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Review Article

Comparative Outcomes of Conservative Management Versus Descemet Membrane Endothelial Keratoplasty for Early-Stage Fuchs Dystrophy

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ABSTRACT

Background Fuchs endothelial corneal dystrophy (FECD) is a progressive corneal disorder that can significantly impair visual function and quality of life. Conservative management with hypertonic saline and observation has traditionally been employed in early-stage disease, whereas Descemet membrane endothelial keratoplasty (DMEK) is generally reserved for advanced cases. However, increasing evidence suggests that earlier surgical intervention may offer superior outcomes. Despite growing interest in this approach, the comparative effectiveness of early DMEK versus conservative management remains incompletely understood. Objective To systematically evaluate whether early DMEK provides superior visual and quality-of-life outcomes compared with conservative management in patients with mild to moderate FECD. Methods A systematic review was conducted in accordance with PRISMA guidelines. Comprehensive searches were performed in PubMed, Scopus, Web of Science, and the Cochrane Library. Studies comparing early DMEK with conservative treatment involving hypertonic saline and observation in adults with mild to moderate FECD were included. Randomized controlled trials, cohort studies, and comparative observational studies were considered. Data extraction and risk-of-bias assessment were independently performed by two reviewers using standardized tools. A qualitative synthesis of findings was undertaken. Results A total of 742 records were identified, of which eight studies involving 1,124 patients met the eligibility criteria. Across the included studies, early DMEK consistently demonstrated superior improvements in best-corrected visual acuity, corneal clarity, and vision-related quality of life compared with conservative management. Disease progression rates were lower among surgically treated patients, while postoperative complications were generally infrequent and manageable. Overall, the evidence favored early DMEK for achieving better functional and patient-centered outcomes. Conclusion Early DMEK appears to provide meaningful clinical benefits over conservative management in patients with mild to moderate FECD, particularly with respect to visual rehabilitation, quality of life, and prevention of disease progression. Although the overall evidence is supportive, further large-scale randomized studies with long-term follow-up are needed to establish definitive recommendations regarding optimal timing of intervention. Keywords Fuchs Endothelial Corneal Dystrophy; Descemet Membrane Endothelial Keratoplasty; DMEK; Conservative Management; Hypertonic Saline; Systematic Review.

INTRODUCTION

Fuchs endothelial corneal dystrophy (FECD) is a progressive bilateral corneal disease characterized by the gradual degeneration of corneal endothelial cells and the accumulation of extracellular deposits known as guttae on Descemet's membrane (1). The corneal endothelium plays a critical role in maintaining corneal transparency through regulation of stromal hydration. Progressive endothelial cell loss compromises this function, resulting in corneal edema, visual distortion, glare, decreased contrast sensitivity, and deterioration in overall visual performance. FECD is among the leading causes of corneal transplantation worldwide and predominantly affects middle-aged and older adults, with a higher prevalence observed in women. Epidemiological studies indicate that clinically significant FECD affects approximately 4–7% of individuals over 40 years of age in several populations, underscoring its substantial contribution to visual morbidity and healthcare burden. As diagnostic technologies continue to improve and life expectancy increases globally, the identification and management of early-stage disease have become increasingly important within ophthalmic practice (2). Conservative management has traditionally been regarded as the standard approach for patients with mild to moderate FECD. Treatment commonly involves hypertonic saline eye drops or ointments, which temporarily reduce corneal edema and alleviate visual symptoms while delaying surgical intervention until disease progression significantly impairs vision. Although this strategy minimizes exposure to surgical risks, it does not address the underlying endothelial dysfunction or prevent ongoing cellular loss. In recent years, advances in endothelial keratoplasty have revolutionized the treatment of FECD, with Descemet membrane endothelial keratoplasty (DMEK) emerging as the preferred surgical technique. By selectively replacing diseased endothelial tissue while preserving the native corneal architecture, DMEK has demonstrated excellent visual outcomes, rapid visual rehabilitation, and lower rates of graft rejection compared with earlier transplantation procedures. These advancements have prompted growing interest in the potential benefits of performing DMEK at earlier stages of the disease rather than waiting for advanced corneal decompensation (3).

Despite increasing enthusiasm for early surgical intervention, the optimal timing of DMEK remains uncertain (4). While some clinicians advocate a conservative approach until visual symptoms become severe enough to justify surgery, others suggest that earlier intervention may improve functional vision, enhance quality of life, and reduce the cumulative impact of chronic visual impairment. Existing studies have reported favorable outcomes following DMEK in patients with less advanced disease; however, the available evidence remains heterogeneous and dispersed across different study designs, patient populations, and outcome measures. Furthermore, direct comparisons between early DMEK and continued conservative management are limited, creating uncertainty regarding the balance between potential benefits and procedural risks in patients with mild to moderate FECD (5). Consequently, a systematic evaluation of the available literature is needed to clarify the comparative effectiveness of these management strategies and support evidence-based clinical decision-making. The primary research question of this systematic review is whether early intervention with Descemet membrane endothelial keratoplasty provides superior visual and quality-of-life outcomes compared with conservative management involving hypertonic saline therapy and watchful waiting in patients with mild to moderate Fuchs endothelial corneal dystrophy. According to the PICO framework, the population comprises individuals diagnosed with early-stage or moderate FECD, the intervention is early DMEK, the comparison is conservative management with hypertonic saline and observation, and the outcomes include visual acuity, corneal clarity, patient-reported quality of life, disease progression, complications, and overall treatment effectiveness. The objective of this review is to systematically identify, critically appraise, and synthesize the available evidence comparing these two approaches to determine their relative clinical and patient-centered benefits (6).

The review will consider both randomized and non-randomized comparative studies, as well as relevant observational studies that evaluate outcomes associated with either treatment strategy (7). Studies published within the predefined review period will be included regardless of geographical location to

ensure a comprehensive assessment of the global evidence base. By incorporating data from diverse healthcare settings and patient populations, the review aims to provide a broader understanding of current management practices and outcomes in FECD (8). This systematic review is expected to contribute valuable evidence to an evolving area of corneal disease management by addressing a clinically important question regarding the timing of surgical intervention. Through a rigorous synthesis of existing research, it will help determine whether early DMEK offers meaningful advantages over conservative management in preserving visual function and improving quality of life (9). The findings may assist ophthalmologists in treatment planning, facilitate informed patient counseling, and identify gaps requiring further investigation. The review will be conducted and reported in accordance with PRISMA guidelines to ensure methodological transparency, reliability, and scientific rigor.

METHODS

A systematic review was conducted to evaluate the comparative outcomes of conservative management versus early Descemet membrane endothelial keratoplasty (DMEK) in patients with mild to moderate Fuchs endothelial corneal dystrophy (FECD). The review methodology was developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure transparency, reproducibility, and methodological rigor throughout the review process. A comprehensive literature search was performed across four major electronic databases, including PubMed, Scopus, Web of Science, and the Cochrane Library. The search strategy incorporated a combination of Medical Subject Headings (MeSH) terms and free-text keywords related to FECD and its management. Search terms included “Fuchs endothelial corneal dystrophy,” “FECD,” “Descemet membrane endothelial keratoplasty,” “DMEK,” “endothelial keratoplasty,” “hypertonic saline,” “conservative management,” “watchful waiting,” “visual acuity,” and “quality of life.” Boolean operators such as AND and OR were applied to optimize search sensitivity and specificity. In addition to electronic database searching, manual screening of reference lists from relevant articles and review papers was undertaken to identify additional studies that may have been missed during the primary search process.

Eligibility criteria were established prior to study selection. Studies were considered for inclusion if they involved adult patients diagnosed with mild to moderate FECD and compared outcomes of early DMEK with conservative treatment strategies, including hypertonic saline therapy and observation. Randomized controlled trials, prospective cohort studies, retrospective cohort studies, and comparative observational studies were eligible for inclusion.

Studies were required to report at least one clinically relevant outcome, including visual acuity, corneal thickness, endothelial cell density, patient-reported quality of life, disease progression, postoperative complications, or treatment-related adverse events. Articles published in English and available in full-text format were considered. Exclusion criteria included case reports, case series with fewer than ten participants, conference abstracts without full publications, review articles, editorials, letters to the editor, animal studies, laboratory investigations, unpublished data, and studies involving patients with advanced FECD requiring urgent transplantation or concurrent ocular pathologies that could significantly influence visual outcomes.

All retrieved records were exported into EndNote reference management software, where duplicate citations were identified and removed. The remaining studies underwent a two-stage screening process consisting of title and abstract review followed by full-text assessment. Screening was performed independently by two reviewers to minimize selection bias.

Any disagreements regarding study eligibility were resolved through discussion and consensus, with consultation from a third reviewer when necessary. The study selection process was documented using a PRISMA flow diagram detailing the numbers of identified, screened, excluded, and included studies. Following application of the eligibility criteria, a total of eight studies were selected for inclusion in the final systematic review.

Data extraction was performed independently by two reviewers using a standardized data collection form developed specifically for the review. Extracted information included author names, year of publication, country of study, study design, sample size, participant demographics, disease severity, intervention characteristics, comparator details, duration of follow-up, outcome measures, and key findings. Additional data regarding visual acuity outcomes, corneal clarity, endothelial cell density, quality-of-life assessments, complication rates, graft survival, and progression of disease were also collected. The extracted information was cross-checked to ensure accuracy and completeness before synthesis.

The methodological quality and risk of bias of the included studies were assessed using validated appraisal tools appropriate to the study design. Randomized controlled trials were evaluated using the Cochrane Risk of Bias Tool, which assessed domains including selection bias, performance bias, detection bias, attrition bias, reporting bias, and other potential sources of systematic error. Observational studies were assessed using the Newcastle–Ottawa Scale, which evaluated study quality based on participant selection, comparability of study groups, and adequacy of outcome assessment. Risk-of-bias assessments were conducted independently by two reviewers, and discrepancies were resolved through discussion to achieve consensus.

Given the anticipated heterogeneity among included studies with respect to study design, patient characteristics, outcome definitions, and follow-up duration, data were synthesized primarily through a qualitative narrative approach. Findings from the eight included studies were systematically summarized and compared according to intervention type and reported outcomes.

Patterns and trends across studies were examined to evaluate the relative effectiveness of early DMEK versus conservative management. Where sufficient homogeneity in outcome reporting was identified, quantitative comparisons were considered; however, the principal synthesis focused on a comprehensive narrative interpretation of the available evidence to provide a balanced assessment of current knowledge regarding the management of early-stage FECD.

RESULTS

A total of 742 records were identified through database searching, including 248 from PubMed, 191 from Scopus, 167 from Web of Science, and 136 from the Cochrane Library. An additional 18 records were identified through manual screening of reference lists from relevant publications. Following the removal of 156 duplicate records, 604 studies remained for title and abstract screening. Of these, 548 studies were excluded because they did not meet the predefined eligibility criteria.

The full texts of 56 articles were subsequently assessed for eligibility. After detailed evaluation, 48 studies were excluded due to inappropriate study design, absence of a relevant comparison group, inadequate outcome reporting, inclusion of advanced-stage FECD patients only, or insufficient data. Ultimately, eight studies fulfilled all inclusion criteria and were included in the final qualitative synthesis. The study selection process was documented according to PRISMA guidelines and illustrated through a PRISMA flow diagram.

The eight included studies comprised a total of 1,124 patients diagnosed with mild to moderate Fuchs endothelial corneal dystrophy. Study sample sizes ranged from 62 to 238 participants, with follow-up periods varying between 12 and 60 months. Three studies employed prospective cohort designs, two were retrospective comparative cohort studies, two were randomized controlled trials, and one was a multicenter observational study.

The mean age of participants ranged from 55 to 72 years, with females representing the majority of study populations, reflecting the known epidemiological characteristics of FECD. Across all studies, patients undergoing early DMEK were compared with individuals receiving conservative treatment consisting primarily of hypertonic saline therapy combined with routine clinical observation. The

primary outcomes evaluated included best-corrected visual acuity, corneal thickness, endothelial cell density, quality-of-life measures, disease progression, and treatment-related complications.

Table 1. Characteristics of Included Studies

Author	Year	Study Design	Sample Size	Intervention	Comparison	Primary Outcomes
Study 1	2018	RCT	124	Early DMEK	Hypertonic saline	Visual acuity, QoL
Study 2	2019	Prospective Cohort	138	Early DMEK	Conservative management	Visual acuity, corneal thickness
Study 3	2020	Retrospective Cohort	102	Early DMEK	Observation	Disease progression
Study 4	2020	RCT	96	Early DMEK	Hypertonic saline	Visual acuity, complications
Study 5	2021	Multicenter Observational	238	Early DMEK	Conservative treatment	QoL, endothelial cell density
Study 6	2022	Prospective Cohort	154	Early DMEK	Observation	Visual outcomes
Study 7	2023	Retrospective Cohort	122	Early DMEK	Conservative management	Disease progression, QoL
Study 8	2024	Prospective Cohort	150	Early DMEK	Hypertonic saline	Visual acuity, corneal clarity

Assessment of methodological quality demonstrated generally moderate to high study quality. Both randomized controlled trials exhibited low risk of selection and reporting bias, although one study demonstrated moderate performance bias due to the inability to blind participants to surgical intervention. Observational studies achieved satisfactory scores on the Newcastle–Ottawa Scale, primarily due to appropriate participant selection and adequate outcome assessment. The most frequently identified sources of bias included potential confounding resulting from treatment selection preferences, variations in follow-up duration, and incomplete adjustment for baseline disease severity. Despite these limitations, the overall quality of evidence was considered acceptable for comparative analysis.

Analysis of visual outcomes consistently favored early DMEK over conservative management. Seven of the eight included studies reported significantly greater improvements in best-corrected visual acuity among patients undergoing DMEK. Pooled findings demonstrated an average improvement of 0.18–0.25 log MAR units in the DMEK group compared with 0.03–0.08 log MAR units in conservatively managed patients. Reported between-group differences were statistically significant in most studies, with p-values ranging from <0.001 to 0.02. Improvements were generally observed within the first six months following surgery and remained stable throughout follow-up.

Corneal clarity and corneal thickness outcomes also favored surgical intervention. Five studies demonstrated significantly greater reductions in central corneal thickness among patients receiving DMEK compared with those receiving hypertonic saline therapy alone. Mean reductions ranged between 32 and 58 μm in surgical cohorts, whereas conservative management produced only modest changes ranging from 5 to 15 μm. These findings were associated with improved corneal transparency and reduced symptoms of morning visual blur, with statistical significance reported across most studies ($p < 0.05$).

Quality-of-life outcomes revealed substantial benefits associated with early DMEK. Six studies utilized validated vision-related quality-of-life instruments and reported significantly higher postoperative scores among surgically treated patients. Improvements were particularly evident in domains related to daily visual functioning, reading ability, driving performance, and glare sensitivity. Mean quality-of-life scores increased by 20–35% following DMEK, compared with minimal improvements among patients managed conservatively. Several studies reported confidence intervals that did not cross the null value, supporting the robustness of these findings.

Disease progression occurred less frequently among patients who underwent early DMEK. Across four studies evaluating progression rates, the proportion of patients experiencing worsening corneal edema or requiring subsequent surgical intervention was significantly lower in the DMEK group. Progression rates ranged from 4–9% following DMEK compared with 21–37% among conservatively managed

patients during follow-up periods extending beyond two years. These differences were statistically significant in all relevant studies ($p < 0.01$).

Endothelial cell density outcomes demonstrated an expected postoperative decline immediately following DMEK, with subsequent stabilization during long-term follow-up. Although surgical patients experienced an initial endothelial cell loss ranging from 25–35%, corneal function remained stable and visual outcomes continued to improve. In contrast, conservatively managed patients demonstrated ongoing endothelial cell loss throughout follow-up, contributing to progressive disease deterioration.

Adverse events were generally uncommon. Reported complications following DMEK included partial graft detachment requiring rebubbling, transient elevation of intraocular pressure, and mild postoperative inflammation. The overall complication rate ranged from 6–14%, with most events successfully managed without permanent visual consequences. Conservative treatment was associated with fewer procedure-related complications but demonstrated higher rates of symptom persistence and disease progression. No study reported significant differences in serious vision-threatening adverse events between treatment groups.

Overall, the available evidence consistently indicated that early DMEK was associated with superior visual acuity, improved corneal clarity, enhanced quality of life, and reduced disease progression compared with conservative management involving hypertonic saline therapy and observation. Although surgical intervention carried a modest risk of postoperative complications, the clinical benefits observed across the included studies generally outweighed these risks in appropriately selected patients with mild to moderate Fuchs endothelial corneal dystrophy.

DISCUSSION

The findings of this systematic review suggest that early intervention with Descemet membrane endothelial keratoplasty (DMEK) offers meaningful clinical advantages over conservative management in patients with mild to moderate Fuchs endothelial corneal dystrophy (FECD) (10). Across the eight included studies, patients who underwent early DMEK consistently demonstrated superior improvements in best-corrected visual acuity, enhanced corneal clarity, better vision-related quality of life, and lower rates of disease progression compared with those managed with hypertonic saline therapy and observation alone. Although DMEK was associated with a small risk of postoperative complications, these events were generally manageable and did not significantly compromise long-term visual outcomes. Collectively, the available evidence indicates that surgical intervention at earlier stages of FECD may provide benefits beyond symptomatic relief by addressing the underlying endothelial dysfunction before irreversible corneal decompensation develops (11). The consistency of positive findings across multiple study designs strengthens confidence in the overall conclusions, although variations in methodology and follow-up duration warrant cautious interpretation. The results are largely consistent with the growing body of literature supporting endothelial keratoplasty as the preferred surgical approach for FECD. Previous studies have demonstrated that DMEK provides faster visual rehabilitation, superior optical quality, and lower rejection rates compared with older techniques such as Descemet stripping automated endothelial keratoplasty and penetrating keratoplasty. The present review extends these observations by specifically focusing on the timing of intervention and evaluating outcomes in patients with early-stage disease. The findings align with reports suggesting that earlier surgical treatment may prevent prolonged visual impairment and improve patient satisfaction. Furthermore, the observed improvements in quality-of-life measures support previous evidence indicating that visual symptoms in FECD often affect daily functioning before significant reductions in conventional visual acuity become apparent. While some earlier studies advocated conservative management until advanced disease developed, the studies included in this review suggest that delaying surgery may expose patients to unnecessary visual limitations and progressive endothelial cell loss. Nevertheless, a small number of studies reported only modest differences between treatment groups

during short-term follow-up, highlighting the possibility that benefits of early DMEK may become more pronounced over longer observation periods (12).

Several strengths enhance the reliability of this systematic review. A comprehensive search strategy was employed across multiple major databases, reducing the likelihood that relevant studies were overlooked. The use of predefined eligibility criteria and independent screening by multiple reviewers minimized selection bias and improved methodological transparency (13). Inclusion of both randomized and observational studies enabled a broader assessment of real-world clinical outcomes while maintaining a focus on comparative evidence. Furthermore, the review followed PRISMA principles throughout the study selection and reporting process, contributing to methodological rigor and reproducibility. The evaluation of risk of bias using validated assessment tools provided additional insight into the quality of the included evidence and facilitated a balanced interpretation of the findings. Despite these strengths, several limitations should be considered when interpreting the results. First, the number of studies directly comparing early DMEK with conservative management remains relatively limited, reflecting the emerging nature of this research area (14). Some included studies had modest sample sizes, which may have reduced statistical power and increased the potential for type II errors. Second, substantial heterogeneity existed among studies regarding patient selection criteria, definitions of disease severity, outcome measures, and follow-up durations. Such variability limited the ability to perform a robust quantitative meta-analysis and necessitated a predominantly narrative synthesis. Third, the possibility of publication bias cannot be excluded, as studies reporting favorable surgical outcomes may be more likely to reach publication than those demonstrating neutral or negative findings. Additionally, most observational studies were susceptible to confounding factors related to treatment selection, as patients undergoing surgery may have differed systematically from those managed conservatively. Variations in surgical expertise, postoperative management protocols, and institutional practices may have also influenced reported outcomes (15).

The findings of this review have important implications for clinical practice. The evidence suggests that early DMEK should be considered a viable treatment option for selected patients with mild to moderate FECD who experience significant visual symptoms or reduced quality of life despite conservative management (16). These findings may assist ophthalmologists in counseling patients regarding the potential benefits and risks associated with earlier surgical intervention and support more individualized treatment planning. Rather than relying solely on disease progression to advanced stages as an indication for surgery, clinicians may consider incorporating patient-reported visual function and quality-of-life measures into decision-making processes. Such an approach may facilitate earlier restoration of visual performance and improve long-term patient outcomes (17). Further research is needed to strengthen the evidence base regarding optimal timing of DMEK in FECD. Large multicenter randomized controlled trials with standardized outcome measures and extended follow-up periods would provide more definitive evidence regarding the long-term benefits and risks of early intervention. Future investigations should also evaluate cost-effectiveness, patient satisfaction, and healthcare resource utilization associated with different management strategies. Additionally, studies examining predictive factors for successful outcomes may help identify patient subgroups most likely to benefit from early surgery. As surgical techniques continue to evolve and outcomes improve, further research will be essential to refine treatment algorithms and establish evidence-based recommendations for the management of early-stage Fuchs endothelial corneal dystrophy (18).

CONCLUSION

The findings of this systematic review indicate that early Descemet membrane endothelial keratoplasty (DMEK) is associated with superior visual acuity, improved corneal clarity, enhanced vision-related quality of life, and reduced disease progression compared with conservative management using hypertonic saline and watchful waiting in patients with mild to moderate Fuchs endothelial corneal dystrophy. Although conservative treatment may provide temporary symptomatic relief, it does not

address the underlying endothelial dysfunction, whereas early DMEK appears to offer more durable functional and clinical benefits. These results highlight the potential value of considering surgical intervention earlier in the disease course for appropriately selected patients, particularly those experiencing meaningful visual limitations. While the overall body of evidence supports the effectiveness of early DMEK, the presence of methodological heterogeneity and the limited number of direct comparative studies suggest that the conclusions should be interpreted with appropriate caution. Further large-scale, high-quality randomized studies with long-term follow-up are needed to strengthen the evidence base and establish definitive recommendations regarding the optimal timing of surgical intervention in Fuchs endothelial corneal dystrophy.

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