·Clinical Research·

Efficacy and tolerability of one-site versus two-site phacotrabeculectomy: a meta-analysis

He-Nan Liu, Xun Li, Qing-Zhu Nie, Xiao-Long Chen

Department of Ophthalmology, Shengjing Hospital, China Medical University, Shenyang 110004, Liaoning Province, China

Correspondence to: He-Nan Liu. Department of Ophthalmology, Shengjing Hospital, China Medical University, Shenyang 110004, Liaoning Province, China. liuhn@sj-hospital.org

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Abstract

• AIM: To evaluate the efficacy and tolerability of one-site versus two-site phacotrabeculectomy in the treatment of patients with coexisting cataract and glaucoma.

• METHODS: A comprehensive literature meta-analysis was performed according to the Cochrane Collaboration methodology to identify controlled clinical trials comparing one-site with two-site phacotrabeculectomy. The studies meeting the predefined criteria were reviewed systematically by meta-analysis. Efficacy estimates were measured by standardised mean difference (SMD) for the percentage intraocular pressure (IOP) reduction from baseline to end point, odds ratio (OR) for the percentage having a best-corrected visual acuity (BCVA) of 0.5 or better after surgery and relative risk (RR) for complete success rates. Tolerability estimates were measured by RR for adverse events. All of outcomes were reported with 95% confidence interval (CI). Data were synthesised by Stata 10.1 for Windows.

• RESULTS: Two-site phacotrabeculectomy was associated with numerically greater, and significant efficacy than one-site in lowering IOP (SMD, -0.19; 95% CI, -0.33 to -0.04; P= 0.01). Numerically greater, but nonsignificant proportions of two-site patients than one-site patients had a BCVA of 0.5 or better (OR, 0.65; 95% CI, 0.30 to 1.39; P=0.26).Numerically greater, but nonsignificant proportions of two-site patients than one-site patients achieved the target IOP without anti-glaucoma medication at the end point (RR, 0.94; 95% CI, 0.84 to 1.04; P =0.22). Furthermore, there was nonsignificant difference in adverse events between two surgical procedures.

• CONCLUSION: The efficacy of two-site phacotrabeculectomy appears to be superior to one-site phacotrabeculectomy. One-site and two-site phacotrabeculectomy are similarly tolerable in postoperative adverse events.

• KEYWORDS: phacotrabeculectomy; one-site; two-site; meta-analysis

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INTRODUCTION

With the increasing elderly population and concurrent longevity in life expectancy, there has been an increase in the incidence of coexisting visually significant cataract and glaucoma. One of the challenges in the management of surgical procedure is difficulty in solving these two problems simultaneously. Phacoemulsification alone may be beneficial in some cases, which results in better intraocular pressure (IOP) than planned extracapsular cataract extraction procedures, and performing the glaucoma filtering surgery first and the cataract surgery later may best serve others [1]. However, there has been a widespread shift towards the use of combined phacotrabeculectomy as the surgical treatment of choice for coexisting cataract and glaucoma in recent years[2-4].

Phacotrabeculectomy can be performed either using one-site or two-site incisions [5]. The earliest clinical studies of phacotrabeculectomy which is known as a one-site procedure reported surgical results using the same the scleral tunnel incision for both the phacoemulsification and trabeculectomy parts of the surgery. The introduction of the temporal incision for phacoemulsification has allowed surgeons to perform two-site procedure, with a prelimbal filtering incision for the trabeculectomy and a separate clear cornea incision for phacoemulsification[5]. Comparing of the two surgical procedures, previous studies generally had small sample sizes and showed conflicting results, which greatly hindered researchers drawing correct conclusions.

A meta-analysis of controlled clinical trials (prospective or retrospective) was conducted to assess the efficacy and tolerability of two surgical procedures for the management of coexisting cataract and glaucoma: one-site and two-site phacotrabeculectomy. This meta-analysis was designed to help resolve ambiguity regarding optimal management of

coexisting cataract and glaucoma by pooling the outcome of available studies. Our analysis controlled for differences in study sizes and patient characteristics. However, we recognize the limitations introduced by differences in study protocols, publication bias, and the quality of studies.

MATERIALS AND METHODS

Search Strategy A computerized literature search was conducted in the PubMed, EMBASE, Scientific Citation Index and Cochrane Controlled Trials Register for relevant articles published up to May 2009. And extensive search for meeting archives, including the annual meeting abstracts of American Association of Ophthalmology (AAO) and Association for Research in Vision and Ophthalmology (ARVO) was also carried out up to May 2009. These databases were searched systematically using the following key words: phacotrabeculectomy, phacoemulsification and trabeculectomy, combined phacoemulsification and trabeculectomy, combined phaco/trabeculectomy, combined cataract and glaucoma surgery, combined cataract-glaucoma surgery, one-site phacotrabeculectomy, two-site phacotrabeculectomy. The search strategy used both keywords and Medical Subject Headings (MeSH) terms. There were no limits placed on the language of publication. All potentially relevant non-English publications were to be translated into English for further assessment. Literature reference proceedings were searched manually at the same time. The title and abstract of all potentially relevant articles were screened to determine their relevance. Then, full articles were scrutinized if the title and abstract were ambiguous. References identified from bibliographies of pertinent articles or books also were retrieved. References of included publications were reviewed until no further relevant studies were found.

Inclusion and exclusion criteria Only controlled clinical trials directly comparing between one-site and two-site phacotrabeculectomy in patients with coexisting cataract and glaucoma were included, anti-metabolites could be used intraoperatively. Studies needed to have measured efficacy, tolerability or both in humans. Outcome variables included at least one of the following primary outcome variables: intraocular pressure reduction (IOPR), the percentage having a best-corrected visual acuity (BCVA) of 0.5 or better after surgery, complete success rates and adverse events, or relevant data. Abstracts from conferences and full texts without raw data available for retrieval, duplicate publications, letter and review were excluded.

Studies selection The assessment of the titles and abstracts for eligibility was conducted by two independent reviewers (Liu HN and Nie QZ). Articles of potential interest were retrieved and their inclusion was reassessed. Disagreement at each step was resolved with discussion between the two reviewers. We obtained the full article of any study that seemed to fit the inclusion criteria.

Data extraction Two reviewers (Liu HN and Nie QZ) performed the data extraction that were included independently. Any differences were resolved by discussion to reach consensus among the investigators. A customized form was used to record authors of study, publication year, location, design, follow-up time, sample size, patient characteristics, interventions, baseline and endpoint values, and adverse events.

Outcome measures For efficacy, we used the percentage intraocular pressure reduction (IOPR%) in preoperative to postoperative IOP. Secondary efficacy measure was the percentage having a postoperative BCVA of 0.5 or better and complete success rate, which was defined as the proportion of patients achieved the target IOP without anti-glaucoma medication at the end point. We assessed tolerability to phacotrabeculectomy by considering the proportions of patients with adverse events, including hyphema, choroidal detachment, bleb leak, hypotony, posterior capsule opacification and shallow anterior chamber.

Statistical Analysis Extracted data were pooled for summary estimates using Stata 10.1 for Windows (StataCorp LP, College Station, TX, USA). Continuous outcomes were expressed as standardised mean difference (SMD), with values <0 favouring two-site phacotrabeculectomy, and dichotomous outcomes as odds ratio (OR) or relative risk (RR). Both outcomes were reported with 95% confidence interval (CI). P<0.05 was considered statistically significant on the test for overall effect. Intertrial statistical heterogeneity was explored using the DerSimonian and Laird Q test, with calculated I^2 indicating the percentage of the total variability in effect estimates among trials that is due to heterogeneity rather than chance. If heterogeneity tests were non-significant, fixed effects models were used, as they provide narrower 95% CIs than the equivalent random effects models, which are more appropriate where significant heterogeneity is detected. The Begg and Egger tests were used to assess for publication bias.

For studies that only reported absolute values for IOP at baseline and end point, the IOPR, standard deviation (SD) of the IOPR (SD_{IOPR}), IOPR% and SD of the IOPR% ($SD_{IOPR\%}$) were calculated as follows: $IOPR = IOP_{baseline} - IOP_{end\ point}$, $SD_{IOPR} = (SD_{baseline}^2 + SD_{end\ point}^2 - SD_{baseline}(SD_{end\ point})^{1/2}$, $IOPR\% = IOPR/IOP_{baseline}$, $SD_{IOPR\%} = SD_{IOPR}/IOP_{baseline}$. The difference of IOPR and its SD between groups was then calculated for each individual study.

Table 1 Characteristics of included studies

Authors	Year	Country	Design	Follow-up (χ, mo)	Participants (n)	Age (χ, yr)	M/F	Eyes(n)	
								1-site	2-site
Wyse *et al* [6]	1998	USA	Pro	16.5	33	75.0	7/26	20	13
el Sayyad *et al* [7]	1999	Saudi Arabia	Pro	12	76	65.5	NA	37	39
Borggrefe *et al* [8]	1999	Germany	Pro	19	50	74.3	16/34	25	25
Mandić *et al* [9]	2000	Croatia	Pro	12	55	71.6	17/22	27	31
Zou *et al* [10]	2001	China	Retro	18.9	45	61.2	29/16	29	18
Isasi-Saseta *et al* [11]	2002	Spain	Retro	6	35	76.4	16/19	19	16
Dong *et al* [12]	2004	China	Retro	12	35	60.9	16/19	15	25
Shingleton *et al* [13]	2006	USA	Retro	12	130	NA	NA	71	64
Cotran *et al* [14]	2007	USA	Pro	36	76	75.4	26/50	43	43
Buys *et al* [15]	2008	Canada	Pro	24	79	70.9	29/50	39	40
Nassiri *et al* [16]	2008	Iran	Retro	18	113	68.8	55/58	61	52

NA: not available

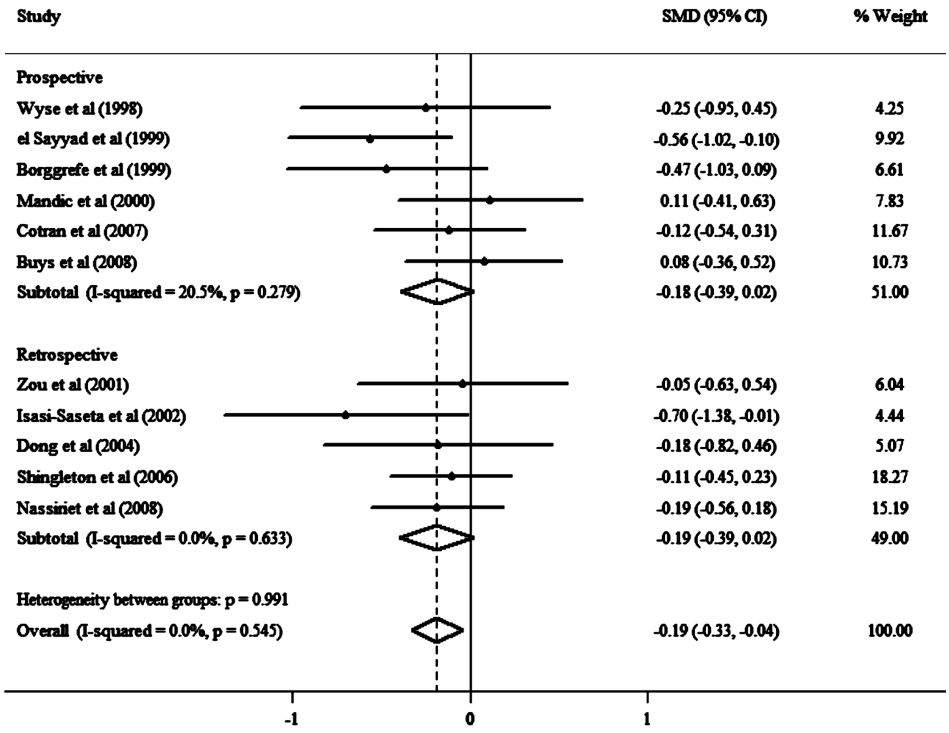

Figure 1 SMD in patients with one-site and two-site phacotrabeculectomy on IOPR% from the fixed effects model

RESULTS

Description of studies Seventeen potentially relevant controlled clinical trials associated with one-site and two-site phacotrabeculectomy in the treatment of coexisting cataract and glaucoma were identified through the literature search. Among these, four articles without exact raw data available for retrieval according with the exclusion criteria were excluded; two abstract reports were found in the annual meeting abstracts of ARVO; eleven controlled clinical trials that fulfilled the eligibility criteria were included in the present meta-analysis [6-16]. These were published in 8 different journals in English, Chinese and Spanish and no unpublished data were identified(Table 1).

Efficacy Effect sizes (SMD in patients with one-site and two-site phacotrabeculectomy on IOPR%) from the fixed effects model for all are prospective and retrospective studies, respectively (Figure 1).Two-site phacotrabeculectomy was associated with numerically lower IOPR% relative to one-site in all studies, except for those by Mandic *et al* [9] and Buys *et al* [15]. Both surgical procedures significantly decreased IOP. The pooled summary estimate for all 11 studies favoured two-site procedure, and showed two-site phacotrabeculectomy was more effective than one-site in lowering IOP (SMD,-0.19; 95% CI,-0.33 to -0.04; P= 0.01). No significant heterogeneity was presented between studies in the one-site versus two-site groups(χ^2 = 8.86, P= 0.55, I^2 =0.0%). Then, we divided the studies into two subgroups according to study design (prospective and

Table 2 Adverse events between one-site and two-site phacotrabeculectomy

Adverse events	Studies (*n*)	Crude event rate, *n*/*n*		RR (95%CI)	Heterogeneity			Overall effect	
		One-site	Two-site		*Q*	*P*	I^2 (%)	*Z*	*P*
Hyphema	8	25/266	24/271	1.03 (0.61, 1.75)	3.04	0.88	0.0	0.11	0.92
Choroidal detachment	4	10/166	12/159	0.80 (0.36, 1.80)	0.96	0.81	0.0	0.53	0.59
Hypotony	4	13/124	12/123	1.03 (0.55, 1.92)	6.27	0.10	52.1	0.09	0.93
Bleb leak	3	21/175	11/159	1.74 (0.87, 3.48)	0.82	0.66	0.0	1.57	0.12
Posterior capsule opacification	2	13/98	10/91	1.26 (0.59, 2.70)	0.12	0.73	0.0	0.60	0.55
Shallow anterior chamber	2	4/66	4/57	0.90 (0.27, 2.95)	2.70	0.10	63.0	0.18	0.86

retrospective). Both prospective and retrospective subgroups showed that two-site approach was associated with numerically lower IOPR relative to one-site procedure, but no significant difference was found. There was no significant heterogeneity in these analysis. Publication bias was also tested using the Begg test (P= 0.28) and the Egger test(P=0.34), and both produced non-statistically significant results, providing no evidence of publication bias.

Three studies involving 166 eyes compared one-site with two-site procedure in visual acuity after phacotrabeculectomy (69% one-site and 78% two-site) [7,8,12]. No statistical heterogeneity was observed between studies (χ^2= 0.10, P=0.95, I^2=0.0%). The combined result showed there was nonsignificant statistically difference in the percentage having a BCVA of 0.5 or better (OR, 0.65; 95% CI, 0.30 to 1.39, P=0.26).Seven studies, involving 426 eyes, reported the proportions of two-site patients than one-site patients achieved the target IOP without anti-glaucoma medication at the end point (73% one-site and 79% two-site)[6-10,14,15]. No statistical heterogeneity was showed between studies (χ^2= 8.71, P=0.19, I^2=31.1%), and the difference between groups was not statistically significant (RR, 0.94; 95% CI, 0.84 to 1.04; P= 0.22).

Tolerability Adverse events in controlled clinical trials comparing between one-site and two-site phacotrabeculectomy are showed in Table 2. Hyphema was one of the most commonly reported postoperative adverse events. However, no significant differences comparing between one-site and two-site phacotrabeculectomy were found in the incidence of hyphema, choroidal detachment, hypotony, bleb leak, posterior capsule opacification and shallow anterior chamber, with the pooled RRs being 1.03 (95% CI 0.61 to 1.75), 0.80 (95% CI 0.36 to 1.80), 1.03 (95% CI 0.55 to 1.92), 1.74 (95% CI 0.87 to 3.48), 1.26 (95% CI 0.59 to 2.70) and 0.90 (95% CI 0.27 to 2.95), respectively.

DISCUSSION

Two-site phacotrabeculectomy now is used frequently as a primary intervention for the management of coexisting cataract and glaucoma [5]. However, it remains controversial as to whether it provides a better outcome than one-site phacotrabeculectomy in the treatment of coexisting cataract and glaucoma [6-16]. Previous studies have prospectively evaluated the efficacy and tolerability of one-site phacotrabeculectomy compared with two-site procedure [6-9,14,15]. The overwhelming majority of studies presented that two-site procedure was associated with a numerically lower but nonsignificant reduction in IOP efficaciously compared with one-site approach [6-8,14]. Variations of sample sizes and follow-up time within these studies prohibit attribution of treatment outcome to one type of intervention in these reports and make it difficult to draw a valid conclusion regarding the superiority of one procedure over another. We identified various studies that provided comparative treatment outcomes of one-site and two-site procedure and controlled for variations in study characteristics to identify a preferred intervention for the management of coexisting cataract and glaucoma.The results of this meta-analysis imply that, with available evidence from controlled clinical trials, the efficacy of two-site phacotrabeculectomy appears to be superior to one-site for the management of coexisting cataract and glaucoma, and there is nonsignificant difference in tolerability between two surgical procedures. Two-site phacotrabeculectomy was associated with numerically greater, and significant, efficacy than one-site in lowering IOP, numerically greater, but nonsignificant, proportions of two-site patients than one-site patients had a BCVA of 0.5 or better, and numerically greater, but nonsignificant, proportions of two-site patients than one-site patients achieved the target end point IOP. Two-site procedure was comparable with one-site in lowering adverse events. However, the greater IOPR effect and slightly greater

BCVA increase effect of two-site procedure over one-site that we have shown does not necessarily indicate a greater surgical effect with two-site procedure. This is because IOP and BCVA merely are surrogate measures for phacotrabeculectomy, and the two surgical procedures may act through pathways independent of this mechanism. There are many preoperative and postoperative key factors to determine which surgical approach to carry out. Factors that may favor a one-site procedure are faster surgical time, less corneal endothelial cell loss, and surgeon experience with a superior approach. Factors that may favor a two-site approach are surgeon familiarity with temporal phacoemulsification, orbital physiognomy, reduced the surgically-induced astigmatism, conjunctival scar, limited superior access, ergonomic comfort for the surgeon, and absence of irrigation outflow underneath the conjunctival flap during phacoemulsification that might potentially affect intraoperative anti-metabolite effect.

The results of our meta-analysis should be interpreted with caution because there may be some limitations in this meta-analysis. One limitation of our meta-analysis is that the analysis of clinically relevant outcome measures that were based on data pooled from trials and follow-up periods were not uniform. Another potential source of heterogeneity in the results is the assessment criteria of success. Success was defined as target end point IOP, and there were several different criteria of the normal IOP, such as IOP $\leqslant$ 18, $\leqslant$ 20, and $\leqslant$21mm Hg. Although such assessments of success are widely used as outcome measures in clinical trials, further research is still needed to fully determine their validity, reliability, and sensitivity to choose the best one. A third limitation of this meta-analysis is that publication bias cannot be excluded fully, because with no sufficient studies, the Begg and Egger tests have a low power to detect publication bias. Finally, some of the controlled clinical trials included in the analysis are not prospective randomized controlled trials, but retrospective or prospective nonrandomized, which may fail to detect actual results. The likelihood of bias was minimized by developing a detailed protocol before initiating the study, by performing a meticulous search for published and unpublished studies, especially published in other languages, and by using explicit methods for study selection, data extraction, and statistical analysis.

In summary, based on the findings of this meta-analysis, we conclude that the efficacy of two-site phacotrabeculectomy appears to be superior to one-site in IOP control, and the proportions of patients in both surgical procedures achieving BCVA of 0.5 or better were comparable, as well as complete success rate. Both two-site and one-site procedure were well tolerated. Pragmatic randomized controlled trials are needed to further evaluate the efficacy and tolerability of two-site phacotrabeculectomy in the treatment of patients with coexisting cataract and glaucoma. In particular, multicenter, long-term, large sample size, randomized, controlled trials are warranted.

REFERENCES

1 Shingleton BJ, Pasternack JJ, Hung JW, O'Donoghue MW. Three and five year changes in intraocular pressures after clear corneal phacoemulsification in open angle glaucoma patients, glaucoma suspects, and normal patients. *J Glaucoma* 2006;15(6):494-498

2 Tham CC, Li FC, Leung DY, Kwong YY, Yick DW, Lam DS. Microincision bimanual phacotrabeculectomy in eyes with coexisting glaucoma and cataract. *J Cataract Refract Surg* 2006;32(11):1917-1920

3 Bayer A, Erdem U, Mumcuoglu T, Akyol M. Two-site phacotrabeculectomy versus bimanual microincision cataract surgery combined with trabeculectomy. *Eur J Ophthalmol* 2009;19(1):46-54

4 Tham CC, Kwong YY, Leung DY, Lam SW, Li FC, Chiu TY, Chan JC, Lam DS, Lai JS. Phacoemulsification versus combined phacotrabeculectomy in medically uncontrolled chronic angle closure glaucoma with cataracts. *Ophthalmology* 2009; 116(4):725-731

5 Kobayashi H, Kobayashi K. Randomized comparison of the intraocular pressure-lowering effect of phacoviscocanalostomy and phacotrabeculectomy. *Ophthalmology* 2007;114(5):909-914

6 Wyse T, Meyer M, Ruderman JM, Krupin T, Talluto D, Hernandez R, Rosenberg LF. Combined trabeculectomy and phacoemulsification: a one-site *vs* a two-site approach. *Am J Ophthalmol* 1998;125(3):334-339

7 el Sayyad F, Helal M, el-Maghraby A, Khalil M, el-Hamzawey H. One-site *vs* 2-site phacotrabeculectomy: a randomized study. *J Cataract Refract Surg* 1999;25 (1):77-82

8 Borggrefe J, Lieb W, Grehn F. A prospective randomized comparison of two techniques of combined cataract-glaucoma surgery. *Graefes Arch Clin Exp Ophthalmol* 1999;237(11):887-892

9 Mandic Z, Ivekovic R, Petric I, Zoric-Geber M. Glaucoma triple procedure: a one-site *vs* a two-site approach. *Coll Antropol* 2000;24(2):367-371

10 Zou Y, Lin Z, Zhou J. Comparison between one-site and two-site incision in phacotrabeculectomy. *Chin J Ophthalmol* 2001;37(5): 335-337

11 Isasi-Saseta MB, Urcelay-Segura JL, Zamora-Barrios J, Ortega-Usobiaga J, Moreno Garc í a-Rubio B, Cort é s-Vald é s C. Trabeculectomy and phacoemulsification. One site *vs* two site approach. A comparative study. *Arch Soc Esp Oftalmol* 2002;77(12):677-680

12 Dong DQ, Chen G, Hou XW. Clinical observation of the combination of phacoemulsification and trabeculectomy. *Chin J Ophthalmol* 2004;40(5):295-298

13 Shingleton BJ, Price RS, O'Donoghue MW, Goyal S. Comparison of 1-site *vs* 2-site phacotrabeculectomy. *J Cataract Refract Surg* 2006;32(5):799-802

14 Cotran PR, Roh S, McGwin G. Randomized comparison of 1-site and 2-site phacotrabeculectomy with 3-year follow-up. *Ophthalmology* 2008;115 (3): 447-454

15 Buys YM, Chipman ML, Zack B, Rootman DS, Slomovic AR, Trope GE. Prospective randomized comparison of one- *vs* two-site Phacotrabeculectomy two-year results. *Ophthalmology* 2008;115(7):1130-1133

16 Nassiri N, Nassiri N, Rahnavardi M, Rahmani L. A comparison of corneal endothelial cell changes after 1-site and 2-site phacotrabeculectomy. *Cornea* 2008;27(8):889-894