

Five-Year Real-World Outcomes of iStent inject W® Combined with Phacoemulsification in Ocular Hypertension and Primary Open-Angle Glaucoma

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Abstract

Purpose:

To evaluate the long-term real-world efficacy, safety, and functional and structural outcomes in patients with ocular hypertension (OHT) or primary open-angle glaucoma (POAG) undergoing trabecular micro-bypass surgery with the iStent inject W®.

Methods:

This retrospective longitudinal study included 149 eyes of 149 patients with OHT or POAG who underwent implantation of the iStent inject W®, combined with phacoemulsification, and were followed for up to five years. Outcomes included intraocular pressure (IOP), number of hypotensive medications, best-corrected visual acuity (BCVA), optical coherence tomography (OCT) structural parameters, and visual field indices. Follow-up data were available at 1 year (n=123), 2 years (n=94), 3 years (n=61), 4 years (n=35), and 5 years (n=15).

Results:

BCVA improved significantly after surgery ($p<0.01$). A mild but statistically significant decline in visual field index (VFI) was observed over time ($p=0.03$), consistent with expected long-term glaucoma progression. OCT structural parameters remained stable throughout follow-up. IOP was significantly reduced at all postoperative visits except at years 3 and 5, where reductions did not reach statistical significance despite a sustained downward trend. Medication burden was significantly reduced at all time points ($p<0.01$). Men exhibited lower postoperative IOP than women ($p=0.02$), and OHT patients had higher IOP levels than those with POAG ($p<0.01$).

Conclusions:

In a real-world clinical setting, the iStent inject W® provided sustained IOP reduction, durable medication burden reduction and long-term structural stability over five years. These findings support its long-term clinical effectiveness in the management of OHT and POAG.

Keywords: iStent inject W®, MIGS, glaucoma, ocular hypertension, intraocular pressure, real-world evidence, long-term outcomes

Introduction

Primary open-angle glaucoma (POAG) and ocular hypertension (OHT) remain leading causes of irreversible visual impairment worldwide. Elevated intraocular pressure (IOP) is the principal modifiable risk factor for disease onset and progression, making effective long-term pressure control central to glaucoma management [1–4]. Traditional treatment strategies, including topical therapy, laser trabeculoplasty, and filtering surgery, are effective but limited by adherence challenges, ocular surface toxicity, and surgical morbidity.

Minimally invasive glaucoma surgery (MIGS) has emerged as an important therapeutic option, offering meaningful IOP reduction with a favorable safety profile and rapid postoperative recovery [5–9]. Among MIGS procedures, trabecular micro-bypass techniques targeting Schlemm’s canal aim to enhance physiological aqueous outflow while preserving conjunctival integrity [10–14].

The second-generation iStent inject W® has demonstrated efficacy in reducing IOP and medication burden in both randomized trials and real-world studies [10,12,15–18]. However, evidence regarding outcomes beyond four years remains limited [19–21]. The present study provides a five-year real-world evaluation of clinical, functional, and structural outcomes following implantation of the iStent inject W® in patients with OHT and POAG.

Methods

To address the limited availability of long-term real-world evidence on the outcomes of trabecular micro-bypass surgery, we conducted a retrospective longitudinal study evaluating the efficacy, safety, and structural and functional outcomes of the iStent inject W® in patients with OHT or POAG.

This retrospective longitudinal study reviewed clinical data from 149 eyes with OHT or POAG who underwent implantation of the iStent inject W® as a standalone surgery (10,09%) or combined with phacoemulsification (89,9%) at a single tertiary center. Inclusion criteria comprised a diagnosis of OHT or POAG and availability of at least one year postoperative follow-up. Eyes with prior incisional glaucoma surgery were excluded. When both eyes of a patient met inclusion criteria, both were included in the analysis, consistent with prior real-world MIGS studies

Outcome measures and endpoints were aligned with previously published MIGS investigations [5,6,9,20].

Outcomes

Primary endpoints were postoperative IOP and number of hypotensive medications, as defined in prior iStent studies [10,12,15].

Secondary endpoints included:

- best-corrected visual acuity (BCVA)

- visual field index (VFI), mean deviation (MD) and pattern standard deviation (PSD)
- OCT- derived structural parameters, including retinal nerve fiber layer thickness (RNFL) and cup / disc ratio (C/D)

all of which are validated markers of glaucomatous damage and progression [3,4,22,23].

Statistical Analysis

Descriptive statistics were used to summarize patients' demographic characteristics. The study included 149 eyes (sample size, $n = 149$); however, some variables contained missing data. The normality of continuous variables was assessed using the Kolmogorov–Smirnov test for samples larger than 50 subjects. Longitudinal repeated-measures models were applied to evaluate changes over time. Statistical significance was defined as a p value < 0.05 .

Ethics approval and consent to participate

The study adhered to the Declaration of Helsinki and was approved by ethics committee of the Virgen Macarena University Hospital. Written informed consent was obtained from all participants.

Results

A total of 149 eyes of 149 patients with OHT or POAG were included in the analysis and followed for up to five years after combined or standalone iStent inject W® implantation. The following sections describe the baseline characteristics of the study population and the longitudinal changes in intraocular pressure, glaucoma medication burden, visual acuity, structural OCT measurements, and visual field parameters, together with subgroup analyses according to sex and glaucoma diagnosis. The decreasing number of eyes available at later time points should be considered when interpreting the five-year outcomes.

BCVA improved significantly following surgery (pre $0,5 \pm 0,2$; post. $0,8 \pm 0,2$ $p < 0,01$), consistent with outcomes reported in combined cataract and iStent procedures [16,17]. A mild but statistically significant decline in VFI was observed over follow-up, although this finding should be interpreted cautiously given the observational design and the variable number of available examinations (pre 84 ± 17 (15, 100); post 82 ± 23 (2, 100) $p = 0,03$), reflecting the expected long-term functional trajectory of glaucoma under treatment [3,23]. Importantly, this functional change occurred in the context of stable OCT structural parameters (pre 73 ± 18 ; post 73 ± 16 $p = 0,92$), suggesting preservation of retinal architecture (table 1) .

IOP showed a sustained downward trend throughout follow-up, although statistical significance was not reached at years 3 and 5 (fig 1 and table 2). This pattern aligns with long-term real-world MIGS literature [10,12,18,20]. Medication burden was significantly reduced at all follow-up visits, demonstrating durable reduction in reliance on topical therapy (fig 2).

Men (48%) exhibited lower postoperative IOP than women (52%), and OHT patients (15%) demonstrated higher baseline and postoperative IOP than those with POAG. These findings represent secondary analyses and likely reflect known anatomical and physiological variability in aqueous outflow pathways rather than differences in surgical efficacy (tables 3 and 4) [24].

As expected in long-term real-world studies, attrition increased over time, with reduced sample size at later follow-up intervals due to routine discharge, loss to follow-up, or transfer of care.

Discussion

This five-year real-world study demonstrates sustained efficacy and safety of the iStent inject W® in patients with OHT and POAG. Beyond IOP reduction, the stability of OCT structural parameters and the modest functional decline observed are consistent with the natural history of glaucoma under effective pressure control.

Long-term preservation of retinal nerve fiber layer and macular parameters suggests that trabecular micro-bypass surgery may contribute to structural stabilization, particularly when implemented early in the disease course or in patients with ocular hypertension. These findings support the growing role of MIGS as part of a stepwise and individualized approach to glaucoma management.

The durable reduction in hypotensive medications observed throughout follow-up carries important clinical implications, including improved adherence, reduced ocular surface toxicity, and enhanced quality of life. Such benefits are especially relevant in chronic diseases like glaucoma, where long-term treatment tolerance remains a major challenge.

Sex-related differences in postoperative IOP and higher pressure levels in OHT compared with glaucomatous eyes likely reflect underlying anatomical and physiological variability rather than differences in surgical response. These findings should therefore be interpreted cautiously.

Our findings are consistent with previous long-term studies evaluating trabecular micro-bypass surgery with the iStent inject W® system. Salimi et al. reported sustained reductions in IOP and medication burden over 5 years in a prospective cohort of 125 eyes, with a 40% reduction in IOP and a 71% reduction in the number of medications, while visual field parameters, retinal nerve fiber layer thickness, and cup-to-disc ratio remained stable [25]. Similarly, Neuhann et al. reported favorable 5-year outcomes following trabecular micro-bypass implantation combined with phacoemulsification in patients with glaucoma or ocular hypertension, with sustained reductions in IOP and medication use [26]. More recently, Hengerer et al. reported favorable efficacy and safety outcomes over 7 years following iStent inject implantation, further supporting the long-term durability of this approach [19]. In addition, Guedes et al. reported 5-year real-world outcomes in 271 eyes with mild-to-moderate open-angle glaucoma treated with iStent inject W®, either as a standalone procedure or combined with phacoemulsification, demonstrating sustained reductions in IOP and topical medication burden [27]. In our real-world cohort, iStent inject W® implantation was likewise associated with a sustained reduction in IOP and a significant decrease in the number of hypotensive medications, while OCT-derived structural parameters remained stable throughout follow-up. The mild

decline observed in VFI should be interpreted cautiously and does not necessarily indicate treatment failure, particularly given the observational design and the decreasing number of eyes available at later follow-up visits. Overall, our findings provide additional real-world evidence supporting the long-term clinical effectiveness of iStent inject W® in reducing treatment burden while maintaining structural stability.

Limitations of our study include the retrospective design and reduced sample size at extended follow-up, a common feature of long-term real-world MIGS studies. Nevertheless, the consistency of outcomes over five years enhances the relevance of these findings for everyday clinical practice.

Conclusions

In a real-world clinical setting, implantation of the iStent inject W® resulted in sustained intraocular pressure reduction, durable decrease in medication burden, improved visual acuity, and long-term structural stability over five years in patients with ocular hypertension and primary open-angle glaucoma.

These results reinforce the role of trabecular micro-bypass surgery as a safe and effective long-term strategy for pressure control while minimizing dependence on topical therapy. The favorable safety profile and stability of functional and structural outcomes support the use of the iStent inject W® as part of an earlier, individualized interventional approach in glaucoma management.

Tables

Table 1: The following is a descriptive statistical analysis of the patients' preoperative and postoperative variables.

Variable (n = 149)	Preoperative (Mean ± DS [Min, Max])	Postoperative (Mean ± DS [Min, Max])	p-value
RNFL	73 ± 18 (12, 125)	73 ± 16 (33, 126)	0,92
C/D	0,7 ± 0,2 (0,0, 1,0)	0,7 ± 0,2 (0,0, 1,0)	0,18
VFI	84 ± 17 (15, 100)	82 ± 23 (2, 100)	0,03*
MD	-7,07 ± 5,70 (-25,69, 0,18)	-7,48 ± 7,24 (-31,09, 0,36)	0,14
PSD	5,04 ± 3,81 (-8,62, 13,39)	6,21 ± 11,09 (1,23, 95,00)	0,217
BCVA	0,5 ± 0,2 (0,1, 1,0)	0,8 ± 0,2 (0,1, 1,0)	< 0,01*

Table 2: The results show that IOP was lower in all postoperative assessments compared to preoperative values.

Visit	IOP (Media $\pm$ SD [Min, Max])	P-value
Preoperative (n = 149)	16.5 $\pm$ 4.5 (9, 33)	/
24 hours (n = 148)	14.0 $\pm$ 4.9 (2, 30)	< 0,01*
1 week (n = 127)	15.0 $\pm$ 5.1 (2, 34)	< 0,01*
1 month (n = 127)	15.4 $\pm$ 3.9 (7, 28)	0,04*
6 months (n = 128)	15.2 $\pm$ 4.1 (8, 28)	< 0,01*
1 year (n = 123)	14.6 $\pm$ 3.2 (8, 24)	< 0,01*
2 years (n = 94)	15.3 $\pm$ 3.2 (7, 26)	0,01*
3 years (n = 61)	15.7 $\pm$ 3.1 (9, 23)	0,07
4 years (n = 35)	14.4 $\pm$ 3.5 (9, 22)	0,01*
5 years (n = 15)	15.1 $\pm$ 3.4 (7, 20)	0,35

Tables 3 and 4: Variables that influence average IOP fixed effects = visit, age, sex, diagnosis, severity; random effects = patient id.

Variable	p – value
Age	0,36
Sex	0,02*
Diagnosis	< 0,01*
Severity	0,52
Visit	<0,01*

Tables 3

Interaction	p – value
Sex * Visit	0,64
Diagnosis * Visit	0,17

Table 4

Table 5: Number of Drugs in each visit

Visit	N° of Drugs (Mean ± DE [Min, Max])	P-value
Preoperative	1.9 ± 0.8 (0, 4)	/
1 year	0.4 ± 0.8 (0, 3)	< 0,01*
2 years	0.5 ± 0.8 (0, 3)	< 0,01*
3 years	0.5 ± 0.8 (0, 3)	< 0,01*
4 years	0.4 ± 0.7 (0, 3)	< 0,01*
5 years	0.2 ± 0.5 (0, 2)	< 0,01*

Figures

Figure 1: The results show that IOP was lower in all postoperative assessments compared to preoperative values.

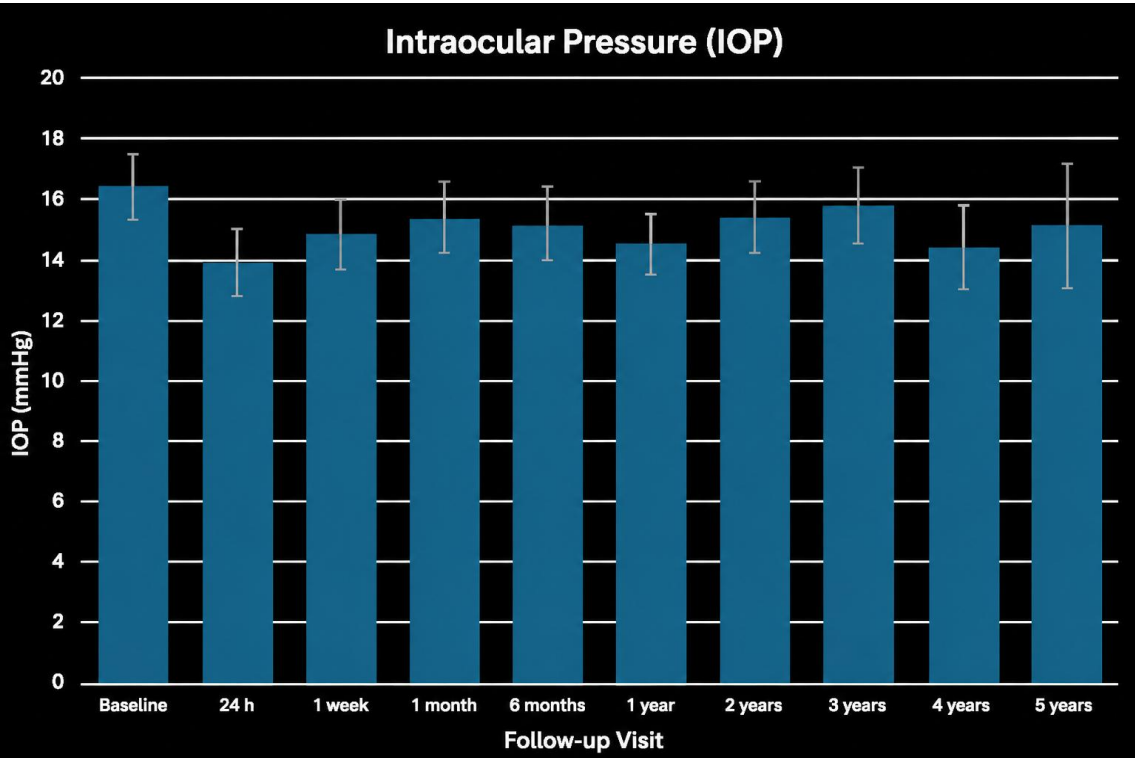
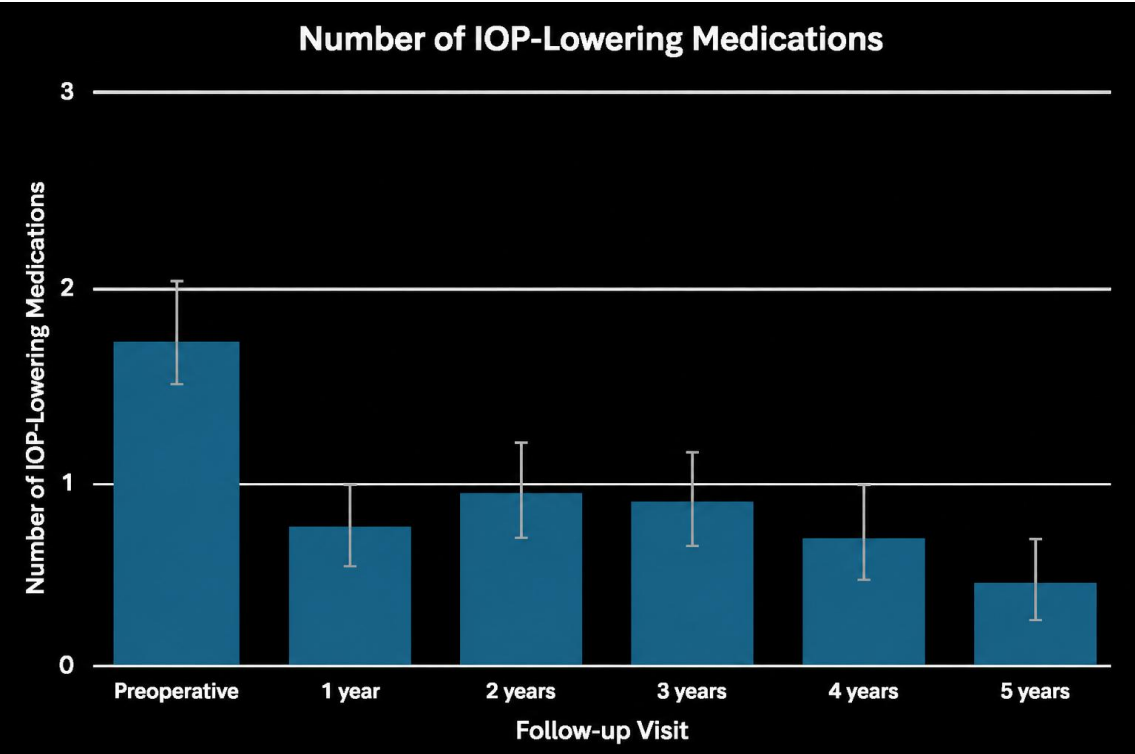


Figure 2: The number of medications decreased significantly at all post-surgical visits compared to the preoperative assessment.



References

1. Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. **Br J Ophthalmol.** 2006;90(3):262–267.
2. Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: a review. **JAMA.** 2014;311(18):1901–1911.
3. Heijl A, Leske MC, Bengtsson B, et al. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. **Arch Ophthalmol.** 2002;120(10):1268–1279.
4. Leske MC, Heijl A, Hussein M, et al. Factors for glaucoma progression and the effect of treatment: the Early Manifest Glaucoma Trial. **Arch Ophthalmol.** 2003;121(1):48–56.
5. Saheb H, Ahmed I. Micro-invasive glaucoma surgery: current perspectives and future directions. **Curr Opin Ophthalmol.** 2012;23(2):96–104.
6. Francis BA, Singh K, Lin SC, et al. Novel glaucoma procedures: a report by the American Academy of Ophthalmology. **Ophthalmology.** 2011;118(7):1466–1480.
7. Kerr NM, Wang J, Barton K. Minimally invasive glaucoma surgery as primary stand-alone surgery for glaucoma. **Clin Exp Ophthalmol.** 2017;45(4):393–400.
8. Pillunat LE, Erb C, Jünemann AG, Kimmich F. Micro-invasive glaucoma surgery (MIGS): a review of surgical procedures using stents. **Clin Ophthalmol.** 2017;11:1583–1600.
9. Richter GM, Coleman AL. Minimally invasive glaucoma surgery: current status and future prospects. **Clin Ophthalmol.** 2016;10:189–206.
10. Samuelson TW, Sarkisian SR Jr, Lubeck DM, et al. Prospective, randomized, controlled pivotal trial of iStent inject trabecular micro-bypass in primary open-angle glaucoma. **Ophthalmology.** 2019;126(6):811–821.
11. Grant WM. Experimental aqueous perfusion in enucleated human eyes. **Arch Ophthalmol.** 1963;69:783–801.
12. Voskanyan L, García-Feijó J, Belda JI, et al. Prospective unmasked evaluation of the iStent inject system for open-angle glaucoma: Synergy Trial. **Adv Ther.** 2014;31(2):189–201.
13. Bahler CK, Smedley GT, Zhou J, Johnson DH. Trabecular bypass stents decrease intraocular pressure in cultured human anterior segments. **Am J Ophthalmol.** 2004;138(6):988–994.
14. Fea AM, Consolandi G, Zola M, et al. Micro-bypass implantation for primary open-angle glaucoma combined with phacoemulsification: long-term results. **J Ophthalmol.** 2015;2015:795357.
15. Fea AM, Belda JI, Rêkas M, et al. Prospective unmasked randomized evaluation of the iStent inject versus two ocular hypotensive agents in primary open-angle glaucoma. **Clin Ophthalmol.** 2014;8:875–882.
16. Craven ER, Katz LJ, Wells JM, Giamporcaro JE. Cataract surgery with trabecular micro-bypass stent implantation in patients with mild-to-moderate open-angle glaucoma. **J Cataract Refract Surg.** 2012;38(8):1339–1345.
17. Ferguson TJ, Swan R, Ibach M, Schweitzer J. Evaluation of iStent inject implantation with cataract surgery in a real-world clinical setting. **Clin Ophthalmol.** 2020;14:185–193.
18. Lindstrom R, Sarkisian SR Jr, Lewis R, et al. Long-term outcomes of iStent inject trabecular micro-bypass implantation with cataract surgery. **Clin Ophthalmol.** 2021;15:409–420.

19. Hengerer FH, Auffarth GU, Conrad-Hengerer I. iStent inject trabecular micro-bypass with cataract surgery: 5-year outcomes. **J Cataract Refract Surg.** 2019;45(7):929–936.
20. Gillmann K, Mansouri K. Minimally invasive glaucoma surgery: where is the evidence? **Asia Pac J Ophthalmol (Phila).** 2020;9(3):203–214.
21. Ansari E. An update on implants for minimally invasive glaucoma surgery (MIGS). **Ophthalmol Ther.** 2017;6(2):233–241.
22. Hood DC, Raza AS. On improving the use of OCT imaging for detecting glaucomatous damage. **Br J Ophthalmol.** 2014;98(Suppl 2):ii1–ii9.
23. Bengtsson B, Heijl A. A visual field index for calculation of glaucoma rate of progression. **Am J Ophthalmol.** 2008;145(2):343–353.
24. Allingham RR, de Kater AW, Ethier CR. Schlemm's canal and the collector channels in normal and glaucomatous eyes. **Invest Ophthalmol Vis Sci.** 1996;37(4):814–823.
25. Salimi A, Watt H, Harasymowycz P. iStent inject Trabecular Micro-Bypass with or Without Cataract Surgery Yields Sustained 5-Year Glaucoma Control. **Adv Ther.** 2022;39:1417–1431. doi:10.1007/s12325-021-02039-4.
26. Neuhann TH, Hornbeak DM, Neuhann R, Giamporcaro JE. Long-term effectiveness and safety of trabecular microbypass stent implantation with cataract surgery in patients with glaucoma or ocular hypertension: Five-year outcomes. **J Cataract Refract Surg.** 2019;45(3):312–320. doi:10.1016/j.jcrs.2018.10.029.
27. Guedes RAP, Gravina DM, Guedes VMP, Guedes Moraes DA, Chaoubah A. Five-Year Outcomes of iStent inject Implantation With or Without Phacoemulsification in Eyes with Open-Angle Glaucoma. **Ophthalmol Ther.** 2025;14(6):1219–1235. doi:10.1007/s40123-025-01134-x

Declarations

Ethics approval and consent to participate This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of the Virgen Macarena University Hospital.

Consent for publication: Informed consent was obtained from all individual participants included in the study.

Competing interests: The authors have no relevant financial or non-financial interests to disclose.

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