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REVIEW

Comparing the Efficacy and Safety of Femtosecond Laser-Enabled Keratoplasty and Conventional Penetrating Keratoplasty: A Systematic Review and Meta-Analysis

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Background: Femtosecond laser-assisted keratoplasty (FLKP) has recently emerged as an alternative to conventional penetrating keratoplasty (CPK). By enabling precise and reproducible corneal incisions, FLKP may offer improved visual outcomes and fewer complications.

Methods: A systematic review was conducted using Google Scholar, PubMed, and Web of Science from inception to July 12, 2024. Included studies were nonrandomized controlled trials, retrospective cohort studies, or prospective observational cohorts comparing FLKP with CPK. Eligible studies reported at least one of the following outcomes: topographic astigmatism, visual acuity, spherical equivalent, endothelial cell density, graft rejection/failure, or complications. Non-English articles, studies comparing other keratoplasty techniques, or lacking relevant outcome data were excluded. Risk of bias was assessed using the MINORS tool. A random-effects model was used to calculate mean differences.

Results: Out of 517 records, 9 studies met the inclusion criteria. FLKP was significantly superior in reducing postoperative topographic astigmatism ($Z = 3.23$, $P = 0.001$, $I^2 = 35\%$) and in improving best-corrected visual acuity (BCVA) ($Z = 5.03$, $P = 0.00001$, and I2 = 4%). No significant difference was found in uncorrected visual acuity (UCVA) or spherical equivalent. FLKP also preserved endothelial cell density more effectively than CPK ($Z = 2$, $P = 0.05$, $I^2 = 67\%$). While most complication rates were similar, FLKP was associated with a lower incidence of wound dehiscence.

Conclusion: FLKP offers better postoperative astigmatism correction, improved BCVA, and greater endothelial cell preservation compared to CPK. It also reduces certain complications, such as wound dehiscence. However, the findings are limited by the retrospective nature and geographic focus of the included studies, underscoring the need for future long-term randomized trials.

Keywords: FLKP, CPK, postoperative astigmatism, BCVA, UCVA, complications

Introduction

Background

Corneal transplantation, often referred to as keratoplasty, is a well-established surgical procedure. It is used for treating a range of corneal disorders, including keratoconus, corneal scarring, and endothelial dysfunction.[1] Traditionally, the most commonly employed technique used for corneal transplantation is conventional penetrating keratoplasty (CPK), where the cornea is manually excised and replaced with a donor cornea using sutures. However, this procedure can be

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technically challenging and may result in complications, such as suture-related issues, graft rejection, and irregular astigmatism.[2] FLKP could be indicated in cases where precise graft-host alignment is critical. The conventional keratoplasty is used mostly in resource-limited areas. Conventional keratoplasty is mostly used due to its long-term outcomes and accessibility, while FLKP is less accessible and more expensive than conventional methods, but it has more precision, better wound architecture, and potential for faster visual recovery.

Scientific Rationale

In recent years, the development of femtosecond laser-enabled keratoplasty (FLKP) has emerged as a promising alternative to CPK. FLKP utilizes a femtosecond laser to create precise, reproducible corneal cuts, which may potentially improve the accuracy and stability of the graft-host interface, leading to better visual outcomes and reduced complications. Multiple studies have evaluated the effectiveness and safety of FLKP and CPK, but the findings have been inconsistent.

A systematic review by Riau AK et al[3] have indicated that FLKP was associated with faster visual recovery, lesser rates of rejected grafts, and better refractive outcomes in comparison to CPK. In contrast, a meta-analysis by Cheng et al[4] reported no significant variations in visual acuity or graft survival comparing the two methods. Similarly, a retrospective study by Busin et al[5] observed comparable outcomes in regard to visual acuity and graft survival for FLKP versus CPK.

These differing results highlight the importance of a thorough systematic review and meta-analysis to provide a more robust evaluation of the available evidence and clarify the relative merits and drawbacks of FLKP and CPK. It is important to note that the abbreviation FLEK (Femtosecond Laser-Enabled Keratoplasty) is used throughout this manuscript only when referring to previous literature or search terms. To improve clarity, we refer to Femtosecond Laser Keratoplasty as FLKP while describing and discussing the surgical approach in this study.

Aims and Objectives

The main objective of this systematic review and meta-analysis is to assess and compare the efficacy and safety of FLKP and CPK in terms of visual acuity, refractive outcomes, graft survival, and postoperative complications. By synthesizing the available evidence, the study aims to provide a thorough evaluation of the relative merits and drawbacks of these two corneal transplantation techniques, thereby informing clinical decision-making and guiding future research in this field.

Methods

Literature Search Strategy

This systematic review was carried out in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards and was prospectively registered in PROSPERO CRD42024546504.[6] A comprehensive electronic search for research published without a date restriction was done using the PubMed, Google Scholar, and Web of Science databases. The search strategy includes terms related to Femtosecond Laser-Enabled Keratoplasty, Conventional Penetrating Keratoplasty, and randomized controlled trials. Keywords include Femtosecond laser-enabled keratoplasty, FLEK, conventional penetrating keratoplasty, CPK, keratoplasty, corneal transplantation, astigmatism, visual acuity, endothelial cell density, graft rejection, graft failure. The search strategy combined keywords associated with FLEK, CPK, and corneal transplantation with controlled vocabulary (MeSH terms). To ensure that the research addressed both FLEK and CPK, Boolean operators ("AND") were used in the search process. The full search strategy and syntax for each database are detailed in (Table 1).

Eligibility Criteria

This review retained all clinical studies comparing FLKP and CPK. Outcomes must include at least one of the following: topographic astigmatism, visual acuity, spherical equivalent, endothelial cell density, graft rejection, graft failure, or complications. Prospective observational cohort studies, retrospective cohort studies, and randomized control trials were all included. Studies that were excluded were studies not comparing FLKP with CPK directly, studies focusing only on other types of keratoplasty like endothelial keratoplasty or anterior lamellar keratoplasty, non-English publications, and

Table 1 Search Syntax by Database

Database	Search Syntax	Records Identified
PubMed	("Femtosecond Laser-Assisted Keratoplasty"[MeSH] OR "FLEK") AND ("Penetrating Keratoplasty"[MeSH] OR "CPK") AND ("Corneal Transplantation"[MeSH] OR "keratoplasty") AND ("Graft Rejection"[MeSH] OR "Graft Failure") AND ("Astigmatism"[MeSH] OR "Visual Acuity"[MeSH] OR "Endothelial Cell Density"[MeSH])	268
Web of Science	TS = ("Femtosecond laser-assisted keratoplasty" OR "FLEK") AND TS = ("conventional penetrating keratoplasty" OR "CPK") AND TS = ("corneal transplantation" OR "keratoplasty") AND TS = ("graft rejection" OR "graft failure") AND TS = ("astigmatism" OR "visual acuity" OR "endothelial cell density")	50
Google Scholar	"femtosecond laser keratoplasty" OR "FLEK" AND "penetrating keratoplasty" OR "CPK" AND "corneal transplantation" AND "graft rejection" OR "graft failure" AND "visual acuity" OR "astigmatism" OR "endothelial cell density"	199

studies lacking the primary outcome of postoperative topographic astigmatism or lacking sufficient secondary outcomes for analysis.

Study Selection

Two groups of two reviewers independently screened titles and abstracts, the same process was used by Group A (O. M. and A.K.) and Group B (A.R. and R.R.) to independently assess the full texts of potentially eligible research. Disagreements were settled through discussion or a third reviewer (D.B.).

Data Collection Process

Four independent reviewers (R.A., J.A., D.B., and O.M.) extracted the data using a standardized form. Extracted data included study characteristics, participant demographics, interventions, comparisons, and outcomes.

Risk of Bias Assessment

The Methodological Index for Non-Randomized Studies (MINORS) tool[7] was utilized to evaluate the potential risk of bias in the non-randomized comparative studies that were included. It consists of 8 items for non-comparative studies and 12 items for comparative studies, each scored on a 0–2 scale, with a maximum score of 16 for non-comparative studies and 24 for comparative studies. Disagreements were resolved by discussion after each study was assessed independently by two reviewers, (Z.Q and A.B).

Meta-Analysis of the Included Data

Statistical analysis was performed using Review Manager (RevMan) Version 5.4.1 (Copenhagen: The Nordic Cochrane Center, The Cochrane Collaboration, 2020). For continuous variables such as topographic astigmatism, we calculated the mean difference. RevMan was also utilized as a tool for data analysis to determine the risk ratio (RR) with a 95% confidence interval (CI). Complication rates were recorded as the number of events per total number of patients in each group. The total patient count in each group was obtained for outcome parameters, and a quantitative evaluation on the basis of clinical and patient-reported outcomes was carried out. As for the meta-analysis, a random effects model was applied, and a value of $P < 0.05$ was determined statistically significant. For all outcomes, the direction of the forest plot ("favours FLEK" or "favours CPK") reflects the clinically favorable result, not just the numerical sign. For instance, in outcomes like endothelial cell density, higher values indicate better preservation, so a positive mean difference favors FLEK.

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Results

Literature Findings

A total of 517 articles were found and retrieved from 3 distinct databases: PubMed (n = 268), Web of Science (n = 50), and Google Scholar (n = 199). Of that, 157 duplicates were found and removed, and 360 studies underwent title and abstract screening. As a result, 326 articles were excluded mainly because they were irrelevant or did not meet the inclusion criteria. The remaining 34 articles were screened for full-text eligibility, with 25 studies being excluded mainly for various reasons. Finally, 9 studies fulfilled the inclusion criteria and were integrated into the systematic review. The described selection criteria are summarized in the PRISMA flow diagram illustrated in Figure 1. A list of excluded studies with reasons for exclusion is presented in (Table 2).

Characteristics of the Included Studies

Table 3 shows the characteristics of the included studies. The included studies were all retrospective comparative except for one prospective study.[32] Four of the studies were conducted in the USA,[33–36] and the remaining were conducted in various countries. The indications for both FLKP and CPK were exclusively keratoconus in two of the studies,[36,37] the

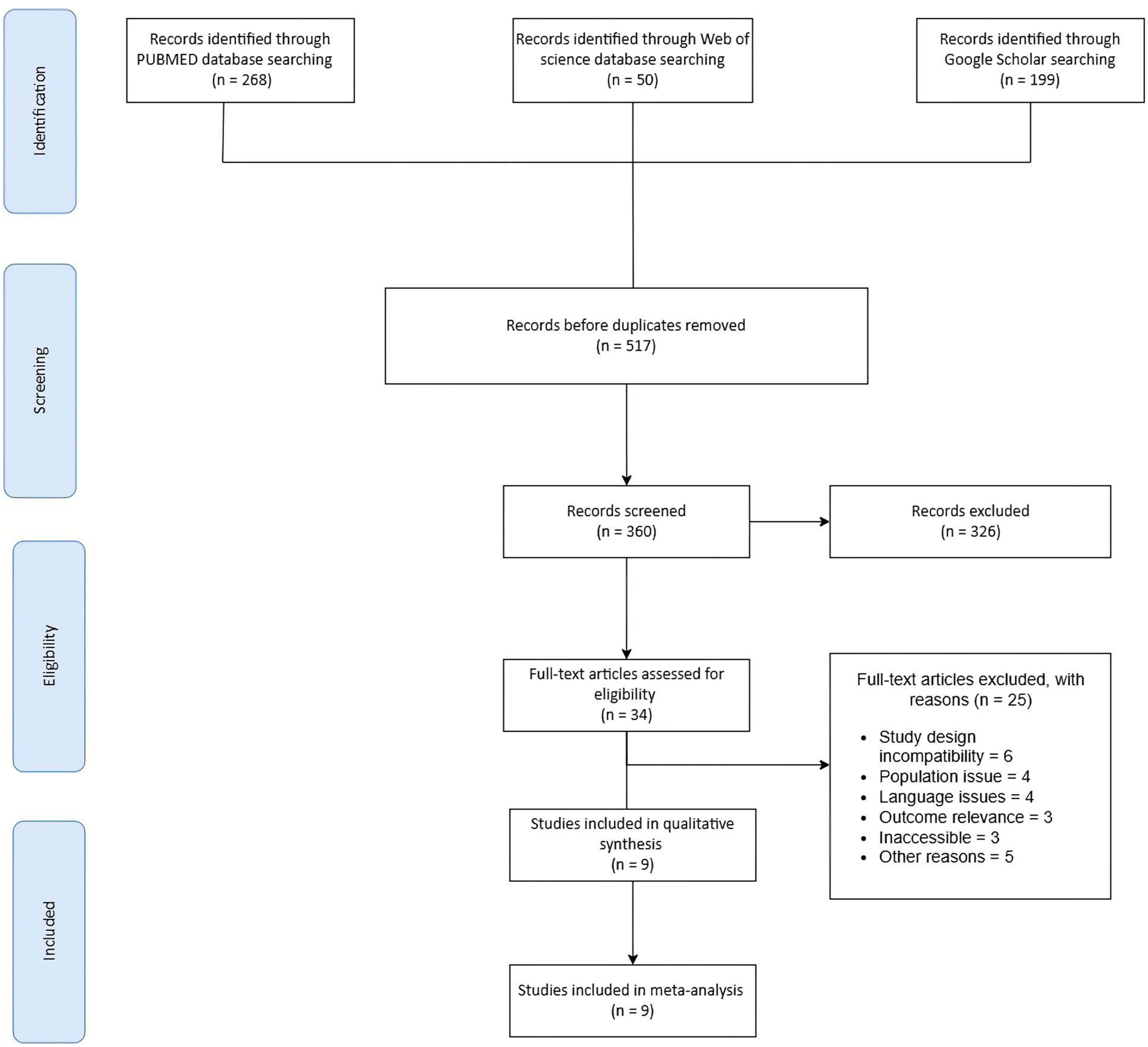

Figure 1 PRISMA flow diagram. PRISMA figure adapted from Page MJ, McKenzie JE, Bossuyt PM et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. Creative Commons.

Table 2 Excluded Studies and the Reason for Their Exclusion

Study	Link (DOI)	Reason for Exclusion
Morales-Wong et al (2023)[8]	10.4103/tjo.TJO-D-23-00083	Study Design Incompatibility
Wade et al. (2019)[9]	10.1097/ICO.0000000000001783	Study do not include targeted comparison group
Chang. (2018)[10]	10.1186/s40662-018-0099-9	Study Design Incompatibility
Farid et al. (2010)[11]	10.1097/ICU.0b013e32833a8dbc	Study do not include the targeted population
Monterosso et al. (2021)[12]	10.1177/11206721211059023	Study do not include targeted comparison group
Gadhvi et al. (2020)[13]	10.1016/j.ajo.2020.07.023	Study do not include targeted comparison group
Birnbaum et al. (2010)[14]	10.1007/s00347-009-2092-0	Non-English study
Holzer et al. (2006)[15]	10.1016/j.ajo.2006.08.029	Study that do not measure primary or secondary outcomes based on aim
Sorkin et al. (2019)[16]	10.1016/j.jcjo.2019.04.003	Study do not include targeted comparison group
Tolba et al. (2021)[17]	10.4103/1319-4534.325785	Study that do not measure primary or secondary outcomes based on aim
Cheng et al. (2009)[4]	10.1097/TP.0b013e3181bc419c	Other reason
Birnbaumet al. (2012)[18]	10.1007/s00417-012-2054-0	Study do not include the targeted population.
Hoffart et al. (2008)[19]	10.1016/j.ajo.2008.02.025	Study Design Incompatibility
Sorkin et al. (2023)[20]	10.1038/s41433-023-02387-1	Study do not include the targeted population
Cheng et al. (2011)[21]	10.1016/j.ajo.2011.03.012	Study do not include the targeted population
Jung et al. (2010)[22]	10.3341/jkos.2010.51.8.1054	Non-English study
Wang et al. (2014)[23]	10.3980/j.issn.1672–5123.2014.12.23	Non-English study
So et al. (2020)[24]	https://doi.org/10.3341/jkos.2020.61.12.1424	Non-English study
Omid et al. (2008)[25]	https://iovs.arvojournals.org/article.aspx?articleid=2377755	Inaccessible Full Text
Yoo et al. (2011)[26]	10.1016/j.ajo.2010.10.008	Study Design Incompatibility
Rafii et al. (2012)[27]	10.1136/bjophthalmol-2012-302196	Study Design Incompatibility
Van Rij et al. (2010)[28]	10.1016/j.ophtha.2010.03.012	Inaccessible Full Text
Fung et al. (2011)[29]	10.1136/bjophthalmol-2011-301035	Study that do not measure primary or secondary outcomes based on aim
Menabuoni et al. (2013)[30]	https://doi.org/10.1111/aos.12144	Inaccessible Full Text
Rij et al. (2009)[31]	10.1136/bjo.2009.160663	Study Design Incompatibility

other studies included a variety of diseases like bullous keratopathy, Fuchs dystrophy, prior ulcer or scarring, failed previous graft, corneal dystrophy, herpetic disease, repaired rupture, and aniridia. The wound configurations for FLKP varied between studies, including Zig-zag, Mushroom, Top-hat, in addition to Straight-cut.

Risk of Bias Assessment

The quality of the non-randomized studies that were included in this review was assessed using the MINORS tool.[7] The total score ranged from 11 to 19 out of a possible 24 points, with a mean score of 16.7. The retrospective study by El Kadi et al[39] had a total score of 11, indicating a higher risk of bias. The cohort studies by Bahar et al[32] and Kamiya et al[40] each had a total score of 19, suggesting a lower risk of bias. The most common methodological limitation was the unbiased assessment of the study endpoint (score of 0 in all studies). The items with the highest scores were the Inclusion of consecutive patients, and the Adequate statistical analyses (score of 2 in all studies). Overall, the included studies had high methodological quality. Thus, it is strongly suggested to interpret the findings with confidence. (Table 4).

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Table 3 Characteristics of the Included Studies

Study	**Chamberlain et al[33]**	**Daniel et al[38]**	**Bahar et al[32]**	**El Kadi et al[39]**	**Kamiya et al[40]**	**Levinger et al[37]**	**Chamberlain et al[34]**	**Gaster et al[36]**	**Farid et al[35]**
Study Design	Retrospective	Retrospective	Prospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective	Retrospective
Region	USA	Germany	Canada	Egypt	Japan	Israel	USA	USA	USA
Sample (Eyes)	FLEK = 34 CPK = 11	TH FLEK = 107 MR FLEK = 34 CPK = 1254	FLEK = 23 CPK = 35	FLEK = 20 CPK = 20	FLEK = 20 CPK = 20	FLEK = 26 CPK = 33	FLEK = 50 CPK = 50	FLEK = 66 CPK = 71	FLEK = 49 CPK = 17
Age (year) (mean ± SD)	FLEK = 61.1 (17.1) CPK = 66.1 (12.4)	TH FLEK = 58 ± 18 MR FLEK = 38 ± 12 CPK = 62 ± 18	FLEK = 42.2 (18.7) CPK = 63.6 (20.2)	N/A	FLEK = 63.7 ± 23.2 CPK = 64.3 ± 14.8	FLEK = 26 CPK = 29	FLEK = 46.26 CPK = 51.88	FLEK = 38.7 CPK = 44.5	FLEK = 60.39 CPK = 59.82
Female/Male	N\A	N\A	FLEK = 11/12 TH CPK = 11/25 CPK = 16/19	Total = 18/20	FLEK = 8/12 CPK = 10/10	FLEK = 7/19 CPK = 6/23	FLEK = 17/33 CPK = 17/33	FLEK = 17/49 CPK = 31/40	FLEK = 17/26 CPK = 6/8
Diagnosis	KC, BK, FD	TH FLEK = KC, BK, FD MR FLEK = KC CPK = KC, BK, FD	FLEK = KC, BK, CS, FG CPK = KC, BK, CS, FD, FG	KC, DC, CD, CO	KC, HD, BK, CS, FD, CD	KC	KC, RR, HSK, BK, CS, FG, CD	KC	FLEK = KC, BK, CS, FD, FG CPK = KC, CS, FD, FG
Cutting profile	Zig-zag	Top-hat Mushroom	Top-hat	Mushroom, Top-hat, straight cut	Straight cut	Mushroom	Zig-zag	Zig-zag	Zig-zag
Apparatus	FLEK: IntraLase FS laser CPK: Recipient: Barron vacuum Trephine. Donor: punch trephine on a Troutman guide	FLEK: IntraLase FS Laser CPK: Guided Trephine System	N\A	N\A	FLEK: VisuMax FS laser system CPK: Hessburg Barron vacuum trephine	N\A	FLEK: IntraLase FS Laser CPK: N/A	FLEK: IntraLase FS Laser CPK: N/A	FLEK: IntraLase FS Laser CPK: N/A
Suturing apparatus	Single 24-bite running 10–0 nylon suture	TH: single-running suture, single-running suture and interrupted sutures, double-running 8-bite suture, 8 interrupted sutures MR: double-running 8-bite suture, 8 interrupted sutures CPK: double-running suture	16 interrupted (8 sutures of 10–0 nylon, 8 sutures of 10–0 vicryl) and a single continuous 16-bite 11–0 of nylon suture, or 8 interrupted sutures (10–0 nylon) and a single continuous 16-bite 10–0 of nylon suture	N\A	16 interrupted sutures (10–0 nylon), or 8 Interrupted sutures and a single continuous 16-bite suture (10–0 nylon)	16-interrupted suturing technique	Either 16-interrupted or 24-interrupted	12 interrupted 10–0 nylon sutures followed by a running suture in between the interrupted sutures	Single, 24-bite running 10–0 nylon
Follow-up	1.5–19 months	Average 33 months	1 day, 1 week and 1, 3, 6 and 12 months	12 months	6 months	12 months	Mean for FLEK = 11.85 Mean for CPK = 19.64	3 - 6 months	FLEK = 1–12 months CPK = 3–12 months

Abbreviations: USA, United States of America; TH, Top-hat; MR, Mushroom; KC, Keratoconus; BK, Bullous Keratopathy; FD, Fuchs Dystrophy; cs, corneal scar; CD, Corneal Dystrophy; HD, Herpetic Disease; FG, Failed Graft; DC, Decompensated Cornea; CO, Corneal Opacity.

Table 4 MINORS Risk of Bias Assessment

Articles	Clearly Stated Aim	Inclusion of Consecutive Patients	Prospective Collection of Data	Endpoints Appropriate to the Aim of the Study	Unbiased Assessment of the Study Endpoint	Follow-Up Period Appropriate to the Aim of the Study	Loss to Follow Up Less Than 5%	Prospective Calculation of the Study Size	An Adequate Control Group	Contemporary Groups	Baseline Equivalence of Groups	Adequate Statistical Analyses	Total Score
Farid et al[35]	2	2	2	2	0	2	0	2	1	2	1	2	18
Gaster et al[36]	2	2	2	2	0	2	0	2	1	0	2	2	17
Chamberlain et al[34]	2	2	2	2	0	2	1	2	1	0	1	2	17
Levinger et al[37]	2	2	2	2	0	2	0	2	1	0	2	2	17
Kamiya et al[40]	2	2	2	2	0	2	2	2	1	0	2	2	19
El Kadi et al[39]	1	2	1	1	0	1	0	1	1	0	1	2	11
Bahar et al[32]	2	2	2	2	0	2	0	2	1	2	2	2	19
Daniel et al[38]	2	2	2	2	0	2	0	2	1	0	1	2	16
Chamberlain et al[33]	2	2	2	2	0	0	0	2	1	2	1	2	16

Meta-Analysis

As evident in Figure 2, at the end of the follow-up FLKP provides a significant improvement compared to CKP in terms of postoperative Topographic Astigmatism (Z = 3.23, P = 0.001, and I2 = 35%). Regarding the Best Spectacle Corrected Visual Acuity (BCVA) outcomes after keratoplasty, it is statistically significant that FLKP is better than CPK at the end of the follow-up period (Z = 5.03, P = 0.00001, and I2 = 4%), Figure 3. Uncorrected Visual Acuity (UCVA) was reported only in 2 studies and did not show any significance (Z = 0.4, P = 0.69, and I2 = 0%) Figure 4. Moreover, Figure 5 demonstrates the mean Spherical Equivalent (SE) was insignificant in regard to FLKP or CPK (Z = 0.14, P = 0.89, and I2 = 3%). When comparing the two techniques for postoperative endothelial cell density, CPK was inferior at preserving the cell count (Z = 2, P = 0.05, and I2 = 67%) Figure 6.

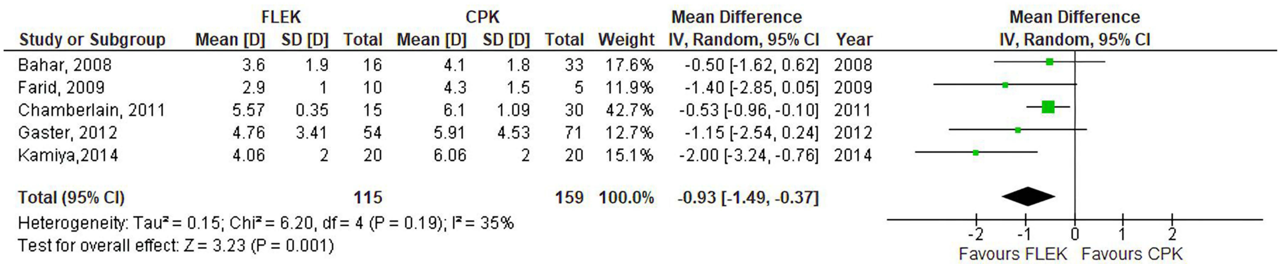

Figure 2 Forest plot showing postoperative topographic astigmatism.

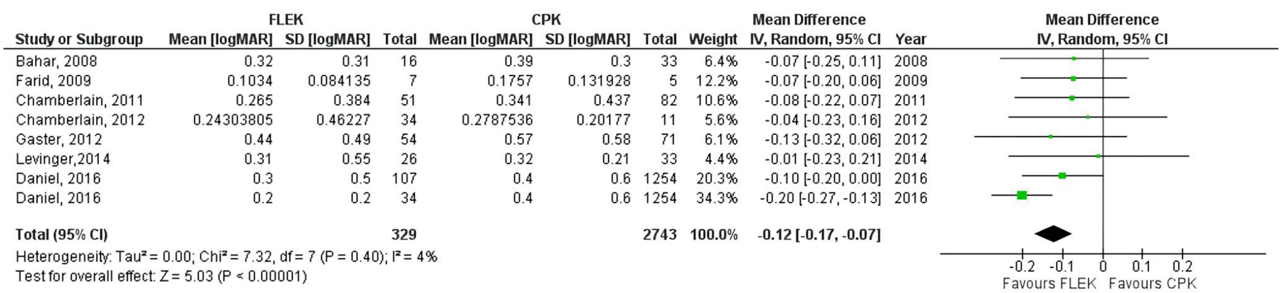

Figure 3 Postoperative Best Spectacle Corrected Visual Acuity.

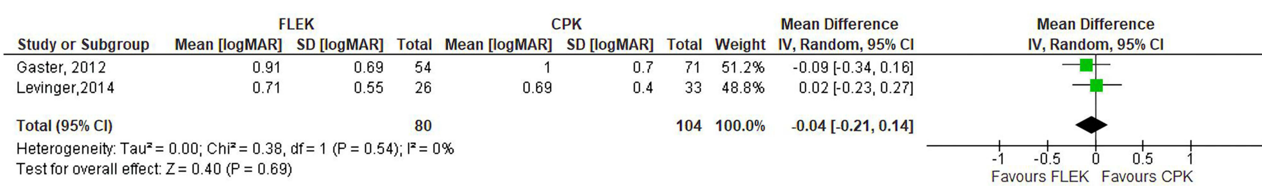

Figure 4 Forest plot for Uncorrected Visual Acuity.

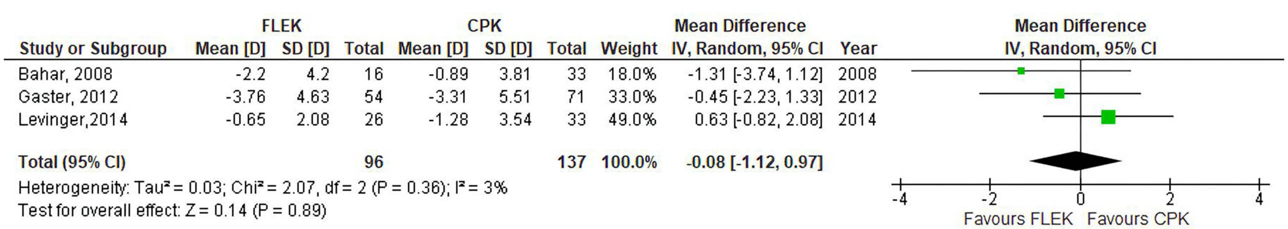

Figure 5 Forest plot for the Mean Spherical Equivalent.

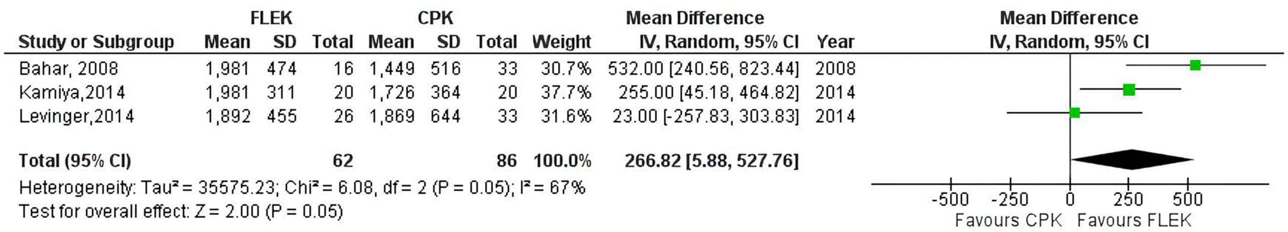

Figure 6 Postoperative endothelial cell density.

A sensitivity analysis was performed by sequentially removing each study from the endothelial cell density meta-analysis to assess the robustness of the results and explore sources of heterogeneity. In all cases, the direction of the pooled effect remained consistent, favoring FLPK over CPK. When Levinger et al[37] was excluded, the effect estimate increased and became more statistically significant (MD = 374.28, 95% CI [105.45, 643.10], $p = 0.006$), with moderate heterogeneity ($I^2 = 56\%$). Removing Bahar et al[32] and Kamiya et al[40] led to nonsignificant results with I^2 values of 41% and 84%, respectively. These findings indicate that while heterogeneity exists, the overall direction and magnitude of the effect are stable and support the conclusion that FLPK better preserves endothelial cell density.

Complications after the two procedures were mentioned in several studies, mostly mentioning graft failure, graft rejection, secondary astigmatism, glaucoma, infectious keratitis, and wound dehiscence/extrusion. All of these were insignificant for either FLKP or CPK except for wound dehiscence/extrusion as demonstrated in Figure 7.

Systematic Review

Certain complications were not mentioned in all studies; thus, it was not appropriate to perform a meta-analysis. Instead, a descriptive summary has been conducted. Table 5.

Discussion

In this meta-analysis, we systematically reviewed studies that compared FLKP with CPK and conducted a comprehensive meta-analysis emphasizing data related to topographic astigmatism, (BCVA - UCVA - SE), post-operative endothelial cell density, and complications after the two procedures.

We found that FLKP is significantly better than CPK upon completion of the follow-up period regarding Postoperative Topographic Astigmatism, BCVA, endothelial cell counts, and wound dehiscence/extrusion. Interestingly, when comparing the two techniques for UCVA, SE, and the mentioned complications (graft failure, graft rejection, secondary astigmatism, glaucoma, infectious keratitis) all of which were insignificant for either FLKP or CPK.

(FLPK) provides precise matching between donor and recipient corneal incisions, improving wound stability and making the graft more resistant to intraocular pressure spikes and less ocular trauma. This technique reduces suture tension and improves corneal alignment, leading to less optical distortion and astigmatism. Compared to (CPK), FLPK causes less tissue trauma, allows faster resolution of wound edema, and enables earlier suture removal. The larger posterior graft diameter in FLPK also helps preserve more endothelial cells, while the manual rotation in CPK may result in more damage and loss.

Femtosecond laser technology has illustrated its capability to attain better donor/recipient wound incision compatibility in terms of accuracy and precision in contrast to the standard manual blade trephination technique.[11,36,37,41–43] Moreover, when compared to the conventional manual blade trephination technique, the perfect apposition of the donor/recipient incision achieved by the femtosecond laser resulted in improved stability of the surgical wound and higher resistance against both elevated intraocular pressure (which can result in graft wound leakage or dehiscence) and ocular trauma.[11,37,41,43,44]

In our study, we found that FLKP is significantly advanced to CPK in terms of postoperative Topographic Astigmatism (Z = 3.23, P = 0.001, and I2 = 35%) at the end of the follow-up. As for BCVA outcomes after keratoplasty, it is statistically significant that FLKP is better than CPK upon completion of the follow-up period (Z = 5.03, P =

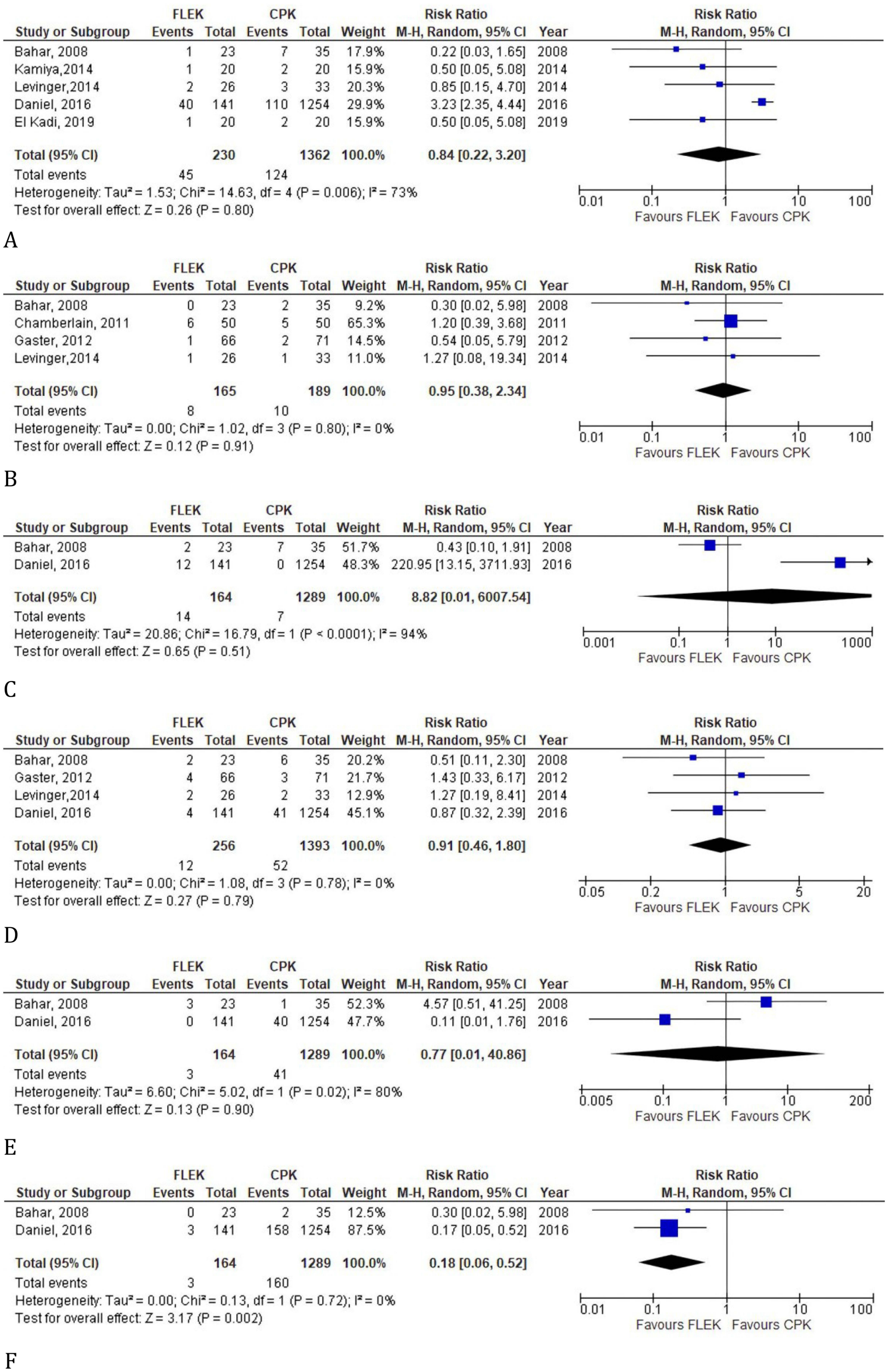

Figure 7 Postoperative Complications.

Notes: (**A**) Graft rejection, (**B**) Graft Failure, (**C**) Secondary Astigmatism, (**D**) Glaucoma, (**E**) Infectious Keratitis, and (**F**) Wound Dehiscence/Extrusion.

Table 5 Descriptive Analysis of Complications

Study	No. of Eyes FLEK/CPK	Main Outcome	P Value
Wound Leakage			
Daniel 2016 (15)	141/1254	9 cases in FLEK	N/A
Graft Ulcerations			
Daniel 2016 (15)	141/1254	3 cases in FLEK	N/A

0.00001, and I2 = 4%). These findings came in accordance with previous studies that stated, the angled zig-zag edges used in FLKP achieve a seamless transition between donor and recipient; which results in improved alignment and reduced suture tension, both will produce less optical distortion and induced astigmatism. Moreover, there will be less tissue interference and trauma in FLKP compared to CPK, which may explain the rapid remission of wound edema in patients treated with FLKP. Furthermore, stronger wounds and earlier suture removal may arise from the larger surface area of the incision in FLKP with higher collagen fibrosis stimulated by laser compared with CPK.[11]

UCVA was reported only in 2 studies and did not show any significance (Z = 0.4, P = 0.69, and I2 = 0%) Figure 4. Moreover, Figure 5 demonstrates the mean SE was insignificant in regard to FLKP or CPK (Z = 0.14, P = 0.89, and I2 = 3%).

Interestingly, when comparing the two techniques for postoperative endothelial cell density, CPK was significantly inferior at preserving the cell count (Z = 2, P = 0.05, and I2 = 67%). This could be explained by the larger diameter of the posterior donor surface used in FLKP compared to CPK (8.5 or 8.87 mm diameter of corneal endothelium in the top hat groups vs 7.75 mm in the CPK group), loaded a larger posterior endothelial layer and more endothelial cells. Furthermore, mechanical rotatory forces exerted by hands in CPK may result in more damage and loss in endothelial cell count after the surgery.[41]

Surprisingly, complications after the two procedures were mentioned in several studies, mostly mentioning graft failure, graft rejection, secondary astigmatism, glaucoma, infectious keratitis, and wound dehiscence/extrusion. All of these were insignificant for either FLKP or CPK except for wound dehiscence/extrusion.

Regarding Daniel et al's[38] study comparing the Long-Term Outcomes of Femtosecond Laser-Assisted Keratoplasty with Conventional Keratoplasty in cases of bullous keratopathy, after 35 months, the rates of graft rejection were greater in patients treated with FLKP (37% vs 28% in the CPK) (P = 0.204). After 35 months, the rates of graft rejection among the patients with Fuchs endothelial dystrophy were 11% in the FLKP group and 13% in the CPK group (P = 0.921). After 35 months, the keratoconus group experienced 25% graft rejection in the FLKP (TH) group and 31% in the CPK group.[38]

According to a study by Levinger et al,[37] the outcomes of traditional CPK and "mushroom" FLKP (M-FLKP) were compared in eyes with Keratoconus. In the M-FLKP group, graft rejection resulted in graft failure in 1 eye (3.8%) and occurred in 2 eyes (7.7%). In the CPK group, graft rejection happened in 3 eyes (9%) and resulted in graft failure in 1 eye (3%). Two patients (7.7% and 6% of each group) had postoperative new-onset secondary glaucoma, which was effectively managed with topical medicines alone.[37]

Another study compared the clinical results of traditional CPK with FLKP utilizing the VisuMax femtosecond laser system. They discovered that one eye (5%), in the FLKP group, experienced graft rejection. Graft rejection, elevated IOP, and suture-oriented infection occurred in 2 (10%), 3 (15%), and 1 (5%), of the eyes in the CPK group, respectively.[40] As far as we are aware, this meta-analysis and systematic review serve as a strong study for evaluating the effectiveness and safety of CPK with FLKP.

The particular inclusion and exclusion criteria, noncommercial nature, and protocol-compliant reporting that closely follows PRISMA recommendations are the strengths of this systematic review and meta-analysis. Bias was assessed in each study's synthesis and methodological quality. As of the time of writing, the most comprehensive data pool was available for analysis in this study, which reviewed the most recent keratoplasty studies.

However, there are a number of limitations to our study. First, the majority of included studies are retrospective studies and may be subjected to recall, observer bias, confounding variables (surgeon experience and patient selection)

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and the small number of studies per outcome all of which have the potential to weaken the validity of the conclusions. Second, the results might not generalize to other locations because the majority of the research that was included in our study came from North America and Europe. Third, because there are not many published papers on this subject, not all of the studies that are part of this systematic review are recent. Finally, not all trials had a long enough follow-up period, which is necessary to measure an accurate prediction. Prospective randomized trials are necessary to provide light on the various surgical techniques for keratoplasty because of heterogeneity and the lack of data from several research and health advancements.

Conclusion

Femtosecond laser technology is one of the most innovative techniques used in keratoplasty nowadays. Our findings emphasize that the postoperative topographic astigmatism outcomes following FLKP surgery are significantly better compared to CPK. It is demonstrated that FLKP has advantages over CPK, in terms of preserving the postoperative endothelial cell density, in addition to BCVA outcomes. However, there is no significant difference in UCVA or spherical equivalent among both groups. For the complications, neither technique showed any significance except for wound dehiscence, where FLKP had lower rates of incident. Therefore, the FLKP procedure substantially provides faster visual recovery and decreases postoperative astigmatism. Notwithstanding the FLKP technique's advantages, its high cost and restricted accessibility in resource-constrained locations should be considered. Future research on FLKP ought to look into whether its benefits outweigh the need for more resources in some locations.

One of the prominent limitations of this study is the retrospective nature of most of the included series. Also, only English-language studies were included, which may introduce language bias and limit the generalizability of the findings to non-English speaking populations. Moreover, the results cannot be generalized to the population as a whole, as the majority of study participants were from North America and Europe. Hence, future long-term randomized, prospective studies will be able to further confirm our findings and elucidate different surgical techniques used in keratoplasty in more detail.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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