Review

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Ultrathin DSAEK versus DMEK – Review of systematic reviews

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Abstract

The efficacy and safety of Descemet's membrane endothelial keratoplasty (DMEK) and ultrathin Descemet stripping automated endothelial keratoplasty (UT-DSAEK) have been recently compared in several systematic reviews (SRs). The aim of this study was to assess the evidence quality of such SRs, in order to obtain a scientifically rigorous comparison between the two techniques. We performed a systematic review of SRs and meta-analyses comparing the efficacy and safety between UT-DSAEK and DMEK up to 24th March 2023, using 3 electronic databases (PubMed, Cochrane Library, Google Scholar) plus manual reference search. Specific outcomes analyzed included best-corrected visual acuity (BCVA), endothelial cell density (ECD), rebubbling rate, and other postoperative complications. Of 90 titles/abstracts screened, four SRs met the inclusion criteria. All SRs adequately analyzed potential bias of the included studies. One SR raised concern for potential literature search bias and two SRs have heterogeneity in some outcomes analyzed. All SRs found higher BCVA after DMEK, but one SR reported significant heterogeneity. All SRs found significant heterogeneity in ECD analysis, with one SR providing inconsistent analysis of this outcome. Three SRs analyzed rebubbling rates, favoring UT-DSAEK over DMEK. Three SRs concluded a higher overall complication rate after DMEK, although rebubbling may be a confounding factor. This systematic review clarifies the strengths and weaknesses of published SRs and reinforces the conclusion that DMEK leads to superior visual outcomes compared to UT-DSAEK, with the trade-off of higher rebubbling rates and possibly other postoperative complications. Studies with longer follow-up are needed to ascertain these differences between procedures.

Keywords

Descemet, descemet membrane endothelial keratoplasty, ultrathin, descemet stripping automated endothelial keratoplasty, systematic review

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Introduction

Descemet's membrane endothelial keratoplasty (DMEK) has gradually become the gold standard technique for the treatment of corneal endothelial failure, having now matched "traditional" Descemet stripping (automated) endothelial keratoplasty (DSEK/DSAEK) as the most widely performed keratoplasty techniques in the United States.[1] The reasons underlying this trend include the superior profile of DMEK compared with traditional DSEK/DSAEK in terms of visual outcomes, refractive results, and safety.[2–6] Although DMEK has a higher graft detachment (GD) rate,[2,3] most GDs are partial and self-limited, rebubbling rates decrease with surgeon experience, and the implications of rebubbling in graft survival are

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controversial.[7,8] Some corneal surgeons advocate that DMEK may be more technically challenging than DSEK/DSAEK, especially in complex eyes; this is currently disputed.[9]

Ultrathin DSAEK (UT-DSAEK), using refined graft preparation techniques to achieve lenticules with graft thickness (GT) below 130 μm,[10] and its recent variations which produce progressively thinner grafts (microthin DSAEK (MT-DSAEK) and nanothin DSAEK (NT-DSAEK),[11] have shown better visual outcomes and lower rejection rates compared with traditional DSAEK.[11] Until recently, there was limited evidence as to whether DMEK is superior to UT-DSAEK, which could be important from clinical and economical/political decision-making standpoints. However, increasing interest has arisen in the topic, and in a short period of time several systematic reviews (SRs) have emerged.

The aim of this paper is to provide a quality appraisal of the SRs comparing the outcomes of UT-DSAEK and its variations versus DMEK, as well as a synthesis of their evidence.

Methods/literature search

Eligibility criteria and search strategy

We conducted a systematic review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We performed a review of all SRs comparing outcomes of ultra-thin DSAEK (and its variant designations NT-DSAEK or MT-DSAEK) versus DMEK for corneal endothelial failure using three electronic databases (MEDLINE, Cochrane Database of Systematic Reviews, Google Scholar), in addition to a manual search of references in main articles up to 24th March 2023. We used search terms by title and abstract using variations of the terms ultra-thin DSAEK / UT-DSAEK / NT-DSAEK / nanothin DSAEK / microthin DSAEK / MT-DSAEK and Descemet membrane endothelial keratoplasty / DMEK. No restrictions by journal, year of publication and language were applied in the literature search.

Population

Patients with corneal endothelial failure who underwent endothelial keratoplasty.

Intervention

UT-DSAEK and its variations.

Comparator

DMEK.

Outcomes

All outcomes analyzed were eligible, including BCVA, residual spherical equivalent refractive error (SphEq), rebubbling rates, primary graft failure and secondary graft failure rates, immune rejection rates, endothelial cell density (ECD), central corneal thickness (CCT), and adverse events including postoperative elevated intraocular pressure (IOP).

Study design

Inclusion. SRs were included if they specified search strategy in at least two literature databases and included primary research; no restrictions were placed on the study design of the primary studies.

Exclusion. We excluded SRs without clearly defined research questions, search strategy or defined process of article selection. We also excluded articles other than SRs comparing UT-DSAEK vs DMEK, and we excluded articles retrieved in the literature search that were not written in English language.

Selection

We created a database of the search results of each database into a Microsoft Excel® sheet and eliminated duplicate results. Two researchers (NM-C, RP-V) independently screened the retrieved titles and abstracts, and the full-text articles of those classified as potentially eligible by either reviewer were independently analyzed by both reviewers. Where a consensus could not be reached by both reviewers, the senior author (JLG) reviewed disagreements.

Data extraction

We collected data including study authors, journal and year of publication patient baseline characteristics and differences, intervention and comparator, outcome measures, duration of follow-up, effect estimates – mean differences (MD) and odds ratios (OR) or risk ratios (RR) with confidence intervals as available –, and study design. One researcher (NM-C) completed data extraction, and a second researcher cross-checked (JPC).

Quality assessment and risk of bias

Two researchers (NM-C, AR) used the ROBIS tool for quality assessment and risk of bias analysis. Where a consensus could not be reached by both reviewers, the senior author (JLG) reviewed disagreements.

Data synthesis

Each outcome was narratively synthesized, including number of SRs using each outcome and effect estimates with confidence intervals (95%CI) from the source review. All outcomes that were reported in the SRs were included in our work, to avoid reporting bias.

Results

Database search identified 90 records, resulting in 71 studies after de-duplication (Supplemental Table 1). Four full-text articles were retrieved and analyzed after the initial screening of titles and abstract, and all four SRs were eligible for inclusion.[12–15] The PRISMA study flow diagram is presented in Supplemental Figure 1.

Review characteristics

Four SRs and meta-analyses met the inclusion criteria. The summary of reviews is presented in Table 1. All SRs included the randomized controlled trial (RCT) by Dunker et al.;[16] all SRs included the *Descemet Endothelial Thickness Comparison Trial* (DETECT) RCT, but while Maier et al.,[12] Dimtsas et al.[13] and Singh et al.[14] included the publication by Chamberlain et al.,[17] Hurley et al.[15] included the publication by Rose-Nussbaumer et al.[18] which analyzed the 2-year results in the same cohort. Three SRs[12,13,15] included the RCT by Matsou et al. which compared "MT-DSAEK" (all grafts had GT $\leq$ 130 µm, although a high proportion had a GT below 100-µm) to DMEK[19]; and only one SR[12] included the RCT by Kurji et al. comparing "NT-DSAEK" (with GT $\leq$ 50 µm) to DMEK.[20] All SRs included the retrospective fellow-eye study of Mencucci et al.,[21] and all SRs included the retrospective study by Romano et al.;[22] three SRs[12,14,15] included the fellow-eye study by Torras-Sanvicens et al.;[23] two SRs[14,15] included the retrospective study by Tourabaly et al. where DMEK was compared with DSAEK grafts of different GT and also compared with NT-DSAEK[24]; and one SR[13] included the retrospective study by Machalińska et al.[25]

Quality assessment and risk of bias

Risk of bias was assessed using the ROBIS tool, a validated tool designed specifically to assess the risk of bias in systematic reviews.[26] No SRs included in this study were considered at a "High risk of bias" (Table 2). All studies provided adequate analysis of risk of bias for the studies included. However, the SR by Singh et al. raised concerns for potential bias and was rated as "Unclear risk of bias" (Table 2). The remaining three SRs were considered as having a "Low risk of bias", although some concerns for potential bias were raised mainly related to the synthesis of findings.

Outcome evaluation. All SRs undertook a narrative synthesis and included meta-analyses for the outcomes.[12–15] All SRs evaluated postoperative BCVA.[12–15] Other outcomes included rebubbling rate (three studies),[12,13,15] ECD (four studies),[12–15] CCT (one study),[13] SphEq (one study),[13] rejection rate (one study),[12] graft survival (one study),[12] postoperative elevation of IOP (two studies),[12,13] and overall complications three studies).[13–15] Dimtsas et al. considered DMEK as the "intervention" and the UT-DSAEK as the "comparator",[13] whereas Maier et al., Singh et al. and Hurley et al. considered UT-DSAEK the "intervention" and DMEK the "comparator".[12,14,15]

Visual outcomes

The SRs by Maier et al.,[12] Dimtsas et al.[13] and Hurley et al.[15] included a meta-analysis of visual outcomes at different time points, focusing particularly on 12-month follow-up. Singh et al. performed a meta-analysis of postoperative BCVA, but time points analyzed in the studies included were variable from 12 to 32 months.[14] There were differences in the studies included in each SR, and as such there were variations in the pooled estimates for this outcome (Table 3). The largest difference in BCVA was reported by Maier et al., who observed a pooled MD of 0.50 (95%CI = 0.27–0.74, $p < 0.0001$) in BCVA 12-month follow-up.[12] This was different than the pooled MD estimates from the other three studies, who observed pooled MD of 0.06–0.07 in BCVA.[13–15] Dimtsas et al. also performed a meta-analysis of the 12-month SphEq and found a pooled estimate favoring DMEK over UT-DSAEK (MD = −0.12, 95%CI = −0.42–0.00, $p =$ 0.049); however, heterogeneity analysis for this outcome was not presented by the authors.[13] The study by Singh et al. observed high heterogeneity in their BCVA meta-analysis, which the authors considered to be likely due to the differences in postoperative time points analyzed in the studies included.[14] The SR by Hurley et al. concluded that the level of quality of evidence for the BCVA analysis was "High" using the GRADE system.[15]

Rebubbling

Only the studies by Maier et al., Dimtsas et al. and Hurley et al. performed a meta-analysis of the rebubbling rates.[12,13,15] There were differences in the studies included in each SR, and as such there were variations in the pooled estimates for this outcome (Table 4).The largest difference in rebubbling rate was reported by Dimtsas et al., who observed a 2.37-fold increase in risk of rebubbling defined by a fixed effects model after DMEK compared with UT-DSAEK.[13] In the other two SRs comparing

Table 1. Summary of systematic review of systematic reviews comparing ultrathin Descemet stripping automated endothelial keratoplasty (UT-DSAEK) to Descemet's membrane endothelial keratoplasty (DMEK).

Review and Year	Aim (participants)	Intervention / Comparator	Search strategy	No. of studies included	Studies included	Total no. of participants		F-U time after intervention (months)	Risk of bias assessment	Outcomes analyzed	Comments
						UT-DSAEK	DMEK				
Maier et al. (2023)[12]	Patients with FED and BK	UT-DSAEK / DMEK	MEDLINE, EMBASE, CDSR, LILACS	7 studies (3 RCT | 1 prospective study | 1 retrospective study | 2 retrospective fellow-eye studies)	Dunker et al. (2020) | Chamberlain et al. - DETECT (2019) | Matsou et al. (2021) | Kurji et al. (2018) | Torras-Sanvicens et al. (2021) | Mencucci et al. (2020) | Romano et al. (2020)	165	163	12	Clear quality appraisal of the studies	Primary outcome: BCVA | Secondary outcomes: ECD, rebubbling, rejection, graft failure, postoperative IOP elevation	
Dimtsas et al. (2023)[13]	Patients with FED and PBK	DMEK / UT-DSAEK	MEDLINE, CDSR	6 studies (4 RCT | 1 retrospective study | 1 retrospective fellow-eye study)	Chamberlain et al. DETECT (2019) | Dunker et al. (2020) | Matsou et al. (2021) | Machalinska et al. (2021) | Mencucci et al. (2020) | Romano et al. (2020)	151	149	12	Clear quality appraisal of the studies	BSCVA, ECD, Spherical equivalent, rebubbling, adverse events	Intervention DMEK, comparator UT-DSAEK
Singh et al. (2023)[14]	Patients with corneal endothelial failure	UT-DSAEK / DMEK	MEDLINE, EMBASE, SCOPUS	6 studies (2 RCT | 2 retrospective studies | 1 retrospective fellow-eye study | 1 cross-sectional comparative case series)	Chamberlain et al. DETECT (2019) | Dunker et al. (2020) | Mencucci et al. (2020) | Tourabaly et al. (2019) | Romano et al. (2020) | Torras-Sanvicens et al. (2021)	151	135	Unclear*	Good quality appraisal of the studies, but primary research method raises concern for potential bias (See ROBIS tool)	Primary outcome: BCVA | Secondary outcomes: ECD, complications	* A specific time point for analysis was not defined by the authors
Hurley et al. (2023)[15]	Patients with corneal endothelial failure	UT-DSAEK / DMEK	MEDLINE, EMBASE, CDSR	7 studies (3 RCT | 2 retrospective studies | 2 retrospective fellow-eye studies)	Rose-Nussbaumer et al. DETECT (2021) | Dunker et al. (2020) | Matsou et al. (2021) | Mencucci et al. (2020) | Romano et al. (2020) | Torras-Sanvicens et al. (2021) | Tourabaly et al. (2019)	189	173	12	Clear quality appraisal of the studies	BCVA, ECD, rebubbling, complications	

Legend: UT-DSAEK: ultrathin Descemet stripping automated endothelial keratoplasty; DMEK: Descemet's membrane endothelial keratoplasty; FED: Fuchs' endothelial dystrophy; BK: bullous keratopathy; MEDLINE: Medical Literature Analysis and Retrieval System Online; EMBASE: Excerpta Medica Database; CDSR: Cochrane Database of Systematic Reviews; LILACS: Latin American & Caribbean Health Sciences Literature; RCT: randomized controlled trial; BCVA: Best-corrected visual acuity; ECD: endothelial cell density; IOP: intraocular pressure; PBK: pseudophakic bullous keratopathy; BSCVA: best spectacle-corrected visual acuity.

Table 2. ROBIS tool assessment of risk of bias in the reviews included in this overview of systematic reviews.

Studies	Study eligibility criteria	Identification and selection of studies	Data collection and study appraisal	Synthesis and findings	Risk of bias in the review	Rationale for concern		
Maier et al.	LOW	LOW	LOW	LOW	LOW	-	-	-
Dimtsas et al.	LOW	LOW	LOW	LOW (*)	LOW	(*) Analyzing overall postoperative complications without including rebubbling would have provided more relevant findings.	No forest plot and heterogeneity analysis were made for some of the outcomes analyzed (CCT, postoperative elevated IOP).	-
Singh et al.	LOW	UNCLEAR*	LOW	UNCLEAR (*) **	UNCLEAR	* The primary search was limited by year, language, and country of publication, which may raise potential bias.	** Some inconsistency between manuscript body and forest plot results; unclear conclusions regarding ECD; significant heterogeneity in BCVA outcome analysis	(*) Analyzing overall postoperative complications without including rebubbling would have provided more relevant findings.
Hurley et al.	LOW	LOW	LOW	LOW (*)	LOW	(*) Analyzing overall postoperative complications without including rebubbling would have provided more relevant findings.	-	-

Legend: CCT: central corneal thickness; IOP: intraocular pressure; ECD: endothelial cell count; BCVA: best-corrected visual acuity.

Table 3. Visual outcome analysis of ultrathin DSAEK versus DMEK.

	No. studies	Total no. of participants		Time point analysis of BCVA	MD	95% CI of MD	p-value	Heterogeneity (I-square)	Conclusion	Comments
		UT-DSAEK	DMEK							
Maier et al. (2023)	7	154	152	12 months	0.50	0.27–0.74	$p <$ 0.0001	9%%	In favour of DMEK	-
Dimtsas et al. (2023) **	5	127	121	12 months	−0.075	−0.12 - −0.03	$p =$ 0.001	49%	In favour of DMEK	12-month analysis SphEq favouring DMEK MD -0.12 (95%CI -0.42 - 0.00) ($p = 0.049$)
Singh et al. (2023)	4	120	110	12–32 months	0.06	0.04–0.09	$p <$ 0.0001	52% (*)	In favour of DMEK	(*) Significant heterogeneity
Hurley et al. (2023)	7	189	173	12 months	0.07	0.04–0.10	$p <$ 0.001	32%	In favour of DMEK	GRADE Quality of Evidence: High

Legend: UT-DSAEK: ultrathin Descemet stripping automated endothelial keratoplasty; DMEK: Descemet's membrane endothelial keratoplasty; BCVA: best-corrected visual acuity; MD: mean difference; CI: confidence interval; SphEq: spherical equivalent.
**Intervention DMEK, comparator UT-DSAEK.

Table 4. Rebubbling rate comparison between ultrathin DSAEK and DMEK.

Review and Year	No. studies	Total no. of participants		RR	95% CI of RR	p-value	Heterogeneity (I-square)	Conclusion
		UT-DSAEK	DMEK					
Maier et al. (2023)	6	154	153	0.33	0.16–0.67	$p =$ 0.0025	0%	Rebubbling rate is lower after UT-DSAEK compared with DMEK
Dimtsas et al. (2023) **	6	151	149	2.37	1.25–4.49	$p = 0.008$	0%	Rebubbling rate is 2.37 times higher after DMEK compared with UT-DSAEK
Hurley et al. (2023)	5	119	117	0.40	0.22–0.73	$p = 0.003$	0%	Rebubbling rate is lower after UT-DSAEK compared with DMEK (GRADE Quality of Evidence: High)

Legend: UT-DSAEK: ultrathin Descemet stripping automated endothelial keratoplasty; DMEK: Descemet's membrane endothelial keratoplasty; RR: risk ratio; CI: confidence interval.
**Intervention DMEK, comparator UT-DSAEK

Table 5. Postoperative complications comparison between ultrathin DSAEK and DMEK.

Review and Year	Type of AE	No. studies	Total no. of participants		Time point analysis of AEs	RR	95% CI of RR	p-value	Heterogeneity (I-square)	Conclusion	Comments
			UT-DSAEK	DMEK							
Maier et al. (2023)	Graft failure	6	133	138	Unclear	0.65	0.18–2.30	$p=0.50$	0%	No significant differences in graft failure risk between procedures	Graft failure 2 UT-DSAEK / 5 DMEK
	Graft rejection	5	123	128	Unclear	1.40	0.27–7.30	$p=0.69$	0%	No significant differences in graft rejection rates between procedures	Graft rejection 1 UT-DSAEK / 0 DMEK
	Postoperative elevated IOP	4	95	100	Unclear	1.14	0.60–2.18	$p=0.69$	0%	No significant differences in postoperative elevated IOP rate between procedures	-
Dimtsas et al. (2023) **	Overall (including donor preparation failure, rebubbling, retransplantation, rejection, postoperative elevated IOP)	6	151	149	Unspecified	1.49	1.02–4.49	$p=0.039$	0%	DMEK group had 1.48 times greater risk for AEs; with comparable postoperative elevated IOP rate	Retransplantation 3 DMEK / 0 UT-DSAEK; Rejection 1 DMEK / 0 UT-DSAEK
	Postoperative elevated IOP	6	151	149	Unspecified	0.91	0.45–1.78	$p=0.790$	N/R		
Singh et al. (2023)	Overall (including graft displacement, rebubbling, graft rejection, graft failure, postoperative elevated IOP)	3	68	72	12 months	0.27	0.12–0.59	$p=0.001$	0%	Lower complication rate in UT-DSAEK	Complications 21 UT-DSAEK / 48 DMEK
Hurley et al. (2023)	Overall (including donor preparation failure, rebubbling, postoperative elevated IOP, graft failure, graft rejection, retransplantation, posterior synechiae, retinal tears and cystoid macular edema)	5	119	117	Unclear	0.57	0.36–0.90	$p=0.02$	39%	Lower complication rate in UT-DSAEK	Complications 33 UT-DSAEK / 59 DMEK; (GRADE Quality of Evidence: Moderate)

Legend: UT-DSAEK: ultrathin Descemet stripping automated endothelial keratoplasty; DMEK: Descemet's membrane endothelial keratoplasty; AE: adverse event; RR: risk ratio; CI: confidence interval; IOP: intraocular pressure.

**Intervention DMEK, comparator UT-DSAEK.

rebubbling rates, UT-DSAEK was associated with a 60–67% lower risk of rebubbling (RR = 0.33 to 0.40).[12,15] Hurley et al. concluded that the quality of evidence for the rebubbling analysis was "High" using the GRADE system.[15]

Other postoperative complications

The studies by Dimtsas et al., Singh et al. and Hurley et al. performed meta-analyses to compare DMEK and UT-DSAK in "overall complications" (Table 5).[13–15] The largest difference in complication rate was reported by Singh et al., who observed that patients undergoing UT-DSAEK had 73% less risk of postoperative complications compared with patients undergoing DMEK (OR = 0.27, 95%CI = 0.12–0.59, $p = 0.001$).[14] Hurley et al. concluded that UT-DSAEK was associated with 43% less risk of complications compared with DMEK (RR = 0.57, 95%CI = 0.36–0.90, $p = 0.02$),[15] and Dimtsas et al. reported a 1.49-fold increased risk of complications after DMEK (RR = 1.49, 95%CI = 1.02–4.49, $p = 0.039$).[13] The analysis of "overall complications" raises concern for potential interpretation bias, since a large proportion of complications in all studies were rebubblings. This means that other individual postoperative complications may not conform to the findings of their meta-analyses. For instance, Dimtsas et al. also performed a meta-analysis of postoperative elevation of IOP, and found no significant differences between DMEK and UT-DSAEK (RR = 0.91, 95%CI = 0.45–1.78, $p = 0.790$),[13] comparable with the findings of Maier et al. (RR = 1.14, 95%CI = 0.60–2.18, $p = 0.69$).[12] Only the study by Maier et al. analyzed the rejection rates and graft failure as standalone parameters, and found no significant differences between both procedures (graft failure RR = 0.65, 95%CI = 0.18–2.30, $p = 0.50$ | graft rejection RR = 1.40, 95%CI 0.27–7.30, $p = 0.69$).[12] Hurley et al. found that the GRADE level of quality of evidence for the comparison of "overall complications" between UT-DSAEK and DMEK was "Moderate".[15]

Endothelial cell density

All SRs included in this overview included a meta-analysis of the ECD at 12-month postoperative follow-up.[12–15] There were differences in the studies included in each SR, and as such there were variations in the pooled estimates for this outcome (Supplemental Table 2). Maier et al. found that pooled estimates could not be interpreted for ECD due to significant heterogeneity,[12] and the other SRs similarly found significant heterogeneity for this analysis.[13–15] The SR by Dimtsas et al. also included a meta-analysis of the 12-month CCT, and found a pooled estimate in favor of DMEK (MD = −47.1, 95% CI = −62.0–32.0, $p < 0.001$)[13]; however, this analysis raises concern for potential interpretation bias, since heterogeneity was not reported, and particularly since this difference may be at least partly explained by the differences in donor lenticule graft thickness between DMEK and UT-DSAEK.[13] The meta-analysis for ECD by Singh et al. has some inconsistencies which raise concern for potential bias (Supplemental Table 2).[14]

Conclusions

This is the first systematic review of SRs specifically addressing the outcomes of corneal endothelial grafting. The relevance of this type of overviews of SRs is highlighted by the findings that only 28–70% of SRs in ophthalmology are considered reliable.[27–30] This is in line with our findings that 25% of the SRs analyzed had an unclear risk of bias after applying the ROBIS tool, that 50% raised potential concerns due to heterogeneity and inconsistent reporting of data, and that three SRs compared "overall complications" rather than reporting each complication individually. Given the weight that rebubbling has in the complication rates after DMEK, at least this outcome should not have been included among other less frequent complications. Besides, the rejection and graft failure rates ought to have been analyzed independently, since these are important outcomes to analyze when two techniques of corneal transplantation are compared.

This summary of SRs provides the highest level of evidence that DMEK leads to higher levels of BCVA in comparison with UT-DSAEK and its variations. The favorable visual outcomes after DMEK are likely due to the lack of posterior stromal tissue in the donor graft, which also leads to lower levels of posterior corneal HOAs compared with UT-DSAEK.[25,31] However, it is unclear whether differences BCVA after 1 year of follow-up are relevant, since the study with the longest follow-up after UT-DSAEK observed a mean BCVA of 0.09 logMAR and that 53.4% of eyes achieved BCVA > 20/20 Snellen,[32] which is comparable with the results of long-term series of DMEK surgery.[5,6]

Rebubbling rates after UT-DSAEK are lower than those after DMEK. However, as previously stated, the implications for rebubbling on graft survival are unclear.[7,8,33] ECD after UT-DSAEK and DMEK were comparable, although significant heterogeneity was observed by all SRs. Endothelial cell loss after DMEK and UT-DSAEK is likely comparable, and this is also true when comparing the endothelial cell loss after conventional DSEK/DSAEK. Although no comparative studies are available for follow-up longer than 1 year, reported 5-year endothelial cell loss rates after UT-DSAEK are also comparable with those of DMEK and those of DSEK/DSAEK.[5,33–36]

Importantly, this systematic review of SRs found that immune rejection rates and other postoperative complications after UT-DSAEK may be comparable with those

after DMEK during the first postoperative year. However, we consider that this is a short follow-up period to establish definite conclusions regarding rejection risk. Although most rejection episodes occur during the first two years after EK,[37] the cumulative rejection risk increases with time after endothelial keratoplasty, and studies with longer follow-ups have reported up to 7% rejection rates at 5 years in UT-DSAEK,[32] compared with 2.5–4% rejection rates at 5 to 10 years after DMEK.[5,6,37]

The main strength of our overview is that we identified the relevant differences and contrasts between the SRs. The main limitation of our systematic review of SRs is that we used few electronic databases, although relevant ones. One important limitation of current SRs of UT-DSAEK versus DMEK is that no review compared the cost-effectiveness of the two techniques, which should be relevant for decision makers. DMEK showed to be cost-effective in comparison to conventional DSAEK in the United States,[38] but a recent multicenter RCT conducted in the Netherlands found that UT-DSAEK was cost-effective compared with DMEK, as DMEK had higher costs (mainly caused by higher rebubbling and regraft rates) while quality-adjusted life years were lower.[39]

In conclusion, there is an overall good quality of evidence on the comparison of outcomes between DMEK and UT-DSAEK and its variations, although a quarter of SRs had an unclear risk of bias, and potential concerns for heterogeneity and inconsistency in reporting of data were found in this overview of SRs. DMEK eyes may expect to reach higher levels of BCVA compared with eyes undergoing UT-DSAEK and its variations, with the trade-off of a higher rebubbling rate. It is unclear whether the rate of other postoperative complications is comparable between the two techniques (apart from rebubbling). Comparative studies with longer follow-up are crucial to elucidate the differences in BCVA, as well as in cumulative rejection rates and graft failure after the first year postoperatively.

Authorship

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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Supplemental material

Supplemental material for this article is available online.

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