, detail, and reliability of the findings. Unlike conventional aggregate-level meta-analyses, IPD allows for more nuanced subgroup analyses and covariate adjustments, resulting in more robust and clinically relevant insights.

However, the study is not without limitations. (1) The relatively small number of patients included across the selected studies may limit the generalizability of the results to the broader AAK population. (2) The lack of prospective, interventional trials and the limited duration of follow-up among the included studies reduce the overall strength of the evidence and increase the potential for bias. (3) The absence of standardized clinical guidelines for the surgical management of AAK introduces variability in both treatment selection and outcome reporting, potentially contributing to selection and reporting bias. (4) Heterogeneity in study design, baseline characteristics, surgical techniques, and outcome definitions across studies may have influenced the pooled estimates and should be considered when interpreting the findings.

• **IMPLICATION FOR PRACTICE, RESEARCH, AND POLICYMAKERS:** This meta-analysis underscores the necessity of individualized surgical planning for patients with AAK, taking into account patient-specific risk factors, underlying ocular pathologies, and long-term visual prognosis. Clinicians are encouraged to carefully weigh the potential benefits and limitations of each surgical approach—particularly PK and KPro—while prioritizing rigorous postoperative monitoring and follow-up care.

To strengthen the current evidence base, future studies should focus on conducting large-scale, prospective trials comparing the long-term efficacy and safety of different surgical techniques in this rare patient population. The development of standardized treatment algorithms and a deeper understanding of the pathophysiological mechanisms underlying AAK are essential for optimizing therapeutic outcomes and halting disease progression.

Furthermore, the engagement of policymakers and funding agencies is critical in promoting research on rare diseases such as AAK. This includes supporting multicenter collaborative studies and the establishment of harmonized clinical guidelines, ultimately aiming to enhance the quality of care and visual outcomes for individuals affected by congenital aniridia.[41,42]

CONCLUSIONS

In terms of surgical outcomes, KPro may offer superior anatomical success compared to graft survival following PK in individuals with AAK. However, postoperative visual improvement does not significantly differ between the two interventions. Importantly, the incidence of postoperative complications is similar for both procedures, reinforcing the need for tailored surgical decisions based on patient profiles rather than procedural risk alone. Further studies with longer follow-up periods are needed to better assess long-term outcomes and treatment durability, as current surgical options remain suboptimal, underscoring the need for continued advancements in our therapeutic armamentarium.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

GÁBOR TÓTH: Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **SHANHE LIU:** Writing – review & editing, Methodology, Formal analysis, Data curation. **SHUAILIN LI:** Writing – review & editing, Methodology, Formal analysis, Data curation. **SZILÁRD VÁNCSA:** Writing – review & editing, Methodology, Formal analysis, Conceptualization. **MÁTYÁS PACZKÓ:** Writing – review & editing, Visualization, Methodology, Formal analysis. **TAMÁS KÓI:** Writing – review & editing, Visualization, Methodology, Formal analysis. **PÉTER HEGYI:** Writing – review & editing, Conceptualization. **NÓRA SZENTMÁRY:** Writing – review & editing, Supervision, Project administration, Methodology, Formal analysis, Conceptualization.

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