What is the role of iStent in glaucoma management in 2019?

Helen Chan FRANZCO¹ and Anne Brooks PhD FRANZCO^{1,2}

1. Royal Victorian Eye and Ear Hospital, Melbourne, Australia
2. Centre for Eye Research Australia, Melbourne, Australia

Correspondence: Helen Chan, Royal Victorian Eye and Ear Hospital, Melbourne, Australia

Helen.Chan@eyeandear.org.au

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Use of minimally invasive glaucoma surgery (MIGS) has grown over recent years and has now become mainstream. Of the MIGS devices, the iStent has received special attention for several reasons: it was the first device to market; its ease of implantation and lack of bleb formation make it attractive to general ophthalmologists and glaucoma specialists alike; and an MBS item number in conjunction with cataract surgery has been made available. Medicare data show 4,271 cataract surgeries with trans-trabecular devices performed in Australia in the last financial year alone.

The quality of evidence continues to improve, with recent publication of meta-analyses of the first-generation iStent – both combined with phacoemulsification(1-3) and as standalone surgery(1, 2, 4) – and a two-year prospective randomised control trial of the second-generation iStent inject.(5) The safety of these devices is well-established in the short term(1-5) – the most common adverse events are transient hyphema, stent malposition or blockage – and long-term data are awaited.

One of the main questions regarding the efficacy of the iStent is: what is the additional effect of the device in a combined surgery compared to cataract surgery alone? A meta-analysis of 1,767 eyes from 28 studies has shown significantly greater reduction in intraocular pressure (IOP) (6.3 compared to 4.62mmHg reduction, weighted mean difference 1.68mmHg and 95% confidence interval 1.11-2.25mmHg), a greater reduction in number of glaucoma drops (-1.4 drops compared to -0.6 drops, WMD 0.80, 95% CI 0.75-0.85) after phaco-iStent compared to phacoemulsification alone.(2) More recently, a large randomised trial of 500 eyes showed that 63.2% of eyes undergoing phacoemulsification plus iStent inject achieved an IOP ≤ 18 mmHg off all medications compared to only 50% undergoing phacoemulsification alone at 2 years.(5) Patients receiving the iStent inject had a greater mean reduction in number of drops (-1.2 drops at 2 years) compared with

phacoemulsification alone (-0.8 drops). These effects are modest but clinically significant – the Early Manifest Glaucoma Trial showed that every 1mmHg reduction is associated with a 10% decreased risk of progression.⁽⁶⁾ Moreover, medication reduction improves conjunctival health in the event that later filtration surgery is required. It is a particular advantage if the number of drops can be safely reduced to ≤ 1 – patient adherence reduces to less than 50% with >1 medication.⁽⁷⁾ Cost-effectiveness studies have been performed using health econometric data from the United Kingdom, Canada and New Zealand,^(8, 9) and quality of life analyses are in progress.

Since 2016, only the iStent inject has been available in Australia, having replaced the first-generation iStent. There have been no randomised trials comparing the first- and second-generation devices. In this issue Hooshmand et al. report the first prospective study comparing iStent versus iStent inject, in combination with cataract surgery.⁽¹⁰⁾ In this case series, each eye received either 1 iStent or 2 iStent injects (there are two preloaded stents in each second-generation injector). The results are similar in each group, with 56.0% of iStent and 51.3% of iStent inject eyes achieving IOP ≤ 18 mmHg without medications at 12 months. The mean IOP was reduced from 18.9 to 16.6mmHg in the iStent group and 18.9 to 16.9mmHg in the iStent inject group. The mean number of glaucoma drops was reduced compared to baseline in both groups, from 1.7 to 0.6 in the iStent group and 1.6 to 0.7 in the iStent inject group, and approximately one-third of patients in both groups were drop-free at 12 months.

By contrast, the only other study comparing iStent and iStent inject reported a significant difference between the two devices. Guedes et al. reported a greater IOP reduction in eyes following phaco-iStent inject compared to phaco-iStent (26.6 vs. 15.8%) and a greater reduction in average number of drops (from 2.3 to 0.4 for

phaco-iStent inject vs. 1.8 to 0.4 for phaco-iStent eyes).(11) However this was a retrospective series and the groups were not evenly matched at baseline, with the iStent inject group starting with a higher preoperative IOP and number of medications.

The effect size reported by Hooshmand et al. is smaller than reported separately for the phaco-iStent(1, 3) or phaco-iStent inject(2, 5, 12). This may reflect a “real-world” setting compared to that of a clinical trial – for example pre- and post-operative drop washout periods were not included. The authors are also early adopters of this technology and it is unclear if there may have been an initial learning effect.

Is there a difference between the iStent and iStent inject? The postoperative IOP and mean number of drops were similar between groups. Interestingly, of those who did restart drops, the mean time to drop initiation was shorter in the iStent inject group than the iStent group (7 vs. 12 months). The authors hypothesise that the larger-sized iStent allowed greater drainage compared to two smaller-sized iStent injects, however ex vivo studies of cultured human anterior segments have shown increased outflow facility with iStent inject compared to iStent(13, 14), and increased outflow facility with 2x iStent injects compared to 1x iStent inject.(13) Ex vivo studies of course cannot account for postoperative scarring and perhaps a smaller stent is more vulnerable to narrowing or occlusion – histopathological studies have demonstrated fibrous material in and around explanted iStents.(15) Hopefully, there will be continued improvement in stent design to address this issue.

Lastly, Hooshmand et al. should be congratulated for this comparative study. Further comparative data examining the relative efficacy of the different MIGS devices are required. Ahmed et al. have recently published a prospective

randomised trial comparing iStent with the Hydrus microstent, as standalone surgery.⁽¹⁶⁾ However there are no comparisons of the iStent with the XEN Gel-Stent and only retrospective data comparing iStent with Cypass, Trabectome and Kahook dual blade.

Overall, the iStent and iStent inject are useful additional therapeutic options. Patient selection is critical and evidence is available to support its use in patients with mild-moderate glaucoma on 1-2 agents. Although the expected IOP reduction is not as large as that of traditional filtration surgery, for this population these devices give significant additional IOP lowering and medication reduction without significant additional risk compared to cataract surgery alone. There is increasing interest in expanding future indications for the device, including angle closure, uveitic and refractory glaucomas, and we await further developments with the standalone iStent which also appears promising.

REFERENCES

1. Lavia C, Dallorto L, Maule M, Ceccarelli M, Fea AM. Minimally-invasive glaucoma surgeries (MIGS) for open angle glaucoma: A systematic review and meta-analysis. PLoS One. 2017;12(8):e0183142.
2. Popovic M, Campos-Moller X, Saheb H, Ahmed IIK. 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.
3. Malvankar-Mehta MS, Iordanous Y, Chen YN, Wang WW, Patel SS, 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.

4. Malvankar-Mehta MS, Chen YN, Iordanous Y, Wang WW, Costella J, Hutnik CM. iStent as a Solo Procedure for Glaucoma Patients: A Systematic Review and Meta-Analysis. PLoS One. 2015;10(5):e0128146.
5. Samuelson TW, Sarkisian SR, Jr., Lubeck DM, Stiles MC, Duh YJ, Romo EA, 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.
6. Heijl A, Leske MC, Bengtsson B, Hyman L, Bengtsson B, Hussein M, et al. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. Arch Ophthalmol. 2002;120(10):1268-79.
7. Saini SD, Schoenfeld P, Kaulback K, Dubinsky MC. Effect of medication dosing frequency on adherence in chronic diseases. Am J Manag Care. 2009;15(6):e22-33.
8. Agrawal P, Bradshaw SE. Systematic Literature Review of Clinical and Economic Outcomes of Micro-Invasive Glaucoma Surgery (MIGS) in Primary Open-Angle Glaucoma. Ophthalmol Ther. 2018;7(1):49-73.
9. Ngan K, Fraser E, Buller S, Buller A. A cost minimisation analysis comparing iStent accompanying cataract surgery and selective laser trabeculoplasty versus topical glaucoma medications in a public healthcare setting in New Zealand. Graefes Arch Clin Exp Ophthalmol. 2018;256(11):2181-9.
10. Hooshmand J, Rothschild P, Allen P, Kerr NM, Vote BJ. Minimally invasive glaucoma surgery: Comparison of iStent with iStent *inject* in primary open angle glaucoma. Clin Experiment Ophthalmol 2019; 47: pp-pp .
11. Guedes RAP, Gravina DM, Lake JC, Guedes VMP, Chaoubah A. Intermediate Results of iStent or iStent inject Implantation Combined with Cataract Surgery in a Real-World Setting: A Longitudinal Retrospective Study. Ophthalmol Ther. 2019;8(1):87-100.
12. Arriola-Villalobos P, Martinez-de-la-Casa JM, Diaz-Valle D, Morales-Fernandez L, Fernandez-Perez C, Garcia-Feijoo J. Glaukos iStent inject(R) Trabecular Micro-

Bypass Implantation Associated with Cataract Surgery in Patients with Coexisting Cataract and Open-Angle Glaucoma or Ocular Hypertension: A Long-Term Study. *J Ophthalmol.* 2016;2016:1056573.

13. Bahler CK, Hann CR, Fjield T, Haffner D, Heitzmann H, Fautsch MP. Second-generation trabecular meshwork bypass stent (iStent inject) increases outflow facility in cultured human anterior segments. *Am J Ophthalmol.* 2012;153(6):1206-13.

14. 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):988-94.

15. Capitenia Young CE, Ammar DA, Seibold LK, Pantcheva MB, SooHoo JR, Kahook MY. Histopathologic Examination of Trabecular Meshwork Changes After Trabecular Bypass Stent Implantation. *J Glaucoma.* 2018;27(7):606-9.

16. Ahmed IIK, Fea A, Au L, Ang RE, Harasymowycz P, Jampel H, et al. A Prospective Randomized Trial Comparing Hydrus and iStent Microinvasive Glaucoma Surgery Implants for Standalone Treatment of Open-Angle Glaucoma: The COMPARE Study. *Ophthalmology.* 2019.

1. Lavia C, Dallorto L, Maule M, Ceccarelli M, Fea AM. Minimally-invasive glaucoma surgeries (MIGS) for open angle glaucoma: A systematic review and meta-analysis. *PLoS One.* 2017;12(8):e0183142.

2. Popovic M, Campos-Moller X, Saheb H, Ahmed IIK. 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.

3. Malvankar-Mehta MS, Iordanous Y, Chen YN, Wang WW, Patel SS, 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.

4. Malvankar-Mehta MS, Chen YN, Iordanous Y, Wang WW, Costella J, Hutnik CM. iStent as a Solo Procedure for Glaucoma Patients: A Systematic Review and Meta-Analysis. *PLoS One*. 2015;10(5):e0128146.
5. Samuelson TW, Sarkisian SR, Jr., Lubeck DM, Stiles MC, Duh YJ, Romo EA, 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.
6. Heijl A, Leske MC, Bengtsson B, Hyman L, Bengtsson B, Hussein M, et al. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. *Arch Ophthalmol*. 2002;120(10):1268-79.
7. Saini SD, Schoenfeld P, Kaulback K, Dubinsky MC. Effect of medication dosing frequency on adherence in chronic diseases. *Am J Manag Care*. 2009;15(6):e22-33.
8. Agrawal P, Bradshaw SE. Systematic Literature Review of Clinical and Economic Outcomes of Micro-Invasive Glaucoma Surgery (MIGS) in Primary Open-Angle Glaucoma. *Ophthalmol Ther*. 2018;7(1):49-73.
9. Ngan K, Fraser E, Buller S, Buller A. A cost minimisation analysis comparing iStent accompanying cataract surgery and selective laser trabeculoplasty versus topical glaucoma medications in a public healthcare setting in New Zealand. *Graefes Arch Clin Exp Ophthalmol*. 2018;256(11):2181-9.
10. Guedes RAP, Gravina DM, Lake JC, Guedes VMP, Chaoubah A. Intermediate Results of iStent or iStent inject Implantation Combined with Cataract Surgery in a Real-World Setting: A Longitudinal Retrospective Study. *Ophthalmol Ther*. 2019;8(1):87-100.
11. Arriola-Villalobos P, Martinez-de-la-Casa JM, Diaz-Valle D, Morales-Fernandez L, Fernandez-Perez C, Garcia-Feijoo J. Glaukos iStent inject(R) Trabecular Micro-Bypass Implantation Associated with Cataract Surgery in Patients with Coexisting Cataract and Open-Angle Glaucoma or Ocular Hypertension: A Long-Term Study. *J Ophthalmol*. 2016;2016:1056573.

12. Bahler CK, Hann CR, Fjield T, Haffner D, Heitzmann H, Fautsch MP. Second-generation trabecular meshwork bypass stent (iStent inject) increases outflow facility in cultured human anterior segments. *Am J Ophthalmol*. 2012;153(6):1206-13.
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):988-94.
14. Capitena Young CE, Ammar DA, Seibold LK, Pantcheva MB, SooHoo JR, Kahook MY. Histopathologic Examination of Trabecular Meshwork Changes After Trabecular Bypass Stent Implantation. *J Glaucoma*. 2018;27(7):606-9.
15. Ahmed IIK, Fea A, Au L, Ang RE, Harasymowycz P, Jampel H, et al. A Prospective Randomized Trial Comparing Hydrus and iStent Microinvasive Glaucoma Surgery Implants for Standalone Treatment of Open-Angle Glaucoma: The COMPARE Study. *Ophthalmology*. 2019.

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Author/s:

Chan, HHL;Brooks, AMV

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