Original Investigation

Efficacy and Safety of Trabeculectomy vs Nonpenetrating Surgical Procedures
A Systematic Review and Meta-analysis

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IMPORTANCE To date, only a few studies have directly compared nonpenetrating surgery (NPS) and trabeculectomy (TE). Therefore, there is no strong evidence as to which surgical technique leads to the best results in terms of ocular hypotensive effect and safety.

OBJECTIVE To compare the hypotensive effect and safety of NPS and TE in terms of intraocular pressure (IOP) reduction and incidence of complications.

DATA SOURCES The MEDLINE and EMBASE databases were searched for studies potentially eligible in any language published up to March 31, 2013.

STUDY SELECTION Systematic review and meta-analysis of comparative studies of 2 or more surgical techniques (1 of which had to be TE), including patients with open-angle glaucoma.

DATA EXTRACTION AND SYNTHESIS The considered interventions were TE, deep sclerectomy (DS), viscocanalostomy, and canaloplasty.

MAIN OUTCOMES AND MEASURES The primary outcome was the mean between-group difference in the reduction in diurnal IOP from baseline to the 6- or 12-month follow-up evaluation. We also considered the incidence of complications, expressed as relative risk.

RESULTS Eighteen articles, accounting for 20 comparisons, were selected for data extraction and analysis. Analysis of the 6-month follow-up data showed that the pooled estimate of the mean between-group difference was −2.15 mm Hg (95% CI, −2.85 to −1.44) in favor of TE. There was no difference between the NPS subgroups. In the subgroup antimetabolite analysis, the addition of mitomycin C to TE and DS decreased the difference in the reduction in IOP (TE and DS without mitomycin C: −2.65 mm Hg [95% CI, −3.90 to −1.39]; TE and DS with mitomycin C: −0.83 mm Hg [95% CI, −2.40 to 0.74]). In the subgroup analysis by implant addition, no significant difference induced by DS with or without drainage devices was detected (test for subgroup differences: $\chi^2_1 = 0.24$; $P = .62$). The absolute risk of hypotony, choroidal effusion, cataract, and flat or shallow anterior chamber was higher in the TE group than in the NPS group.

CONCLUSIONS AND RELEVANCE Trabeculectomy seems to be the most effective surgical procedure for reducing IOP in patients with open-angle glaucoma. However, as expected, it was associated with a higher incidence of complications when compared with NPS.

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Trabeculectomy (TE) involves draining aqueous humor from the anterior chamber into the subconjunctival spaces through a sclerostomy and requires full-thickness penetration of the anterior chamber under a partial-thickness scleral flap.[1] It is considered to be the standard procedure for lowering intraocular pressure (IOP) in patients with glaucoma,[1-3] but it is frequently accompanied by short- and long-term complications such as hypotony,[4,5] bleb leaks,[6-9] accelerated cataract progression,[10] choroidal effusion and hemorrhaging,[11] and prolonged or permanent visual impairment due to hypotony maculopathy.[4,12] These complications are generally increased by the use of antifibrotics (also called antimetabolites) such as 5-fluorouracil or mitomycin C (MMC), but without them, the incidence of short-term failure is relatively high.[13,14]

There has recently been renewed interest in nonpenetrating surgery (NPS) for glaucoma, which was developed to improve the safety of conventional filtering procedures. The 3 main variations of NPS are deep sclerectomy (DS),[15-18] viscocanalostomy (VCO),[19] and canaloplasty (CP).[20,21] Deep sclerectomy is a filtering procedure for which success often requires bleb formation, which is infrequent in the case of VCO and CP as the reduction in IOP is mainly due to the opening of previously nonfunctional areas of the Schlemm canal. Antifibrotics are frequently used in DS but never in VCO and CP. Moreover, it has been suggested that the use of collagen drainage devices positioned under the scleral flap would improve aqueous humor filtration.[22-24]

As only a few studies have directly compared NPS and TE, there is no strong evidence as to which surgical technique leads to the best results in terms of hypotensive effects and safety. The aim of this systematic review and meta-analysis of aggregate data is to fill this gap.

Methods

To avoid the bias induced by post hoc decisions, the eligibility criteria and methods of analysis were specified in advance and documented in a protocol described here. As this is a systematic review analyzing data already published, we did not enroll patients and institutional review board approval was not required.

Eligibility Criteria

We selected experimental and observational comparative studies of 2 or more surgical techniques (1 of which had to be TE).

Patients

The studies involved patients with open-angle glaucoma (OAG), regardless of age, race/ethnicity, or sex. Open-angle glaucoma was defined as the following: (1) an untreated mean IOP greater than 21 mm Hg; (2) open drainage angles detected by gonioscopy; (3) typical optic disc damage with glaucomatous cupping and loss of the neuroretinal rim; and (4) visual field defects compatible with glaucomatous optic neuropathy.[25] Studies including patients with exfoliative glaucoma (XFG) or pigment dispersion syndrome were considered eligible, whereas those including patients with neovascular glaucoma, secondary glaucoma, or normal-tension glaucoma were excluded. Mixed study populations of patients with OAG and patients with chronic angle-closure glaucoma were also considered eligible.

Interventions

The considered interventions were TE, DS, VCO, and CP, including TE and DS with intraoperative antimetabolite augmentation and DS with a scleral implant. Studies including combined cataract and glaucoma surgery were excluded, unless the data relating to glaucoma surgery were described separately.

Outcome Measures

The primary outcome was the mean between-group difference (MeD) in the reduction in diurnal IOP from baseline to the 6- or 12-month follow-up evaluation. Unfortunately, even if progression of visual field damage is the main outcome of glaucoma treatments, there is a lack of literature on comparison of surgical techniques (TE vs NPS) and progression of visual field. Thus, it was not possible to perform such systematic review with this outcome. Six months was considered to be the minimal follow-up period to ensure IOP stabilization after surgery; therefore, studies with a shorter follow-up were excluded. We also considered the incidence of complications, expressed as relative risk (RR). Significant complications (including hypotony, choroidal effusion, cataract, and flat or shallow anterior chamber) were prespecified in the data extraction form.

Search Strategies

The MEDLINE and EMBASE databases were searched for studies in any language published up to March 31, 2013 (eTable 1 in Supplement). However, non-English-language articles for which no full-text translation or evaluation was available were excluded during the screening phase. The reference lists of trial reports as well as narrative and systematic reviews were hand

Figure 1. Study Selection

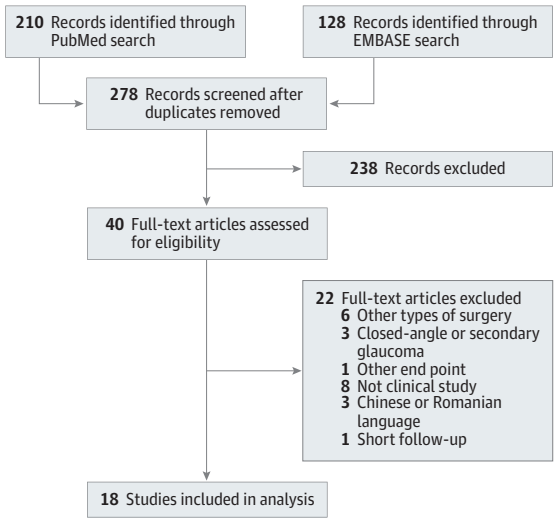


Table 1. Description of Studies and Patients

Source	Design	Masking	Withdrawals and Dropouts Described	Diagnosis	Patients Enrolled/ Analyzed, No.	Eyes Enrolled/ Analyzed, No.	Male, %	Age, Mean (SD), y	White, %
Ayyala et al,[33] 2011	Observational	Open label	Yes	POAG	79/79	79/79	54	66.1 (11.0)	46
Gilmour et al,[40] 2009	Experimental (randomized)	Not reported	No	POAG + XFG	43/U	50/42	67	64.4 (10.3)	100
Russo et al,[45] 2008	Experimental (randomized)	Not reported	Yes	POAG	93/93	93/93	51	67.3 (2.7)	U
Yarangümeli et al,[48] 2004	Experimental (randomized)	Not reported	Yes	POAG + XFG + CACG	22/22	44/44	45	64.3 (10.5)	U
Cillino et al,[36] 2004	Experimental (randomized)	Outcome assessor masked	Yes	POAG + XFG	35/35	35/35	49	70.0 (1.5)	U
Yalvac et al,[47] 2004	Experimental (randomized)	Not reported	U	POAG	50/50	50/50	72	60.2 (11.5)	U
Schwenn et al,[46] 2004	Experimental (randomized)	Open label	Yes	POAG	22/22	22/22	50	68.3 (11.7)	U
Egrilmez et al,[38] 2004	Experimental (randomized)	Not reported	Yes	POAG + XFG + PDS	34/30	34/30	57	61.7 (10.9)	100
Carassa et al,[34] 2003	Experimental (randomized)	Outcome assessor masked	Yes	POAG + XFG	50/49	50/49	40	67.7 (13.4)	100
Kobayashi et al,[42] 2003	Experimental (randomized)	Not reported	U	POAG	25/25	50/50	44	62.5 (7.4)	100
Lüke et al,[43] 2002	Experimental (randomized)	Not reported	U	POAG + XFG + PDS	60/60	60/60	48	61.4 (17.6)	95
Ambresin et al,[32] 2002	Experimental (nonrandomized)	Not reported	U	POAG + XFG + PDS	20/20	40/40	50	68.0 (12.6)	95
Chiselita,[35] 2001	Experimental (randomized)	Outcome assessor masked	U	POAG	17/17	34/34	53	60.17 (7.3)	U
El Sayyad et al,[39] 2000	Experimental (randomized)	Not reported	U	POAG	39/39	78/78	63	53.4 (9.6)	U
Mermoud et al,[44] 1999	Observational	Not reported	Yes	POAG + XFG	93/88	93/88	51	68.8 (13.0)	99
Cillino et al,[37] 2008	Experimental (randomized)	Not reported	U	POAG + XFG	40/40	40/40	50	70.3 (6.7)	U
Jonescu-Cuypers et al,[41] 2001	Experimental (randomized)	Not reported	U	POAG	20/20	20/20	55	62.5 (13.1)	100
Mesci et al,[49] 2012	Experimental (randomized)	Outcome assessor masked	Yes	POAG + XFG	99/91	99/91	48	68.0 (10.2)	U

Abbreviations: CACG, chronic angle-closure glaucoma; PDS, pigment dispersion syndrome; POAG, primary open-angle glaucoma; U, unknown; XFG, exfoliative glaucoma.

searched to identify additional studies. Three reviewers (a biostatistician [I.F.] and 2 ophthalmologists [L.Q. and I.R.]) independently checked the titles, abstracts, and keywords of the identified studies to ensure eligibility and then read the full articles to identify those that met the inclusion criteria; any disagreements were resolved by consensus. A κ statistic was calculated for measuring agreement between the reviewers.[26]

Data Extraction

The study design, patient characteristics, interventions, and outcomes were independently recorded by 2 reviewers (I.D.S. and G.G.) using a data extraction form that had been pilot tested on 4 randomly selected studies and subsequently refined. Any differences in data extraction were resolved by a third reviewer (I.R.), who referred back to the original article.

Risk of Bias Assessment

The quality of the studies was independently evaluated by 2 reviewers (E.R. and E.B.) using the approach proposed by the Cochrane Collaboration for the experimental studies[27] and the Newcastle-Ottawa Scale for the observational studies.[28]

Statistical Analysis

The reduction in IOP in each eligible arm of the individual studies was calculated as the difference between the values at baseline and the different follow-up times, and its variance was computed as the weighted mean of their variances. The MeD was then computed as the between-treatment difference in the IOP reduction from baseline.

For studies with more than 2 eligible groups to be included in the same meta-analysis, the control group was split into 2 or more groups with smaller sample size to overcome a unit of analysis error.[27]

To evaluate the assumptions in the variance computation, the ρ correlation coefficient for paired data (baseline and follow-up IOP) was calculated and assessed using the approach suggested by the Cochrane Collaboration.[27]

The absolute value of the MeD indicates the size of the effect difference, whereas the sign indicates the direction of this effect. A value of 0 suggests no difference in efficacy between the groups. Pooled MeD estimates were calculated using the 2-step method for the random-effects model proposed by DerSimonian and Kacker.[29]

Table 2. Surgery Characteristics

Source	TE	NPS	Postoperative Treatment	Goniopuncture	Implant
Ayyala et al,[33] 2011	With MMC (0.4 mg/mL × 45 s)	CP	MMC (TE only)	No	No
Gilmour et al,[40] 2009	No antimetabolite	VCO	5-FU	Yes	No
Russo et al,[45] 2008	With MMC (0.2 mg/mL × 2 min)	DS + MMC (0.2 mg/mL × 2 min)	5-FU	No	SK-Gel
Yarangümeli et al,[48] 2004	No antimetabolite	VCO	None	Yes	No
Cillino et al,[36] 2004	No antimetabolite	DS (no antimetabolite)	None	No	No
Yalvac et al,[47] 2004	No antimetabolite	VCO	None	No	No
Schwenn et al,[46] 2004	With MMC (0.2 mg/mL × 5 min)	DS + MMC (0.2 mg/mL × 5 min)	5-FU	No	SK-Gel
Egrilmez et al,[38] 2004	No antimetabolite	DS (no antimetabolite), VCO	None	No	T-Flux
Carassa et al,[34] 2003	No antimetabolite	VCO	5-FU	Yes	No
Kobayashi et al,[42] 2003	With MMC (0.4 mg/mL × 3 min)	VCO	None	Yes	No
Lüke et al,[43] 2002	No antimetabolite	VCO	None	No	No
Ambresin et al,[32] 2002	No antimetabolite	DS (no antimetabolite)	5-FU	Yes	SK-Gel
Chiselita,[35] 2001	No antimetabolite	DS (no antimetabolite)	None	No	no
El Sayyad et al,[39] 2000	No antimetabolite	DS (no antimetabolite)	5-FU	Yes	no
Mermoud et al,[44] 1999	No antimetabolite	DS (no antimetabolite)	5-FU	Yes	SK-Gel
Cillino et al,[37] 2008	With MMC (0.2 mg/mL × 2 min)	DS + MMC (0.2 mg/mL × 2 min)	None	Yes	No
Jonescu-Cuypers et al,[41] 2001	No antimetabolite	VCO	None	No	No
Mesci et al,[49] 2012	No antimetabolite	DS + MMC (0.2 mg/L × 2 min)	MMC	Yes	SK-Gel, no

Abbreviations: CP, canaloplasty; DS, deep sclerectomy; MMC, mitomycin C; NPS, nonpenetrating surgery; TE, trabeculectomy; VCO, viscocanalostomy; 5-FU, 5-fluorouracil.

Safety was assessed in terms of the incidence of intraoperative and postoperative complications in each group. The difference between groups was expressed as the RR.

All results were expressed as a point estimate and its 95% confidence interval.

Statistical heterogeneity was quantified using the I^2 statistic, which indicates the percentage of variability due to heterogeneity rather than to chance alone: 0% indicates no heterogeneity, greater values indicate increasing heterogeneity, and values greater than 50% imply substantial heterogeneity.[30]

We also used χ^2 tests for homogeneity. The assumption of homogeneity was deemed not valid if $P < .10$.

All of the statistical analyses were performed using Review Manager version 5.1 software (Nordic Cochrane Centre, Cochrane Collaboration).

Efficacy Analysis

The primary analysis compared TE and NPS after 6 and 12 months of follow-up in terms of the MeD. In the case of studies with no 6- or 12-month assessment, we considered the IOP recorded at the nearest subsequent evaluation. Subgroup analyses were made by type of NPS (DS, VCO, and CP), antimetabolite augmentation during surgery (only for studies comparing TE and DS), and the use of implants (only for studies comparing TE and DS). To verify the robustness of the results of the primary analysis, the analyses were repeated by excluding the studies not assessing IOP at 6 or 12 months and by excluding nonrandomized studies.

Safety Analysis

The safety analysis compared TE with one of the NPS procedures in terms of the incidence of complications. Each complication was analyzed separately.

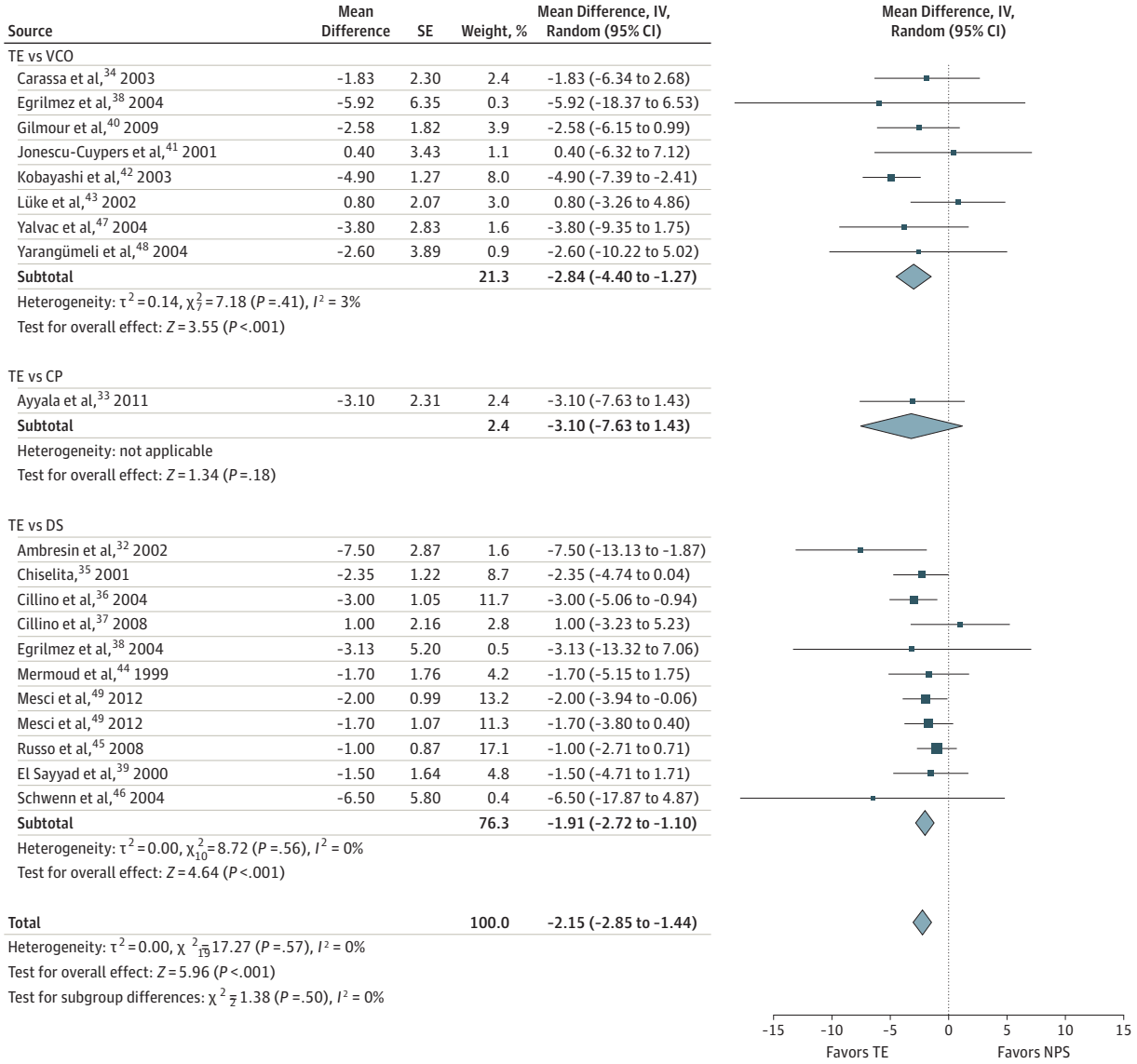
Publication Bias Assessment

To exclude the presence of publication bias (ie, the bias due to the fact that studies with positive results are more likely to be published than those with negative results) and small-study effects (the tendency for treatment effect estimates to be different in small and larger studies), we visually explored any asymmetry using a funnel plot in which study size was plotted as a function of the measure of interest.[31]

Results

Figure 1 shows the study selection process. The electronic searches identified 278 abstracts, 238 of which did not meet the eligibility criteria; the full texts of the remaining 40 articles were examined. No additional studies were identified from the references of the selected articles, and no relevant

Figure 2. Trabeculectomy vs Nonpenetrating Surgery at 6-Month Follow-up



CP indicates canaloplasty; DS, deep sclerectomy; IV, inverse-variance method; NPS, nonpenetrating surgery; TE, trabeculectomy; and VCO, viscocanalostomy.

unpublished studies were found. A further 22 studies were subsequently excluded (eTable 2 in Supplement): 6 because they investigated other types of surgery, 3 because they included patients with secondary glaucoma or closed-angle glaucoma, 1 because it had a different end point, 8 because they were not clinical studies, 1 because the follow-up was too short, and 3 because they were not written in English and no full-text translation or evaluation was available. For the abstract screening, the agreement was good (κ = 0.70); regarding the full-text article screening, we obtained full agreement between the reviewers.

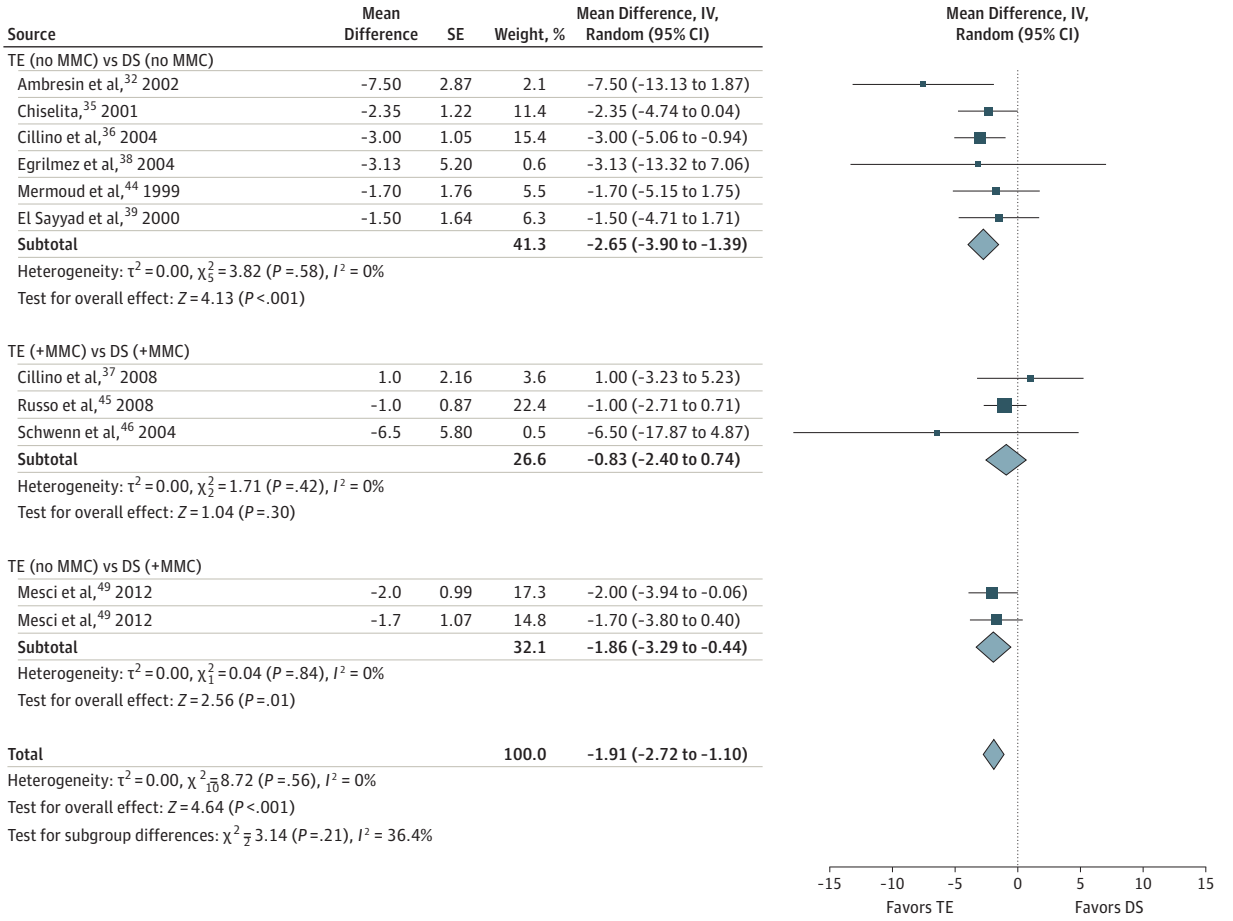
Eighteen articles were therefore selected for data extraction and analysis,[32-49] but as 2 of them provided 2 comparisons,[38,49] the total number of comparisons was 20.

Study Characteristics

Table 1 shows the characteristics of the 18 studies. Fifteen were randomized clinical trials,[34-43,45-49] 1 was a nonrandomized experimental study,[32] and 2 were observational studies.[33,44]

Information about the blindness assessment was not clearly described in 12 articles.[32,37-45,47,48] One article[40] did not describe withdrawals or dropouts, and 8 articles[32,35,37,39,41-43,47] did not clearly indicate the presence of withdrawals or dropouts. Eight studies[33,35,39,41,42,45-47] only included patients with primary OAG (POAG), 6 studies[34,36,37,40,44,49] included patients with POAG and XFG, 3 studies[32,38,43] included patients with POAG, XFG, and pigment dispersion syndrome, and 1 study[48] included patients with POAG, XFG, and chronic angle-

Figure 3. Subgroup Analysis of Antimetabolite Addition for Trabeculectomy vs Deep Sclerectomy at 6-Month Follow-up



DS indicates deep sclerectomy; IV, inverse-variance method; MMC, mitomycin C; and TE, trabeculectomy.

closure glaucoma. There were more men than women in 9 studies, and the patients' ages ranged from 53.4 to 70.3 years.

Risk of Bias

Selection bias could not be excluded in 15 of the 16 experimental studies because of the absence of adequate sequence generation or concealed allocation (3 studies)[32,36,45] or lack of information (12 studies).[34,35,37-41,43,46-49] Attrition bias could be excluded in 6 experimental studies[34,38,45,46,48,49] that addressed the question of incomplete outcome data; the rates of follow-up and the number of withdrawals were similar between the groups. Only 4 of the 16 experimental studies[34-36,49] stated that the outcome assessors were unaware of the assigned intervention.

The 2 observational studies[33,44] had a low risk of bias, but the observational design limitations should be taken into consideration.

Effects of Interventions

The 18 studies made a total of 20 comparisons and involved 945 eyes: 7 studies[34,40-43,47,48] compared TE with VCO (315 eyes); 1 study[33] compared TE with CP (79 eyes); 8 studies[32,35-37,39,44-46] compared TE with DS (430 eyes); 1 study[38] compared TE with DS and VCO (30 eyes); and 1 study[49] compared TE with DS with or without an implant (91 eyes). Mitomycin C was the only antimetabolite added at the time of surgery in 7 comparisons of TE and DS (**Table 2**).

TE vs NPS

Analysis of the 6-month follow-up data showed that the pooled estimate of the MeD was −2.15 mm Hg (95% CI, −2.85 to −1.44; test for overall effect: $Z = 5.96$, $P < .001$); no heterogeneity was detected ($I^2 = 0\%$; test for heterogeneity: $\chi^2_{19} = 17.27$, $P = .57$) (**Figure 2**).

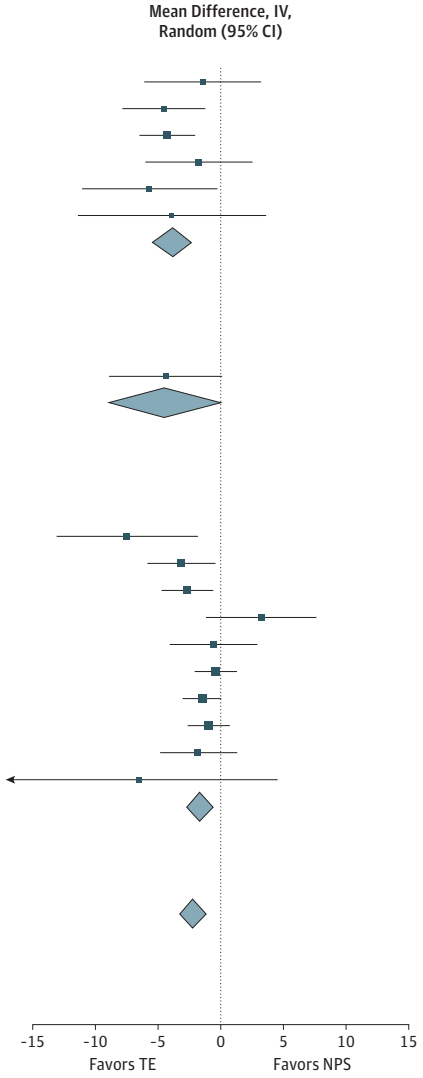
There was no difference between the surgical subgroups indicating that TE led to a greater IOP reduction.

In the subgroup antimetabolite analysis (**Figure 3**), 6 studies[32,35,36,38,39,44] compared TE and DS without MMC (MeD = −2.65 mm Hg [95% CI, −3.90 to −1.39]), 3 studies[37,45,46] compared TE and DS with MMC (MeD = −0.83 mm Hg [95% CI, −2.40 to 0.74]), and 1 study[49] compared TE without MMC with DS with MMC (MeD = −1.86 mm Hg [95% CI, −3.29 to −0.44]).

In the subgroup analysis of the studies in which an implant was added to DS, there were 5 studies[35-37,39,49] of DS with-

Figure 4. Trabeculectomy vs Nonpenetrating Surgery at 12-Month Follow-up

Source	Mean Difference	SE	Weight, %	Mean Difference, IV, Random (95% CI)
TE vs VCO				
Carassa et al,[34] 2003	-1.47	2.37	3.4	-1.47 (-6.12 to 3.18)
Gilmour et al,[40] 2009	-4.56	1.70	5.6	-4.56 (-7.89 to -1.23)
Kobayashi et al,[42] 2003	-4.30	1.14	9.1	-4.30 (-6.53 to -2.07)
Lüke et al,[43] 2002	-1.80	2.19	3.9	-1.80 (-6.09 to 2.49)
Yalvac et al,[47] 2004	-5.70	2.77	2.6	-5.70 (-11.13 to -0.27)
Yarangümeli et al,[48] 2004	-3.90	3.84	1.5	-3.90 (-11.43 to 3.63)
Subtotal			**26.1**	**-3.84 (-5.34 to -2.34)**
Heterogeneity: $\tau^2 = 0.00$, $\chi^2_5 = 2.66$ ($P = .75$), $I^2 = 0\%$				
Test for overall effect: $Z = 5.01$ ($P < .001$)				
TE vs CP				
Ayyala et al,[33] 2011	-4.40	2.29	3.6	-4.40 (-8.89 to 0.09)
Subtotal			**3.6**	**-4.40 (-8.89 to 0.09)**
Heterogeneity: not applicable				
Test for overall effect: $Z = 1.92$ ($P = .05$)				
TE vs DS				
Ambresin et al,[32] 2002	-7.50	2.87	2.5	-7.50 (-13.13 to -1.87)
Chiselita,[35] 2001	-3.16	1.37	7.4	-3.16 (-5.85 to -0.47)
Cillino et al,[36] 2004	-2.70	1.08	9.5	-2.70 (-4.82 to -0.58)
Cillino et al,[37] 2008	3.20	2.24	3.8	3.20 (-1.19 to 7.59)
Mermoud et al,[44] 1999	-0.60	1.78	5.3	-0.60 (-4.09 to 2.89)
Mesci et al,[49] 2012	-0.40	0.87	11.4	-0.40 (-2.11 to 1.31)
Mesci et al,[49] 2012	-1.50	0.81	12.0	-1.50 (-3.09 to 0.09)
Russo et al,[45] 2008	-1.00	0.87	11.4	-1.00 (-2.71 to 0.71)
El Sayyad et al,[39] 2000	-1.80	1.57	6.3	-1.80 (-4.88 to 1.28)
Schwenn et al,[46] 2004	-6.60	5.68	0.7	-6.60 (-17.73 to 4.53)
Subtotal			**70.2**	**-1.53 (-2.59 to -0.47)**
Heterogeneity: $\tau^2 = 0.99$, $\chi^2_9 = 14.48$ ($P = .11$), $I^2 = 38\%$				
Test for overall effect: $Z = 2.83$ ($P = .005$)				
Total			**100.0**	**-2.22 (-3.18 to -1.27)**
Heterogeneity: $\tau^2 = 1.33$, $\chi^2_{16} = 26.10$ ($P = .05$), $I^2 = 39\%$				
Test for overall effect: $Z = 4.56$ ($P < .001$)				
Test for subgroup differences: $\chi^2_2 = 8.96$ ($P = .01$), $I^2 = 77.7\%$				



CP indicates canaloplasty; DS, deep sclerectomy; IV, inverse-variance method; NPS, nonpenetrating surgery; TE, trabeculectomy; and VCO, viscocanalostomy.

out an implant and 6 studies[32,38,44-46,49] of DS with an implant. There was no between-group difference in the comparison of TE and DS without an implant (MeD = −2.10 mm Hg [95% CI, −3.20 to −1.00]) or in the comparison of TE and DS with an implant (MeD = −1.79 mm Hg [95% CI, −3.13 to −0.45]). The result of the test for subgroup difference was $\chi^2_1 = 0.24$ ($P = .62$).

Two studies[38,41] were excluded from the analysis of the 12-month follow-up data because of an insufficient duration of follow-up. Overall, TE led to a greater reduction in IOP than NPS (**Figure 4**). There was a difference between the subgroups defined by type of surgery ($\chi^2_2 = 8.96$; $P = .01$): the MeD decreased in favor of TE in the VCO group (from −2.84 mm Hg [95% CI, −4.40 to −1.27] at 6 months to −3.84 mm Hg [95% CI, −5.34 to −2.34] at 12 months) and the CP group (from −3.10 mm Hg [95% CI, −7.63 to 1.43] at 6 months to −4.40 mm Hg [95% CI, −8.89 to 0.09] at 12 months) but increased in favor of DS in the DS group (from −1.91 mm Hg [95% CI, −2.72 to −1.10] at 6 months to −1.53 mm Hg [95% CI, −2.59 to −0.47] at 12 months).

Sensitivity Analysis

Two studies[32,45] in which the first IOP evaluation was made after 6 months were excluded from the 6-month sensitivity analysis, and 1 study[45] in which the first IOP evaluation was made after 12 months was excluded from the 12-month sensitivity analysis. A further 3 studies[32,33,44] were excluded from the analyses of only randomized clinical trials. The results of these sensitivity analyses were always consistent with those of the primary analysis.

Safety Evaluation

The results of the analysis of postoperative complications are shown in **Table 3**. The absolute risk of hypotony (RR = 2.3 [95% CI, 1.3-3.8]), choroidal effusion (RR = 3.9 [95% CI, 2.0-7.5]), cata-

Table 3. Complications

Subgroup	Hypotony		Choroidal Effusion		Cataract		Flat or Shallow Anterior Chamber	
	Studies, No. (Eyes, No.)	RR (95% CI)	Studies, No. (Eyes, No.)	RR (95% CI)	Studies, No. (Eyes, No.)	RR (95% CI)	Studies, No. (Eyes, No.)	RR (95% CI)
TE vs VCO	6 (303)	2.6 (1.2-5.6)	3 (159)	6.0 (1.1-33.8)	4 (204)	3.8 (1.5-9.5)	3 (154)	5.5 (1.2-25.1)
TE (no MMC) vs VCO	5 (253)	2.3 (1.1-5.0)	3 (159)	6.0 (1.1-33.8)	3 (154)	3.6 (1.4-9.7)	2 (104)	4.7 (0.7-32.6)
TE (+MMC) vs VCO	1 (50)	11.0 (0.6-188.9)	NA	NA	1 (50)	5.0 (0.3-99.2)	1 (50)	9.0 (0.5-158.9)
TE vs DS	7 (399)	2.1 (0.9-4.6)	7 (409)	3.8 (1.6-9.0)	6 (424)	3.3 (1.8-5.8)	9 (521)	4.1 (2.1-8.0)
TE (no MMC) vs DS (no MMC)	3 (153)	2.2 (0.5-8.8)	3 (163)	6.1 (1.9-19.9)	4 (240)	3.0 (1.3-6.6)	5 (275)	8.3 (2.6-26.7)
TE (no MMC) vs DS (+MMC)	1 (91)	3.1 (1.6-6.3)	1 (91)	15.6 (0.9-281.3)	1 (91)	3.5 (1.3-9.4)	1 (91)	2.8 (1.0-7.9)
TE (+MMC) vs DS (+MMC)	3 (155)	1.7 (0.4-6.3)	3 (155)	2.4 (0.6-9.8)	1 (93)	3.9 (0.9-17.0)	3 (155)	3.1 (0.6-16.7)
TE vs CP	NA	NA	1 (79)	12.3 (0.7-205.9)	NA	NA	NA	NA
TE vs NPS	13 (702)	2.3 (1.3-3.8)	11 (647)	3.9 (2.0-7.5)	10 (628)	3.4 (2.1-5.5)	12 (675)	4.3 (2.3-8.0)

Abbreviations: CP, canaloplasty; DS, deep sclerectomy; MMC, mitomycin C; NA, not applicable; NPS, nonpenetrating surgery; RR, relative risk; TE, trabeculectomy; VCO, viscocanalostomy.

ract (RR = 3.4 [95% CI, 2.1-5.5]), or a flat or shallow anterior chamber (RR = 4.3 [95% CI, 2.3-8.0]) was higher in the TE group than in the NPS group.

In the comparison of TE and VCO, the RRs for all of the considered complications increased when MMC was added to TE (RR of hypotony increased from 2.3 to 11.0; RR of cataract increased from 3.6 to 5.0; and RR of a flat or shallow anterior chamber increased from 4.7 to 9.0).

In the comparison of TE and DS, the RRs of all of the considered complications except cataract (RR increased from 3.0 to 3.9) decreased when MMC was added to both (RR of hypotony decreased from 2.2 to 1.7; RR of choroidal effusion decreased from 6.1 to 2.4; and RR of a flat or shallow anterior chamber decreased from 8.3 to 3.1).

Discussion

To our knowledge, this is the first meta-analysis that assesses efficacy and safety of TE vs all of the available NPS procedures. The results of this systematic review suggest that TE is more effective in reducing IOP than NPS 6 and 12 months after surgery (−2.15 mm Hg [95% CI, −2.85 to −1.44] and −2.22 [95% CI, −3.18 to −1.27], respectively). The significance of such differences in IOP is likely to be clinically relevant especially in patients requiring a greater IOP reduction or those at greater risk for glaucoma progression. Among the NPS procedures, there was less difference in efficacy between DS and TE, although the superiority of TE was statistically significant.

These results are in line with what is generally believed about so-called canal surgery (VCO and CP), which cannot be expected to lower IOP as much as the bulk flow of the full-thickness perforation created in the eye by means of TE. Deep sclerectomy seems to be a clinically reasonable compromise in terms of reducing IOP.

With regard to the efficacy of TE and DS with or without MMC, the addition of MMC to both decreased the difference in the reduction in IOP: TE and DS without MMC, −2.65 mm Hg (95% CI, −3.90 to −1.39); TE and DS with MMC, −0.83 mm Hg (95% CI, −2.40 to 0.74). This indicates that the use of MMC is advisable when performing DS because the nature of the procedure (filtering surgery: filtration of aqueous humor into the subconjunctival spaces) means that antimetabolites can avoid conjunctival healing and optimize surgical outcomes.

The implantation of drainage devices during DS has been advocated as a means of increasing the success rate of the procedure,[50,51] but our meta-analysis shows no significant difference in the reduction in IOP induced by DS with or without drainage devices (test for subgroup differences: $\chi^2_1 = 0.24$; $P = .62$). This finding has important implications in clinical practice because the use of implants significantly increases the cost of DS, which is otherwise the same as that of standard TE.

As expected, TE was associated with a higher incidence of short- and long-term complications. Viscocanalostomy had a better safety profile than TE, although the evidence concerning CP was not sufficient to draw any conclusion.

It has been claimed that the additional use of intraoperative MMC increases surgery-related complications. Our findings show that without MMC, TE led to a higher incidence of complications than DS, but when both procedures were supplemented with MMC, the rate of complications (except cataract progression) increased in the DS group. One possible explanation is that DS has not been modified from the original technique (with or without the use of MMC), whereas standard TE has been substantially improved since the advent of antimetabolites. The term *safe trabeculectomy* reflects a development that can be considered as optimizing the technique and postoperative management (suture lysis, bleb manipulation).[52-54]

In conclusion, TE still offers the possibility of obtaining excellent IOP control at the long-term follow-up in patients with OAG. Success may vary depending on glaucoma form, ie, it may work better in XFG, whereas NPS procedures are not a viable option in chronic angle-closure glaucoma. Moreover, NPS procedures are more difficult to perform, require a long learning curve even for an experienced glaucoma surgeon, and are more costly. Despite a higher incidence of postoperative complica-

tions when compared with NPS, the advent of the safe trabeculectomy technique offers the possibility of tailoring the IOP postoperatively with minimal postoperative complications. Therefore, further studies are needed to assess the safety profile of the current TE procedure compared with NPS techniques.

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OPHTHALMIC IMAGES

Entopic Image of Dislocated Intraocular Lens

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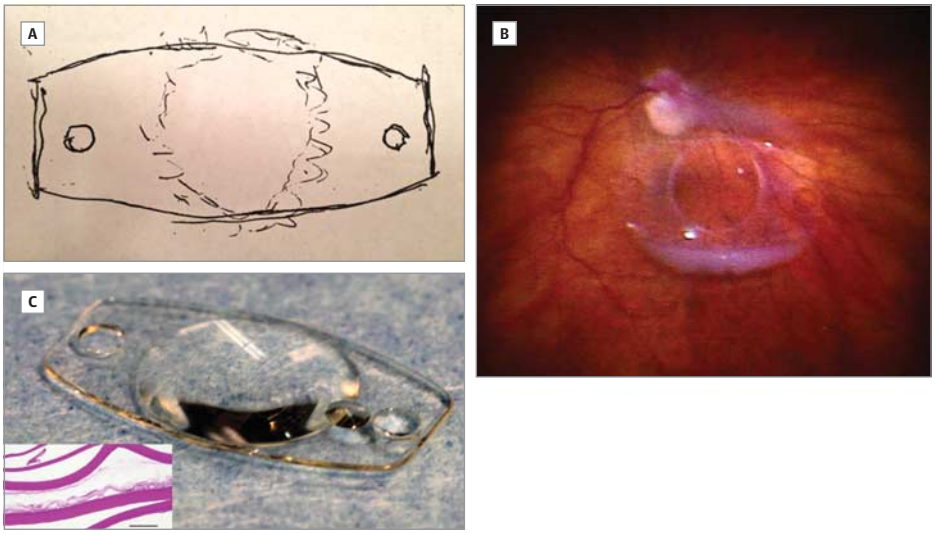

A 67-year-old man, with history of right cataract extraction surgery 10 years earlier then retinal detachment with therapeutic vitrectomy 1 year later, experienced severe blurred vision in the eye for 1 week. Visual blur was interrupted with the transient image of a "gasket," which he could draw better than explain verbally (A). Visual acuity was 20/25 with +8-diopter correction. On reclined fundus examination, a plate haptic intraocular lens (IOL) was observed floating in front of the macula (B). The dislocated IOL was removed surgically (C) and replaced with an anterior chamber IOL. The cloudy edge of the entopic image corresponded to adherent lens capsule to the IOL (C, insert; periodic acid–Schiff; bar = 20 μm).