

Comparison of hydrophobic and hydrophilic intraocular lens in preventing posterior capsule opacification after cataract surgery

An updated meta-analysis

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Abstract

Background: Posterior capsular opacification (PCO) is a common long-term complication of cataract surgery. Intraocular lens design and material have been implicated in influencing the development of PCO. This study evaluated the association of hydrophobic and hydrophilic intraocular lenses on preventing PCO.

Methods: Medline, Cochrane, EMBASE, and Google Scholar databases were searched until August 3, 2016, using the following search terms: cataract, posterior capsule opacification, and intraocular lens. Eligible studies included randomized controlled trials (RCTs), retrospective, and cohort studies.

Results: Eleven studies were included in the study with a total of 889 eyes/patients. The overall analysis revealed that hydrophobic intraocular lenses were associated with lower Nd:YAG laser capsulotomy rates than hydrophilic lenses [odds ratio (OR) = 0.38, 95% confidence interval (95% CI) = 0.16–0.91, $P = .029$]. Hydrophobic intraocular lenses were also associated with lower subjective PCO score (diff. in means: -1.32 , 95% CI = -2.39 to -0.25 , $P = .015$) and estimated PCO score (diff. in means: -2.23 ; 95% CI, -3.80 to -0.68 , $P = .005$) as compared with hydrophilic lenses. Objective PCO score was similar between lens types. (diff. in means: -0.075 ; 95% CI, -0.18 to 0.035 ; $P = .182$). Pooled analysis found that visual acuity was similar between hydrophobic and hydrophilic intraocular lenses (diff. in means: -0.016 ; 95% CI, -0.041 to 0.009 , $P = .208$).

Conclusion: In general, PCO scores and the rate of Nd:YAG laser capsulotomy were influenced by intraocular lens biomaterial. Lens made of hydrophobic biomaterial were overall superior in lowering the PCO score and the Nd:YAG laser capsulotomy rate, but not visual acuity.

Abbreviations: CI = confidence intervals, Nd:YAG = neodymium-doped yttrium aluminum garnet, OR = odds ratio, PCO = posterior capsular opacification, RCTs = randomized controlled trials, SD = standard deviations.

Keywords: biomaterial, cataract, hydrophilic, hydrophobic, intraocular lens, Nd:YAG laser capsulotomy, posterior capsule opacification

1. Introduction

Patients having cataract surgery with intraocular lens implantation have great benefit from the development of surgical techniques and new types of lens materials.^[1] However,

posterior capsular opacification (PCO) remains a common long-term complication of the procedure. PCO can result in reduction of visual performance 1 or 2 years postcataract surgery.^[2] The rates of PCO following cataract surgery are estimated to be 12% at year 1, 21% at year 3, and 28% at 5 years after surgery.^[2] Treatment of PCO with neodymium-doped yttrium aluminum garnet (Nd:YAG) laser capsulotomy is effective; however, complications, including retinal detachment, macular edema, and increases in intraocular pressure, may also occur.^[3]

Studies have found that several surgical- and intraocular lens related factors may play a role in the development of PCO.^[1,4–11] Two aspects of the intraocular lenses seem important: the biomaterials and the edge design of the lenses. Acrylic intraocular lenses that have hydrophobic or hydrophilic surfaces have a long history in clinical practice and are associated with lower PCO and rates of Nd:YAG laser capsulotomy than lenses made of other biomaterials such as silicone or hydrogel.^[6,8,12] Acrylic material has a relative low propensity to induce cell proliferation in the capsular bag.^[9] In addition, studies have shown that lenses with sharp edge design inhibit lens epithelial cell migration resulting in a reduced rate of PCO.^[4,5]

Only a limited number of studies have compared hydrophobic and hydrophilic lenses in relationship to development of PCO or the rate of Nd:YAG laser capsulotomy. Most of the studies are limited by the small sample size. Three prior meta-analyses

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assessed the efficacy of different intraocular lens material in preventing PCO lowering the rate of Nd:YAG laser capsulotomy.^[1,10,11] The aim of the current study was to provide an updated evaluation on the efficacy of hydrophobic and hydrophilic intraocular lens materials in preventing PCO and reducing the rate of Nd:YAG laser capsulotomy.

2. Methods

2.1. Search strategy

The following terms were used to search Medline, Cochrane, EMBASE, and Google Scholar databases until August 3, 2016: cataract, posterior capsule opacification, intraocular lens. Eligible studies included randomized controlled trials (RCTs), retrospective studies, and cohort studies. In addition, references of papers were hand-searched to identify other potential studies.

Studies had to have evaluated patients >18 years of age who had age-related (senile) cataracts and who had undergone cataract surgery that included either a hydrophobic or hydrophilic intraocular lens (1, 2, or 3 pieces). Eligible studies had to have reported quantitatively outcomes of interest. Excluded studies included case series, case reports, letters, comments, and personal communications. Studies that investigated patients with congenital cataract or traumatic cataract, or who studied pediatric patients were excluded. Studies were identified and considered for inclusion and the data were extracted by 2 independent reviewers, and a third reviewer was consulted to decide any differences in opinions.

2.2. Study selection and data extraction

The following information/data were extracted from studies that met the inclusion criteria: the name of the first author, year of publication, study design, number of patients in each group, patient age and gender, and the major outcomes.

2.3. Quality assessment

The quality of the included studies was assessed using the Cochrane Collaboration tool for assessing risk of bias.^[13]

2.4. Outcome measures

The primary outcomes were Nd:YAG laser capsulotomy rate, PCO score (subjective, estimated, and objective), and visual acuity.

2.5. Statistical analysis

Study characteristics were summarized as mean, mean \pm standard deviations (SD), mean (range: min., max.), or median (min., max.) for continuous variables and n (%) for gender. The primary outcomes were summarized as n or n (%) for categorical data and mean \pm SD or mean (range: min, max) or median (interquartile range, IQR: 1st and 3rd quartiles) or mean with P values for continuous data. An effect size, odds ratio (OR) with corresponding 95% confidence intervals (95% CIs) for categorical data and difference in means with 95% CI for continuous data were calculated for each individual study and for all studies combined.

For Nd:YAG capsulotomy rate, OR >1 indicated patients with hydrophobic treatment had a higher rate than patients who

received hydrophilic treatment; OR <1 indicated patients with hydrophobic treatment had a lower rate of Nd:YAG capsulotomy than those with hydrophilic treatment; OR = 1 indicated the Nd:YAG capsulotomy rate was similar between treatments. For PCO score and visual acuity, a difference in means >0 indicated patients with hydrophobic treatment had higher PCO score or visual acuity than patients with hydrophilic treatment; a difference in means <0 indicated patients with hydrophobic treatment had lower values than those with hydrophilic treatment; and a difference in means of 0 indicated the PCO score and visual acuity were similar between lens types.

A χ^2 test for homogeneity was conducted, and an inconsistency index (I^2) and Q statistics were determined. If the I^2 statistic was >50%, a random-effects model (DerSimonian–Laird method) was used. Otherwise, a fixed-effects model (Mantel–Haenszel method) was employed. Combined effects were calculated, and a 2-sided P value of <.05 was considered significant. A sensitivity analysis was conducted using a leave-one-out approach. Publication bias was not performed due to <10 studies being included in the meta-analyses.^[14] All data were arranged using Microsoft Office Excel2007 (Microsoft Corp, Redmond, WA) and all analyses performed using Comprehensive Meta-Analysis statistical software, version 2.0 (Biostat, Englewood, NJ).

2.6. Ethics

This study did not involve human subjects, so informed consent was not required. In addition, no approval was required from an institutional review board.

3. Results

The search identified 503 potential studies, of which 448 were excluded after initial abstract and title review for not meeting the inclusion/exclusion criteria (Fig. 1). Fifty-five studies underwent full-text review and 44 were excluded for not comparing hydrophobic and hydrophilic lenses, not reporting outcomes of interest, being a single-arm study, did not quantitatively compare the 2 types of lenses, and the data could not be analyzed.

A total of 11 studies were included in the study with a total of 889 eyes/patients (Table 1).^[3,12,15–23] All included studies were RCTs. The number of patients in each study ranged from 24 to 120. The mean age at the time of the operation ranged from 65.8 to 75 years and the length of follow-up ranged from 1 to 9 years. Among the studies, all intraocular lenses were acrylic and the piece number were either 1 or 3. The optic edge of the intraocular lenses varied across the studies.

Treatment outcomes are summarized in Table 2. In general, the PCO score (i.e., subjective, objective, and estimated score) was lower with hydrophobic intraocular lenses than with hydrophilic lenses for across the studies. In addition, hydrophobic lenses result in lower rate of Nd:YAG capsulotomy than hydrophilic lenses in most of the included studies.

3.1. Meta-analysis

3.1.1. Nd:YAG capsulotomy rate. Eight studies (Chang et al [2017], Shcriefl et al,^[21] Iwase et al,^[18] Vasavada et al,^[19] Kang et al,^[20] Kugelberg et al,^[16] Kang et al,^[15] and Kugelberg et al^[3]) reported complete data for rate of Nd:YAG capsulotomy for each type of lens. A random-effects model of analysis was used as high heterogeneity was seen (Q statistic = 19.77, I^2 = 64.6%, P = .006). The overall pooled analysis indicated that the hydrophobic

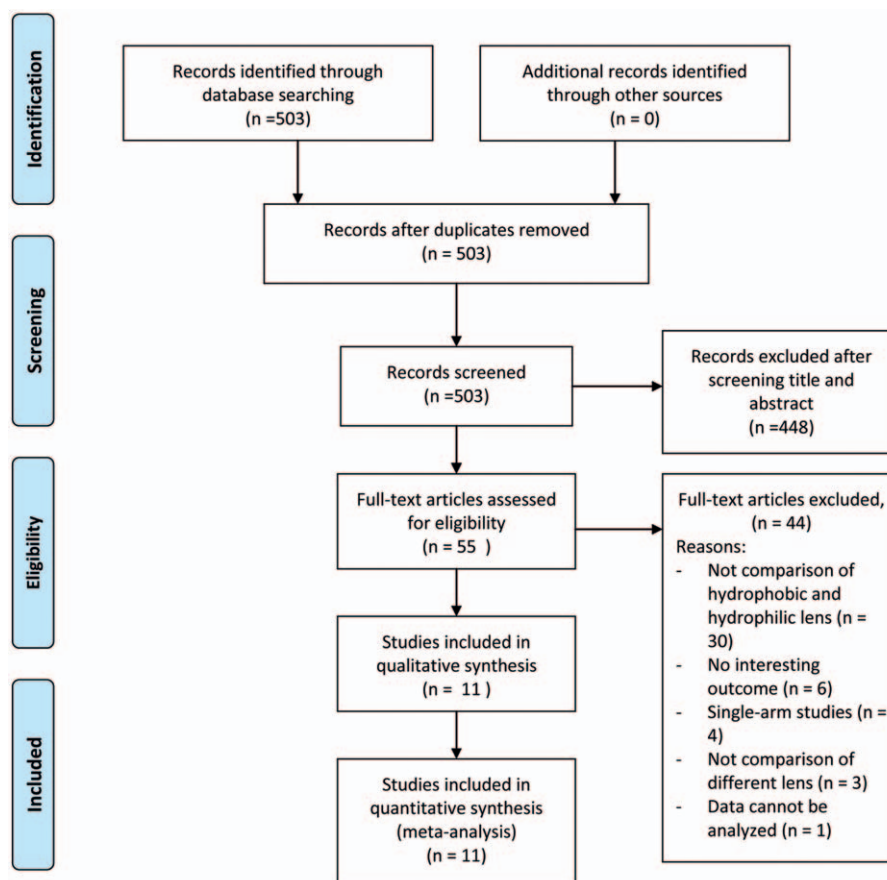


Figure 1. Study selection flow diagram.

intraocular lenses resulted in a lower rate of Nd:YAG capsulotomy than hydrophilic lenses. (OR: 0.38; 95% CI, 0.16–0.91; $P=.029$) (Fig. 2).

3.1.2. PCO score. Two studies had complete data for subjective PCO score (Schrieffl et al^[21] and Gangwani et al^[23]), 5 had full data for objective PCO score (Chang et al [2016], Schrieffl et al [2015], Kang et al,^[20] Kang et al,^[15] and Healy et al [2005]) and 2 (Schrieffl et al^[21] and Vasavada et al^[19]) reported complete data for estimated PCO score. These studies were included in the pooled analysis. A random effect model was performed due to the presence of large heterogeneity in the data (subjective PCO score: Q statistic=2.39, $I^2=58.26\%$, $P=.122$; objective PCO score: Q statistic=44.37, $I^2=90.99\%$, $P<.001$; estimated PCO score: Q statistic=7.90, $I^2=87.34\%$, $P=.005$). Pooled analysis found that hydrophobic lenses were associated with lower subjective PCO score (diff. in means: -1.32 , 95% CI= -2.39 to -0.25 , $P=.015$) and estimated PCO score (diff. in means: -2.23 ; 95% CI, -3.80 to -0.68 , $P=.005$) as compared with hydrophilic intraocular lenses. Objective PCO score was similar between lens types. (diff. in means: -0.075 ; 95% CI, -0.18 to 0.035 ; $P=.182$) (Fig. 3).

3.1.3. Visual acuity (LogMAR). Six studies (Chang et al [2016], Schrieffl et al,^[21] Kang et al,^[20] Cleary et al,^[17] Kugelberg et al,^[16] and Kang et al^[15]) reported full data for visual acuity and were included in the analysis. A random effect model was performed due to the high degree of heterogeneity observed in the data (Q statistic=49.16, $I^2=89.83\%$, $P<.001$). Pooled analysis found that visual acuity was similar between hydrophobic and

hydrophilic intraocular lenses (diff. in means: -0.016 ; 95% CI, -0.041 to 0.009 , $P=.208$) (Fig. 4).

3.2. Sensitivity analysis

Sensitivity analysis was performed using the leave-one-out approach in which separated meta-analyses were done with each study is left out in turn. The direction and magnitude of the combined estimates did not markedly differ with the removal of and one study (Supplemental Figure 1, 2, 3, <http://links.lww.com/MD/B923>) indicating that the meta-analysis had good reliability and that the data were not overly influenced by any study.

3.3. Quality assessment

All 11 included studies were RCTs and used random sequence generation for randomization of patients (Fig. 5). The 11 studies had no selective reporting and low risk of reporting bias. However, only 4 studies had allocation concealment and 3 used double blinding. Six studies had no incomplete outcome data and had a low risk of attrition bias. None of the studies used intent-to-treat analysis. Overall, the studies were of good quality.

4. Discussion

PCO is a common long-term complication of cataract surgery. Intraocular lens design and material have been implicated in influencing the development of PCO. The current study, which

Table 1

Summary of the clinical characteristics of enrolled studies.

Ref.	Study design	Bilateral/ unilateral	n (eyes/patients)	Group	IOL				Length of follow-up, y	
					Piece number	Optic material	Optic edge	Mean age, y		Male (%)
Chang (2016)	RCT	Unilateral	60/60	Hydrophobic	NA	Acrylic	sharp-edged	73.4	38%	9
Schrieff et al ^[21]	RCT	Bilateral	60/60	Hydrophilic	3	Acrylic	Square edge	72.1	32%	4
Gangwani et al ^[23]	RCT	Bilateral	60/60	Hydrophilic	1	Acrylic	6.0 mm optic diameter	72	NA	4
Iwase et al ^[18]	RCT	Bilateral	35/35	Hydrophobic-hydrophobic copolymer	1	Acrylic	Double-square edged	73.4	32%	4
Vasavada et al ^[19]	RCT	Bilateral	63/63	Hydrophobic	1	Acrylic	Sharp square edge	65.8	70%	3
			33/33	Hydrophilic		Acrylic				
			31/31	Hydrophobic		Acrylic	Sharp square edge	67.3	65%	3
			31/31	Hydrophilic		Polyhydroxyl copolymer	Double-squared edge			
Cleary et al ^[17]	RCT	Bilateral	24/24	Hydrophobic	3	Acrylic	NA	73.5	46%	2
			24/24	Hydrophilic	1					
Kang et al ^[20]	RCT	Unilateral, simple cataract group	28/28	Hydrophilic	3	Acrylic	Double squared edge	68.2	NA	1
			30/30	Hydrophobic			Double round edge			
			37/37	Hydrophilic			Double squared edge	67.1		
			39/39	Hydrophobic			Double round edge			
Kang et al ^[15]	RCT	Unilateral	50/50	Hydrophobic	3	Acrylic	NA	66.5	46%	1
			50/50	Hydrophilic				69.5	42%	
Kugelberg et al ^[16]	RCT	Unilateral	58/60	Hydrophobic	1	Acrylic	NA	72	32%	2
			57/60	Hydrophilic				73	46%	
Kugelberg et al ^[3]	RCT	Unilateral	59/59	Hydrophobic	1	Acrylic	Square-edged	73	NA	1
			57/57	Hydrophilic				72		
Heatley et al ^[12]	RCT	Bilateral	53/53	Hydrophobic	1	Acrylic	NA	NA	NA	1
			53/53	Hydrophilic						

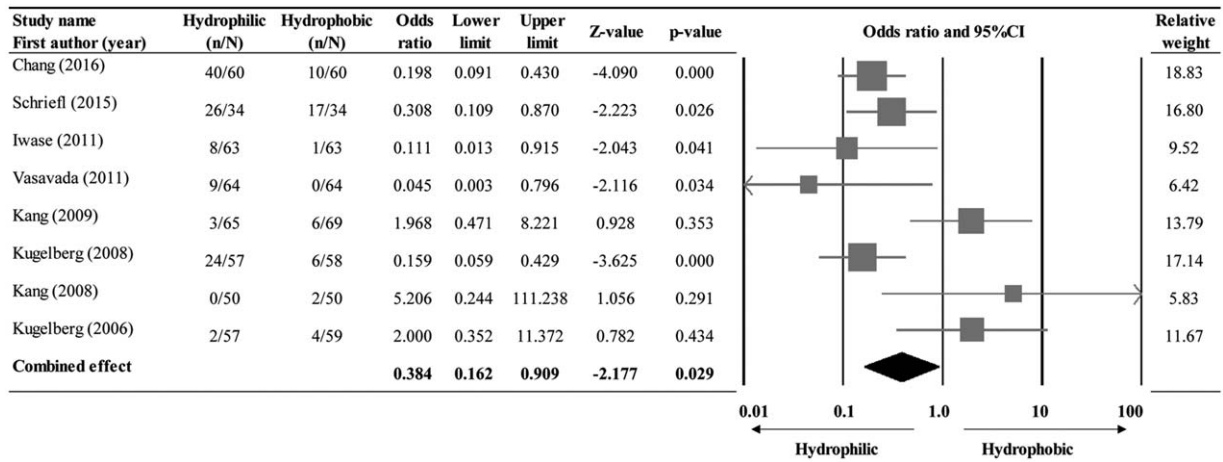
RCTs = randomized controlled trial.

Table 2

Summary of the results of PCO scores, visual acuity, and Nd:YAG capsulotomy among the enrolled studies.

Ref.	hydrophobic/hydrophilic	Subjective PCO score	Objective PCO score	Estimated PCO score	CDVA or BDVA, best corrected distance visual acuity (logMAR)	Nd:YAG capsulotomy, n (%)
Chang (2016)	Hydrophobic	NA	Median = 0.26 (IQR: 0–3)	NA	Median = 0 (IQR: -0.08 to 0.13)	17/60 (28%)
Schriefel et al ^[21]	Hydrophilic	20 mo: 0.9±1.2	Median = 3 (IQR:1–3)	4 y: 2.4±2.4	Median = 0 (IQR: -0.08 to 0.11)	40/60 (67%)
	Hydrophobic	4 y: 1.9±2.0	20 mo: 1.2±1.4	4 y: 2.4±2.4	4 y: median = 0.097 (range: 0–0.22)	20 mo: 4/39 (10%)
	Hydrophilic	20 mo: 2.3±2.1	4 y: 2.0±2.0	4 y: 5.5±3.7	4 y: median = 0.2 (range: 0–1.0)	4 y: 17/34 (50%)
	Hydrophobic	4 y: 3.7±3.0	20 mo: 2.1±1.8	NA	NA	20 mo: 12/39 (31%)
Gangwani et al ^[23]	Hydrophobic	1.9±1.9	4 y: 3.0±2.2	NA	NA	4 y: 26/34 (77%)
	Hydrophilic-Hydrophobic copolymer	2.6±2.0	NA	NA	NA	NA
Ivase et al ^[18]	Hydrophobic	NA	NA	NA	NA	2 y: 1 (2%)
Vasavada et al ^[19]	Hydrophobic	NA	NA	1 mo: 0.00±0.08	3 y: 0.18 (20/30)	2 y: 8 (13%)
	Hydrophobic	NA	NA	1 y: 0.02±0.11	NA	0
	Hydrophilic (Group C)	NA	NA	2 y: 0.02±0.14	3 y: 0.30 (20/40)	4/31 (12.9%)
Cleary et al ^[17]	Hydrophobic	NA	NA	3 y: 0.03±0.52	3 y: 0.18 (20/30)	0
	Hydrophobic	NA	NA	1 mo: 0.00±0.20	3 years: 0.40 (20/50)	5/31 (16.1%)
	Hydrophilic (group A)	NA	NA	1 y: 0.23±0.47	NA	NA
Kang et al ^[20]	Hydrophobic	NA	NA	2 y: 0.46±1.21	6 mo: 0.004±0.092	1 (3.6%)
	Hydrophilic	NA	NA	3 y: 0.93±1.37	12 mo: 0.005±0.110	2 (6.7%)
	Hydrophobic	NA	NA	1 mo: 0.00±0.11	24 mo: -0.009±0.093	2 (6.7%)
	Hydrophilic	NA	NA	1 y: 0.01±0.32	6 mo: 0.031±0.091	2 (5.4%)
	Hydrophobic	NA	NA	2 y: 0.00±0.13	12 mo: 0.040±0.094	4 (10.3%)
Kang et al ^[15]	Hydrophobic	NA	NA	3 y: 0.01±0.14	24 mo: 0.023±0.107	2 (4%)
	Hydrophilic	NA	NA	1 mo: 0.00±0.14	0.029±0.094	NA
Kugelberg et al ^[16]	Hydrophobic	NA	0.081±0.043	1 mo: 0.00±0.14	0.031±0.089	NA
	Hydrophilic	NA	0.075±0.052	2 y: 1.30±1.35	0.232±0.210	NA
	Hydrophobic	NA	0.181±0.108	3 y: 2.18±1.45	0.270±0.240	NA
	Hydrophilic	NA	0.110±0.141	NA	Baseline: 0.582±0.366	NA
Kugelberg et al ^[3]	Hydrophobic	NA	Mean = 0.076, P = .288	NA	6 mo: 0.046±0.086	0 (0%)
	Hydrophilic	NA	Mean = 0.041	NA	12 mo: 0.084±0.077 P = .554	NA
Heatley et al ^[12]	Hydrophobic	NA	NA	NA	baseline: 0.592±0.407	6/58 (10%)
	Hydrophilic	NA	Median = 0.055 (P < .001)	NA	6 mo: 0.039±0.062	24/57 (42%)
Heatley et al ^[12]	Hydrophobic	NA	Median = 0.18	NA	12 mo: 0.032±0.082	4 (6.8%)
	Hydrophilic	NA	0.08±0.13	NA	-0.017±0.099	2 (3.5%)
Heatley et al ^[12]	Hydrophobic	NA	0.12±0.14	NA	0.051±0.14	NA
	Hydrophilic	NA	0.12±0.14	NA	NA	NA

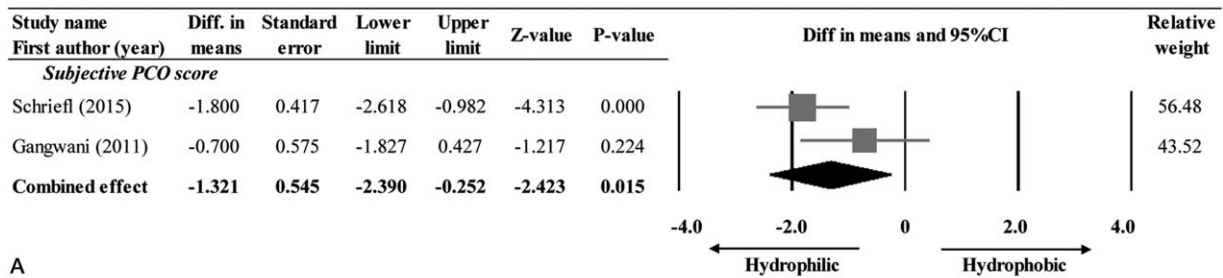
BDVA = best distance visual acuity, CDVA = corrected distance visual acuity, Nd:YAG = neodymium-doped yttrium aluminum garnet, PCO = posterior capsule opacification.



Heterogeneity test: Q-value = 19.77, df=7, p-value=0.006, I-squared=64.6%

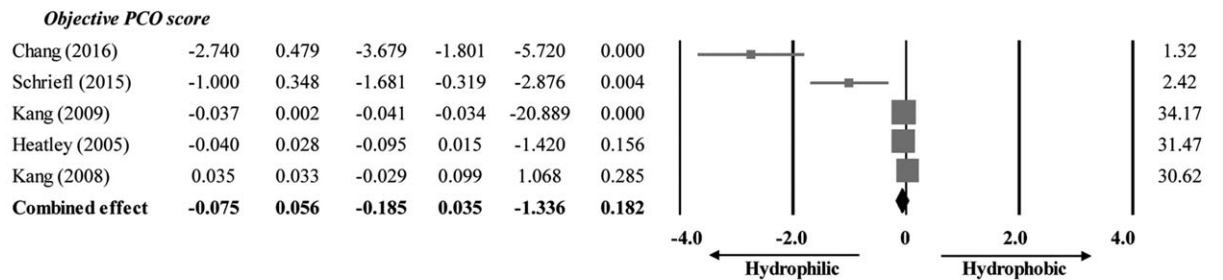
Abbreviations: n, number of eyes had Nd:YAG capsulotomy; N, number of total eyes at the last follow-up; CI, confidence intervals (lower and upper limit) of Odds ratio.

Figure 2. Forrest plot of Nd:YAG capsulotomy rate of patients received hydrophobic and hydrophilic lens.



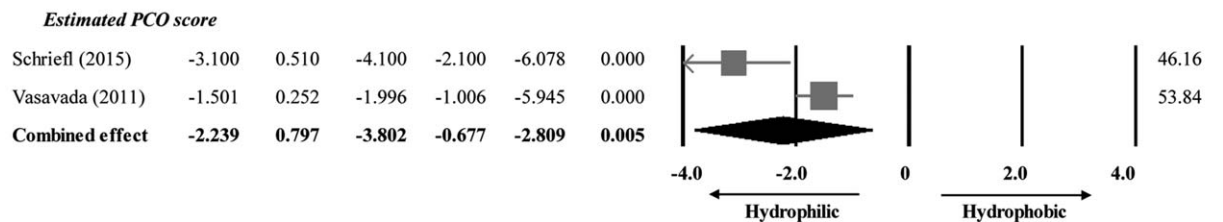
A

Heterogeneity test: Q-value = 2.396, df=1, p-value=0.122, I-squared=58.26%



B

Heterogeneity test: Q-value = 44.37, df=4, p-value<.001, I-squared=90.99%

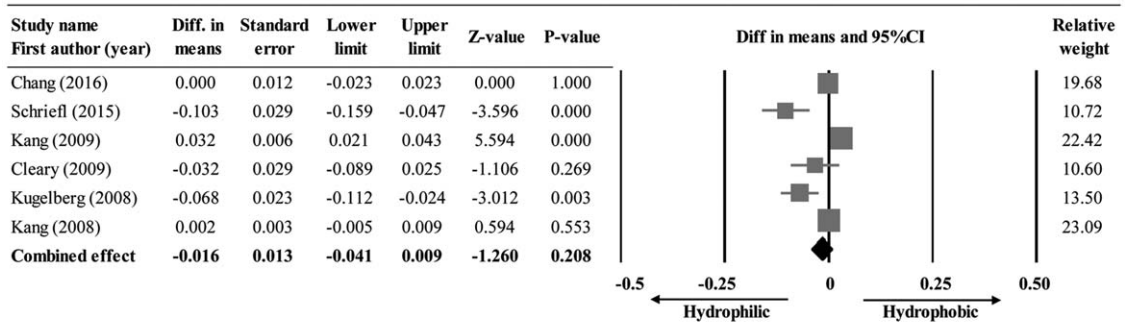


C

Heterogeneity test: Q-value = 7.90, df=1, p-value=0.005, I-squared=87.34%

Abbreviations: CI, confidence intervals (lower and upper limit) of difference in means.

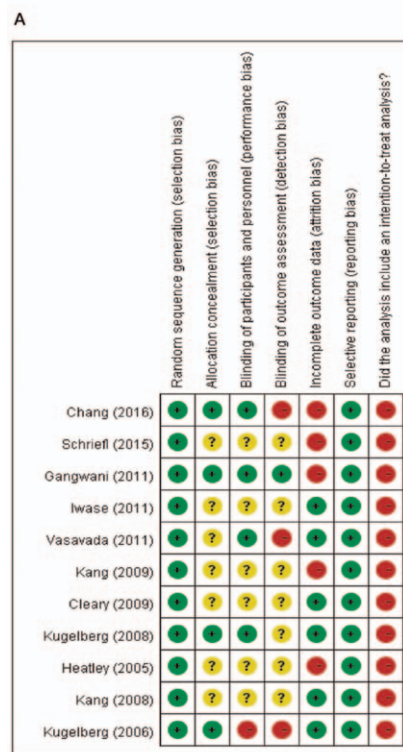
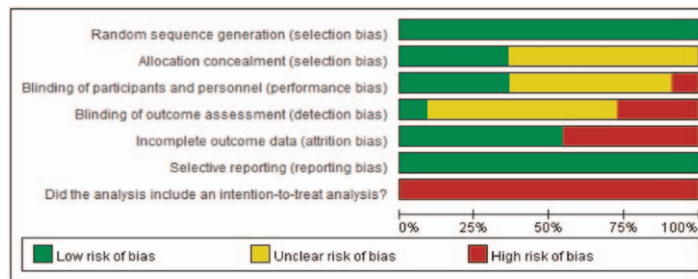
Figure 3. Forrest plot of difference in means of subjective PCO score (A), objective PCO score (B), and estimated PCO score (C) of patients received hydrophobic and hydrophilic lens.



Heterogeneity test: Q-value = 49.16, df=5, p-value<.001, I-squared=89.83%

Abbreviations: Diff, difference; CI, confidence intervals (lower and upper limit) of difference in means.

Figure 4. Forrest plot of difference in means of visual acuity of patients received hydrophobic and hydrophilic lens.



B

Figure 5. Quality assessment.

included only RCTs, was an updated evaluation of the association of hydrophobic and hydrophilic intraocular lenses on preventing PCO and reducing Nd:YAG laser capsulotomy rate. The overall pooled analysis found that hydrophobic lenses had lower rate Nd:YAG laser capsulotomy than hydrophilic treatment. (OR=0.38; $P=.029$). Hydrophobic lenses compared with hydrophilic lenses were also associated with better (lower) subjective and estimated PCO score ($P \leq .015$). The objective PCO score and visual acuity were similar between lens types ($P \geq .182$).

The findings of the current study are consistent with a prior meta-analysis that assessed the effect of hydrophilic and hydrophobic acrylic intraocular lens on posterior capsule opacification.^[10] The study of Li et al^[10] included 9 RCTs with a total of 861 eyes. They found that the hydrophobic acrylic intraocular lens showed benefit with respect to PCO severity at 1-year (standard mean diff: 1.72; $P=.0002$) and 2-year (standard mean diff: 1.79; $P < .0001$) follow-up. Hydrophilic acrylic lenses were associated with about a 7-fold higher risk of Nd:YAG laser capsulotomy than hydrophobic acrylic lenses; the pooled relative risk of Nd:YAG laser capsulotomy rates 2 years postsurgery was 6.96 (hydrophilic vs hydrophobic; $P < .00001$).

Another prior meta-analysis also found the rates of PCO and Nd:YAG laser capsulotomy was influenced by different intraocular lens biomaterial.^[11] The study of Cheng et al^[11] included 23 RCTs and compared the effect of acrylic, polymethylmethacrylate, hydrogel, silicone, and PMMA lenses. They also examined sharp and rounded-edge designs. The study found that acrylic and silicone intraocular lenses were more effective than PMMA and hydrogel lenses in lowering the rates of Nd:YAG laser capsulotomy and PCO. In addition, they found that sharp optic edges were superior at lowering PCA and the rate of Nd:YAG laser capsulotomy than lenses with round-edge design. In contrast, a meta-analysis performed by Findl et al,^[11] which included 66 studies, found no influence of the intraocular lens optic material (i.e., PMMA, hydrogel, hydrophobic acrylic, and silicone) on the development of PCO, although they did observe that silicone-based lenses tended to have lower PCO scores and hydrogel higher PCO scores than the other materials.

The molecular and cellular reasons for the difference in effectiveness between hydrophobic and hydrophilic intraocular lenses are not well understood. The difference may at least in part involve the fact that hydrophobic intraocular lens can adhere to collagen membrane resulting in tight opposition of the lens in the posterior capsular bag, and increased adhesiveness through fibronectin.^[12,24] These molecular interactions may result in less space between the intraocular lens and posterior capsule where the lens epithelial cells migrate.^[10] In addition, the hydrophilic surface properties have been shown to promote proliferation and migration of lens epithelial cells from the equatorial area to the visual region.^[25] Hydrophilic intraocular lenses were also found to have less sharp edges, possibly due to manufacturing methods, which may also increase PCO.^[18,26]

The study has several limitations. One limitation is the small sample of included studies. In addition, the studies themselves had small patient populations. The follow-up time varied across studies that may have impacted the findings, as PCO and Nd:YAG laser capsulotomy rate are influenced by length of time following surgery.^[10] Also, the lenses differed with respect to edge design, which may have influenced the findings as edge design has been found to impact PCO and Nd:YAG laser capsulotomy rate.^[11] Long-term randomized controlled studies, with large sample sizes, are needed to further evaluate the effects

of various intraocular lens biomaterials on PCO and the rate of Nd:YAG capsulotomy.

In conclusion, hydrophobic intraocular lenses may have lower Nd:YAG capsulotomy rate and lower subjective and estimated PCO score as compared with hydrophilic intraocular lenses. Further studies are needed to further explore this issue.

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