

# Surgical treatment for primary angle closure – glaucoma: a Meta analysis

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## Abstract

• **AIM:**To evaluate the efficacy and safety of trabeculectomy, phacotrabeculectomy plus intraocular lens implantation (phacotrab+IOL group) and phacoemulsification with IOL (phaco+IOL) in primary angle-closure glaucoma(PACG).

• **METHODS:** It was a systematic review and meta-analysis, randomized controlled trials(RCT) and clinical controlled trials (CCT) were collected through electronic searches of the Cochrane Library, PubMed, EMBASE, Wanfang Database online, Chinese journal Full-text Database, Chinese Scientific Journals Full-text Database (from the date of building the database to October 2010) We also checked the bibliographies of retrieved articles. All the related data that matched our standards were abstracted. The quality of included trials was evaluated according to the Dutch Cochrane Centre. RevMan 5.0 software was used for Meta-analysis.

• **RESULTS:** A total of 5 RCT and 11 CCT involving 1495 eyes were included. The results of meta-analysis showed that phacotrab+IOL group was superior than trabeculectomy(trab group) (MD -3.93,95% CI [-7.31, -0.54]) which was also superior than phaco+IOL group(MD 0.52,95%CI [0.10, 0.95]) in decreasing Intraocular Pressure(IOP). Phacotrab group(MD -1.45,95%CI [-1.68, -1.22])and phaco group (MD-1.12,95% CI [-1.87, -0.37])are both deeper than trab group in the anterior chamber depth. In increasing the coefficient of

outflow facility of aqueous humor (C values) there was no statistical difference in the three groups. And there was no statistical difference between phacotrab groups and phaco groups in visual acuity but phacotrab group was superior than phaco group (MD 1.07, 95%CI [0.73, 1.40])in the use of IOP-lowering drugs. There was no statistical difference among three groups.

• **CONCLUSION:** Current evidence suggests that phacotrab+IOL group was superior than trab group which was also superior than phaco+IOL group in decreasing IOP. Phacotrab group and phaco group are both deeper than trab group in the anterior chamber depth. Phacotrab group was superior than phaco group in the use of IOP-lowering drugs.

• **KEYWORDS:** trabeculectomy; phacoemulsification; phacotrabeculectomy;primary angle-closure glaucoma; meta-analysis  
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## INTRODUCTION

**G**laucoma is the second important cause of blindness. There are 67 million patients all over the world<sup>[1]</sup>. Specific structural abnormalities of optic nerve head and patterns of visual field loss are irreversible. It causes heavy burden on patients and society.

The primary glaucomas can be classified as open angle glaucoma (POAG) or angle-closure glaucoma (PACG). Angle-closure glaucoma is prevalent in Eastern Asian and China where the patients is more common than western country<sup>[2]</sup>. In China, PACG is mainly in the old which have 3.5 million patients. More than 25% patients can be caused blindness<sup>[3]</sup>. The main therapy of PACG is surgery. Three surgeries involving trabeculectomy, phacotrabeculectomy plus intraocular lens implantation (phacotrab+IOL group) and phacoemulsification with IOL(phaco+IOL) are common used in treating PACG. But there are still some controversies in efficacy, safety and complications<sup>[4-8]</sup>. We use Meta-analysis to collect articles which include

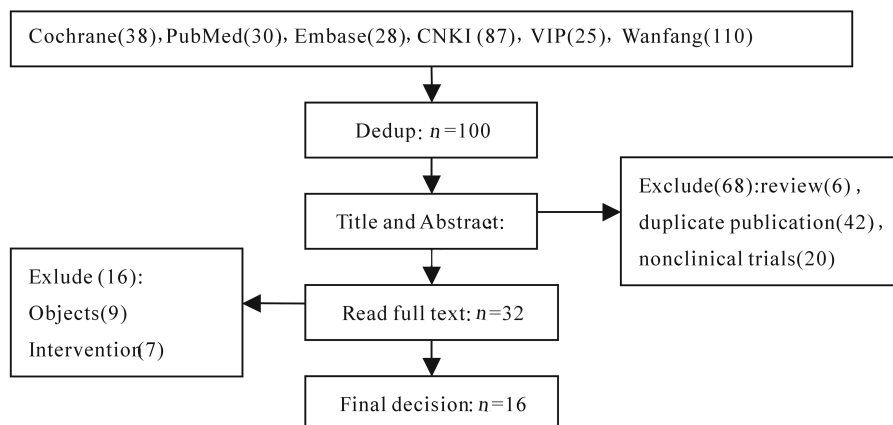


Table 1 Selection flowchart

randomized controlled trials and clinical controlled trials to evaluate the efficacy and safety of the three surgeries.

## MATERIALS AND METHODS

### Inclusion and Exclusion Criteria

**Types of studies** All randomized and clinic controlled trials were eligible for inclusion.

**Types of participants** Participants in the trials were people with a diagnosis of acute and chronic angle closure glaucoma. The trials with patients who were cyclopia, got uveitis, ocular operation, laser therapy and combined other ocular and systemic disease were not included. There were no restrictions with respect to age, gender, ethnicity, co-morbidities, use of adjunctive medications or the number of participants.

**Types of interventions** All trials include trabeculectomy *vs* phacotrab+IOL group or trabeculectomy *vs* phaco+IOL or phacotrab+IOL group *vs* phaco+IOL (Table 1).

**Types of outcome measures** Main outcomes: intraocular pressure (IOP) reduction, coefficient of outflow facility (C-values), anterior chamber depth(ACD), visual acuity.

Other outcomes: surgery success rate, adjunctive therapy (AT), trabecular iris angle (TIA), angle opening distance (AOD500), trabecular ciliary processes distance(TCPD).

**Search Methods for Identification of Studies** We combined uncontrolled terms and mesh terms with "primary angle closure glaucoma, trabeculectomy, phacoemulsification, cataract extraction, lens extraction" to search PUMED (1966-2010.11), EMBASE(1974-2010.11), Cochrane library (2010; issue 12), CNKI, (1994-2010.11), VIP(1989-2010.11), Wanfang (1997-2010.11), Google and we also searched conference paper and abstract of American Association of Ophthalmology and Association for Research in Vision and Ophthalmology.

**Data Collection and Assessment of Methodological Quality** Two authors independently assessed the methodological quality of each included study according to

the guidelines developed by the Netherlands 24 Dutch Cochrane Collaboration <sup>[9]</sup>, the quality involved methods of baseline, allocation, masking, intend to treat, collection of data, losses to follow up, adjunctive therapy when data were difficult to determine from the paper the authors were contacted for more information. The three authors compared the extracted data and the discrepancies were resolved by discussion.

**Data Analysis** We will calculate a summary risk ratio for dichotomous outcomes. The mean difference will be calculated for continuous outcomes. Standardized mean difference will be reported if outcomes are measured using different scales. We will attempt to quantify the proportion of variability within included studies that is explained by heterogeneity using the I2 statistic (Higgins 2002). If the I2 statistic is greater than 50% we will consider it as statistical heterogeneity, if there is no substantial heterogeneity, we combine the study results in a meta-analysis using a random-effects model. We will examine funnel plot symmetry for evidence of other sources of heterogeneity. If there is no substantial heterogeneity and statistical heterogeneity as per the I2 statistic we will combine the results of the included studies in a meta-analysis using a fix-effects model. If there is substantial heterogeneity and statistical heterogeneity, instead we will take subgroup analysis or present the studies in a tabulated or narrative summary. The software we used is RevMan5.0<sup>[10]</sup>.

## RESULTS

**Results of the Search** Sixteen eligible trials were included in our final meta-analysis (Table 2). It involved 5 randomized controlled trials <sup>[19-22,25]</sup> and 11 nonrandomized controlled trials <sup>[11-18, 23, 24, 26]</sup>. The total sample capacity is 1495 eyes. 3 trials <sup>[11-13]</sup> involved trabeculectomy (trab), phacotrab+IOL group and phaco+IOL. Two trials <sup>[16,26]</sup> compared trab with phacotrab, 5 trials <sup>[14, 15, 23-25]</sup> compared trab with phaco, 6 trials<sup>[17-22]</sup> compared phacotrab with phaco.

**Table 2 Study characteristic and quality assessment**

Trials	Study type	Eyes	Intervention	Baseline	Allocation concealment	Intent to treat	Masking	Followup (month)	Completefollowup (%)	Adjunctive therapy	Outcome measures
Tham,C.C.Y.2008	RCT	72	Phacotrab. Phaco	YES	YES	YES	YES	24	100%	YES	IOP, VA, AT
Tham,C.C.Y.2009	RCT	51	Phacotrab. Phaco	YES	YES	YES	YES	24	100%	YES	IOP, VA, AT
Tham,C.C.Y.2010	RCT	72	Phacotrab. Phaco	YES	YES	YES	YES	12	100%	YES	ACD, AOD500, TCPD
Tham,C.C.Y.2010	RCT	123	Phacotrab. Phaco	YES	YES	YES	YES	24	100%	YES	complication
Peng 2009	RCT	70	Trab. Phaco	YES	Unclear	Unclear	Unclear	6	100%	YES	IOP, AOD500, ACD, VA, AT
Zhang 2006	NONRCT	72	Trab Phacotrab Phaco	YES	NO	NO	NO	20	100%	YES	IOP, AOD500, ACD, VA, C-values, VA, AT, complication
Zhang 2007	NONRCT	97	Trab Phacotrab Phaco	YES	NO	NO	NO	16	100%	YES	IOP, AOD500, ACD, VA, C-values, AT, complication
Wang 2007	NONRCT	48	Trab Phacotrab Phaco	YES	NO	NO	NO	24	100%	YES	IOP, surgery success rate, AOD500, AOD, AT, VA, complication
Lv 2010	NONRCT	138	Trab Phacotrab	YES	NO	NO	NO	<1	100%	YES	IOP, ACD, VA, complication
Du 2007	NONRCT	160	Trab Phacotrab	YES	NO	NO	NO	6	100%	YES	ACD, TIA, AOD500, TCPD
Zhang 2004	NONRCT	100	Trab Phaco	YES	NO	NO	NO	20	100%	YES	IOP, AOD500, ACD, VA, complication
Tang 2008	NONRCT	145	Trab Phaco	YES	NO	NO	NO	1	100%	YES	IOP, AOD500, ACD, VA, C-values, complication
Hu 2010	NONRCT	65	Trab Phaco	YES	NO	NO	NO	1	100%	YES	IOP, ACD, VA, complication
Song 2010	NONRCT	129	Trab Phaco	YES	NO	NO	NO	6	100%	YES	IOP, surgery success rate, AOD500, AT, VA, complication
Sheng 2004	NONRCT	37	Phacotrab Phaco	YES	NO	NO	NO	6	100%	YES	IOP, ACD, AT, complication
Chu 2008	NONRCT	116	Phacotrab Phaco	YES	NO	NO	NO	3	100%	YES	IOP, AOD500, ACD, complication

**Study Quality Assessment** Five trials<sup>[19-22, 25]</sup> which did not mentioned location and masking were randomized controlled trials, in which 4 trials<sup>[19-22]</sup> used table of random number, 1 trials<sup>[25]</sup> did not account for the particular method. The other 11 trials<sup>[10-25]</sup> were nonrandomized controlled trials.

**Intraocular Pressure** Ten trials<sup>[11-15, 17, 19, 20, 23, 24]</sup> reported the intraocular pressure

**Trab vs Phacotrab**

Three CCTs<sup>[11-13]</sup> reported the intraocular pressure. The results of meta-analysis was [MD=3.93, 95%CI(-7.31,-0.54),  $P=0.02$ ]. There was statistical difference between the two surgeries (Table 3).

**Phacotrab vs Phaco**

Two RCTs<sup>[19, 20]</sup> and 4 CCTs<sup>[11-13, 17]</sup> reported the intraocular pressure. The results of Meta-analysis was [SMD=0.34, 95% CI (-0.02,0.70),  $P=0.06$ ] (RCT), there was no statistical difference between the two surgeries; [SMD 1.37, 95%CI [0.69, 2.05],  $P=0.003$ ] (CCT), there is statistic difference between the two surgeries (Table 3).

**Trab vs Phaco**

Seven CCTs<sup>[11-15, 23, 24]</sup> reported the intraocular pressure. The results of meta-analysis was [SMD=0.52, 95% CI (0.10, 0.95),  $P=0.02$ ]. There is statistical difference between the two surgeries (Table 3).

**Anterior Chamber Depth(ACD)**

Eight trials<sup>[11-17, 23]</sup> reported the change of anterior chamber depth(ACD)

**Trab vs Phacotrab**

Three CCTs<sup>[11,13,16]</sup> reported the anterior chamber depth. The result of meta-analysis was [MD=-1.45, 95%CI(-1.68,-1.22),  $P< 0.00001$ ]. There is statistic difference between the two surgeries (Table 3).

**Phacotrab vs Phaco**

Four CCTs<sup>[11-13,17]</sup> reported the anterior chamber depth. The result of meta-analysis was [MD=-0.07, 95%CI(-0.19,-0.06),  $P=0.29$ ]. There is statistical difference between the two surgeries (Table 3).

**Trab vs Phaco**

Five CCTs<sup>[11,13,15,23]</sup> reported the anterior chamber depth. The result of meta-analysis was [MD=-1.12, 95%CI(-1.87,-0.37),  $P=0.003$ ]. There was statistical difference between the two surgeries (Table 3).

**Coefficient of Outflow Facility(C-values)**

Three trials<sup>[11,13,23]</sup> reported the change of coefficient of outflow facility(C-values)

**Trab vs Phacotrab**

Two CCTs<sup>[11,13]</sup> reported coefficient of outflow facility. The result of meta-analysis was [MD=-0.03, 95%CI(-0.06,-0.00),  $P=0.03$ ]. There is statistic difference between the two surgeries.(Table 3).

**Phacotrab vs Phaco**

Two CCTs<sup>[11,13]</sup> reported coefficient of outflow facility. The result of meta-analysis was [MD=0.03, 95%CI(-0.00,0.06),  $P=0.06$ ]. There is no statistic difference between the two surgeries (Table 3).

**Trab vs Phaco**

Three CCTs<sup>[11,13,23]</sup> reported coefficient of outflow facility. The result of meta-analysis was [MD=0.01, 95%CI(-0.01,0.03),  $P=0.06$ ]. There is no statistic difference between the two surgeries (Table 3).

**Visual Acuity**

Two RCTs<sup>[19,20]</sup> reported visual acuity. The result of meta-analysis was [MD=-0.10, 95%CI(-0.23,0.03),  $P=0.13$ ]. There is no statistic difference between Phacotrab and Phaco (Table 3).

**Table 3 Result of Meta Analysis**

outcome	group	Study type	Study quantum	eyes	Tests for heterogeneity		Result of Meta analysis			
					$I^2(\%)$	$P$	Statistical method	Effectsize and 95% credibility interval	$P$	
Primary outcome	Intraocular pressure	Trab	non-RCT	3	152	0	0.97	Fixed (IV)	MD -3.93 [-7.31,-0.54]	0.02
		Phacotrab	non-RCT	4	174	74	0.009	Random (IV)	SMD 1.37[0.69,2.05]	0.003
		Phacotrab Phaco	RCT	2	123	0	0.80	Random (IV)	SMD 0.34 [-0.02, 0.70]	0.06
		total	non-RCT RCT	7	297	81	<0.0001	Random (IV)	SMD 1.00 [0.41, 1.58]	0.008
	Chamber depth	Trab Phaco	non-RCT	7	584	83	<0.00001	Random (IV)	SMD 0.52 [0.10, 0.95]	0.02
		Trab Phacotrab	non-RCT	3	275	79	0.008	Random (IV)	MD -1.45 [-1.68, -1.22]	<0.00001
		Phacotrab Phaco	non-RCT	4	174	0	0.82	Fixed (IV)	MD- 0.07 [-0.19, 0.06]	0.29
	C-values	Trab Phaco	non-RCT	5	429	99	<0.00001	Random (IV)	MD -1.12 [-1.87, -0.37]	0.003
		Trab Phacotrab	non-RCT	2	115	0	1.00	Fixed (IV)	MD-0.03 [-0.06, -0.00]	0.03
		Phacotrab Phaco	non-RCT	2	104	0	1.00	Fixed (IV)	MD0.03 [-0.00, 0.06]	0.06
		Trab Phaco	non-RCT	3	264	0	0.89	Fixed (IV)	MD0.01 [-0.01, 0.03]	0.43
	Visual acuity	Phacotrab Phaco	RCT	2	123	0	1.00	Fixed (IV)	MD-0.10 [-0.23, 0.03]	0.13
	Adjunctive therapy	Phacotrab Phaco	RCT	2	123	0	0.78	Fixed (IV)	MD1.07 [0.73, 1.40]	<0.00001
	Secondary outcome	Surgery success rate	Trab Phacotrab	non-RCT	2	102	0	0.98	Fixed (M-H)	RR0.95[0.86,1.05]
Phacotrab Phaco			non-RCT	2	93	5	0.31	Fixed (M-H)	RR1.11[0.97,1.28]	0.12
Trab Phaco		non-RCT	3	224	0	0.59	Fixed (M-H)	RR1.03[0.97,1.09]	0.37	

### Adjunctive Therapy

Two RCTs <sup>[19,20]</sup> reported adjunctive therapy. The result of meta-analysis was [MD=1.07, 95%CI(0.73,1.40),  $P<0.00001$ ]. There is no statistic difference between phacotrab and phaco (Table 3).

### Surgery Success Rate

Three CCTs <sup>[12,13,24]</sup> reported the success rate of surgery (involve conditional success). There were 274 eyes. 105 eyes were successful in Trab group which involved 109 eyes ; 48 eyes were successful in Phacotrab group which involved 50 eyes; 109 eyes were successful in Phaco group which involved 115 eyes. There is no statistic difference between Phacotrab and Phaco (Table 3).

### Trab vs Phacotrab

The result of meta-analysis was [RR=0.95[0.86,1.05],  $P=0.34$ ]. There is no statistic difference between Trab and Phacotrab (Table 3).

### Phacotrb vs Phaco

The result of meta-analysis was [RR1.11[0.97,1.28],  $P=0.12$ ]. There is no statistic difference between Phacotrab and Phaco (Table 3).

### Trab vs Phaco

The result of meta-analysis was [RR1.03[0.97,1.09],  $P=0.37$ ]. There is no statistic difference between Trab and Phaco (Table 3).

### Trabecular Iris Angle

One nonRCT <sup>[16]</sup> reported trabecular iris angle of Trab surgery, which showed there was no significant improvement after surgery ( $P>0.05$ ); 1 nonRCT <sup>[16]</sup> and 1RCT<sup>[22]</sup> reported trabecular iris angle of Phacotrab surgery, which showed

there was significant improvement after surgery ( $P<0.05$ ); 1RCT <sup>[22]</sup> reported trabecular iris angle of Phaco surgery, which showed there was significant improvement after surgery ( $P<0.001$ ).

### Angle Opening Distance(AOD500)

One nonRCT <sup>[16]</sup> reported angle opening distance of Trab surgery, which showed there was no significant improvement after surgery ( $P>0.05$ ); 1 nonRCT <sup>[16]</sup> and 1RCT<sup>[22]</sup> reported angle opening distance of Phacotrab surgery, which showed there was significant improvement after surgery ( $P<0.05$ ); 1 RCT <sup>[22]</sup> reported angle opening distance of Phaco surgery, which showed there was significant improvement after surgery ( $P<0.001$ ).

### Trabecular Ciliary Processes Distance

One nonRCT <sup>[16]</sup> reported trabecular ciliary processes distance of Trab surgery, which showed there was no significant improvement after surgery ( $P>0.05$ ); 1 nonRCT<sup>[16]</sup> and 1RCT <sup>[22]</sup> reported angle trabecular ciliary processes distance of Phacotrab surgery, which showed there was significant improvement after surgery ( $P<0.05$ ); 1RCT <sup>[22]</sup> reported trabecular ciliary processes distance of Phaco surgery, which showed there was significant improvement after surgery ( $P<0.001$ ).

### DISCUSSION

The meta-analysis showed that: (1) the three surgeries can decrease intraocular pressure, in which Phacorab is superior than Trab which is superior than Phaco; (2) the three surgeries can deep anterior chamber depth, in which Phacorab is superior than Trab which is superior than Phaco. Phaco trab group and phaco group are both deeper

than trab group in the anterior chamber depth; (3)coefficient of outflow facility: the three surgeries can increase coefficient of outflow facility, but there was no statistic difference in the three surgeries; (4)the three surgeries can improve visual acuity. 2 RCT showed that there was no statistic difference between Phacotrab and Phaco. (5) adjunctive therapy: Phacotrab was superior than Phaco, there lacked Trab trials in current evidences. (6)the three surgeries had no statistic difference in surgery success rate. Phaco trab and Phaco were superior than Trab in angle opening, trabecular iris angle (TIA), angle opening distance (AOD500), trabecular ciliary processes distance; (7) complications: the primary complications in Trab were low intraocular pressure, shallow of anterior chamber, choroidal detachment, hyphema; the primary complications in Phacotrab were shallow of anterior chamber, corneal bedewing, descemets membrane wrinkle, hyphema; the primary complications in Phaco were corneal bedewing, descemets membrane wrinkle, chamber fibrin exudation. Phaco was superior to Trab and Phacotrab in complications. There still existed some disadvantages and limitations in our meta-analysis: we only involved 5RCTs which did not reported the location and masking, so there existed performance and measurement bias. According to current evidence, most of trials did not used randomized controlled methods strictly. We should adopt appropriate randomized controlled methods, location, masking to decrease bias; we should make accurate standard of follow-up time to improve quality and applicability.

Current evidence showed that Phacotrab was superior than the other two surgeries in intraocular, chamber depth, visual acuity, adjunctive therapy, Trab is superior than Phaco in intraocular pressure, it is not superior than the other two surgeries in chamber depth, Trab and Phacotrab were not superior than Phaco.

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