

Meta-analysis of the efficacy and safety of combined surgery in the management of eyes with coexisting cataract and open angle glaucoma

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Abstract

• **AIM:** To conduct a systematic review and quantitative Meta-analysis of the efficacy and safety of combined surgery for the eyes with coexisting cataract and open angle glaucoma.

• **METHODS:** We performed a systematic search of the related literature in the Cochrane Library, PubMed, EMBASE, Web of Science databases, CNKI, CBM and Wan Fang databases, with no limitations on language or publication date. The primary efficacy estimate was identified by weighted mean difference of the percentage of intraocular pressure reduction (IOPR%) from baseline to end-point, the percentage of number of glaucoma medications reduction from pre- to post-operation, and the secondary efficacy evaluations were performed by odds ratio (OR) and 95% confidence interval (CI) for complete and qualified success rate. Besides, ORs were applied to assess the tolerability of adverse incidents. Meta-analyses of fixed or random effect models were performed using RevMan software 5.2 to gather the consequences. Heterogeneity was evaluated by Chi² test and the I² measure.

• **RESULTS:** Ten studies enrolling 3108 patients were included. The combined consequences indicated that both glaucoma and combined cataract and glaucoma surgery significantly decreased IOP. For deep sclerectomy vs deep sclerectomy plus phacoemulsification and canaloplasty vs phaco-canaloplasty, the differences in IOPR% were not all statistically significant while trabeculotomy was detected to gain a quantitatively greater IOPR% compared with trabeculotomy plus phacoemulsification. Furthermore, there was no statistical significance in the complete and qualified success rate, and the rates of adverse incidents for trabeculotomy vs trabeculotomy plus phacoemulsification.

• **CONCLUSION:** Compared with trabeculotomy plus phacoemulsification, trabeculectomy alone is more effective in lowering IOP and the number of glaucoma medications, while the two surgeries can not demonstrate statistical differences in the complete success rate, qualified success rate, or incidence of adverse incidents.

• **KEYWORDS:** open angle glaucoma; cataract; glaucoma surgery; phacoemulsification; combined surgery; Meta-analysis
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INTRODUCTION

Glaucoma is the most important cause of irreversible blindness worldwide. At least 70 million people are suffering from glaucoma of which 10% are bilaterally blind^[1]. Elevated intraocular pressure (IOP) is the most important risk factor in the development of the disease, although up to 30% of the patients never exceed an IOP within the normal range. Lowering the IOP is most important for glaucoma nowadays. Cataract is an age-related disease. According to the WHO, cataract is the main cause of reversible blindness worldwide. Within the aging population, it is increasingly frequent for cataract and glaucoma to coexist in the same patient. The treatment of coexistent cataract and glaucoma is a prevalently clinical challenge. The treatment of either condition can influence the course of the other.

In recent years, changes in surgical technique have greatly impacted the surgical method to patients with coexisting cataract and glaucoma. Especially, there has been an extensive tendency toward the application of combined phacoemulsification with intraocular lens (IOL) implantation and trabeculectomy (phacotrabeulectomy) as one choice of the surgical management for this situation^[2].

This review article will evaluate the different aspects that affect the choice and result of surgical treatment in patients coexisting open angle glaucoma and cataract. The influence of trabeculectomy on the IOP will be discussed, and the most

Table 1 Characteristics of included studies

First author (year)	Country	Design	No. of patients	No. of eyes	Mean age±SD (y)		M/F (n)		Intervention regimen	Follow up (mo)
					Glaucoma surgery	Combined surgery	Glaucoma surgery	Combined surgery		
Bilgin (2014)	Turkey	CCT	49	52	69.6±7.1	66.6±9.5	15/11	12/11	NPDS vs phaco-NPDS	30.9/28.7
Bull (2011)	Germany	RCT	101	101	67.3±9.9	67.3±9.9	-	-	Canaloplasty vs phacocanaloplasty	36/36
Cillino (2004)	Italy	RCT	65	65	68.6±1.7	71.7±2.0	9/8	8/7	NPDS vs phaco-NPDS PT vs phaco-PT	24/24 24/24
					71.3±1.2	74.6±1.1	8/10	9/6		
D'Eliseo (2003)	Italy	RCT	42	42	71.5	79	15/6	8/13	DS vs Phaco-DS	12/12
Ting (2012)	USA	Pro	713	713	68±15	74±9	181/256	104/155	Trabeculectomy vs cataract extraction and trabeculectomy	12/12
Wishart (2003)	England	Pro	151	192	66.9±10.1	78.9±12.3	13/7	23/33	VC vs phaco-VC DS vs phaco-DS	36.4/32.2 36.3/35.1
					67±11.7	77±8.9	21/22	17/18		
Wishart (2002)	UK	Pro	73	101	75.2	75.2	-	-	VC vs phaco-VC	36/36
Parikh (2016)	USA	Retro	753	753	69±11	72±9	-	-	Trabeculectomy vs phaco-trabeculectomy	12/12
Tetz (2015)	Germany	Retro	112	112	63.5±9.9	74.8±9.0	44/38	12/18	Canaloplasty vs phacocanaloplasty	36/36
Salaga-Pylak (2013)	Poland	Retro	122	122	70.8±6.3	70.7±7.0	32/40	12/38	TrabMMC vs phaco-trabMMC	18/18
Chihara (2011)	Japan	Retro	789	789	60.2±17.6	68.7±13.9	-	-	TrabMMC vs phaco-trabMMC VC vs phaco-VC	6/6
					60.2±17.6	71.4±9.6				
Rotchford (2007)	UK	Retro	63	63	72.8±7.6	79.2±7.5	17/13	16/16	MT vs phaco-MT	43.5/41.8
Marek (2006)	Poland	Retro	35	67	-	-	-	-	DS vs phaco-DS	12/12
Uretmen (2003)	Turkey	Retro	40	40	71.8±7.7	71.1±6.4	10/10	12/8	VC vs phaco-VC	12/12

CCT: Clinical controlled trial; RCT: Prospective randomized controlled trial; Pro: Prospective non-randomized; Retro: Retrospective; NPDS: Non-penetrating deep sclerectomy; Phaco: Phacoemulsification; DS: Deep sclerectomy; VC: Viscocanalostomy; MT: Microtrabeculectomy; PMT: Phaco-microtrabeculectomy; TrabMMC: Trabeculectomy with mitomycin C; PT: Punch trabeculectomy.

recent surgical pressure lowering techniques in combination with phacoemulsification will be reviewed.

MATERIALS AND METHODS

Search Strategy Our Meta-analysis and systematic review were performed in accordance with the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines^[3]. To evaluate relevant studies, we searched the Cochrane Library, PubMed, EMBASE, Web of Science databases, CNKI, CBM and Wan Fang databases for observational studies of the comparison of effect on IOP between combined surgery and anti-glaucoma surgery in the patients with coexisting cataract and open angle glaucoma, with no limitations on language or publication date. The search period was through December 2016. Keywords included open angle glaucoma, glaucoma, combined glaucoma/ataract surgery, canaloplasty, non-penetrating glaucoma surgery, penetrating glaucoma surgery, punch trabeculectomy, deep sclerectomy, viscocanalostomy, glaucoma surgery, filtering surgery, trabeculectomy, bleb, filtering surgery, nonfiltering surgery, eye pressure, IOP, intraocular tension, ocular pressure, ocular tension, intraocular tension, eyeball pressure, eye internal pressure, intraocular hypertension, phacoemulsification, cataract extraction, IOP reduction mode. In addition, we also hand searched the reference of identified case reports and trial reports to seek out relevant articles. There were no language limitations in the search for articles.

Literature Selection Two reviewers (Jiang N and Lin J) independently browsed the titles and abstracts to eliminate the articles which were not consistent with the inclusion criteria. Full text reports of the trials that may accord with the inclusion criteria were browsed for further evaluation. They reviewed the results, and decided whether the trial should be included or excluded by the third reviewer or discussion. We also got in touch with the authors to perfect the data.

Inclusion and Exclusion Criteria The inclusion criteria involved:

Type of studies: All randomized and clinic controlled trials were appropriate for inclusion.

Type of participants: Participants with a diagnosis of open angle glaucoma, pseudoexfoliation glaucoma, or ocular hypertension (OH) which had the clinical features of open angle glaucoma and underwent glaucoma surgery or combined glaucoma/ataract surgery were involved in the trials. The trials with patients who were cyclopia, got uveitis, ocular operation and combined other ocular and systemic disease were excluded. There were no limitations concerning age, gender, ethnicity, the number of participants, use of adjunctive medications or co-morbidities.

Type of interventions: All pre- and post-operative trials included glaucoma/ataract surgery (Table 1).

Type of outcome measures: At least one of the following: pre- and post-operative IOP, percentage of intraocular pressure

reduction (IOPR%), visual acuity, complete success rate, qualified success rate and adverse events.

Data Extraction and Analysis Two reviewers (Jiang N and Lin J) separately extracted the data that conformed to the inclusion criteria. The full papers of selected trials were read to estimate whether they contain useful information. The investigators resolved any disagreement by discussion to reach a consensus. The following data were collected from each trial: 1) publication data: the first author's last name, year of publication, country of origin; 2) features of the participants: gender, age, the setting, sample size; 3) interventions: all surgical methods of lens extraction; 4) follow-up time; 5) outcome calculation: the number of IOP reduction, C-values, visual acuity, complete success rate, qualified success rate and complications.

Outcome Measures The primary result for efficacy was IOPR% and the percentage of the number of glaucoma medications reduction from pre- to post-operation. We used mean and standard deviation (SD) of IOP and IOPR reported directly. When these were not found, we would measure these in accordance with the methods described in the Cochrane Handbook for Systematic Reviews of Interventions: $IOPR = IOP_{baseline} - IOP_{end\ point}$, $SD_{IOPR} = (SD_{baseline}^2 + SD_{end\ point}^2 - SD_{baseline} \times SD_{end\ point})^{1/2}$. IOPR% and SD of IOPR% ($SD_{IOPR\%}$) were assessed by $IOPR\% = IOPR / IOP_{baseline}$ and $SD_{IOPR\%} = SD_{IOPR} / IOP_{baseline}$, apartly. For the percentage of the number of glaucoma medications reduction from pre- to post-operation, we used the same data processing. We used the proportions of qualified and complete success to estimate the efficacy. The target end point IOP without medications was regarded as complete success, and the target end point IOP with or without medications was regarded as qualified success. Besides, we estimated the result of the incidence of adverse incidents, including flat anterior chamber, bleb leakage, hypotony and choroidal effusion.

Statistical Analysis Statistical analyses were executed using RevMan 5.2 software. The pooled odds ratio (OR) was measured for dichotomous outcomes, and weighted mean difference (WMD) was for continuous outcomes. We estimated the heterogeneity among trials by examination of graphical presentations and using the χ^2 and I^2 measure^[4]. We defined $P < 0.05$ for Chi-square or the I^2 measure $> 50\%$ as significant heterogeneity. We applied a fixed effects model to collect results when there was no significant heterogeneity; otherwise, a random effects model was applied (inverse of variance method and DerSimonian and Laird method). $P < 0.05$ demonstrated statistical significance on the test for whole effect. We conducted subgroup analysis to estimate the effect of methodological features in study designs, which were distinguished as prospective (Pro), retrospective (Retro), randomized and nonrandomized.

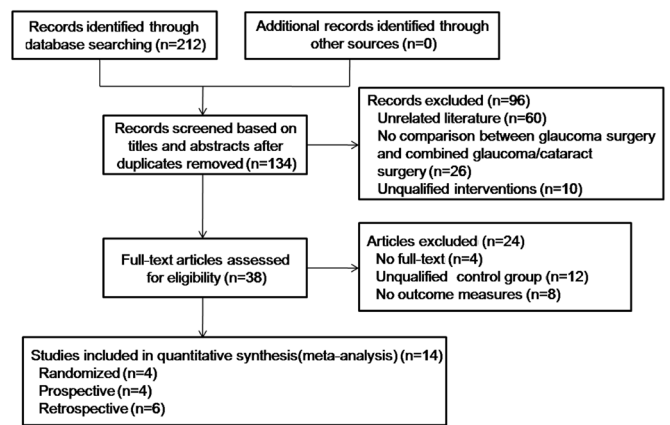


Figure 1 Flow chart of literature search and study selection.

RESULTS

Study Selection In total, 212 papers were determined by the literature search. Of 212, 78 papers were repetitions; thus, these were eliminated. We read the titles and abstracts of the remaining 134 papers and eliminated 96 papers for the reasons outlined in Figure 1. Then, 24 papers were eliminated owing to unqualified control groups and short of required outcomes. At last, 14 appropriate controlled clinical trials that accorded with our inclusion criteria were involved in this systematic review^[5-18].

Quality and Features of the Included Studies Of the 14 included studies, 5 reported the application of deep sclerectomy vs combined deep sclerectomy with phacoemulsification, 5 reported the use of canaloplasty vs phaco-canaloplasty, nevertheless the other 4 reported the trabeculotomy vs combined trabeculotomy with phacoemulsification. The characteristics of the included studies were pooled in Table 1. Four studies were randomized controlled trials (RCTs)^[5-8], which were taken on in Turkey, Germany, Italy, while the other 3 were Pro nonrandomized^[9-10,15] and 7 were Retro^[11-14,16-18]. A sum of 3212 eyes of 3108 patients were included. The follow-up period was from 6 to 43.5mo. The average ages of patients were from 60.2 to 79.2y. As for quality estimation, Downs and Blacks scores of all the included studies were > 16 (50%). Quality assessment was generalized in Table 2.

Results of Meta-analysis

IOPR% (deep sclerectomy vs combined deep sclerectomy with phacoemulsification) Five studies including 254 eyes contrasted deep sclerectomy with deep sclerectomy plus phacoemulsification regarding IOPR%. Moderate heterogeneity was examined between these studies ($P = 0.12$, $I^2 = 46\%$). The combined results indicated the two agents greatly decreased IOP. The differences in IOPR% were not all statistically great (WMD=2.85, 95%CI: -0.69, 6.39; Table 3). We then separated the studies into 3 subgroups in accordance with study design (Pro and Retro nonrandomized, randomized). A statistically significant result was obtained in Retro but not in the Pro randomized and nonrandomized trial (Table 4).

Table 2 Quality scoring components for 14 clinical trials included

First author (year)	Quality score component					Score	
	I	II	III	IV	V	Over all	Percentage (%)
Bilgin (2014)	10	3	5	6	1	25	78.13
Bull (2011)	11	2	5	4	1	23	71.88
Cillino (2004)	11	1	7	5	1	25	78.13
D'Eliseo (2003)	9	1	5	4	1	20	62.5
Ting (2012)	9	1	5	3	1	19	59.36
Wishart (2003)	9	1	5	4	4	23	71.88
Wishart (2002)	9	1	5	3	4	22	68.75
Parikh (2016)	9	1	5	4	4	23	71.88
Tetz (2015)	9	1	5	4	3	22	68.75
Salaga-Pylak (2013)	9	1	5	4	2	21	65.63
Chihara (2011)	10	1	5	3	5	24	75
Rotchford (2007)	10	1	5	3	1	20	62.5
Marek (2006)	9	1	5	3	1	19	59.38
Uretmen (2003)	9	1	4	3	1	18	56.25

Table 3 Percentage IOP decline from baseline comparing glaucoma surgery with combined glaucoma/cataract surgery

Trails	Glaucoma surgery		Combined glaucoma/cataract surgery		WMD (fixed) (95%CI)
	No. of eyes	IOPR% [Mean (SD)]	No. of eyes	IOPR% [Mean (SD)]	
Deep sclerectomy vs combined deep sclerectomy with phacoemulsification ^a					
Bilgin (2014)	26	37.87 (18.85)	23	38.7 (29.76)	0.83 (-13.33, 14.99)
Cillino (2004)	17	41.06 (8.36)	15	41.04 (7.20)	-0.02 (-5.41, 5.37)
D'Eliseo (2003)	21	35.34 (12.4)	21	42.44 (12.58)	7.10 (-0.45, 14.65)
Wishart (2003)	52	40.99 (19.32)	35	38.02 (23.26)	-2.97 (-12.29, 6.35)
Marek (2006)	21	29.59 (17.73)	23	41.39 (13.63)	11.80 (2.39, 21.21)
Total	137		117		2.85 (-0.69, 6.39)
Canaloplasty vs phaco-canaloplasty ^b					
Tetz (2015)	82	33.76 (16.93)	30	42.13 (19.63)	-8.37 (-16.29, -0.45)
Bull (2011)	82	32.61 (17.22)	16	42.39 (21.58)	-9.78 (-20.99, 1.43)
Wishart (2003)	27	35.63 (28.61)	78	30.83 (19.56)	-4.80 (-16.43, 6.83)
Wishart (2002)	26	35.38 (22.52)	75	33.89 (17.57)	1.49 (-8.04, 11.02)
Uretmen (2003)	20	34.45 (20.49)	20	38.4 (24.95)	-3.95 (-18.10, 10.20)
Total	237		219		-3.78 (-8.38, 0.81)
Trabeculotomy vs combined trabeculotomy with phacoemulsification ^c					
Parikh (2016)	255	26.73 (27.94)	498	21.32 (25.74)	5.41 (1.30, 9.52)
Salaga-Pylak (2013)	72	-4.55 (31.37)	50	-13.79 (29.65)	9.24 (-1.72, 20.20)
Ting (2012)	450	34.12 (26.83)	263	21.61 (23.63)	12.51 (8.73, 16.29)
Chihara (2011)	145	52.04 (24.19)	116	24.07 (16.22)	27.97 (23.05, 32.89)
Rotchford (2007)	37	45.12 (28.88)	37	42.98 (18.97)	2.14 (-8.99, 13.27)
Cillino (2004)	18	47.04 (7.29)	15	36.30 (6.94)	10.74 (5.87, 15.61)
Total	977		979		12.65 (10.56, 14.74)

^aTest for heterogeneity $\text{Chi}^2=7.35$, $\text{df}=4$ ($P=0.12$); $I^2=46\%$, Test for overall effect: $Z=1.58$, $P=0.12$; ^bTest for heterogeneity $\text{Chi}^2=5.66$, $\text{df}=4$ ($P=0.23$); $I^2=29\%$, Test for overall effect: $Z=1.61$, $P=0.11$; ^cTest for heterogeneity $\text{Chi}^2=53.56$, $\text{df}=5$ ($P<0.00001$); $I^2=91\%$, Test for overall effect: $Z=11.87$, $P<0.00001$.

Percentage of intraocular pressure reduction (canaloplasty vs phaco-canaloplasty) Five studies including 456 eyes compared canaloplasty with canaloplasty plus phacoemulsification regarding IOPR%. Mild heterogeneity was indicated between studies ($P=0.23$, $I^2=29\%$). The combined results indicated that the two factors greatly declined

IOP. The differences in IOPR% were not all statistically obvious (WMD=-3.78, 95%CI: -8.38, 0.81; Table 3). We then separated the studies into 3 subgroups in terms of the design (Pro and Retro nonrandomized, and randomized). There was statistically significant result in the Retro subgroup (Table 4).

Table 4 Subgroup analysis estimating the effect of trial design on percentage IOP decline

Subgroup	No. of studies	WMD (fixed) (95%CI)	Heterogeneity			Overall effect	
			Chi ²	P	I ² (%)	Z	P
Deep sclerectomy vs combined deep sclerectomy with phacoemulsification							
All trials	5	2.85 (-0.69, 6.39)	7.35	0.12	46	1.58	0.12
RCTs	3	-2.25 (-6.44, 1.95)	2.30	0.32	13	1.05	0.29
Pro	1	2.97 (-6.35, 12.29)	-	-	-	0.62	0.53
Retro	1	-11.80 (-21.21, -2.39)	-	-	-	2.46	0.01
Canaloplasty vs phaco-canaloplasty							
All trials	5	-3.78 (-8.38,0.81)	5.66	0.23	29	1.61	0.11
RCTs	1	-9.78 (-20.99,1.43)	-	-	-	1.71	0.09
Pro	2	2.82 (-4.55, 10.19)	0.19	0.67	0	0.75	0.45
Retro	2	-7.31 (-14.23, -0.40)	0.29	0.59	0	2.07	0.04
Trabeculotomy vs combined trabeculotomy with phacoemulsification							
All trials	6	12.65 (10.56, 14.74)	53.56	<0.00001	91	11.87	<0.00001
RCTs	1	10.74 (5.87, 15.61)	-	-	-	4.33	<0.00001
Pro	1	12.51 (8.73, 16.29)	-	-	-	6.48	<0.00001
Retro	4	13.42 (10.50, 16.35)	52.70	<0.00001	94	9	<0.00001

Table 5 Subgroup analysis estimating the effect of trial design on percentage of the number of glaucoma medications reduction

Subgroup	No. of studies	WMD (fixed) (95%CI)	Heterogeneity			Overall effect	
			Chi ²	P	I ² (%)	Z	P
Canaloplasty vs phaco-canaloplasty							
All trials (Retro)	2	-12.87 (-29.65, 3.91)	3.17	0.07	68	1.5	0.13
Trabeculotomy vs combined trabeculotomy with phacoemulsification							
All trials (Retro)	3	1.55 (-5.06, 8.16)	9.46	0.002	89	0.46	0.65

Percentage of intraocular pressure reduction (trabeculotomy vs combined trabeculotomy with phacoemulsification) Six studies involving 1956 eyes compared trabeculotomy with trabeculotomy plus phacoemulsification regarding IOPR%. High statistical heterogeneity was indicated between studies ($P<0.00001$, $I^2=91\%$). The combined results indicated that the two factors significantly declined IOP. Trabeculotomy obtained a numerically greater IOPR% from baseline, and the differences in IOPR% were statistically significant (WMD=12.65, 95%CI: 10.56, 14.74; Table 3). We then separated the studies into 3 subgroups in line with the design (Retro and randomized). The three subgroups indicated distinct results (Table 4).

Percentage of the number of glaucoma medications reduction in all subgroups Three studies involving 1088 eyes compared trabeculotomy with trabeculotomy plus phacoemulsification regarding percentage of the number of glaucoma medications reduction. Statistical heterogeneity was not applicable between studies. The combined results indicated that both the factors didn't reduce the number of glaucoma medications after surgery. The differences in two retrospective subgroups were not statistically obvious (WMD=1.55, 95%CI: -5.06, 8.16). Two studies including 152 eyes were used to compare canaloplasty with phaco-canaloplasty. There was no

difference between two subgroups (WMD=-12.87, 95%CI: -29.65, 3.91; Table 5).

Complete and Qualified Success (trabeculotomy vs combined trabeculotomy with phacoemulsification) In two researches studied the possibility of complete success, there was no significant difference between the two groups [pooled OR=1.13 (95%CI: 0.51, 2.53); Table 6]. Furthermore, no significant difference was found between trabeculotomy and trabeculotomy plus phacoemulsification in the subgroup analyses in terms of study design [pooled OR=1.43 (95%CI: 0.36, 5.66) for randomized and [pooled OR=1.00 (95%CI: 0.37, 2.71)] for Retro nonrandomized]. Two researches also studied the proportion of patients reaching target IOP with or without medications at follow-up endpoint; the difference in qualified success rate between the two groups was not statistically obvious [pooled OR=0.48 (95%CI: 0.14, 1.72)]. For the subgroup analysis in terms of study design, the difference between groups was not statistically obvious [pooled OR=0.57 (95%CI: 0.05, 7.00)] for randomized and [pooled OR=0.46 (95%CI: 0.10, 1.98)] for Retro nonrandomized] (Table 6).

Adverse Events No significant differences in the incidence of shallow/flat anterior chamber (AC), hyphema and choroid detachment were found between deep sclerectomy and deep

Table 6 Complete success and qualified success comparing trabeculotomy with combined trabeculotomy with phacoemulsification

Trial	Studies (n)	Success rate, n/N		OR (95%CI)	Heterogeneity			Overall effect	
		Trabeculotomy	Phaco-trabe		Chi ²	P	I ² (%)	Z	P
Complete success (≤21 mm Hg)									
All trials	2	36/55	33/52	1.13 (0.51, 2.53)	0.17	0.68	0	0.30	0.77
RCT	1	10/18	7/15	1.43 (0.36, 5.66)	-	-	-	0.51	0.61
Retro	1	26/37	26/37	1.00 (0.37, 2.71)	-	-	-	0	1.00
Qualified success (≤21 mm Hg)									
All trials	2	47/55	48/52	0.48 (0.14, 1.72)	0.02	0.88	0	1.13	0.26
RCT	1	16/18	14/15	0.57 (0.05, 7.00)	-	-	-	0.44	0.66
Retro	1	31/37	34/37	0.46 (0.10, 1.98)	-	-	-	1.05	0.29

Table 7 Subgroup analysis evaluating frequency of postoperative complications in study group

Adverse events	Studies (n)	Crude event rate, n		OR (95%CI)	Heterogeneity			Overall effect	
		Glaucoma surgery	Combined cataract/ glaucoma surgery		Chi ²	P	I ² (%)	Z	P
Deep sclerectomy vs combined deep sclerectomy with phacoemulsification									
Shallow/flat anterior chamber	2	1/69	0/50	2.21 (0.09, 55.42)	-	-	-	0.48	0.63
Hyphema	2	5/69	3/50	1.22 (0.28, 5.38)	-	-	-	0.27	0.79
Choroid detachment	2	3/69	1/50	2.23 (0.22, 22.06)	-	-	-	0.68	0.49
Trabeculotomy vs combined trabeculotomy with phacoemulsification									
Hyphema	2	25/103	24/120	1.28 (0.68, 2.42)	-	-	-	0.77	0.44
Hypotony	2	43/103	45/120	1.19 (0.70, 2.05)	-	-	-	0.65	0.52
Choroid detachment	2	5/103	5/120	1.17 (0.33, 4.17)	-	-	-	0.25	0.80

sclerectomy plus phacoemulsification, with the pooled ORs being 2.21 (95%CI: 0.09, 55.42), 1.22 (95%CI: 0.28, 5.38), and 2.23 (95%CI: 0.22, 22.06) respectively (Table 7). Furthermore, the rates of adverse events did not greatly differ between trabeculotomy and trabeculotomy plus phacoemulsification, with pooled ORs of 1.28 (95%CI: 0.68, 2.42), 1.19 (95%CI: 0.70, 2.05) and 1.17 (95%CI: 0.33, 4.17) for hyphema, hypotony and choroid detachment, respectively.

DISCUSSION

With the emergence of the aging of the population, at least 4% to 10% of the elderly patients with significant cataracts have glaucoma or OH^[19-21]. For glaucoma and cataracts, there are many similar risk elements, including gender, age, smoking, prior trauma, use of topical medication, eye surgery and diabetes. So the question emerges: “How to size up the options for these combined problems of cataract and glaucoma?”

Many surgeries are optional for patients with cataract accompanied with glaucoma. Cataract surgery is a vision-restoring and sometimes life-transforming operation, nevertheless glaucoma filtering procedures were actualized to lessen the IOP in order to lower the risk of visual loss. The surgery of combined phacoemulsification with IOL

implantation and trabeculectomy (phacotrabeculectomy) is extensively used as one surgical treatment for this condition. The advantages of combined surgery are an immediate increase of visual acuity and economical aspects. It may also be important in patients whose medical conditions are too poor to endure multiple surgical procedures.

Systematic reviews of the medical literature can help practitioners determine how to provide the best care^[22]. Nevertheless, there is short of reliable evidence-based conclusions in clinical practice. Therefore, we resorted to Meta-analysis to estimate the clinical safety and efficacy of the combined surgery in patients with coexisting cataract and open angle glaucoma.

In the Meta-analysis, we reviewed the clinically relevant outcome measures of 14 controlled clinical trials. Concerning IOP, this study discovered that both trabeculotomy and trabeculotomy plus phacoemulsification greatly reduced IOP, but in comparison with trabeculotomy plus phacoemulsification, trabeculotomy alone reduced IOP more efficiently, resulting in a greatly higher percentage of IOP and glaucoma medications reduction. One possible reason for the finding may be that combined surgery prolongs the operation time and increases the risk of postoperative complication^[7]. There was no

significant difference in complete and qualified success rates between the two groups. It is difficult to draw credible conclusions due to the reason for the small sample size and short follow-up duration.

In all glaucoma surgical techniques, trabeculectomy has been the most popular surgery to be combined with phacoemulsification. The main risk of trabeculectomy and phacotrabeculectomy is ocular hypotony and its consequences^[5]. Adverse events were similar concerning the two types. It may also be related with a small sample size and short follow-up duration.

Trabeculectomy is the preferred filtration procedure in combined surgery. However, new filtering surgery techniques known as “non-perforating” have been introduced, such as *ab externo* trabeculectomy, deep sclerectomy and Stegmann’s viscocanalostomy^[23]. They all make a scleral ablation towards Schlemm’s canal to create a space for the aqueous humour defluxion^[24]. So, in our Meta-analysis, we observe the IOP lowering efficacy in canaloplasty vs phaco-canaloplasty and deep sclerectomy vs combined deep sclerectomy with phacoemulsification subgroups.

As for IOP assessment, we also found both deep sclerectomy and deep sclerectomy plus phacoemulsification significantly decreased IOP, but for the outcomes of deep sclerectomy alone and deep sclerectomy plus phacoemulsification, there were no statistically significant differences in IOPR%. The result was similar concerning IOP lowering efficacy in canaloplasty and canaloplasty plus phacoemulsification groups. Moreover, no statistical difference was found in evaluating frequency of postoperative complications between deep sclerectomy and combined deep sclerectomy with phacoemulsification group. This may be related with a small sample size and short follow-up duration.

Our study had some advantages. Firstly, we strictly conformed to the Cochrane Handbook for Systematic Reviews of Interventions and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement, involving the literature search, data extraction, quality assessment and statistical analysis. This procedure makes our conclusions more reliable and scientific. Secondly, we actualized the subgroup analysis in accordance with study design in order to make the conclusions credible.

Besides, there were several limitations: 1) Randomization: There were 4 RCTs, 3 Pro nonrandomized, and 7 Retro in the 14 included studies. Only 3 RCT studies included sufficient information on how to actualize RCTs and describe the performance of allocation concealment. The potential selection bias may occur if inappropriate methods of RCTs were performed. 2) Masking: Only 1 study used masking, while others did not find masking, which may lead to measurement and performance bias. 3) Heterogeneity: Significant heterogeneity

in the studies may indicate differences in age, gender, sample size, differences in definition of complete and qualified success, and outcome of measurements. A random effects model was used when statistically significant heterogeneity was fit. 4) Publication bias: We used manual and electronic searches to gather all potential relevant trials to prevent publication bias. Nevertheless, we may not have considered some papers, especially those published in languages other than Chinese or English. Besides, the test for publication bias was not done due to a limited number of trials involved in our Meta-analysis. 5) Follow-up: The short follow-up time may influence the long-term results.

As a result, this Meta-analysis firstly answers the question of whether combined cataract/glaucoma surgery is more effective and safer than glaucoma surgery. The results suggest that trabeculectomy alone is more effective in lowering IOP than trabeculectomy plus phacoemulsification; however, trabeculectomy is comparable with trabeculectomy plus phacoemulsification concerning qualified success rate, complete success rate and incidence of adverse events. Besides, there was no statistically significant concerning IOP lowering efficacy in deep sclerectomy and deep sclerectomy plus phacoemulsification, and there was a similar result in terms of IOP lowering efficacy in canaloplasty and canaloplasty plus phacoemulsification groups. Although there are some limitations, we believe that the results of this Meta-analysis are sufficient credibility and can give enlightenment to future clinical practice. Besides, we require the more RCTs with larger sample sizes and systematic studies to further confirm the presented results.

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