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Review article

Beyond keratoplasty: The role of Descemet stripping only in the management of Fuchs endothelial dystrophy—a systematic review and meta-analysis

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ABSTRACT

The clinical role of Descemet stripping only (DSO) in treating Fuchs endothelial corneal dystrophy (FECD) remains uncertain. The literature varies regarding patient selection, timing of intervention, and use of additional therapies. We evaluate the efficacy and safety of DSO through a systematic review and meta-analysis, focusing on visual outcomes, corneal clearance, and the need for subsequent keratoplasty. It was conducted following PRISMA guidelines and registered with PROSPERO (ID: CRD420251160540). Comprehensive searches of MEDLINE, Scopus, Web of Science, and Embase were performed from inception to August 2025. Eligible studies included prospective or retrospective clinical series with at least 5 patients who underwent DSO for FECD and had a minimum follow-up of 6 months. Data extraction focused on best-corrected visual acuity (BCVA), corneal clearance rates, complications, and reoperation rates. Risk of bias was assessed using the Newcastle-Ottawa Scale and the Egger test.

After a multistage screening process, 15 studies meeting the inclusion criteria were included. The pooled mean difference in BCVA, estimated using a random-effects model, was 0.23 LogMAR (95% Confidence Interval [CI] −0.30 to −0.17). The corneal clearance rate after DSO was found to be 0.91 (95% CI, 0.85–0.96). Subgroup analysis based on postoperative Rho-kinase inhibitor (ROCKi) use showed that the corneal clearance rate was higher in the group that used ROCKi prophylactically than in the group that did not (96% vs. 85%), with a statistically significant difference ($p = 0.0012$). The need for secondary endothelial keratoplasty (EK), considered surgical failure after DSO, was 10 % (95% CI, 0.05–0.15).

In conclusion, DSO presents a promising alternative to EK in certain FECD patients, decreasing dependence on donor tissue and eye banks, reducing immunological risks, and minimizing the need for complex surgeries. Although the results generally support its clinical value, the variation in outcomes emphasizes the importance of patient selection and complementary therapies. We consolidate the available evidence and underscore the necessity for prospective studies to establish standard indications for DSO and enhance its clinical application.

1. Introduction

Fuchs endothelial corneal dystrophy (FECD) is the leading indication for endothelial keratoplasty worldwide and remains a major cause of vision loss among the aging population.[1] Current surgical options mainly involve Descemet membrane endothelial keratoplasty (DMEK) and, to a lesser extent, Descemet stripping automated endothelial keratoplasty (DSAEK).[2] These procedures have significantly improved visual recovery compared to penetrating keratoplasty, but they still depend on donor tissue availability, carry a risk of graft failure, and require advanced surgical expertise.[3]

In this context, Descemet stripping only (DSO)—also termed

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descemetorhexis without endothelial keratoplasty—has become a new, tissue-sparing technique. Inspired by the spontaneous resolution of corneal edema caused by iatrogenic descemetorhexis during phacoemulsification and graft dehiscence following endothelial keratoplasty[4–6], DSO aims to stimulate the eye's natural ability for endothelial cell migration and regrowth by removing the diseased central Descemet membrane while preserving the peripheral endothelium. The procedure is straightforward and avoids the logistical and immune challenges associated with donor tissue transplants.[7,8]

First described by Paufique in 1955[9] and largely overlooked for several decades, this technique has recently gained renewed attention and is increasingly being adopted in clinical practice. Early reports were diverse, with varying rates of corneal clearance, highlighting the importance of appropriate patient selection. Increasing evidence suggests that earlier intervention, in eyes with preserved peripheral endothelial reserve, may improve outcomes and decrease the need for subsequent keratoplasty.[10–13] Recently, adjunctive strategies such as Rho kinase inhibition have been investigated to enhance postoperative recovery, further expanding the potential role of DSO in clinical practice.[14,15]

Nevertheless, the long-term outcomes of DSO are only now beginning to be observed, and its precise role relative to keratoplasty remains to be clarified. A systematic review of the available evidence is therefore both timely and necessary. By consolidating published data on patient selection, surgical technique, efficacy, and safety, this review aims to offer a clearer understanding of the usefulness of DSO. Ultimately, if proven effective and properly integrated into clinical practice, DSO could reduce the need for keratoplasty in carefully selected patients. We guide that process and establish an evidence-based foundation for wider clinical adoption.

2. Methods

2.1. Information sources and literature search

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[16] and was registered with the PROSPERO database (ID: CRD420251160540). Since this review did not involve human subjects, institutional review board approval was not required. A comprehensive literature search was carried out in 4 electronic databases (MEDLINE via Ovid, Embase, Scopus, and Web of Science) from their inception until August 31, 2025. Epub publications were also included. The search strategy combined controlled vocabulary (e.g., MeSH, Emtree) and free-text terms, including: (1) “Descemet stripping only,” “descemetorhexis without endothelial keratoplasty,” “DSO,” “DWEK”; (2) “Fuchs endothelial dystrophy” or “corneal endothelial disease”; and (3) “endothelial keratoplasty,” “keratoplasty,” “Rho kinase inhibitors.” The strategy was developed with input from a medical librarian experienced in systematic reviews and was piloted using key seed articles. Additionally, a manual search of the reference lists of included studies, relevant review articles, and grey literature (Google Scholar) was performed to reduce the risk of missing eligible studies. No restrictions were applied regarding publication year or language; non-English articles were translated when necessary.

2.2. Study selection and data collection

Two reviewers (GSV, ZA) independently reviewed all titles and abstracts based on prespecified eligibility criteria. The full texts of potentially relevant articles were then reviewed by another reviewer (OBS), and data extraction was carried out independently twice. Disagreements were resolved through consensus. A Microsoft Excel database was used to organize the extracted data. The PRISMA flowchart below illustrates each step of the screening process, including the number of records identified, excluded, and included, along with the reasons for exclusion.

2.3. Eligibility criteria

Inclusion criteria were: clinical studies reporting DSO/DWEK results in patients with FECD, including at least 5 eyes, with a minimum of 6 months of postoperative follow-up, and reporting best-corrected visual acuity (BCVA), corneal clearance, endothelial cell density or complications. Exclusion criteria were: reports with fewer than 5 eyes, animal or *in vitro* studies, combined procedures where DSO was not analyzed separately, overlapping datasets, non-original research (reviews, commentaries, letters, editorials), and studies with inaccessible full text.

2.4. Outcomes

The primary outcomes were: (1) postoperative BCVA, (2) the proportion of eyes achieving complete corneal clearance, and (3) the need for subsequent endothelial keratoplasty. Secondary outcomes included: (1) changes in endothelial cell density, (2) time to corneal clearance, and (3) complications such as persistent oedema or graft failure. Subgroup analysis was conducted based on Rho kinase inhibitor use. To further investigate sources of between-study heterogeneity, potential factors affecting corneal clearance rates were examined through meta-regression analysis.

2.5. Risk of bias and quality assessment

The Egger test was used to assess publication bias. Cohort studies were also evaluated using the Newcastle-Ottawa Scale (NOS).[17]

2.6. Statistical analysis

All statistical analyses were conducted using the R (version 4.3.2) programming language and the RStudio (version 2023.09.1) interface. Snellen visual acuity values were converted to the logarithm of the minimum angle of resolution (logMAR) for analysis. Various packages developed in the R environment were used for the meta-analysis process. The meta package was used for pooling proportions for primary and subgroup analyses, creating forest plots, calculating heterogeneity statistics, and conducting meta-regression analyses. The metaphor package was used to generate a contour-enhanced funnel plot to assess publication bias. The dplyr package was utilized for data manipulation tasks such as organizing the dataset, filtering, and generating new variables before and during analysis. The PRISMA 2020 flowchart visualizing the study selection process was created with the DiagrammeR package. A p value of less than 0.05 was considered statistically significant.

3. Results

3.1. Study characteristics

The systematic search initially identified 225 potential studies. After removing duplicates, 180 articles remained for review of their titles and abstracts. At this stage, 147 articles were eliminated for various reasons such as being irrelevant to the focus of the study or having an inappropriate study design. The full text of the remaining 33 articles was thoroughly assessed for eligibility. An additional 18 articles that did not meet the prespecified inclusion criteria were excluded after full-text review. After this rigorous, multistage screening process, 15 studies examining DSO in the treatment of FECD and suitable for inclusion in the quantitative synthesis of this meta-analysis formed the final dataset (Fig. 1). Among the studies, 5 were conducted in the United States[7,14,18–20], 3 in Europe (Spain, Portugal, France)[12,21,22], o1in Russia[23], and 1 in Australia[24]. The remaining 5 studies involved researchers from different continents.[25–29]

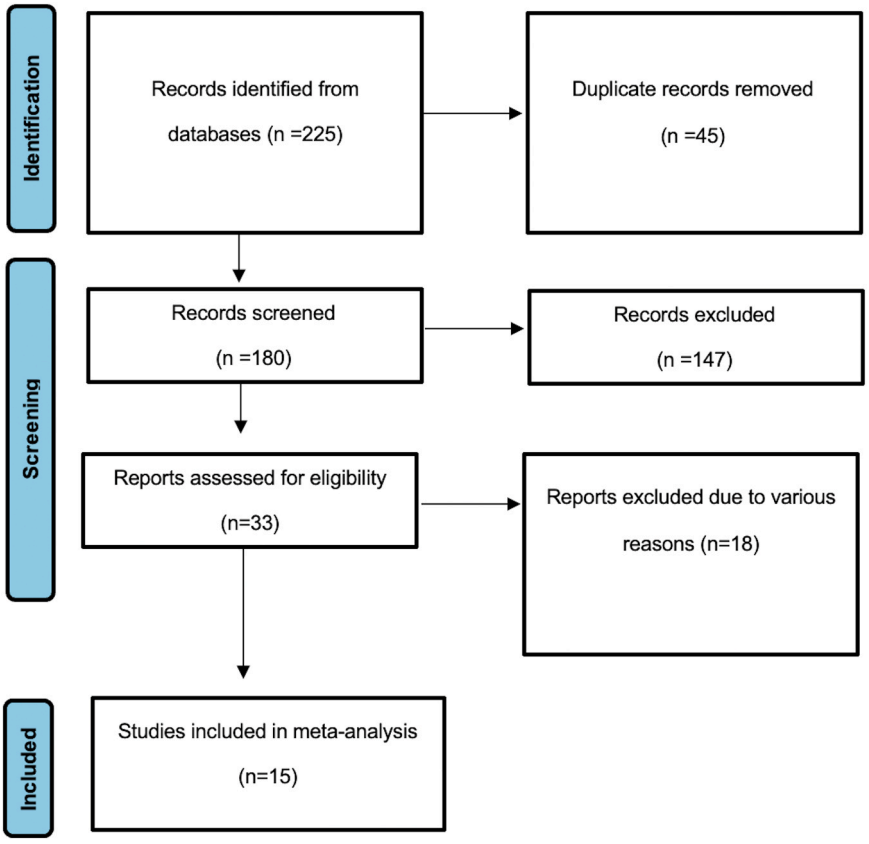

Fig. 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 flow diagram illustrating the search strategy of the meta-analysis.

3.2. Risk of bias

The studies showed some asymmetry around the combined effect size (Fig. 2). Egger regression test results indicated a bias coefficient of −3.43 (1.56), supporting a statistically significant asymmetry [p = 0.0466, t = -2.20 (df = 13)]. This finding suggests a potential risk of publication bias, meaning that studies with positive results may be more likely to be published.

3.3. Visual outcomes

An analysis of 12 studies with pre- and post-operative BCVA data was conducted. Because standard deviations were not directly reported in most studies, a correlation coefficient of 0.5 was assigned to estimate the variance of the mean difference. The forest plot showed a statistically significant improvement; the mean difference was −0.23 LogMAR (95% Confidence Interval [CI] −0.30 to −0.17, $p < 0.0001$). This corresponds to an approximate gain of 2.3 lines on the Snellen chart and represents clinically significant visual rehabilitation for patients (Figure 3).

A very high level of heterogeneity, however, was observed across studies ($I^2 = 93.4\%$, $p < 0.0001$). This indicates that DSO generally improves vision, but the magnitude of this improvement likely varies between studies due to various factors such as disease severity, surgical technique, and follow-up time.

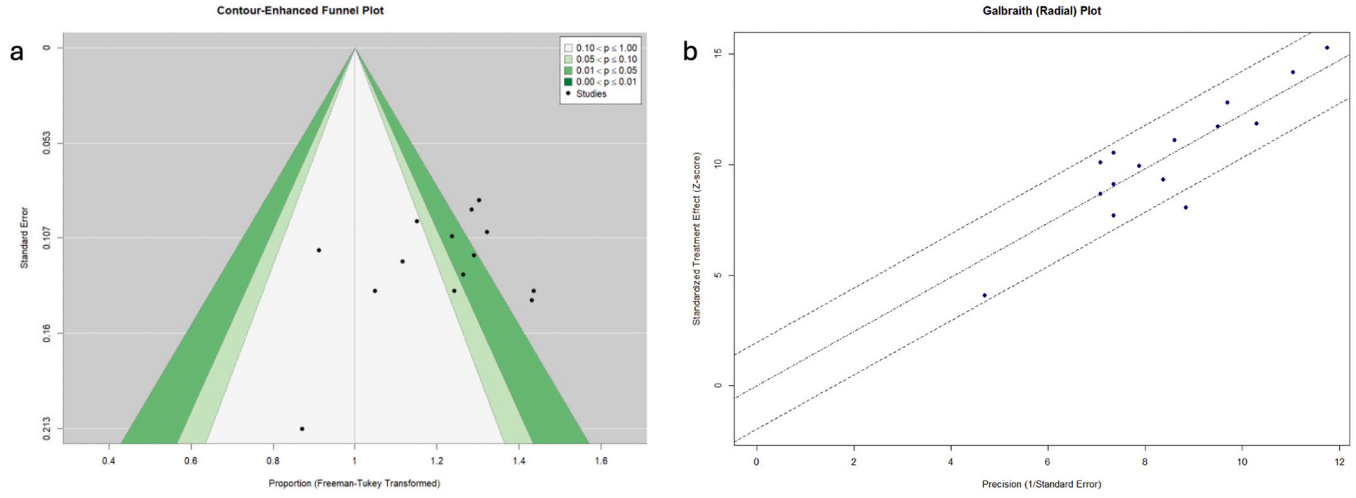

Fig. 2. The funnel plot (a) and radial plot (b) for corneal clearing ratio indicate that the studies show some asymmetry around the combined effect size.

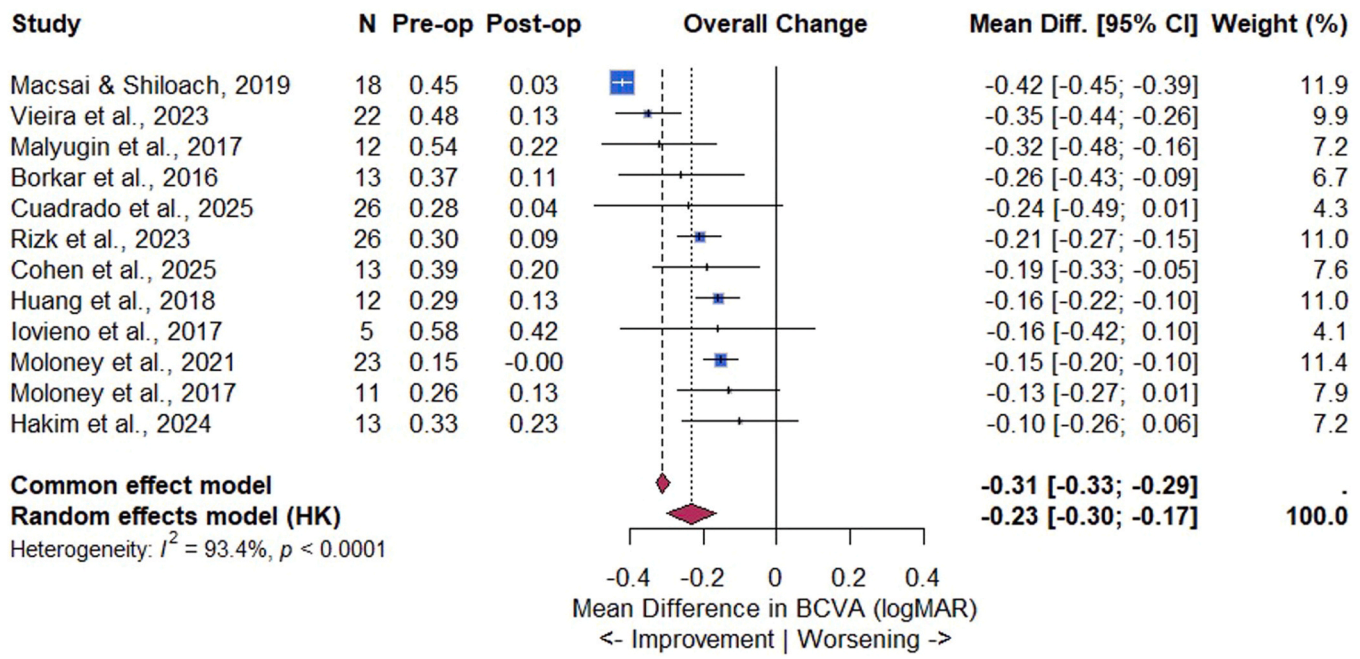

Fig. 3. Forest plot showing the mean difference in best corrected visual acuity (BCVA) after Descemet stripping only.

3.4. *Corneal clearance*

The corneal clearance rate after DSO was found to be 0.91 (95% CI, 0.85–0.96). Low to moderate heterogeneity was observed across the studies ($I^2 = 32.0\%$, $p = 0.1130$). As shown in Fig. 4, individual results generally indicate high success rates, with most reporting clearance rates above 80%. The reviewed literature concludes that DSO is a highly effective procedure for restoring corneal transparency in FECD treatment.

Furthermore, potential factors influencing the corneal clearing rate were examined.

**Effect of publication year*: Analysis revealed a statistically significant positive correlation between publication year and corneal clearance rate ($p = 0.0326$). The positive coefficient (beta = 0.0241) indicates a measurable increase in the success rate of the DSO procedure with each passing year. Remarkably, this pattern explained almost all of the remaining heterogeneity between studies ($R^2 \approx 100\%$) (Fig. 5).

**Effect of patient age:* Analysis of 12 studies reporting age data showed no statistically significant relationship between mean patient age and DSO success rate ($\beta = 0.0105$, $p = 0.0204$) (Fig. 6).

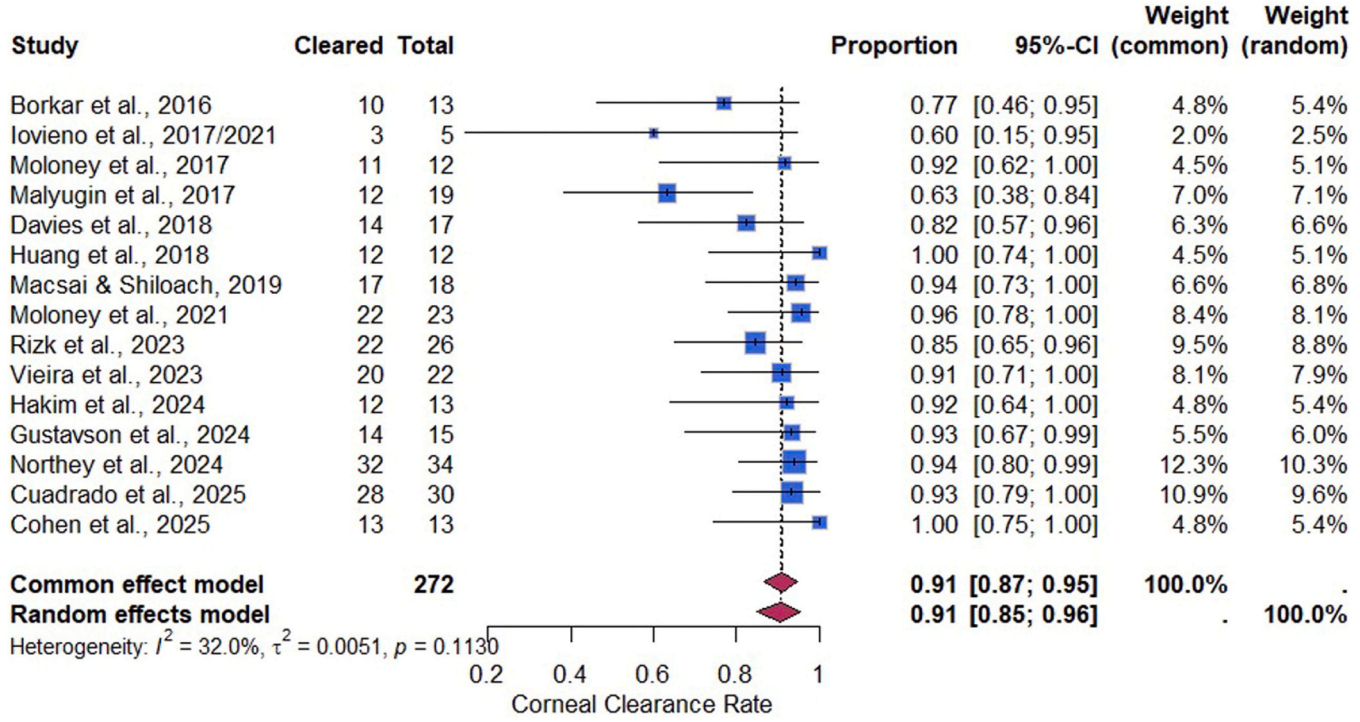

Fig. 4. Forest plot for corneal clearing rates after Descemet stripping only.

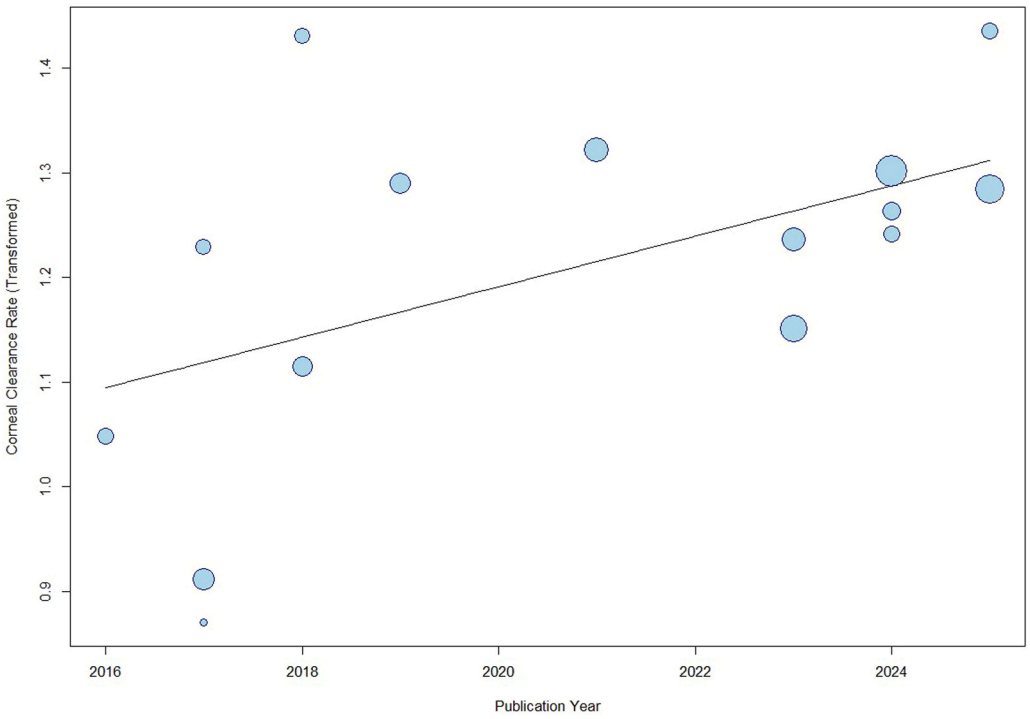

Fig. 5. Bubble plot demonstrating the impact of publication year on corneal clearing rate.

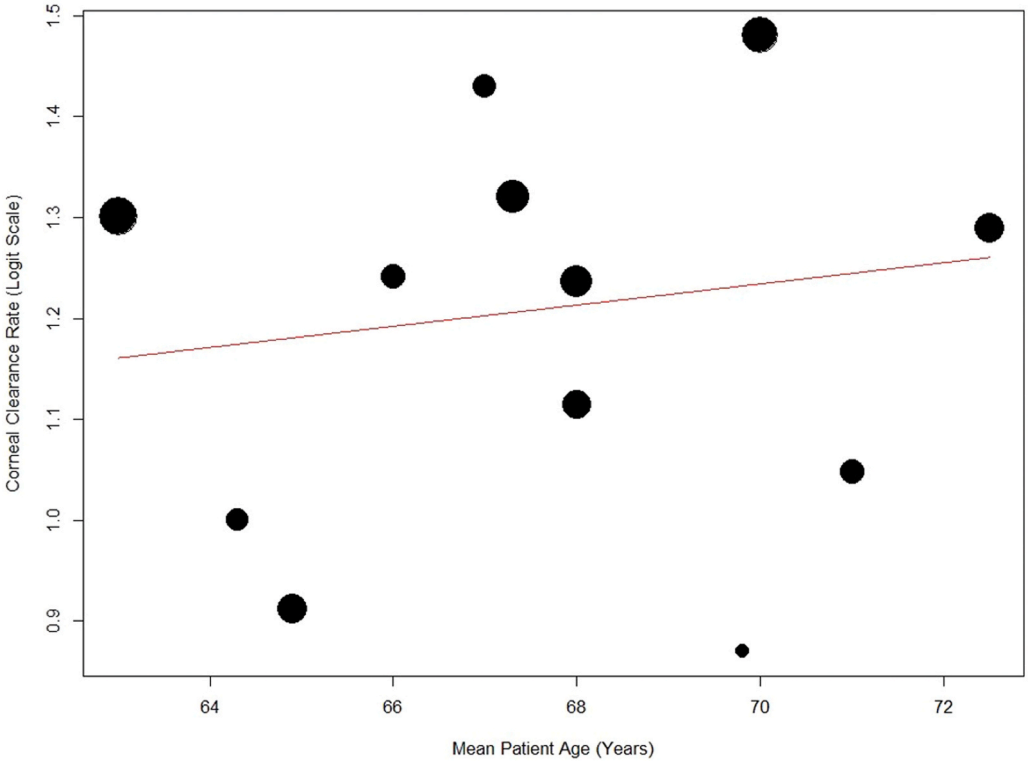

Fig. 6. Bubble plot showing the effect of patient age on corneal clearing rate.

**ROCK inhibitor (ROCKi) use*: Eight studies did not use ROCKi, 1 used it only for salvage in unsuccessful cases, and 6 used it prophylactically. A subgroup analysis based on postoperative ROCKi use revealed that the corneal clearing rate was higher in the group using ROCKi prophylactically (96%, 95% CI, 0.93–0.99) compared to the group not using it (85%, 95% CI, 0.74–0.93), with a statistically significant difference ($p = 0.0012$) (Fig. 7).

The lack of heterogeneity across studies in the prophylactic ROCKi group ($I^2 = 0.0\%$) indicates that the results are quite consistent among studies; however, the moderate heterogeneity observed in the group that did not use ROCKi ($I^2 = 33.1\%$) suggests that other factors may have affected the outcomes in this group.

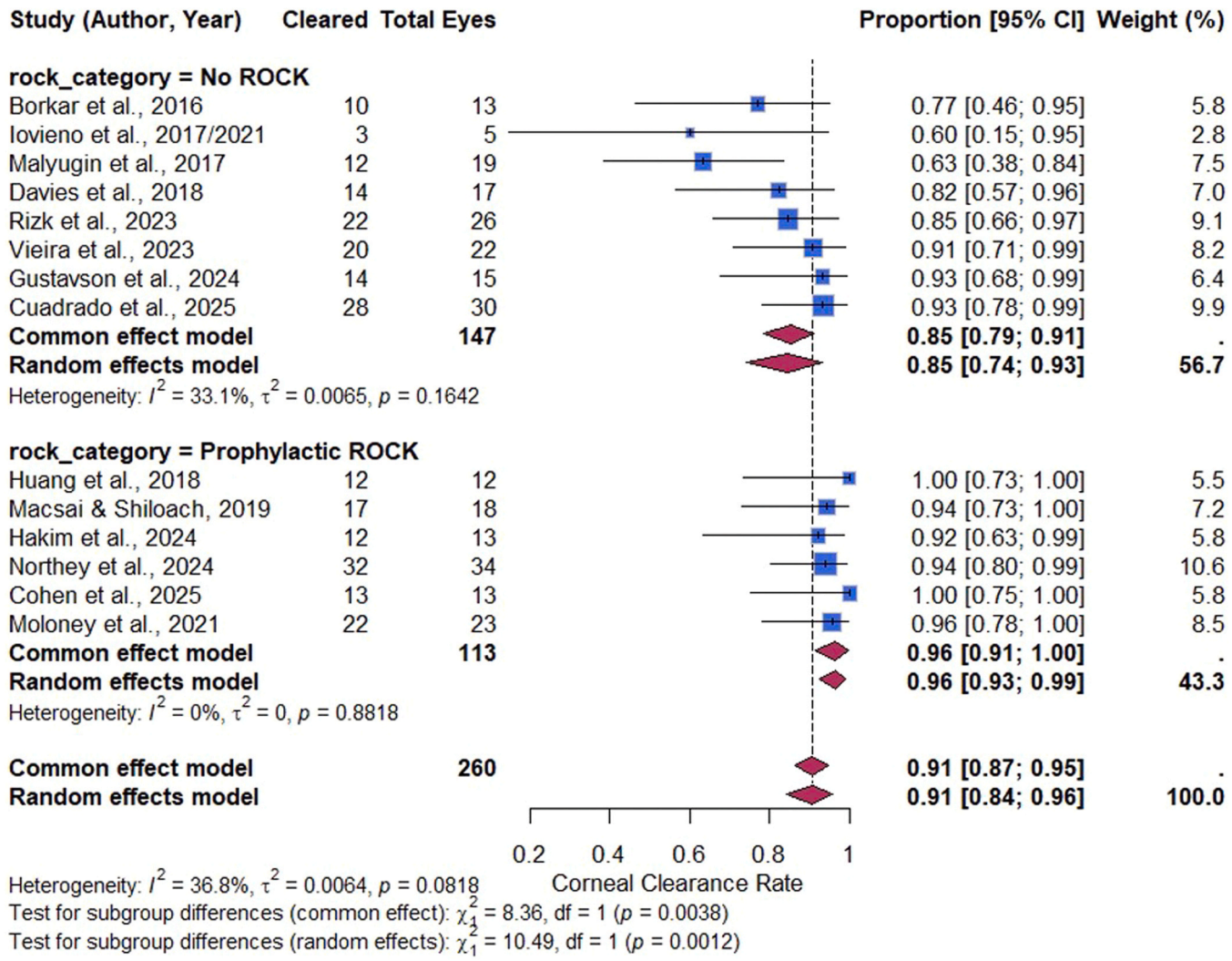

Fig. 7. Subgroup forest plot of clearing rates by ROCK inhibitor use.

3.5. Secondary keratoplasty

The need for secondary endothelial keratoplasty (EK), considered a surgical failure after DSO, was found to be 10 % (95% CI, 0.05–0.15) in a pooled analysis of all studies. Low heterogeneity was observed, but this was not statistically significant (I^2 = 17.6%, p = 0.2566) (Fig. 8).

4. Discussion

4.1. Summary of evidence and clinical implications

In patients with FECD, vision loss and impaired visual quality are the main parameters in both quality of life and surgical indication. In clinical practice, serial corneal thickness measurements are generally used as the main parameter for determining progression and making surgical decisions; however, this parameter alone is insufficient as a definitive indicator. In various studies, guttata have emerged as an important factor affecting visual quality, even in the absence of edema or when adjustments are made for increased corneal thickness.[30] Shah and coworkers[31] found that corneal densitometry values and guttata severity were associated with decreased visual acuity in FECD. In another study, Watanabe and coworkers[32] found that guttata, even without edema, caused higher scattering, affecting visual acuity and contrast sensitivity. Therefore, in addition to visual acuity, guttata severity is also a determining factor for surgery, especially in eyes with mild FECD, and should be considered when establishing surgical indications. Increased awareness that guttae, particularly those affecting the central 2 mm area, impair visual acuity and quality through light scattering has drawn attention to DSO, in which the central 4 mm portion of the Descemet membrane is peeled.[31]

Cumulative evidence from the included studies indicates that DSO is a promising yet evolving treatment option for FECD. In most published series, DSO has shown a clinically meaningful improvement in BCVA. The mean improvement of −0.23 logMAR equates to about 2.3 lines on the Snellen chart, indicating a significant benefit for patients. Additionally, the corneal clearance rate after DSO was found to be 91 %, with most reporting clearance rates above 80%. The need for secondary EK, considered a surgical failure after DSO, was only 10 %; however, the variation in results across studies underscores the importance of appropriate patient selection, surgical technique, and the use of pharmacological agents as adjunct therapy.

ROCKi are considered a useful adjuvant therapy for DSO. Various corneal endothelial cell culture studies have shown that they support cell adhesion, migration, and proliferation. ROCKi can be initiated prophylactically postoperatively or used to salvage cases that have failed to clear.[33,34] Seven of the studies included in this meta-analysis reported the adjunctive use of ROCKi. Predominantly (6 studies), ROCKi were used prophylactically in the postoperative period, 4–6 times daily for 2–8 weeks. In one study, Moloney and coworkers[24] administered ROCKi 6 times daily for 2 weeks as salvage therapy to 3

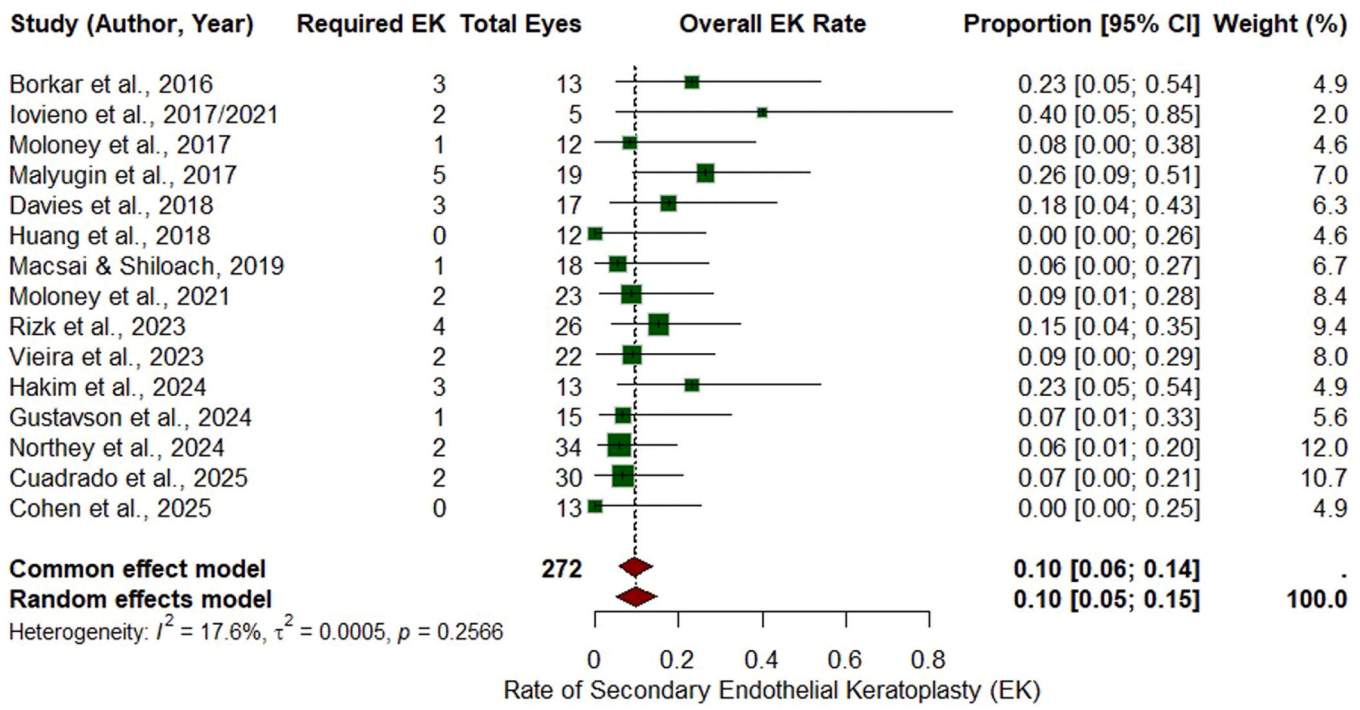

Fig. 8. Forest plot for secondary endothelial keratoplasty (EK) rates following Descemet stripping only.

cases that had not shown improvement over 2–5 months and achieved a positive response in 2 of them. Corneal clearance rates were significantly higher in the prophylactic ROCKi group compared with the non-user group (96 % vs. 85%, p = 0.0012). These pharmacologic agents effectively reduce healing time by promoting endothelial cell migration and proliferation. [35–37] While promising, their application varies across studies, and robust randomized controlled trials are needed to establish standard dosing protocols and confirm long-term benefits.

In the current technique, DSO is performed as follows: The cornea is marked under mesopic conditions. In the operating room, 4-mm-diameter descemetorhexis boundaries are defined, centred on this marking. A 2-mm clear corneal incision, which heals spontaneously, is made, and the anterior chamber is filled with viscoelastic. A flap is created at the edge of the 4-mm circle using an inverted Sinskey hook. The flap is then peeled in a linear, circular manner using gripping forceps. The viscoelastic material is then removed by irrigation/aspiration, and the main wound is hydrated.[38] It is thought that surgical trauma to the stroma triggers an unpredictable healing response, possibly involving stromal keratocytes. This has prompted consideration of modifying the surgical technique. Although cell loss was observed with Descemet trepanization/scoring, the peeling technique was found to preserve cell morphology up to the furthest edge of the wound. This highlights the peeling technique.[19,38] In addition, over time, modifications have been made to the surgical technique regarding the size of the descemetorhexis. Early reports indicated suboptimal visual outcomes with larger descemetorhexis diameters of 6–8 mm, whereas subsequent studies demonstrated successful corneal clearance with smaller descemetorhexis diameters of 4 mm.[18,39,40] The analysis demonstrated a statistically significant positive correlation between publication year and corneal clearance rate, explaining nearly all the heterogeneity among studies. Publication year alone, however, is insufficient to account for all determinants of surgical success and should be interpreted as a surrogate marker reflecting the combined influence of unmeasured factors, including the evolution of surgical techniques, increasing surgeon experience, and improvements in patient selection criteria. This trend likely reflects the global evolution of the DSO technique, greater surgical experience, and optimization of patient selection over the past decade.

Reported complications of DSO are usually infrequent and mild, such as transient stromal edema, Descemet membrane folds, and delayed corneal detachment.[41] No cases of vision-threatening complications or infections directly related to DSO have been reported in the current series; however, it should be noted that the current literature is based on small observational series and includes variable follow-up periods. In some cases, progressive endothelial dysfunction has been reported to develop over the long term, with new guttae formation in the descemetorhexis area of the relocated endothelium.[42] When necessary, secondary EK procedures have yielded positive results, showing that a failed DSO does not prevent successful future keratoplasty.[27]

Additionally, changes in corneal tomography after DSO affect refractive outcomes. Corneal tomography shows posterior float corresponding to the area where Descemet membrane is peeled off. Decentralization of the float, i.e., decentralized descemetorhexis, triggers irregular astigmatism similar to that seen in ectasias. Davies and coworkers documented increased astigmatism in some cases, even when centralized rhexis.[43] Earlier studies have also shown significant irregular corneal astigmatism that limits visual acuity after DSO, but these studies are limited to a few eyes that did not achieve complete corneal clearance after the procedure;[41] however, the predominant literature suggests that post-DSO astigmatism does not affect final visual acuity.[19] Davies and coworkers[43] detected an average hyperopic shift of + 0.65 D after DSO and found that this value decreased to + 0.38 1 month after corneal clearance. Similar refractive deviations after DMEK were reported.[44] Changes in posterior corneal curvature and corneal deturgescence are considered potential pathophysiologic mechanisms.

4.2. *Comparison with alternative approaches*

EK, especially DMEK and DSAEK, remains the standard treatment for FECD due to its high success rate and reliable visual recovery;[45] however, its disadvantages include reliance on donor tissue and eye banks, immunological risks, interface problems, and the need for complex surgical procedures and specialized equipment.[46] Long-term steroid use after EK is also a potential disadvantage. Maier and coworkers[47] investigated the incidence of intraoculr pressure (IOP) elevation and

glaucoma in 352 patients at 12 and 36 months after DMEK. They observed steroid-induced IOP elevation with an incidence of 11.7% at 12 months and 12.9% at 36 months or 3 years. In contrast, DSO avoids these problems and is technically simpler. In their comparative study of DMEK and DSO, Huang and coworkers[20] observed postoperative adverse events, including elevated IOP, anterior chamber inflammation, and graft nonadherence, in 53% of patients in the DMEK group. One of these patients required anterior chamber paracentesis due to extremely high IOP, and another underwent reoperation because of graft nonadherence. No adverse events were seen in the DSO group; however, the results of DSO are less predictable, and recovery takes longer. The same study group found the mean time to reach 20/40 vision was 2.2 ± 2.8 weeks (0.1–10.9 weeks) for DMEK, while this duration was 7.1 ± 2.7 weeks (3.1–12.9 weeks) for DSO ($p < 0.01$). Complications with DSO are usually limited to temporary oedema or delayed deturgescence.[7] While visual recovery tends to be quicker after EK, the lack of donor-related risks makes DSO especially appealing in regions with limited eye bank resources. Moreover, the use of ROCKi might enhance the predictability of DSO, reducing the performance gap between the two methods.

DSO relies on the natural ability of peripheral endothelial cells to migrate and repopulate the central cornea after the diseased Descemet membrane is peeled away. Although this regenerative approach appears promising in theory, its success depends on the remaining endothelial cell reserve and their functional health.[48,49] Mild to moderate stages of the disease, characterized by localized central guttae and relatively intact peripheral endothelial function, tend to have the highest rates of clearance and visual improvement. Conversely, advanced FECD with widespread guttae and low baseline endothelial cell density exhibits slower or incomplete recovery.[50–52] An interesting factor influencing the success of the procedure is the surgical technique used. Davies and coworkers[19] discovered that the density and location of the guttae did not affect postoperative results, but the removal method (descemetorhexis vs. 360-degree scoring and stripping) did impact corneal clarity.

It is important to note that a failed DSO does not influence the outcome of subsequent EKs.[53] This supports a staged approach where DSO is attempted first, followed by EK if no response is observed. Clinicians can adopt a staged approach in which DSO is administered initially, with close postoperative monitoring using slit lamp examination and anterior segment optical coherence tomography to identify early signs of clearance. Lack of deturgescence within the expected timeframe should prompt a timely switch to EK; however, the duration of corneal oedema before EK may affect surgical success. In a recent case series, significant corneal flattening and hyperopia were reported after salvage EK performed 4–7.5 months after 3 failed DSO cases. The study group emphasizes the need to consider salvage therapy at week 8 in cases with severe corneal oedema and to pay close attention to the timing of salvage surgery.[54] Patients should also be informed that healing is slower compared to EK and that there may be a need for secondary keratoplasty.

4.3. Limitations

The current evidence base is constrained by the absence of large randomized controlled trials and the predominance of small retrospective case series, as well as by heterogeneity in inclusion criteria, surgical techniques, outcome definitions, and follow-up durations, all of which limit generalizability. Funnel plot asymmetry suggests a potential risk of publication bias, whereby studies reporting favourable outcomes may be preferentially published. In addition, patient selection, a critical determinant of DSO success, including FECD staging, peripheral endothelial reserve, and timing of intervention, remains inconsistently defined across studies. Included studies report outcomes inconsistently, with varying definitions of success and diverse follow-up periods, limiting the reliability and precision of the combined analysis. Secondary outcomes—changes in endothelial cell density, time to corneal clearance, and complications such as persistent edema or graft failure—are measured and reported inconsistently. This hinders reliable assessment of these parameters. Additionally, since most studies have short follow-up periods, the long-term outcomes of DSO remain uncertain. Although the role of ROCKi is promising, it is not standardized; variations in indications—prophylactic or salvage—dose regimens, and treatment duration prevent definitive conclusions and require further validation. Furthermore, determining the FECD stage in included patients is difficult because of vague definitions.

5. Conclusions, implications for practice, and future directions

Because the procedure is relatively new, the long-term durability of endothelial function and the impact of DSO on disease progression have not yet been fully established. Success largely depends on patient selection, and more research is necessary to define clear criteria, prognostic markers, and standardized outcome measures. The potential of ROCKi appears promising, but still requires further validation. It should also be noted that our results are based on small retrospective case series, and the heterogeneity in inclusion criteria and outcomes limits the interpretation and generalizability of the results. Nevertheless, the current evidence can be interpreted as preliminary results indicating that DSO is a viable early intervention for FECD in selected cases and may help reduce reliance on keratoplasty and donor tissue.

6. Method of literature search

A comprehensive literature search was performed in four electronic databases (MEDLINE, Ovid, Embase, Scopus, and Web of Science). The search strategy integrated controlled vocabulary (e.g., MeSH, Emtree) and free-text terms, including: “Descemet peeling only,” “Descemetorhexis without endothelial keratoplasty,” “DSO,” “DWEK”; “Fuchs endothelial dystrophy” or “corneal endothelial disease”; and “endothelial keratoplasty,” “keratoplasty,” “Rho kinase inhibitors.” Additionally, a manual search of the reference lists of included studies, relevant review articles, and grey literature (Google Scholar) was conducted. Two reviewers (GSV, ZA) independently screened all titles and abstracts. The full texts of potentially relevant articles were then reviewed by another reviewer (OBS), with data extraction performed independently twice. Studies involving fewer than 5 eyes, animal or in vitro studies, combined procedures where DSO was not analysed separately, overlapping datasets, non-original research (reviews, commentaries, letters, editorials), and articles lacking full-text access were excluded.

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CRediT authorship contribution statement

barut selver ozlem: Writing – review & editing, Methodology. **Zeynep Akgun:** Writing – original draft. **sahin vural gozde:** Writing – review & editing, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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