Comparison of tube shunt implantation and trabeculectomy for glaucoma: a systematic review and meta-analysis

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ABSTRACT

Objective To compare the efficacy and safety of tube shunt implantation with trabeculectomy in the treatment of patients with glaucoma.

Methods A systematic literature search was performed for studies comparing tube with trabeculectomy in patients with glaucoma (final search date: 27 February 2022). Comparisons between tube and trabeculectomy were grouped by the type of tube (Ahmed, Baerveldt, Ex-PRESS and XEN). The primary endpoints included intraocular pressure (IOP), IOP reduction (IOPR), IOPR percentage (IOPR%), complete success rate (CSR), qualified success rate (QSR) and adverse events (AEs).

Results Forty-nine studies were included in this meta-analysis and presented data for 3795 eyes (Ahmed: 670, Baerveldt: 561, Ex-PRESS: 473, XEN: 199, trabeculectomy: 1892). Ahmed and Ex-PRESS were similar to trabeculectomy in terms of IOP outcomes and success rate (Ahmed vs trabeculectomy: IOPR%: mean difference (MD)=1.34 (–5.35, 8.02), p=0.69; Ex-PRESS vs trabeculectomy: IOPR%: MD=0.12 (–3.07, 3.31), p=0.94). The IOP outcomes for Baerveldt were worse than those for trabeculectomy (IOPR%: MD=–7.51 (–10.68, –4.35), p=0.00001), but the QSR was higher. No significant difference was shown for the CSR. XEN was worse than trabeculectomy in terms of IOP outcomes (IOPR%: MD=–7.87 (–13.55, –2.18), p=0.007), while the success rate was similar. Ahmed and Ex-PRESS had a lower incidence of AEs than trabeculectomy. Baerveldt had a lower incidence of bleb leakage/wound leakage, hyphaema and hypotonic maculopathy than trabeculectomy but a higher incidence of concurrent cataracts, dioplia/strabisim and tube erosion. The incidence of AEs was similar for the XEN and trabeculectomy procedures.

Conclusion Compared with trabeculectomy, both Ahmed and Ex-PRESS appear to be associated with similar ocular hypotensive effects and lower incidences of AEs. However, Baerveldt and XEN cannot achieve sufficient reductions in IOP outcomes similar to those of trabeculectomy.

PROSPERO registration number CRD42021257852.

INTRODUCTION

Glaucoma, the second most common cause of blindness worldwide, leads to irreversible vision loss.1 The most prominent symptoms of glaucoma are visual field defects and optic nerve damage caused by elevated intraocular pressure (IOP).2 Therefore, lowering the IOP is regarded as a primary and initial treatment option for glaucoma. Among the available surgical treatments, trabeculectomy is regarded as the gold standard and is the most widely practiced, even though it was first introduced in 1968.3 The basic principle of trabeculectomy is to establish an ostium at the limbus to allow the aqueous humour (AH) to flow from the anterior chamber into the subconjunctival space.4 Another type of filtration surgery, tube shunt implantation, has been increasingly performed in recent years, especially as a surgical procedure for refractory glaucoma.5 6 However, these procedures are performed much less frequently than trabeculectomy.7

With the development of tube shunt surgery, also known as AH shunt surgery, glaucoma drainage device (GDD) surgery and glaucoma drainage implantation (GDI), various types of drainage implants have been applied in the clinic. According to their drainage pathway, they can be roughly divided into three categories: the suprachoroidal space (CyPass Micro-Stent, iStent Supra), the subconjunctival space (Ahmed, Baerveldt,
InnFocus MicroShunt, Krupin, Molteno, XEN gel stent, Ex-PRESS) and Schlemm’s canal and trabecular meshwork (Hydrus Microstent, iStent). Among these surgical pathways, subconjunctival drainage is the most common and is the focus of this study. Common subconjunctival tube shunt surgery includes conventional GDD surgery, such as Ahmed glaucoma valve and Baerveldt glaucoma implant placement, and microinvasive glaucoma surgery (MIGS).

Before the Tube versus Trabeculectomy study, few studies had directly compared tube shunt implantation and trabeculectomy. However, controversy remains regarding the relative efficacy and safety of tube shunt implantation and trabeculectomy as glaucoma therapies. Consequently, we conducted this meta-analysis to evaluate the outcomes of the two different surgical approaches for treating glaucoma.

MATERIALS AND METHODS

We conducted this meta-analysis following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (online supplemental table S1).

Search strategy

The following electronic databases were used to retrieve relevant literature: (1) EMBASE; (2) Ovid MEDLINE; (3) PubMed; (4) ScienceDirect; (5) The Cochrane Library; (6) Web of Science and (7) Google Scholar. The following terms were used: “glaucoma”, “trabeculectomy”, “glaucoma drainage implants” and “MIGS”. The last search was performed on 27 February 2022. The detailed search results are shown in online supplemental table S2. The references of the retrieved articles were manually searched for additional eligible studies. There were no language restrictions imposed.

Inclusion and exclusion criteria

The inclusion criteria for eligible studies in this meta-analysis were as follows: (1) population: patients with glaucoma; (2) intervention and comparison: tube shunt implantation versus trabeculectomy; (3) outcome parameters: IOP at final follow-up, IOP reduction (IOPR), IOP reduction percentage (IOPR%), complete or qualified success rate (CSR or QSR); and (4) study design: randomised controlled trial (RCT) or cohort study. If two or more articles were based on the same population, we selected the paper published most recently. In addition, abstracts only, animal research, articles with duplicated data, meta-analyses and reviews without original data were excluded. The screening process was completed by two authors (NL and WZ) independently. If conflicts arose between the two authors during the screening process, a discussion was held to resolve the inconsistencies.

Outcome measures

The following outcomes were recorded as the primary outcome measures for the efficacy of the operation: IOP at the final follow-up, IOPR and IOPR% from baseline to the endpoint, and the CSR and QSR. We used existing IOPR% data directly if they were available in the original study. If not, we applied the following principles for calculation: IOPR=IOP (baseline)−IOP (endpoint) SD IOPR=(SD IOP (baseline)+SD IOP (endpoint))/√2, while the IOPR% and SD of the IOPR% (SD IOPR%) were estimated by IOPR%=IOPR/ IOP (baseline), SD IOPR%=SD IOPR/IOP (baseline). Moreover, we considered the target IOP (<21 mm Hg) at the endpoint without medications to be complete success, while qualified success was defined as the target IOP (<21 mm Hg) at the endpoint with or without medications. For the safety assessment, the proportions of patients with postoperative complications were considered.

Data extraction

Two investigators independently extracted the data. The information included the article characteristics (country, first author, publication year), participant characteristics (number of eyes, age, sex and type of glaucoma), intervention (prior glaucoma surgery, GDD model), study design (RCT, cohort study), duration of follow-up, IOP measurements, postoperative visual acuity, success rate and number of adverse events (AEs). Any disagreements were resolved jointly by discussion.

Quality assessment

The risk-of-bias tool in the Cochrane Handbook for Systematic Reviews of Interventions (version 5.1.0) was used to assess the methodological quality of the RCTs. All the included studies were assessed for selection bias, performance bias, detection bias, attrition bias, reporting bias and other biases. The 5-point Jadad scale was also used for quality assessment, which includes three main aspects: accountability of all patients, masking and randomisation. Studies with scores ≥3 points were defined as being of high quality.

We applied the Newcastle-Ottawa Scale (NOS, 9 points) to appraise the quality of the cohort studies. The scale considers three main items: comparability, exposure and selection. High-quality studies (score 8–9 points) and medium-quality studies (score 6–7 points) were included, while low-quality studies (score ≤5 points) were excluded.

The quality of evidence for the results was measured with the Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines, which consider imprecision, inconsistency, indirectness, publication bias and risk of bias. The evidence was divided into high, medium, low or very low levels. The GRADE guidelines were also applied for pooled RCTs and cohort studies, as described in previous studies. Briefly, data from eligible articles were extracted and used to generate an ‘evidence profile’ by grading the quality of evidence for each separate outcome.

Statistical analysis

We analysed the data with Cochrane Review Manager (RevMan, software V.5.3, Copenhagen, Denmark: The
RESULTS
Study characteristics and quality assessment
In all, 3552 articles were initially identified. After applying the exclusion criteria, 49 articles were included in this meta-analysis, as shown in figure 1.19–67 A total of 3795 eyes were included in this study, which included 670 eyes in the Ahmed group, 561 eyes in the Baerveldt group, 473 eyes in the Ex-PRESS group, 199 eyes in the XEN group and 1892 eyes in the trabeculectomy group. Sixteen of the 49 studies had an RCT design,25–27 29–32 34 35 36 37 39 48 49 51–53 55 56 59 62 64 66 and the others had a retrospective or prospective comparative design.19–24 28–36 38 40–47 50 54 57 58 60 61 63 65 67 Overall, the included RCTs demonstrated a low risk of bias for the majority of domains evaluated (online supplemental figure S1). According to the 5-point Jadad scale, all 16 RCTs were of high quality (online supplemental table S3). According to the NOS, 16 cohort studies were of high quality, and 17 cohort studies were of medium quality (online supplemental table S3). Online supplemental table S4 summarises the characteristics and main assessments of the included studies. Additionally, all of the outcome indicators for therapeutic strategy and study design regarding efficacy and safety were assessed as low

Patient and public involvement
None.

Nordic Cochrane Center, The Cochrane Collaboration, 2014 and the Stata software package (V.16.0; Stata Corp). Comparisons between tube shunt implantation and trabeculectomy were grouped by the type of tube shunt (GDI for Ahmed and Baerveldt, MIGS for Ex-PRESS and XEN). To determine whether the IOPR efficacy of tube shunt implantation versus trabeculectomy among subgroups was consistent with the total results, a subgroup analysis for the IOPR% was assessed within each of the following classifications: nation, age, follow-up, publication time, type of tube shunt implanted, GDD model, prior glaucoma surgery and study design. The mean difference (MD) was measured for continuous variables (IOP, IOPR, IOPR%), while the risk ratio (RR) was measured for dichotomous variables (CSR, QSR, AEs). All of the outcomes are presented with a 95% CI. P<0.05 indicated statistical significance. Heterogeneity was evaluated using the $\chi^2$ test and $I^2$ statistic. If the heterogeneity was acceptable ($p>0.1, I^2<50\%$), a fixed-effects model was applied. Otherwise, we used a random-effects model. Publication bias was assessed with Begg’s and Egger’s tests.17 18

Figure 1 Flow chart of study selection. CSR, complete success rate; IOR, intraocular pressure; IOPR, IOP reduction; IOPR%, IOPR percentage; QSR, qualified success rate.
or very low GRADE quality (online supplemental table S5).

Ahmed versus trabeculectomy

Regarding efficacy, no significant difference between Ahmed and trabeculectomy was observed in terms of IOP (MD=−0.03 (−1.88, 1.83), p=0.98; figure 2), IOPR (MD=1.00 (−1.40, 3.41), p=0.41; figure 3) or IOPR% (MD=1.34 (−5.35, 8.02), p=0.69; figure 4). No significant difference in the CSR was found between Ahmed and trabeculectomy (RR=0.96 (0.79, 1.18), p=0.70; online supplemental figure S2). The QSR of Ahmed was similar to that of trabeculectomy (RR=1.02 (0.92, 1.12), p=0.75; online supplemental figure S3). Moreover, in the subgroup analysis of the IOPR%, no significant difference was observed (online supplemental table S6).

Regarding safety, the only complications that were significantly different were postoperative hypotony (RR=0.69 (0.53, 0.90); p=0.006; online supplemental figure S4) and bleb leakage/wound leakage (RR=0.25 (0.11, 0.58); p=0.001; online supplemental figure S5), and these results favoured tube shunt implantation (online supplemental table S7).

Baerveldt versus trabeculectomy

Regarding efficacy, the IOP (MD=1.40 (0.67, 2.14), p=0.0002; figure 2), IOPR (MD=−1.84 (−3.61, 0.06), p=0.04; figure 3) and IOPR% (MD=−7.51 (−10.68, −4.35), p<0.00001; figure 4) results favoured trabeculectomy over Baerveldt. No significant difference in the CSR was found between Baerveldt and trabeculectomy (RR=0.84 (0.45, 1.55), p=0.57; online supplemental figure S2). The pooled RR for the QSR was in favour of Baerveldt over trabeculectomy (RR=1.17 (1.06, 1.29), p=0.002; online supplemental figure S3). However, in the subgroup analysis, Europe, age <45 years, follow-up <2 years, phacomorphic glaucoma, the 250 mm² model and RCT showed no significant differences between Baerveldt and trabeculectomy (online supplemental table S6).

Regarding safety, the hyphaema (RR=0.59 (0.39, 0.88), p=0.01; online supplemental figure S6), bleb leakage/wound leakage (RR=0.10 (0.04, 0.24), p<0.00001; online supplemental figure S5) and hypotonic maculopathy (RR=0.20 (0.06, 0.66), p=0.008) results favoured tube shunt implantation, while the concurrent cataract (RR=3.28 (1.56, 6.90), p=0.002), diploria/strabismus (RR=3.00 (1.73, 5.23), p<0.0001) and tube erosion...

Ex-PRESS versus trabeculectomy

Regarding efficacy, no significant difference was observed in IOP (MD=0.15 (−0.26, 0.67), p=0.56, figure 5), IOPR (MD=0.06 (−1.14, 1.27), p=0.92, figure 6) or IOPR% (MD=0.12 (−3.07, 3.31), p=0.94, figure 7) between Ex-PRESS and trabeculectomy. Both the CSR and QSR showed no significant difference between the two procedures (CSR: RR=1.17 (0.96, 1.44), p=0.12, online supplemental figure S8; QSR: RR=1.06 (0.96, 1.17), p=0.25, online supplemental figure S9). According to subgroup analysis, there was no statistically significant difference in any item between Ex-PRESS and trabeculectomy (online supplemental table S6).

Regarding safety, the Ex-PRESS group had a significantly lower incidence rate of hyphaema (RR=0.30 (0.17, 0.52), p<0.0001, online supplemental figure SI0), flat anterior chamber (RR=0.44 (0.29, 0.69), p=0.0003, online supplemental figure S11) and choroidal effusion (RR=0.60 (0.41, 0.88), p=0.009, online supplemental table S7) than the trabeculectomy group. No significant difference was detected in hypotony (RR=0.63 (0.34, 1.14), p=0.13, online supplemental figure S12) or bleb leakage/wound leakage (RR=0.81 (0.41, 1.61), p=0.55, online supplemental figure S13) between the two groups.

XEN versus trabeculectomy

Regarding efficacy, the IOP (MD=1.62 (0.66, 2.58), p=0.0010; figure 5), IOPR (MD=−2.05 (−3.86, −0.24), p=0.03; figure 6) and IOPR% (MD=−7.87 (−13.55, −2.18), p=0.007; figure 7) results favoured trabeculectomy over XEN. The CSR of XEN was similar to that of trabeculectomy (RR=0.90 (0.75, 1.08), p=0.25; online supplemental figure S8), as was the QSR (RR=0.96 (0.85, 1.08), p=0.46; online supplemental figure S9). As there were too few studies on XEN versus trabeculectomy, no subgroup analysis was performed (online supplemental table S6).

Safety outcomes were similar between XEN and trabeculectomy, with no significant difference in any AE (online supplemental table S7).
In the analysis of the IOP, IOPR and IOPR% for Ahmed/Ex-PRESS versus trabeculectomy, significant heterogeneity was identified. To assess the stability and sensitivity, the impact of each study on the pooled results was evaluated. A sensitivity analysis of the IOP, IOPR and IOPR% demonstrated that the ultimate outcomes were reliable and robust (online supplemental figures S14 and S15).

**Publication bias**

The results of funnel plot analysis demonstrated no clear evidence of publication bias for the IOP, IOPR or IOPR% in the comparison of Ahmed/Ex-PRESS and trabeculectomy. In addition, Begg’s and Egger’s tests indicated no publication bias (online supplemental figures S16 and S17).

**DISCUSSION**

Glaucoma filtration surgery, such as trabeculectomy, remains the mainstream treatment, although it is associated with some complications. Some studies have demonstrated that the IOPR for tube implantation is comparable to that for trabeculectomy, while fewer postoperative complications are observed after tube implantation than after trabeculectomy. However, it is worth noting that replacing trabeculectomy with tube shunt implantation is still controversial. The current study is a meta-analysis comparing the efficacy and safety of tube shunt implantation with those of trabeculectomy for treating glaucoma. In the present study, we reviewed 16 RCTs and 33 cohort studies. Ahmed and Ex-PRESS appear to be better than trabeculectomy, with similar reductions in IOP outcomes and a lower incidence of AEs. However, Baerveldt and XEN cannot achieve reductions in IOP outcomes similar to those of trabeculectomy. Pooled results comparing Ahmed and trabeculectomy showed similar efficacy in reducing IOP outcomes, which is consistent with Pakravan et al’s and Wilson et al’s studies. However, Wilson et al’s study showed lower IOP in the trabeculectomy group during the initial period after surgery. This may be related to the poor compatibility of the drainage tube with the aqueous circulatory system in the short term after surgery. In our study, when Ex-PRESS was compared with trabeculectomy, the pooled outcomes of both short-term (<2 years) and long-term (2–4 years and >4 years) analyses showed...
similar reductions in IOP outcomes between the two groups according to subgroup analysis. These results are in accordance with the results reported previously by other studies.53 58 However, although no statistically significant difference was found, the pooled result for the QSR favoured Ex-PRESS over trabeculectomy, which is consistent with long-term studies but in contrast to short-term studies.61 63 This demonstrated that although the short-term success rate was similar between the groups, Ex-PRESS may favour the long-term maintenance of a target IOP. Thus, it is advised that further studies focus on comparing efficacy over more than 3 years of follow-up.

The trabeculectomy group showed a better effect in lowering IOP than the Baerveldt and XEN groups, which is in agreement with Gedde et al’s study.25 This could be attributed to the Baerveldt effectively ensuring a watertight closure and providing easy constriction for the prevention of postoperative hypotony.72 Limited AH drainage leads to less IOP reduction than can be achieved with trabeculectomy. Similarly, the XEN gel stent controls the drainage of AH by adjusting the inner diameter of the stent, which plays a similar role as a drainage valve.73

Under the success criteria mentioned above, the QSR was in favour of the Baerveldt group rather than the trabeculectomy group, while the CSR was comparable between the groups. These results are basically consistent with those of previous studies,21 which means that Baerveldt combined with postoperative medication can increase the success rate of IOP control. In the subgroup analysis, Europe, age <45 years, follow-up <2 years, phacomorphic glaucoma, the 250 mm² model and RCT showed no significant difference between Baerveldt and trabeculectomy. However, for the ‘Europe, age <45 years, follow-up <2 years, phacomorphic glaucoma and 250 mm² model’ subgroup analyses in the Baerveldt versus trabeculectomy comparison, only one study was included in each subgroup analysis, so the result was unreliable. However, in the RCT subgroup analysis, Baerveldt was similar to trabeculectomy for the IOPR%, which was due to the inclusion of the 5-year follow-up study reported by Islamaj according to sensitivity analysis. This suggests that further long-term research with at least 5 years of follow-up is warranted, as these long-term findings may differ from outcomes in the literature.

The analysis of total AEs demonstrated that the incidence of complications associated with Ahmed, Baerveldt and XEN was not significantly different from that associated with trabeculectomy, while Ex-PRESS was associated with a significantly lower incidence of AEs. Moreover, a significant difference in the incidence of individual complications was found when comparing trabeculectomy with Ahmed, Baerveldt and Ex-PRESS. In fact, the Ex-PRESS glaucoma device is a non-valved implant that may be placed under a partial-thickness scleral flap adjacent to the limbus to shunt AH from the anterior chamber to the subconjunctival space. Unlike trabeculectomy,
Ex-PRESS implantation does not require a sclerostomy or peripheral iridotomy. This may reduce the intraoperative time and the likelihood of hyphaema, decrease postoperative inflammation and minimise the variability of results. Moreover, it is difficult to predict the filtration volume in traditional trabeculectomy. Consequently, hypotony is much more likely to occur with traditional trabeculectomy than with Ex-PRESS. In contrast, the small internal diameter of the Ex-PRESS tube (50 µm) is unlikely to cause hypotony due to overfiltration. Similar outcomes for Ahmed versus trabeculectomy were observed in the study by Pakravan et al.37 Our results are also consistent with the long-term results of Gedde et al’s study comparing Baerveldt with trabeculectomy.36 Sufficient samples and a more detailed classification of the severity of AEs are needed for further study. Due to the lower IOP in the trabeculectomy group, the incidence of hypotony was higher in the trabeculectomy group than in the Ahmed group. Unlike trabeculectomy, subconjunctival drainage does not require iridectomy, which involves a risk of hyphaema.74 This is especially evident in an eye with neovascular glaucoma that contains many abnormal vessels.65 Otherwise, the sudden lowering of the IOP below the episcleral venous pressure during trabeculectomy increases the incidence of hyphaema.73 The results of the analysis showed that Baerveldt and Ex-PRESS were less likely to cause hyphaema than trabeculectomy. A flat anterior chamber is regarded as a common early complication after glaucoma filtration surgery.76 According to our study, the rate of a flat anterior chamber in Ahmed was similar to that in trabeculectomy. However, a flat anterior chamber was observed significantly more frequently in the trabeculectomy group than in the Ex-PRESS group, which may be caused by overfiltration during the postoperative period that should result in a decrease in the anterior chamber depth. Moreover, choroidal effusion was significantly more common after trabeculectomy than after Ex-PRESS implantation, which was consistent with the findings of previous studies (Maris et al.).61 Among all of the complications related to filtering blebs, the incidence of filtering bleb leakage was the highest.77 Bleb leakage showed a lower incidence in tube shunt implantation than in trabeculectomy. To explain this phenomenon, unlike tube shunt surgery, which produces delayed drainage of AH to the equatorial region of the eye due to the distance between the location of filtration and the conjunctival incision, trabeculectomy causes an immediate filtration of AH near the conjunctival incision that increases the risk of leakage. In addition, the application of antimetabolites such as mitomycin C (MMC) and 5-fluorouracil (5-FU) in trabeculectomy is considered to be related since they are thought to be the cause of an increased probability of bleb leakage.78 Histological studies of MMC blebs have shown an irregular surface epithelium and a largely avascular and acellular subepithelium of loosely arranged connective tissue, which may explain the delayed bleb formation.
leaks seen frequently after MMC-augmented glaucoma surgery. The association between delayed bleb leaks and thin-walled, avascular blebs has been previously reported, with these leaks being more frequent after full-thickness procedures. The use of MMC to enhance trabeculectomy has probably led to an increase in the frequency of thin avascular blebs and consequences such as delayed bleb leaks, hypotony and bleb infections. In fact, fibrosis of subconjunctival and episcleral tissue is considered the most important cause of surgical failure. However, the severity of individual complications varies. In an attempt to prevent this complication, the antifibrotic agents MMC and 5-FU became adjuvant treatments for use in filtration surgeries. Although previous RCTs have provided evidence for the efficacy of both MMC and 5-FU in enhancing surgical success, it remains controversial whether one of these adjunctive therapies is associated with better long-term surgical success and fewer complications than the other. Singh et al found that 5-FU and MMC were equally safe and effective adjuncts to primary trabeculectomy in the short-term and medium-term post-operative periods. Fendi et al found a lower pooled mean IOP and higher complete and qualified success rates in the MMC arm than in the 5-FU arm. Furthermore, epithelial corneal defects are a unique complication reported more frequently with 5-FU treatment than with MMC treatment. Lin et al found that intraoperative MMC is more effective in reducing IOP in trabeculectomy than intraoperative 5-FU but comparable to intraoperative 5-FU in terms of both the QSR and CSR. The intraoperative use of both agents may contribute equally to AEs. Equally controversial as the choice of antimetabolite is the dosage and method of application. For example, there is a 50-fold range in the concentration of MMC used and an 84-fold difference in the exposure time reported among the members of the American Glaucoma Society. Therefore, further studies should focus on the effects of different antimetabolite usages on the efficacy and safety of filtration surgeries. Moreover, it is well known that one of the main disadvantages of shunt surgery is corneal endothelial cell loss (CECL) during follow-up. Trabeculectomy, tube shunt surgery and MIGS are associated with CECL. Obuchowska and Konopińska assumed that increased CECL may result from the chronic presence of a titanium foreign body in the trabecular meshwork, which is rich in phagocytic and antigen-presenting cells; extensive manipulation within the anterior chamber during implantation; and postoperative contact between the blood and endothelium. Olgun et al indicated that XEN gel stent (Allergan, Belfast, Ireland) resulted in a 2.1% reduction in the endothelial cell density at 3 months after surgery. Konopińska et al found that Ex-PRESS mini glaucoma shunt implantation may cause progressive endothelial cell loss, with a significantly higher rate of CECL than trabeculectomy. However, another study suggested that iStent implantation did not significantly

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<td>26.52</td>
<td>61</td>
<td>-3.27 [-11.92, 5.38]</td>
<td></td>
</tr>
<tr>
<td>Shinohara 2017</td>
<td>46.71</td>
<td>26.73</td>
<td>50</td>
<td>56.41</td>
<td>21.31</td>
<td>39</td>
<td>-9.70 [-19.68, 0.28]</td>
<td></td>
</tr>
<tr>
<td>Wadgy 2021</td>
<td>50.57</td>
<td>9.64</td>
<td>14</td>
<td>42.84</td>
<td>13.69</td>
<td>14</td>
<td>7.73 [-1.04, 16.50]</td>
<td></td>
</tr>
<tr>
<td>Wang 2017</td>
<td>43.64</td>
<td>29.55</td>
<td>24</td>
<td>46.35</td>
<td>32.1</td>
<td>24</td>
<td>-2.71 [-20.17, 14.75]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>457</td>
<td>76.0%</td>
<td>657</td>
<td>676</td>
<td>100.0%</td>
<td>-1.79 [-4.58, 0.99]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 7: Forest plot of mean difference of intraocular pressure reduction at final follow-up associated with microinvasive glaucoma surgery versus trabeculectomy.
increase CECL compared with phacoemulsification alone for patients who underwent surgery.35 Therefore, further studies assessing the effect of different types of filtration surgeries on corneal endothelial cell numbers are needed. In this case, the results should be interpreted with caution, especially in the selection of surgery.

Several limitations of this study should be acknowledged. (1) Most of the studies are not RCTs. Instead, they are non-randomised, retrospective or prospective studies with potential sources of selection bias. In addition, all of the data are only from the final follow-up, which causes potential bias. (2) We cannot completely rule out publication bias, although funnel plots and Begg’s and Egger’s tests showed no indication of publication bias. As noted above, we should interpret the outcomes cautiously. (3) As trabeculectomy can be easily distinguished from tube shunt implantation, it is difficult to mask the surgical procedures during the postoperative follow-up period, which may affect the results. (4) Due to the limited number of study cases, further subgroup analysis could not be carried out. (5) The inclusion of non-English literature was insufficient, which may lead to selection bias in terms of language. Existing practice patterns for the selection of these two glaucoma procedures have been established based on the actual clinical situation of the patients. In this way, the application of evidence-based conclusions during the process of guiding treatment decisions should be combined with clinical practice experience. (6) Although indirect comparisons between Ahmed and Baerveldt indicated that the results favoured Ahmed shunt implantation in terms of reductions in IOP outcomes, a more concrete conclusion would better align with the Ahmed versus Baerveldt study. (7) Considering the variations in postoperative interventions among different studies and the lack of clear reports of these interventions in some studies, we cannot completely rule out the bias caused by postoperative interventions. (8) As the indications for various filtration surgeries differ, further studies should focus on comparing efficacy and safety among different surgeries according to the severity of glaucoma (eg, grouped by IOP). (9) Since different models of these glaucoma tube shunts are available in different regions, their effects might differ. The subgroup analyses in our study could not distinguish these differences well.

In conclusion, Ahmed and Ex-PRESS appear to be better than trabeculectomy, with similar reductions in IOP outcomes and a lower incidence of AEs. Baerveldt surpassed trabeculectomy in terms of the QSR. However, Baerveldt and XEN cannot achieve sufficient reductions in IOP outcomes similar to those of trabeculectomy. Generally, the overall benefit of Ahmed and Ex-PRESS is better than that of trabeculectomy. However, although Ahmed and Ex-PRESS demonstrate an advantage in IOP control compared with traditional trabeculectomy, we cannot simply regard these two procedures as a substitution for trabeculectomy due to the results of the GRADE assessment, which indicated a low or very low certainty of evidence for all outcomes. To clarify a more precise basis and criterion for the selection of a more efficient and safer surgical method, RCTs with larger populations and longer follow-up durations are needed. Furthermore, it is believed that a comparison between Ahmed and Ex-PRESS is necessary.

Contributors WZ had full access to all of the data in the manuscript and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors read and approved the final manuscript. All authors contributed to the concept and design, and were responsible for the acquisition, analysis or interpretation of data. NL, ML, MH, RX and FW took responsibility for the drafting of the manuscript. NL and WZ provided critical revision of the manuscript for important intellectual content. NL and WZ participated in statistical analysis and supervision. WZ is acting as guarantor.

Funding This study was supported by National Natural Science Foundation of China (NSFC, grant number: 81563045) and National Science Foundation of Jiangxi Province (grant number: 20181BAB215027). Role of the funding: the funding had no role in the design and conduct of the study; collection, management, analysis and interpretation of the data; preparation, review or approval of the manuscript; and decision to submit the manuscript for publication.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

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REFERENCES


