# LITERATURE REVIEW

# MINIMALLY INVASIVE GLAUCOMA SURGERY (MIGS): COMPARISON OF TRABECULAR VERSUS SUPRACHOROIDAL ROUTE

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#### ABSTRACT

**Introduction:** Because of the high rate of complications associated with traditional glaucoma filtering surgery, various research were launched to develop a new device, such as drainage channels, such as Glaucoma Drainage Devices.

**Objective:** To compare the efficacy and safety of trabecular route and suprachoroidal MIGS in eyes with mild to moderate glaucoma with and without cataract extraction of these two devices.

*Methods:* Literature search was conducted using online database such as Google Scholar, Pubmed, Survey of Ophtalmology, and Clinical Key.

**Result:** Since the IOP-lowering efficacy of these treatments is restricted by episcleral venous pressure, MIGS targeting the trabecular outflow system may be the best option for patients with mild-to-moderate open-angle glaucoma.

**Conclusion:** The implantation of trabecular iStents resulted in a considerable reduction in IOP, particularly in mild and moderate POAG. Both MIGS versions have good efficacy and safety profiles, with only minor problems like microscopic hyphema and stent blockage.

Keywords: glaucoma, Minimally Invasive Glaucoma Surgery (MIGS), iStents, cypas

### **INTRODUCTION**

laucoma is a group of optic nerve diseases, characterized by selective and progressive loss of retinal ganglion cells and their axons. It is well known that glaucoma is the second leading cause of irreversible blindness worldwide and increasing number in

Indonesia.1,2

The global prevalence of glaucoma has been estimated 64.3 million by 2014 and has projected to be 76 million by 2020 and 111.8 million by 2040, with the largest number of glaucoma cases worldwide was counted in Asia.<sup>2</sup> Data from Cipto Mangunkusumo Hospital from July 2013 – June 2014 showed the number of glaucoma patients were 12.801 from 131.465 total of out-patients patients in Kirana Eye Clinic.

Penetrating filtering surgery, that is, trabeculectomy, is currently the most commonly performed incisional surgical procedure for uncontrolled glaucoma on maximal medical treatment. It remains the gold standard surgery and is usually reserved for moderate to severe cases of glaucoma.<sup>3</sup> The success rates of trabeculectomy varies between 40-98%.<sup>9</sup> A shift in accelerating trend to utilize tube shunts more often in many countries and to be use as primary surgery or after trabeculectomy failed.<sup>3,4</sup> Based on TVT study, comparison between trabeculectomy versus tube implant had similar IOP end result in long term period.<sup>5</sup>

Recently, new glaucoma surgical procedures have increased in popularity, these procedures are called Minimally or Micro- Invasive Glaucoma Surgery (MIGS). The era of MIGS had began as technology evolved, demographic pressures increased, and the glaucoma care community recognized that a new interventional strategy needed to exist to take care of patients who required more IOP control than can be provided by medical approaches but who do not need aggressive surgical intervention.<sup>6–8</sup> MIGS can usually be combined with cataract surgery, and most clinical studies have analyzed results of combined surgery. With MIGS, there is a trade-off between enhanced safety and efficacy compared to conventional filtering surgery. MIGS can be classified on the basis of the targeted aqueous outflow pathway: via trabecular, via the suprachoroidal, or via the subconjunctival based. There are 3 devices that target the juxtacanalicular part of the trabecular meshwork (TM), which are iStent, iStent-inject [Glaukos Inc., Laguna Hills.], CA, USA], and Hydrus [Ivantis Inc., Irvine, CA, USA].<sup>9,10</sup>

*iStent* and *iStent-inject* have been used more by surgeon with good result. Principally these procedures like trabeculectomy, which removes the juxtacanalicular trabecular meshwork and inner wall of Schlemm's canal, to remove or bypass the inner wall of Schlemm's canal and allow aqueous directly access from the anterior chamber to the collector channels at the outer aspect of Schlemm's canal. So, these MIGS provide a conduit for aqueous fluid into the Schlemm's canal through the TM, which is thought to be the primary location of outflow obstruction in open-angle glaucoma (OAG). It is commonly used iStent implantation in conjunction with cataract surgery to enhance the benefit greater IOP reduction in glaucoma eyes.<sup>11,12</sup>

While the other options are generating new and probably less physiological outflow pathways into the suprachoroidal space (Cypass), for another safety profile of different approaches needs to be considered, especially the risk for generating hypotony. The supraciliary space is a virtual space lying between the ciliary lying between the ciliary body and the sclera. Posteriorly, it is continuous with the suprachoroidal space. Supraciliary stents are placed in the anterior chamber angle with the device and applicator, making a blunt dissection between the scleral spur and the iris/ciliary body.<sup>12</sup>

This literature review will focus on currently available MIGS strategies and devices such as i-Stent, i-Stent inject and Cypass devices, which categorize as trabecular MIGS and suprachoroidal MIGS to emphasize the efficacy and safety of each types. There is a question to rise, how effective the MIGS is in lowering the IOP in glaucoma patients and is there any adverse event regarding of using MIGS? There are two common device MIGS available in market such as via trabecular; iStent and via suprachoroidal; Cypass.

The aim of this literature review to evaluate comparison the outcome of the efficacy and safety of trabecular pathway and suprachoroidal MIGS with and without cataract extraction of these two devises in eyes with mild to moderate glaucoma.

#### **METHODS**

Literature search was conducted using online database such as Google Scholar, Pubmed, Survey of Ophthalmology, and Clinical Key. Keywords used to search for the relevant articles were: "Minimally invasive glaucoma surgery" OR "Micro invasive glaucoma surgery" OR "MIGS" OR "Phaco-MIGS" OR "Supraciliary Microstent" OR "Trabecular Microbypass" AND "Glaucoma" OR "Open angle glaucoma" OR "Glaucoma and Cataracts".

Based on search results using keywords stated above, articles were considered eligible to be reviewed if the studies met the following inclusion criteria such as primary glaucoma patients, IOP <24 mmHg with 1 or 3 glaucoma eye drops, baseline unmedicated IOP >21 mmHg and less of 34 mmHg who undergo i-Stent (1<sup>st</sup> gen), iStent-inject (2<sup>nd</sup> gen) implantation and Cypass micro stenting with or without cataract surgery with efficacy end point data. The studies with follow-up shorter than 12 months, and any previous glaucoma surgery except laser trabeculoplasty were excluded.

In accordance with the provided definition of MIGS we included studies regarding:

- Trabecular Microbypass Stent (iStent (1<sup>st</sup> gen), iStent-inject (2<sup>nd</sup> gen) [Glaukos Inc., Laguna Hills.], CA, USA]).
- Supraciliary Microstent (Cypass Transcend Medical, Menlo Park, CA, USA)

Baseline characteristics of included studies were highly variable in terms of glaucoma severity, initial visual acuity, washed-out IOP values, all of the reviewed studies use Goldmann applanation as a standard tool for measuring the IOP and number of glaucoma medications.

No.	Authors	Year	LoE	Subject (Eyes)	Mean Age (Year)	Device	Diagnosis
1.	Samuelson et al <sup>13</sup>	2011	II	233	$73 \pm 3.6$	iStent 1G + Phaco	OAG
	Samuelson et al <sup>14</sup>	2019	II	387	$69\pm8.2$	iStent2 G + phaco	OAG
2.	Katz et al <sup>15</sup>	2015	II	120	$68.1\pm0.11$	iStent 1G	OAG
3.	Voskanyan et al <sup>16</sup>	2014	III	99	$66.4 \pm 10.9$	iStent 2G	OAG
4.	Feijoo et al <sup>17</sup>	2015	III	65	$68.3 \pm 10.5$	Cypass	OAG
5.	Vold et al <sup>3</sup>	2016	II	505	$70\pm 8$	Cypass + phaco	OAG
6.	Hoeh et al <sup>12</sup>	2016	IV	23	N/R	Cypass + phaco	OAG
7.	Guedes et al <sup>18</sup>	2019	III	35	$67.8\pm8.9$	iStent 1G + phaco	POAG, PXG,
				23	$73.4\pm7.4$	iStent 2G + phaco	PG
8.	Clement et al <sup>19</sup>	2019	III	165	$71.4\pm7.6$	iStent 2G +phaco	OAG, OH, ACG
9.	Salimi et al <sup>20</sup>	2019	III	118	$68.56\pm8.74$	iStent 2G + phaco	POAG, PACG, NTG, PXG, PG

 Table 1. Studies characteristics

## RESULTS

Using the search strategies mentioned above, there were 566 literatures which related to the keywords. 188 duplicate literatures were removed and the remaining 378 literatures were screened. The full-text literatures for 34 references were assessed for eligibility, then 25 literatures were excluded due to inclusion criteria.

The studies were reviewed in this article were published from year 2011 to 2020. From all 10 studies, 7 were prospective studies, and 3 were case series. Variation of implant used as shown in the table 1; there are 74 studies using iStent implantation, only 2 studies was being reported as solo procedures, meanwhile 5 other studies in conjunction with cataract surgery. Furthermore; 2 studies were combined with phacoemulsification.

No.	Author	Device	Mean IOP at baseline (mmHg)	Follow up Time (month)	Mean IOP at last follow up (mmHg)	Mean IOP reduction (mmHg)
1	Katz et al <sup>15</sup>	1 iStent 1G	$25.0\pm1.1$	18	$15.9\pm0.9$	91
		2 iStent 1G	$25.0\pm1.7$	18	$14.1\pm1.0$	1.,9
		3 iStent 1G	$25.1 \pm 1.9$	18	$12.2\pm1.1$	12.9
2	Guedes et al <sup>18</sup>	iStent 1G+phaco	$16.1\pm3.6$	12	$15.4\pm2.4$	0.7
		iStent 2G+phaco	$16.2\pm3.1$	12	$13.1\pm2.2$	3.1
3	Samuelson et al <sup>13</sup>	iStent 1G+Phaco	$25.4\pm3.6$	12	$14.0\pm3.9$	8,4
	Samuleson et al <sup>14</sup>	iStent 2G+phaco	$24.83 \pm 3.4$	24	15.5	8.5
4	Voskanyan et al <sup>16</sup>	iStent 2G	$26.3\pm3.1$	12	$14.7\pm3.1$	10,2
5	Clement et al <sup>19</sup>	iStent 2G + phaco	$18.3\pm5.4$	12	$14.0\pm3.0$	.,3
6	Salimi et al <sup>20</sup>	iStent 2G + phaco	$17.0\pm3.8$	12	$13.97\pm2.65$	3.0
7	Hoeh et al <sup>12</sup>	CyPass + phaco	$25.5\pm4.9$	24	$15.9\pm3.1$	9.7
8	Feijoo et al <sup>17</sup>	CyPass	$24.5\pm2.8$	12	$16.4\pm5.5$	8.1
9	Vold et al <sup>3</sup>	CyPass + phaco	$24.5\pm3.0$	24	$17.0 \pm 3.4$	7.5

 Table 2. IOP reduction

Katz et al<sup>26</sup> and Voskanyan et al<sup>27</sup> iStent studies as a solo procedure showed that by implanted more iStents will decrease IOP regardless type of iStent. Moreover Samuelson et al<sup>30,31</sup> and Guedes et al<sup>32</sup> had different effect of the mean IOP reduction, when they implanted iStent 1<sup>st</sup> gen combined with phacoemulsification resulting 14.0 and 15.4 mmHg of IOP reduction and 15.5 and 13.1 mmHg by iStent 2<sup>nd</sup> gen combining with cataract extraction.

The study by Katz et al6 compared the efficacy of iStent 1<sup>st</sup> gen with a different number of glaucoma devices implanted, 1,2 or 3 implant. In his study indicated the highest reduction of the mean IOP post-surgically when utilization of 3 implants.

Furthermore, Guedes et al<sup>32</sup> when compared the efficacy of iStent 1<sup>st</sup> gen to iStent 2<sup>nd</sup> gen combined cataract surgery demonstrated the higher mean IOP reduction by iStent 2<sup>nd</sup> gen rather than iStent 1<sup>st</sup> gen. Clement et al<sup>33</sup> and Salimi et al<sup>28</sup> reported when combining iStent 2<sup>nd</sup> gen device with phacoemulsification giving the mean IOP reduction of 14.0 and 13.97 mmHg.

Cypass implanted alone has been reported by Feijoo et al<sup>24</sup> and showed the mean IOP reduction of 8.1 mmHg in one year follow up. Another studies by Hoeh et al<sup>29</sup>and Vold et al<sup>18</sup> studies when cypass combining phacoemulsification had the mean IOP reduction of 9.7 mmHg to 9.5 mmHg.

	Author	Treatment	Mean BCVA pre-op (logMAR)	Mean BCVA post-op (logMAR)
1	Katz et al <sup>15</sup>	1 iStent 1G	$0.28 \pm 0.34$	no significant changes
		2 iStent 1G	$0.39\pm0.40$	no significant changes
		3 iStent 1G	$0.24\pm0.35$	no significant changes
2	Guedes et al <sup>18</sup>	iStent 1G+phaco	20/40	Improve VA
		iStent 2G+phaco	20/40	Improve visual VA
3	Samuelson et al <sup>13</sup>	iStent 1G+phaco	45% eyes	94% improve≥20/40
			BCVA≥20/40	
	Samuleson et al <sup>14</sup>	iStent 2G+phaco		98% imporve≥20/40
4	Voskanyan et al <sup>16</sup>	iStent 2G	0.3	no significant changes
5	Clement et al <sup>19</sup>	iStent 2G + phaco	N/A	N/A
6	Salimi et al <sup>20</sup>	iStent 2G + phaco	$0.17\pm0.22$	$0.10\pm0.17$
7	Hoeh et al <sup>12</sup>	CyPass + phaco	N/A	N/A
8	Feijoo et al <sup>17</sup>	CyPass	N/A	N/A
9	Vold et al <sup>3</sup>	CyPass + phaco	$0.52 \pm 0.26$	N/A

### Table 3. BCVA changes

# **Table 4.** Number of antiglaucoma reduction

No.	Author	Device	Medication used before intervention	Follow- up (month	Medication used after interventio n	Mean antiglaucom a reduction
1	Katz et al <sup>15</sup>	1 iStent 1G	$1.71 \pm 0.16$	12	N/A	N/A
		2 iStent 1G	$1.76\pm0.54$	12	N/A	N/A
		3 iStent 1G	$1.51\pm0.69$	12	N/A	N/A
2	Guedes et al <sup>18</sup>	iStent 1G+phaco	$1.8 \pm 0.8$	12	$0.1 \pm 0.2$	1.7
		iStent 2G+phaco	$1.7\pm0.8$	12	$0.5\pm0.8$	1.2
3	Samuelson et al <sup>13</sup>	iStent 1G+phaco	$1.5\pm0.6$	12	$0.2 \pm 1.0$	$1.4\pm0.8$
	Samuleson et al <sup>14</sup>	iStent 2G+phaco	$1.5 \pm 0.7$	24	$0.8 \pm 0.6$	1.2
4	Voskanyan et al <sup>16</sup>	iStent 2G	$2.21\pm0.44$	12	$1.4 \pm 0.8$	0.1
5	Clement et al <sup>19</sup>	iStent 2G + phaco	$1.65 \pm 1.28$	12	$0.47\pm0.95$	1,2
6	Salimi et al <sup>20</sup>	iStent 2G + phaco	$2.31 \pm 1.33$	12	$1.03 \pm 1.10$	1.28
7	Hoeh et al <sup>12</sup>	CyPass + phaco	2,2	24	1	1.2
8	Feijoo et al <sup>17</sup>	CyPass	$1.5 \pm 1.3$	12	$1.4 \pm 1.3$	0.1
9	Vold et al <sup>3</sup>	CyPass + phaco	1,3	24	0,6	0.7

No.	author	author Device		Number of eyes needed secondary surgery
1	Guedes et al <sup>18</sup> istent 1G+phaco		35	1 (2.86%)
		iStent 2G+phaco	23	0
2	Voskanyan et al <sup>16</sup>	iStent 2G	99	10(10.1%)
3	Samuelson et al <sup>13</sup>	iStent 1G+phaco	240	5 (4.5%)
	Samuelson et al <sup>14</sup>	iStent 2G+phaco	387	24(6.2%)
4	Clement et al <sup>19</sup>	iStent 2G + phaco	165	3 (1.8%)
5	Hoeh et al <sup>12</sup>	Cypass + phaco	23	5 (11%)
6	Feijoo et al <sup>17</sup>	Cypass	65	11 (16.9%)

Table 5. Number of eyes needed secondary surgery

There were 7 studies reported number of eyes needed secondary glaucoma surgery in their study group. Study by Feijoo et al<sup>17</sup> and Hoeh et al<sup>12</sup> which using Cypass implant reported a quiet high number of eye needed secondary glaucoma surgery 11(16.9%) and 5(11%)). The iStent study by Voskanyan et al<sup>16</sup>, Samuelson et al<sup>13,14</sup> and Guedes et al<sup>18</sup> showed the lower number of eyes needed secondary glaucoma surgery 10(10.1%), 5(4.5%), 24(6,6%) and 1(2.86%)). The secondary glaucoma surgeries reported were trabeculectomy, additional MIGS implantation and laser trabeculoplasty.

No	Author	Device	Hypoton y (%)	Elevated IOP (%)	Shallow/ Flat AC (%)	Hyphem a (%)	Cataract Progressi on (%)	Choroidal detachmen t/effusion (%)	Secondary glaucoma surgery (%)	Stent obstruc tion (%)	Endothel touch (%)
1	Katz et al <sup>15</sup>	1 iStent 1G	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
		2 iStent 1G	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
		3 iStent 1G	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
2	Guedes et al <sup>18</sup>	iStent 1G+phaco	N/A	N/A	1	N/A	N/A	N/A	N/A	N/A	N/A
		iStent 2G+phaco	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
3	Samuelson et al <sup>13</sup>	iStent 1G+phaco	1	3	0	0	0	0	4.5	4	0
	Samuelson et al <sup>14</sup>	iStent 2G+phaco	0	1	0	0	0	0	1	6.2	0
4	Voskanyan et al <sup>16</sup>	iStent 2G	0	10.1	0	0	1	0	3	3	0
5	Salimi et al <sup>20</sup>	iStent 2G +phaco	0	11	0	5		0	0	0	0
6	Hoeh et al <sup>12</sup>	CyPass +phaco	13.8		0	1.2	1.8	0	6	5.4	1.2
7	Feijoo et al <sup>17</sup>	CyPass	0	10.8	0	6.2	7.7	0	18.5	0	0
8	Vold et al <sup>3</sup>	CyPass +phaco	2.9	4.3	0	2.7	0	0	5.1	2.1	0

 Table 6. Complications after surgery

No.	Author	Device	Follow up period (month)	Definition of success	Success rate	Safety profile	Significant adverse events
1	Katz et al <sup>15</sup>	1 iStent 1G	18		N/A	acceptable	no significant adverse events
		2 iStent 1G			N/A		
		3 iStent 1G		Highest IOP reduction	N/A		
2	Guedes et	iStent 1G	12	IOP < 18 mmHg	80%	favorable	1 case of PAS
	al <sup>18</sup>	phaco	_	IOP < 15 mmHg	34.3%		occluding the
				IOP < 12 mmHg	0%		internal ostia of iStent
		iStent 2G	12	IOP < 18 mmHg	100%	favorable	no adverse
		phaco	-	IOP < 15 mmHg	73.9%		events
			-	IOP < 12 mmHg	26.1%		
3	Samuelson	iStent 1G	12	IOP < 21 mmHg	72%	acceptable	stent
	et al <sup>13</sup>	phaco		without			obstruction
		iStent 2G	24 -	$\frac{\text{medication}}{\text{IOP reduction} \geq}$	66%		(4%) Vs (6%)
	Samuelson	phaco	24	20% without	84%		
	et al <sup>14</sup>	P		medication	0470		
4	Voskanyan	iStent 2G	12	IOP reduction $\geq$	61%	acceptable	elevated IOP
	et al <sup>16</sup>			30% without			(10%)
			-	$\frac{\text{medication}}{\text{IOP} \le 18 \text{ mmHg}}$	66%		
				without	00 %		
				medication			
5	Clement et al <sup>19</sup>	iStent 2G	12	$IOP \le 18 \text{ mmHg}$	95.76%	acceptable	no significant
	al	+ phaco	_	$IOP \le 15 \text{ mmHg}$	67.27%		adverse events
6	Salimi et	iStent 2G	12	$IOP \le 18 \text{ mmHg}$	93%		no sight-
	$al^{20}$	+ phaco	-	$IOP \le 15 \text{ mmHg}$	70%		threatening
			-	$IOP \le 12 \text{ mmHg}$	29%		adverse events
7	Hoeh et	CyPass	12	IOP < 21 mmHg	65%	acceptable	transient
	al <sup>12</sup>			without			hypotony
0	Esilos at	CyDaga	12	medication	mot	a a a a m ta h la	(13.8%)
8	Feijoo et al <sup>17</sup>	CyPass	12	IOP reduction $\geq$ 30% without	not reported	acceptable	post-operative hyphema
	u			medication	reported		(7.3%)
9	Vold et al <sup>3</sup>	CyPass	24	$IOP \le 21 \text{ mmHg}$	61%	acceptable	BCVA
				without			reduction ≥10
			-	medication	<b>67</b> 07		letters (8%)
				$IOP \le 18 \text{ mmHg}$ without	67%		
				medication			
			-	$IOP reduction \geq$	53%%		
				20% without			
				medication			

Table 7. Surgio	al success rates
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Most studies reported more than 50% surgical success rate in achieving IOP-lowering target effect in the end of follow up. The highest success rate report is achieved from combined

surgery between iStent-inject + phacoemulsification from Clement et  $al^{19}$  and Salimi et  $al^{20}$  studies. The adverse events reported by the included studies were mostly not significant. Significant complications were reported from Cypass studies by Hoeh et  $al^{12}$  and Feijoo et  $al^{17}$ , they were transient hypotony (13.8%) and post-operative hyphema (7.3%), respectively.

## DISCUSSION

MIGS fill a gap that has existed in the treatment algorithm for glaucoma between medical therapy and laser at one end of the spectrum and conventional filtering glaucoma surgeries at the other. In situations where IOP reduction goals are more modest, the glaucoma is newly diagnosed, the optic nerve head damage is only mild to moderate, and/or the medication burden creates the risk of poor adherence, MIGS is a treatment option that should be considered.<sup>1,22,23</sup>

The current definition of MIGS includes 3 anatomical categories. The first is Schlemm's canal, by improving the trabecular outflow. The second is the suprachoroidal space, by improving the uveoscleral outflow through a connection between the anterior chamber and the suprachoroid. The third is the subconjunctival space, by creating an alternative outflow pathway for aqueos humor.<sup>12,21</sup>

Katz et al<sup>15</sup> evaluated the efficacy of the implantation of either one, two or three iStents during solo procedures without PE/IOL in 119 patients with OAG and found an IOP reduction of 20% without ocular hypotensive medication were achieved by 89.2%, 90.2%, and 92.1% of eyes in the one-, two-, and three-stent subgroups, respectively. This prospective study resulted over 80% of subjects attained both the primary end point of month-12 IOP reduction without medication of >20% from baseline unmedicated IOP and the secondary end point of month-12 IOP >18 mmHg without medication, a greater percentage of multiple-stent subjects vs the single-stent group shows month-12 IOP < 15 mmHg.<sup>15</sup>

Reduction of the mean IOP and the number of antiglaucoma medication after surgery was showed as the best result by the iStent 1<sup>st</sup> Gen implanted with more devices as reported by Katz et al<sup>15</sup>. The study from Guedes et al<sup>18</sup> and Salimi et al<sup>20</sup> which use iStent-inject shows smaller IOP reduction compared with the other studies which use iStent 1<sup>st</sup> gen. There is still no study which comparing iStent 1<sup>st</sup> gen and iStent-inject (2<sup>nd</sup> gen) directly head to head, but this IOP reduction results can be rationalized because iStent-inject has smaller in size and tube diameter rather than iStent 1<sup>st</sup> gen. This reason may cause the outflow of aqueous humor debit stream of iStent-inject smaller that iStent 1<sup>st</sup> gen. However samuelson et al<sup>30,31</sup> described iStent combined with phacoemulsification in sequentially study using iStent 1<sup>st</sup> gen followed by

iStent 2<sup>nd</sup> gen showed a better result of using iStent 2<sup>nd</sup> gen in follow 2 years.

Hoeh et al<sup>12</sup> study showed the 2 years outcomes of the Cypass Micro-Stent as adjunct intervention to phacoemulsification cataract surgery in patients with concomitant glaucoma are consistent with the therapeutic profile of a MIGS procedure. Adverse events were infrequent, no sight-threatening complications because of a device-related adverse event. Cypass is also associated with relatively fast recovery and streamlined postsurgical follow-up, more consistent with phaco-cataract surgery rather than conventional glaucoma surgery. It was also showed a sustained effect on both medications and IOP, with 50% reduction in the need of IOP-lowering concurrent with a more than 35% reduction of IOP.<sup>12</sup> It seem that Cypass had a greater effect on decreasing IOP compared to iStent implantation except for those implanted with multiple iStents without cataract extraction, however the *IOP- lowering* effects of all iStent groups and Cypass groups after surgery are various when compare with combined phacoemulsification in all MIGS procedures.<sup>24,25</sup>

Almost all of the studies show none of significant BCVA reduction after surgery. This condition might related with the fact that the subjects which were included in all of the reviewed studies were in cataract progression ages, study by Klamann et al<sup>26</sup> suggested that mini-device implantation in phakic eyes may accelerate cataract progression, this also had correlation with the increase of inflammation reaction in anterior chamber due to device implantation.

Surgical success rates in glaucoma surgical treatment and medical trials is commonly defined as an IOP reduction to < 21 mmHg without medication. According to this definition, all studies reported more than 50% success rate and offered acceptable safety profile. The significant adverse event reported from iStent-inject was elevated IOP which reported from Voskanyan et al<sup>16</sup> study. In term of Safety profile and adverse events of iStent and iStent-inject, blood reflux from Schlemm's canal into the anterior chamber is a common process that occurs intraoperatively. This reflux may be seen as a positive and normal sign which occurs when iStent and iStent-inject are well positioned in the trabecular meshwork. The most common adverse events in all studies were minor, and include temporary obstructions of the iStent, which were resolved in most cases by Nd-YAG laser treatment, and malpositioned micro-stents. No postoperative hypotony, loss of endothelial cells, and no signs of inflammation were being reported in any of the studies. As for all trabecular procedures, caution should be applied in patients with elevated EVP, in patients with lower baseline IOPs and in patients with obesity or metabolic syndrome.<sup>16,27</sup>

The safety profile of these two types of MIGS were favorable. Visual acuity remained stable or improved during follow-up. There were no cases of the complications seen with

filtering surgeries such as endophtalmitis, choroidal detachment or effusion, bleb-related infection or re-needling. Hypotony cases after surgery mostly found in Cypass implantation. The significant adverse events reported from Cypass was transient hypotony by Hoeh et al<sup>12</sup> study and post-operative hyphema by Feijoo et al<sup>17</sup> study.

MIGS technology has potential advantages that could improve the management of glaucoma. These include reducing the medication burden, which enhances patient quality of life, bypassing or delaying the need for more invasive surgery and preserving the conjunctiva if a more-invasive intervention were to be required later on.

The disadvantages as a new design and material, the glaucoma surgeons has to improve their surgical learning curves and skills. The IOP decrease is limited by scarring and encapsulation which difficult to manage and costly for developing country.

Limitation of this review is a bias due to the differences in IOP outcome with MIGS device implantation with or without cataract surgery. It is well documented that cataract surgery alone may have an IOP lowering effect, but implantation of MIGS devices does not alter angle anatomy.

## CONCLUSION

Trebecular iStents implantation significantly offered IOP reduction especially in mild and moderate POAG compare to Cypass. By performing multiple implantation has a greater efficacy rather than single-stent implantation, thus demonstrating stent implantation as a titratable therapy that can be tailored for patients to achieve even lower IOP target depending on severity and/or progression of OAG. Suprachoroidal space MIGS implantation; Cypass probable can offer a good option and maybe still has a potential effect for treatment an advanced cases with good safety profile.

Finally, both MIGS types have favorable efficacy and acceptable safety profiles with complications were mild such as microscopic hyphema and stent occlusion. There were no reports of serious complication, such as choroidal effusions, hypotony and bleb-related complications as for trabeculectomy and tube-shunt surgery being reported.

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References are written according to the rules of the Vancouver authors, numbered according to their appearance in the entire text, not alphabetically. Please use the references software to cite articles for your manuscript references, such as: EndNote, Mendeley, etc. It is written using Times New Rowman 10 with single space.

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