

Phacoemulsification with and without iStent: A Systematic Review and Meta-Analysis of Comparative Studies

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Keywords

Glaucoma · iStent · Intraocular pressure · Microinvasive glaucoma surgeries · Micro-bypass stent

Abstract

Background: The iStent (Glaukos Corporation; Laguna Hills, CA, USA) is one of the minimally invasive glaucoma devices. It can be inserted at the time of phacoemulsification or as a stand-alone procedure to lower the intraocular pressure (IOP). **Objective:** Our aim was to conduct a systematic review and meta-analysis comparing the effect of iStent insertion at the time of phacoemulsification with phacoemulsification alone in patients with ocular hypertension or open-angle glaucoma. **Methods:** We searched EMBASE, MEDLINE (OVID and PubMed), CINAHL, and Cochrane Library for articles published between 2008 and June 2022 (PRISMA 2020 for the checklist). Studies comparing the IOP-lowering effect of iStent with phacoemulsification versus phacoemulsification alone were included. The endpoints were IOP reduction (IOPR) and the mean reduction in the number of glaucoma drops. A quality-effects model was used to compare both surgical groups. **Results:** Ten studies were included, reporting on 1,453 eyes. Eight hundred fifty three eyes had the combined iStent and phacoemulsification, and 600 eyes underwent phacoemulsification alone. IOPR was higher in the combined surgery at of 4.7 ± 2 mm Hg

compared to 2.8 ± 1.9 mm Hg in phacoemulsification alone. A greater decrease in postoperative eye drops was noted in the combined group having a decrease of 1.2 ± 0.3 eye drops versus of 0.6 ± 0.6 drops in isolated phacoemulsification. The quality effect model showed an IOPR weighted mean difference (WMD) of 1.22 mm Hg (confidence interval [CI]: [-0.43, 2.87]; $Q = 315.64$; $p < 0.01$; $I^2 = 97\%$) and decreased eye drops WMD 0.42 drops (CI: [0.22, 0.62]; $Q = 42.6$; $p < 0.01$; $I^2 = 84\%$) between both surgical groups. Subgroup analysis shows that the new generation iStent may be more effective in reducing IOP. **Conclusion:** iStent has a synergetic effect with phacoemulsification. The reduction of IOP and glaucoma eye drops was higher when iStent is combined with phacoemulsification compared with isolated phacoemulsification.

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Introduction

Glaucoma is the leading cause of irreversible vision loss worldwide, affecting more than 80 million individuals, and this number is projected to reach 111 million by 2040 [1]. It is characterized by progressive asymptomatic

This study has not been presented in any meeting.

vision loss due to optic nerve damage and often associated with elevated intraocular pressure (IOP), which remains to be the only modifiable risk factor that prevents its progression [2, 3]. An array of IOP-lowering drops is available, and they serve as the initial treatment option for ocular hypertension (OHT) and open-angle glaucoma (OAG). The limitation of topical treatment is ocular surface irritation and noncompliance, especially when the patient is on a complex regimen involving multiple drops [4]. Selective laser trabeculoplasty can also be used as first-line therapy, but its effectiveness decreases with time, fading at 5 years [5].

For patients with OHT and mild to moderate OAG, different microinvasive glaucoma surgeries can be performed. One of these surgeries is the microstent iStent (Glaukos Corporation) [6]. It is inserted through the trabecular meshwork creating a patent bypass pathway for aqueous humor flow. The first-generation iStent device comprises of a central inlet with multiple outlets allowing multidirectional flow through Schlemm's canal. iStent *inject*, the second-generation device, works using the same mechanism but comprises of two stents and is significantly smaller [7, 8]. iStents can be inserted at the time of cataract surgery or as a stand-alone procedure. Extensive research has been done to assess the various outcomes of iStent and iStent *inject*, such as change in IOP, change in the number and frequency of drops needed, best-corrected visual acuity, structural measures of disability (cup-to-disk ratio, visual fields, retina nerve fiber layer thickness), surgery adverse effects, as well as cost analyses [9–14]. It is known that cataract extraction can, independently, decrease postoperative IOP and the number of glaucoma medication used [13–15]. Although a large number of published studies assessed the effect of iStent on lowering IOP and number of drops when combined with phacoemulsification, many lack the control arm comparing it to phacoemulsification alone in the same setting. In addition, the only published meta-analysis included cases of isolated phacoemulsification surgeries which were performed on different populations and in different settings from the combined surgeries population [16].

Our objective in this systematic review and meta-analysis was to decrease the confounding factors and include only high-quality studies comparing the IOP-lowering effect and subsequent reduction in topical IOP-lowering drops, of iStent combined phacoemulsification versus phacoemulsification alone, in patients diagnosed with OHT or OAG and concomitant cataract.

Methods

A systematic literature review and meta-analysis was conducted in compliance with the PRISMA guideline. The study did not require an IRB review as it did not involve human subjects. We searched EMBASE (OVID), MEDLINE (OVID and PubMed), CINAHL (EBSCO), and the Cochrane Library (Wiley) without any language between 2008 and June 2022. OVID auto-alerts for monthly new literature updates were set. Manual reference search of included articles was done to retrieve potentially relevant studies. Database-specific subject headings and keywords for “open-angle glaucoma,” “ocular hypertension,” “phacoemulsification,” “cataract extraction,” “trabecular microbypass,” and “iStent” were utilized in the search strategy. Unique syntax and terminology were tailored to suit each of the used databases. Detailed search strategy has been provided in the supplementary material (online suppl. Table 1; for all online suppl. material, see <https://doi.org/10.1159/000531077>). Searches were limited to human subjects.

Inclusion and Exclusion Criteria

To be included in the analysis, articles were required to be strictly comparative between isolated phacoemulsification and combined phacoemulsification and iStent to decrease the heterogeneity between the studied populations. Clinical trials, randomized controlled trials, prospective and retrospective cohorts, and case series were included, while meta-analysis, reviews, cost-effectiveness analysis, case reports, editorials, and abstract meeting submissions were excluded. Only OHT and OAG pathologies were included with a minimum total number of patients set for 20 and a minimum age of 19 years. Minimum postoperative follow-up was set at 2 months to avoid the IOP fluctuations observed in the early phase after cataract surgery. When standard deviation (SD) values of the mean IOP and the mean glaucoma drops used were both missing, the study was excluded. Both versions, iStent and/or iStent *inject*, were included. Also, articles including patients with prior history of ocular surgery or laser treatments (selective laser trabeculoplasty and YAG iridotomy) were excluded.

Data Collection

Two reviewers completed the article search independently and extracted the data based on the aforementioned inclusion and exclusion criteria. Conflicting results were discussed and solved through consultation. The extracted data included study design, location, duration of postoperative follow-up, intervention performed, patient mean age and SD, along with baseline and postoperative characteristics such as IOP, best-corrected visual acuity, and the number of pressure lowering drops used. Complications such as iStent malposition and occlusion and hyphema formation were noted. The quality index (QI) of included papers was assessed independently in duplicates using the Downs and Black checklist (online suppl. Table 2) comprising of 27 questions, yielding an overall QI score ranging between zero and 1.

Data Analysis

Statistical analysis was conducted using MetaXL, version 5.3 (EpiGear, 2019, Rotterdam, The Netherlands) [17]. In the articles where reductions were not calculated, mean IOP reduction

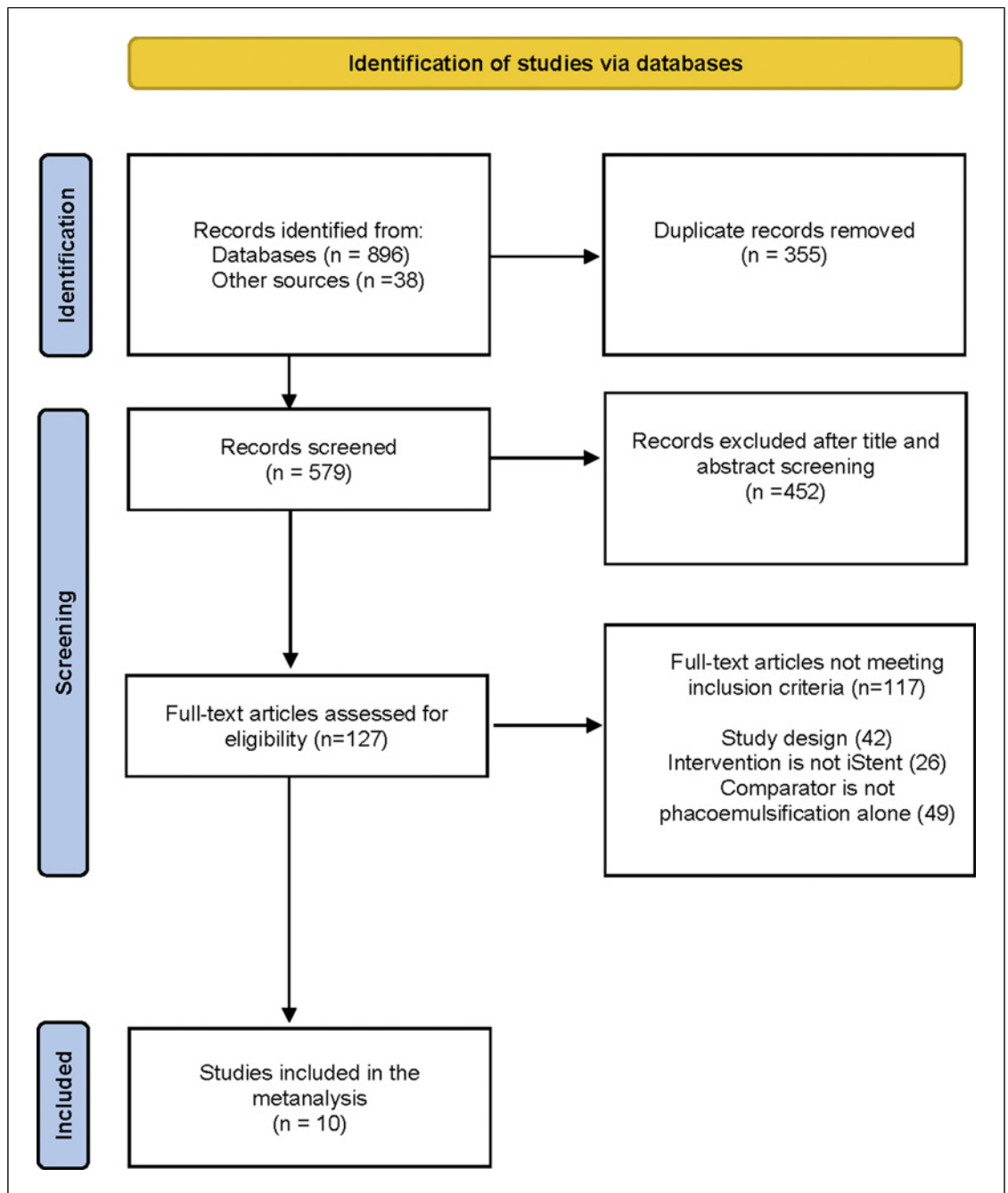


Fig. 1. Prisma flow diagram of the studies comparing combined iStent and phacoemulsification with phacoemulsification alone in patients having glaucoma and cataract.

(IOPR) and glaucoma drop reduction following surgery were calculated by subtracting baseline values from values at the last follow-up, using the following equations:

$$\text{IOPR} = \text{IOP}_{\text{baseline}} - \text{IOP}_{\text{endpoint}}$$

$$\text{Drop reduction mean} = \text{Mean of baseline drops} - \text{Mean of endpoint drops}$$

In articles where the standard error (SE) of IOPR and SE of drop reduction were not reported, the mean was calculated using the following formulae:

$$(\text{SE}_{\text{IOPR}}) = \sqrt{(\text{SE baseline IOP})^2 - (\text{SE post - op IOP})^2}$$

$$(\text{SE}_{\text{IOPR}}) = \sqrt{(\text{SE baseline drops})^2 - (\text{SE post - op drops})^2}$$

Table 1. Baseline characteristics of each of the included studies of phacoemulsification with and without iStent implantation

Study (year)	Location	RCT	iStent, n	Patients, N	Mean follow-up, months	iStent + phacoemulsification		Isolated phacoemulsification		QI	Weight, %
						patients, n	mean age ± SD, years	patients, n	mean age ± SD, years		
Fea [18] (2010)	Italy	RCT	1	36	15	12	64.9±3.1	24	64.5±3.4	0.78	10
Fernandez et al. [19] (2010)	Spain	RCT	2	33	12	17	75.2±7.2	16	-	0.78	10
Samuelson et al. [20] (2011)	United States	RCT	1	240	12	123	73±0.67	117	73±0.67	0.78	10
Craven et al. [21] (2012)	United States	RCT	1	240	24	117	-	123	-	0.71	9.09
Fea et al. [22] (2015)	Italy	Retrospective cohort	1	36	48	12	-	24	-	0.67	8.63
Chansangpetch et al. [23] (2018)	United States	RCT	1	121	12	60	72.9±6.41	61	72.76±9.88	0.57	7.27
Samuelson et al. [24] (2019)	United States	RCT	2	505	24	387	69±8.2	118	70.1±7.7	0.71	9.09
Best et al. [25] (2019)	Germany	RCT	2	65	24	31	-	34	-	0.71	9.09
Lee et al. [26] (2020)	England	Retrospective case series	1	97	24	50	70±8	47	73±9	0.6	7.72
Kozera et al. [15] (2021)	Switzerland	RCT	1	80	24	44	70.9±7.74	36	71.8±6.7	0.75	9.54
Total/Mean				1,453	24.5	853		600			100

N, number; SD, standard deviation; RCT, randomized controlled trial.

Table 2. Pre- and postoperative changes in IOP following phacoemulsification with and without iStent implantation

Study (year)	iStent + phacoemulsification			Phacoemulsification		
	mean baseline IOP±SD, mm Hg	mean postoperative IOP±SD, mm Hg	IOPR + SE IOPR, mm Hg	mean baseline IOP±SD, mm Hg	mean postoperative IOP±SD, mm Hg	IOPR + SE IOPR, mm Hg
Fea [18] (2010)	17.9±2.6	14.8±1.2	3.1±2.3	17.3±3	15.7±1.1	1.6±2.7
Fernandez et al. [19] (2010)	24.2±1.8	17.6±2.8	6.6±2.1	23.6±1.5	19.8±2.3	3.8±1.7
Samuelson et al. [20] (2011)	18.4±3.2	16.9±1.2	1.5±2.9	18.4±3.2	17.4±1.2	1±2.9
Craven et al. [21] (2012)	25.4±3.6	17.1±2.9	8.3±2.1	25.3±3.6	17.8±3.3	7.5±1.4
Fea et al. [22] (2015)	17.8±2.7	15.9±2.3	1.9±1.4	16.7±3	17±2.5	-0.3±1.6
Chansangpetch et al. [23] (2018)	14.5±2.86	14.3±3.04	0.21±1.03	15.1±3.5	13.5±3.3	1.5±1.08
Samuelson et al. [24] (2019)	24.8±3.34	17.8**	7±4	24.5±3.08	19.1**	5.4±3.7
Best et al. [25] (2019)	25.1±1.6	19.3±2.1	5.8±1.3	22±1.7	20±1.7	2±0.01
Lee et al. [26] (2020)	17.9±1.35	13.8**	4.1**	13.6±1.1	12.6**	1**
Kozera et al. [15] (2021)	23.7±1.44	16.1±2.2	7.6±1.66	21.9±1.03	17.2±2.7	4.7±2.1
Weighted mean±SD	21.1±2.4	16.4±2.1	4.7±2.1	20±2.4	17.1±2.1	2.8±1.9

SD, standard deviation; SE, standard error; IOPR, intraocular pressure reduction. **missing SD or SE.

Table 3. Pre- and postoperative changes in the number of glaucoma eye drops following phacoemulsification with and without iStent implantation

Study (year)	iStent + phacoemulsification			Phacoemulsification		
	mean baseline drops±SD	mean postoperative drops±SD	drop reduction mean±SE	mean baseline drops±SD	mean postoperative drops±SD	drop reduction mean±SE
Fea [18] (2010)	2±0.9	0.4±0.7	1.6±0.5	1.9±0.6	1.3±1	0.6±0.7
Fernandez et al. [19] (2010)	1.1±0.5	-	1.1±0.5	1.2±0.6	0.7±1	0.5±0.7
Samuelson et al. [20] (2011)	1.5±0.6	0.2±0.6	1.3±0.01	1.5±0.3	0.2±0.7	1.1±0.6
Craven et al. [21] (2012)	1.6±0.8	0.3±0.6	1.3±0.5	1.5±0.4	0.5±0.7	1±0.5
Fea et al. [22] (2015)	1.9±0.9	0.5±0.8	1.4±0.4	1.8±0.7	0.9±1	0.9±0.6
Chansangpetch et al. [23] (2018)	2±1.5	0.6**	1.32**	1±0.6	0.6**	0.4±0.6
Samuelson et al. [24] (2019)	1.6±0.8	0.4±0.8	1.2±0.01	1.5±0.2	0.8±1	0.7±0.9
Best et al. [25] (2019)	2.8**	1.5**	1.3**	2.6**	2.1**	0.5**
Lee et al. [19] (2020)	2.6±0.2	1.9±0.2	0.7±0.01	2.1±0.1	1.8±0.1	0.3±0.1
Kozera et al. [19] (2021)	1.75±0.67	0.5±0.8	1.23±0.4	1.2±0.4	0.86±0.7	0.34±0.5
Weighted mean±SD	1.8±0.6	0.6±0.6	1.2±0.3	1.6±0.4	0.9±0.7	0.6±0.6

SD, standard deviation; SE, standard error. **missing SD or SE.

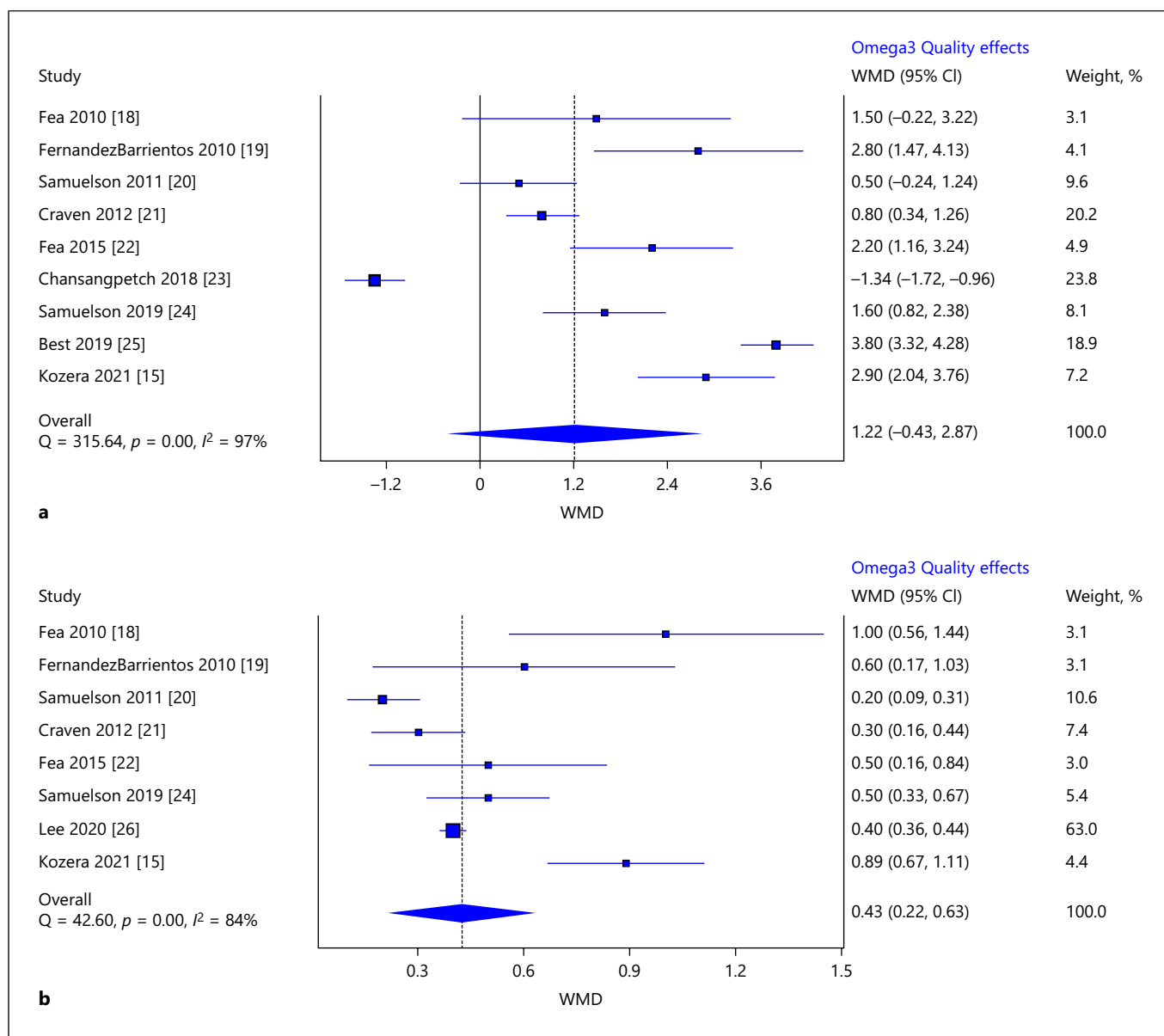


Fig. 2. Forest plot for the difference in intraocular pressure reduction (**a**) and glaucoma medication reduction (**b**) following surgery when comparing combined iStent/phacoemulsification with stand-alone phacoemulsification.

Cochran's Q was calculated using the following formula with the following abbreviations (k = number of groups, R = row totals, C = column totals, and T = grand total [sum of R or sum of C]).

$$Q = \frac{(k-1)(k\sum C^2 - T^2)}{KT - \sum R^2}$$

Given the small number of studies included, we further calculated I^2 to test the percentage of variation among studies due to true heterogeneity and not chance alone. I^2 was calculated using the following formula where df stands for degrees of freedom:

$$I^2 = 100\% \frac{(Q - df)}{Q}$$

The weighted mean difference (WMD) was then calculated by comparing the preoperative with postoperative means for the IOP and number of topical glaucoma medications, taking into consideration the QI and number of patients in each study. As a result, randomized studies were given higher quality than the retrospective studies.

Given the potential superiority of iStent *inject*, a subgroup analysis was performed including only studies with iStent. Graphical representation of publication bias was plotted in the funnel plot.

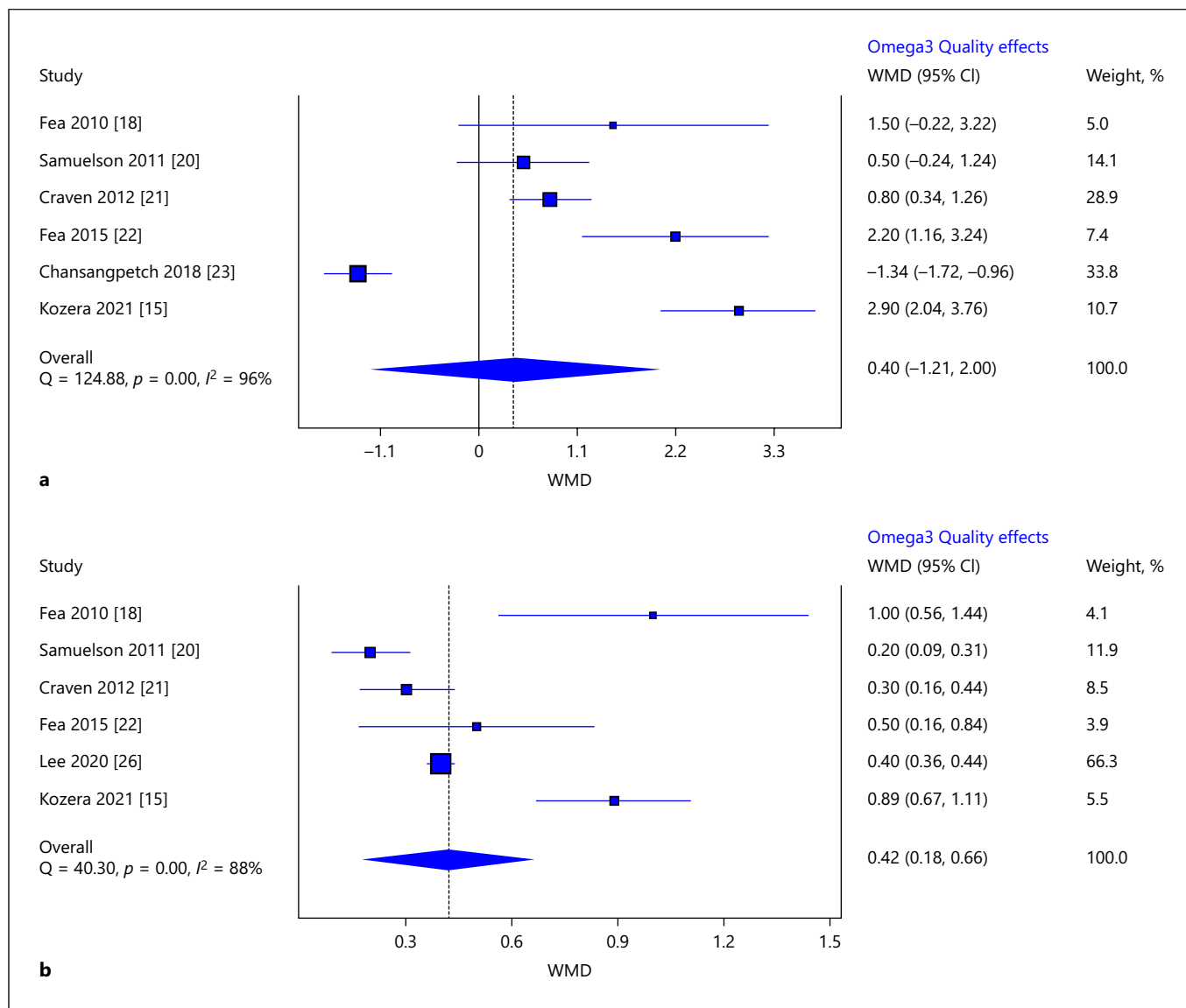


Fig. 3. Forest plot for the difference in intraocular pressure reduction (**a**) and glaucoma medication reduction (**b**) following surgery when comparing combined iStent/phacoemulsification with stand-alone phacoemulsification excluding studies with 2 iStents injection.

Results

A total of 934 records were reviewed, and 10 comparative studies met the abovementioned criteria (Fig. 1). Out of the included studies, eight were randomized controlled trials and two were retrospective studies. (Table 1) [15, 18–26] Three of the studies compared iStent *inject* with phacoemulsification, and the rest assessed iStent. A total number of 853 eyes were subjected to the combined surgery, and 614 eyes underwent phacoemulsification alone. The mean follow-up period

was 21.9 months. All studies except the study by Chansangpetch et al. [23] reported higher IOPR in the combined surgery with a weighted mean IOPR of 4.7 ± 2.1 mm Hg compared with phacoemulsification alone having a weighted mean IOPR of 2.8 ± 1.9 mm Hg (Table 2). All studies reported a larger decrease in the mean number of glaucoma drops use after combined surgery with a weighted mean drop reduction of 1.2 ± 0.3 drops compared with isolated phacoemulsification with a weighted mean drop reduction of 0.6 ± 0.6 drops (Table 3).

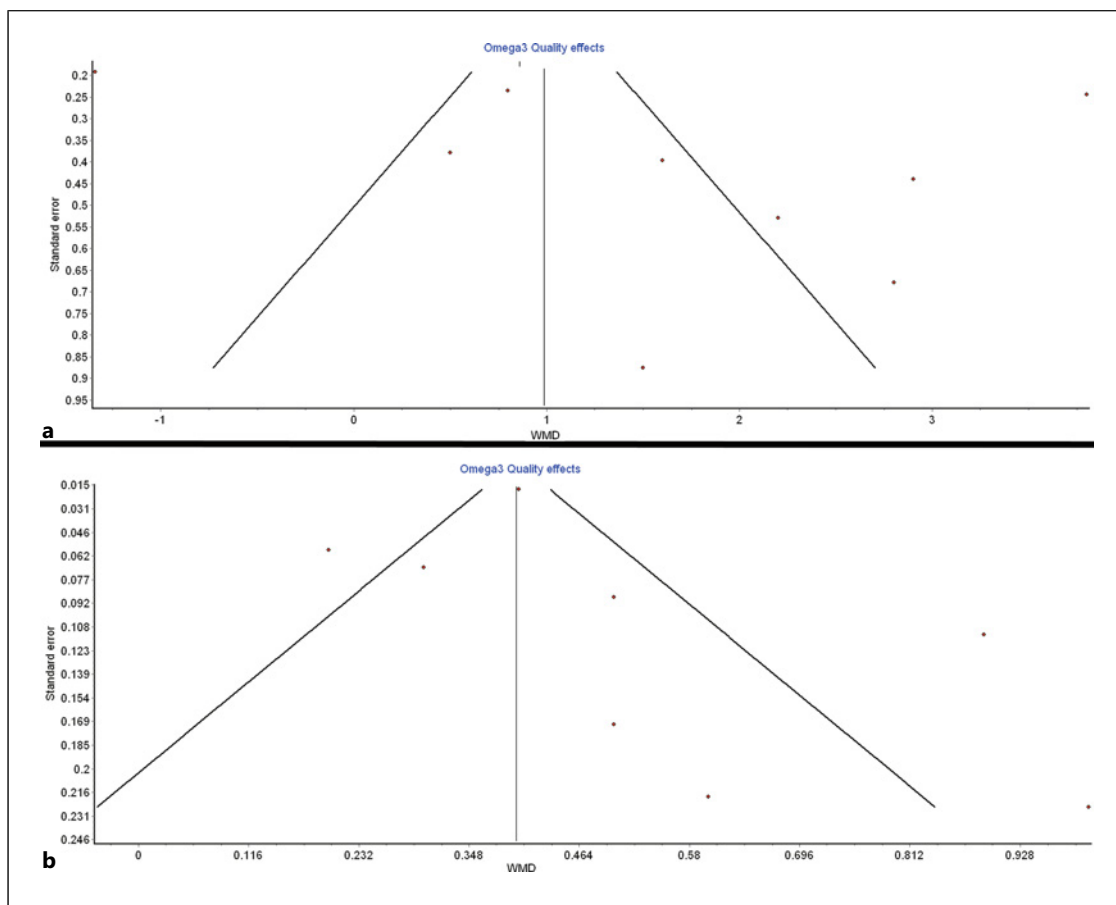


Fig. 4. Funnel plots for intraocular pressure reduction (a) and glaucoma medication reduction (b) following surgery when comparing combined iStent/phacoemulsification with solo phacoemulsification.

Further analysis was performed using omega 3 quality effect, taking into consideration the number of patients in each study and excluding the studies missing SD. The results showed an IOPR by a WMD of 1.22 mm Hg (confidence interval [CI]: [-0.43, 2.87]; $Q = 315.64$; $p < 0.01$; $I^2 = 97\%$) and eye drops by a WMD of 0.42 drops (CI: [0.22, 0.62]; $Q = 42.6$; $p < 0.01$, $I^2 = 84\%$) when comparing combined surgery with isolated phacoemulsification (Fig. 2).

Subgroup analysis including only the first generation iStent (1 stent) showed a lower mean IOPR with a WMD of 0.4 mm Hg (CI: [-1.21, 2]; $Q = 124.8$; $p < 0.01$; $I^2 = 96\%$) and eye drops by WMD of 0.42 drops (CI: [0.18, 0.66]; $Q = 40.3$; $p < 0.01$, $I^2 = 88\%$) when comparing combined surgery with isolated phacoemulsification (Fig. 3). Subgroup analysis including only the second-generation iStent (iStent inject:2 stents) could not be performed with only three identified studies. Using omega 3 quality effect, plotting

SE against WMD of IOPR and of drop reduction showed asymmetry in the included studies in both parameters, indicating potential publication bias (Fig. 4).

Discussion

The cumulative results depicted in this meta-analysis denote that both phacoemulsification alone as well as combined phacoemulsification and iStent implantation lead to a decrease in IOP and the number of topical glaucoma drops needed. The combined surgery outperformed isolated phacoemulsification with further decrease in IOP and the number of eye drops. Our results are in accordance with results of two previous meta-analyses. In the first meta-analysis published by Malvankar-Mehta et al. in 2015 [16], the authors compiled different non-comparative studies evaluating effect of phacoemulsification and iStent on glaucoma where they used

uncontrolled, one-armed studies examining the efficacy of the phacoemulsification-alone group. The second meta-analysis was published by Marko Popovic et al. in 2018 [11]. In their analysis, the authors included only studies with both arms, a stand-alone phacoemulsification arm and the combined surgery arm, but at that time, only a small number of studies with head-to-head comparison between combined surgery and phacoemulsification had been published [18–20].

In both assessed outcomes, the reduction is almost doubled in the combined surgery group, with a 22% IOPR, as compared to phacoemulsification alone having a 14% IOPR. In our subgroup analysis that excluded iStent *inject* (2 stents), the IOPR was smaller following the combined surgery; however, the change in glaucoma eye drops remained constant between both iStent types. On the other hand, a high IOPR was noted in the studies where iStent *inject* was used, but the small number of included studies precludes the opportunity to draw robust conclusion [19, 24, 25].

The heterogeneity (I^2) between studies was found to be high. This can be attributed to both the low number of studies included, as well as the small sample size in these studies [27]. Also, the two outcomes (IOP and glaucoma drops) are interconnected and may increase this heterogeneity. The difference in surgeon skill, geographic location, population, year of conduction of study, number of patients included, and follow-up period are factors that may have contributed to this heterogeneity. In addition, we excluded some studies due to missing SD and other values. This may have affected the final outcome of the meta-analysis. Another limitation of the study is the duration of follow-up that was significantly different among studies ranging between 12 months and 51 months.

Visual inspection of funnel plots for both pre- and postoperative IOPR% and the number of topical medications reveals asymmetry. This serves as an additional limitation indicating possible publication bias [28]. Other potential biases may be related to industry funding due to the difficulty in obtaining peer-reviewed funding for device trials.

Systematic reviews and meta-analysis may serve as evidence-based foundations to draft guidelines that would govern the future standard of care, especially since cost may be a barrier for the access to these treatments. This study's findings support the use of iStent in combination with cataract surgery when further IOPR is desired in patients with OHT or OAG. The second-generation iStent seems more effective in lowering the IOP.

Conclusion

This minimally invasive procedure when combined together with phacoemulsification has a synergistic beneficial effect on both IOPR and glaucoma drop reduction. Although the results were statistically significant with iStent showing a good safety profile and offering the benefit of decreasing the dependence on glaucoma eye drops, the clinical implications are still debatable. Further studies are still needed to assess the long term IOP-lowering effect of iStent, the protective effect on the optic nerve, and how long it may delay the need for future, more invasive, glaucoma surgeries.

Statement of Ethics

An ethics statement is not applicable because this study is based exclusively on the published literature.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Francesca Kahale, Wassef Chanbour, Lulwa El Zein, Jason Brenner, Jae Young You, and Samir Melki contributed to the conception or design of the work, interpretation of data for the work, and revising the article; they all approved the final version to be published and agree to be accountable for all aspects of the work. Francesca Kahale and Wassef Chanbour contributed to the acquisition, analysis, and drafting of the manuscript.

Data Availability Statement

All data generated and analyzed during this study are included in this article and its online supplementary material files. The data that support the findings of this study are available from the corresponding author, W.C., upon reasonable request. Further inquiries can be directed to the corresponding author.

References

- 1 **Glaucoma: Facts and Figures**. Bright Focus Foundation. <https://www.brightfocus.org/glaucoma/article/glaucoma-facts-figures> (accessed March 28, 2022).
- 2 Prum BE, Rosenberg LF, Gedde SJ, Mansberger SL, Stein JD, Moroi SE, et al. Primary open-angle glaucoma preferred practice Pattern® guidelines. *Ophthalmology*. 2016;123(1):P41–111.
- 3 Coleman AL, Kodjebacheva G. Risk factors for glaucoma needing more attention. *Open Ophthalmol J*. 2009;3:38–42.
- 4 Baudouin C, Labbé A, Liang H, Pauly A, Brignole-Baudouin F. Preservatives in eye-drops: the good, the bad and the ugly. *Prog Retin Eye Res*. 2010;29(4):312–34.
- 5 Gazzard G, Konstantakopoulou E, Garway-Heath D, Garg A, Vickerstaff V, Hunter R, et al. Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicentre randomised controlled trial. *Lancet*. 2019;393(10180):1505–16.
- 6 **Inc P. iStent inject® W surgery**. Glaucoma products. <https://www.glaukos.com/glaucoma/products/iStent-inject-w/> (accessed March 28, 2022).
- 7 Hooshmand J, Rothschild P, Allen P, Kerr NM, Vote BJ, Toh T. Minimally invasive glaucoma surgery: comparison of iStent with iStent inject in primary open angle glaucoma. *Clin Exp Ophthalmol*. 2019;47(7):898–903.
- 8 Manasses DT, Au L. The new era of glaucoma micro-stent surgery. *Ophthalmol Ther*. 2016; 5(2):135–46.
- 9 Clement C, Howes F, Ioannidis A, Shiu M, Manning D, Lusthaus J, et al. Two-year multicenter outcomes of iStent inject trabecular micro-bypass stents combined with phacoemulsification in various types of glaucoma and ocular hypertension. *Clin Ophthalmol*. 2020;14:3507–17.
- 10 Salimi A, Watt H, Harasymowycz P. Long-term outcomes of two first-generation trabecular micro-bypass stents (iStent) with phacoemulsification in primary open-angle glaucoma: eight-year results. *Eye Vis*. 2021;8(1):43.
- 11 Popovic M, Campos-Moller X, Saheb H, Ahmed K II. Efficacy and adverse event profile of the iStent and iStent inject trabecular micro-bypass for open-angle glaucoma: a meta-analysis. *J Curr Glaucoma Pract*. 2018;12(2):67–84.
- 12 Guedes RAP, Gravina DM, Lake JC, Guedes VMP, Chaoubah A. One-year comparative evaluation of iStent or iStent inject implantation combined with cataract surgery in a single center. *Adv Ther*. 2019;36(10):2797–810.
- 13 Majstruk L, Leray B, Bouillot A, Michée S, Sultan G, Baudouin C, et al. Long term effect of phacoemulsification on intraocular pressure in patients with medically controlled primary open-angle glaucoma. *BMC Ophthalmol*. 2019;19(1):149.
- 14 Teus M, Belda J, Lavín C, Garcá-a-FeijoÁ J, Falvey H, Buseghin G, et al. Cost-effectiveness analysis of iStent Inject® implantation during cataract surgery compared to cataract surgery alone for mild to moderate open-angle glaucoma patients in Spain. *Expert Rev Ophthalmol*. 2021;16(4):319–28.
- 15 Kozera M, Konopińska J, Mariak Z, Rękas M. Effectiveness of iStent trabecular microbypass system combined with phacoemulsification versus phacoemulsification alone in patients with glaucoma and cataract depending on the initial intraocular pressure. *Ophthalmic Res*. 2021;64(2):327–36.
- 16 Malvankar-Mehta M, Iordanous Y, Chen Y, Wang W, Patel S, Costella J, et al. iStent with phacoemulsification versus phacoemulsification alone for patients with glaucoma and cataract: a meta-analysis. *PLoS One*. 2015; 10(7):e0131770.
- 17 Barendregt JJ, Doi SA, Lee YY, Norman RE, Vos T. Meta-analysis of prevalence. *J Epidemiol Community Health*. 2013;67(11):974–8.
- 18 Fea AM. Phacoemulsification versus phacoemulsification with micro-bypass stent implantation in primary open-angle glaucoma: randomized double-masked clinical trial. *J Cataract Refract Surg*. 2010;36(3):407–12.
- 19 Resende AF, Patel NS, Waisbourd M, Katz LJ. iStent® trabecular microbypass stent: an update. *J Ophthalmol*. 2016;2016:2731856.
- 20 Samuelson TW, Katz LJ, Wells JM, Duh YJ, Giamporcaro JE; US iStent Study Group. Randomized evaluation of the trabecular micro-bypass stent with phacoemulsification in patients with glaucoma and cataract. *Ophthalmology*. 2011;118(3):459–67.
- 21 Craven ER, Katz LJ, Wells JM, Giamporcaro JE; iStent Study Group. Cataract surgery with trabecular micro-bypass stent implantation in patients with mild-to-moderate open-angle glaucoma and cataract: two-year follow-up. *J Cataract Refract Surg*. 2012;38(8):1339–45.
- 22 Fea AM, Consolandi G, Zola M, Pignata G, Cannizzo P, Lavia C, et al. Micro-bypass implantation for primary open-angle glaucoma combined with phacoemulsification: 4-year follow-up. *J Ophthalmol*. 2015;2015: 795357–4.
- 23 Chansangpetch S, Lau K, Perez C, Nguyen N, Porco T, Lin S. Efficacy of cataract surgery with trabecular microbypass stent implantation in combined-mechanism angle closure glaucoma patients. *Am J Ophthalmol*. 2018;195:191–8.
- 24 Samuelson TW, Sarkisian SR, Lubeck DM, Stiles MC, Duh Y; iStent inject Study Group, et al. Prospective, randomized, controlled pivotal trial of an ab interno implanted trabecular micro-bypass in primary open-angle glaucoma and cataract: two-year results. *Ophthalmology*. 2019;126(6):811–21.
- 25 Best UP, Domack H, Schmidt V, Khalifa M. Mikroinvasive Glaukomchirurgie: wirksamkeit von trabekulären Stents bei kombinierten Eingriffen. *Ophthalmol*. 2019;116(8):771–9.
- 26 Lee GA, Porter AJ, Vincent RA, Makk J, Vincent SJ. Combined phacoemulsification and microinvasive glaucoma surgery in comparison to phacoemulsification alone for open angle glaucoma. *Eye*. 2020;34(2):312–8.
- 27 Von Hippel PT. The heterogeneity statistic I^2 can be biased in small meta-analyses. *BMC Med Res Methodol*. 2015;15(1):35.
- 28 Sterne JAC, Sutton AJ, Ioannidis JPA, Terrin N, Jones DR, Lau J, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ*. 2011;343:d4002.