Review Article

Simplifying "target" intraocular pressure for different stages of primary open-angle glaucoma and primary angle-closure glaucoma

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Lowering of intraocular pressure is currently the only therapeutic measure for Glaucoma management. Many longterm, randomized trials have shown the efficacy of lowering IOP, either by a percentage of baseline, or to a specified level. This has lead to the concept of 'Target" IOP, a range of IOP on therapy, that would stabilize the Glaucoma/prevent further visual field loss, without significantly affecting a patient's quality of life. A clinical staging of Glaucoma by optic nerve head evaluation and perimetric parameters, allows a patient's eye to be categorized as having – mild, moderate or severe Glaucomatous damage. An initial attempt should be made to achieve the following IOP range for both POAG or PACG after an iridotomy. In mild glaucoma the initial target IOP range could be kept as 15-17 mmHg, for moderate glaucoma 12-15 mmHg and in the severe stage of glaucomatous damage 10-12 mmHg. Factoring in baseline IOP, age, vascular perfusion parameters, and change on perimetry or imaging during follow up, this range may be reassessed over 6 months to a year. "Target" IOP requires further lowering when the patient continues to progress or develops a systemic disease such as a TIA. Conversely, in the event of a very elderly or sick patient with stable nerve and visual field over time, the target IOP could be raised and medications reduced. An appropriate use of medications/laser/surgery to achieve such a "Target" IOP range in POAG or PACG can maintain visual fields and quality of life, preventing Glaucoma blindness.

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Glaucoma is commonly diagnosed and treated by all ophthalmologists, not glaucoma specialists alone. It is therefore essential that guidelines for the management of primary adult glaucomas – primary open-angle glaucoma (POAG) and chronic primary angle-closure glaucoma (PACG) – should be easy to apply at any level of eye care.

In POAG and chronic PACG after iridotomy, the intraocular pressure (IOP) is the primary risk factor for the development and progression of glaucoma, and studies have shown that IOP reduction can slow/prevent progression of glaucoma. Currently, lowering of IOP is the only therapy available to treat glaucoma, and most ophthalmologists are using the concept of "target" IOP, in one form or the other. However, the extent of IOP reduction is the common dilemma.[1,2]

The average IOP in a normal population without optic nerve head changes has been reported as 14–17 mmHg, but this could be different in different races [Table 1]. Once raised IOP has damaged the optic nerve and ganglion cells, it is logical that such tissues would merit an IOP reduced to at least this level, if not lower. This would maintain/improve function in damaged/dysfunctional cells or the few remaining ones that have been anatomically displaced or physiologically altered and therefore more prone to even moderately raised IOP [Fig. 1].

Target IOP is seen as a guesstimate that will stabilize glaucoma, based on an evaluation of severity of glaucomatous damage in an individual patient, and other known risk factors. In addition, a cost–benefit analysis of the therapy required to achieve that 'target" IOP should be discussed with the patient. Current studies appear to favor a simple, threshold range approach to "target" IOP, based on structural and functional changes due to optic nerve damage.[2]

A suggested range of initial target IOP for different stages of glaucomatous damage to prevent progression and therefore blindness are shown in Fig. 2. These are based on available long-term studies discussed in this review.

There are no uniformly accepted norms for determining target IOP; therefore, this review will discuss:
1. What is "normal" IOP?
2. The concept of "target" IOP

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Table 1: Some population based normal intraocular pressure values from literature

Study	Age group	Mean IOP±SD	Population
Aravind Comprehensive Eye Study[3]	40-49 50-59 60-69	14.7 (3.3) 14.5 (3.7) 14.1 (3.7)	Indians
Central India Eye and Medical Study[4]	>40	13.6±3.4	Indians
Rural South India[5,6]	>40	14.29 3.32	Indians
Fukuoka *et al*.[7]	>40	14.1±2.3	Japan
Tomoyose *et al*.[8]	>40	15.1±3.1	Japan
Leske *et al*.[9]	>40	Black: 18.7±5.2 Mixed: 18.2±3.8 White: 16.5±3.0	USA
Gutenberg Eye Study[10]	>35	14.0±2.6 mmHg	
Beaver Dam Eye Study[11]	>43	15.3/15.5 mmHg	USA

IOP: Intraocular pressure, SD: Standard deviation

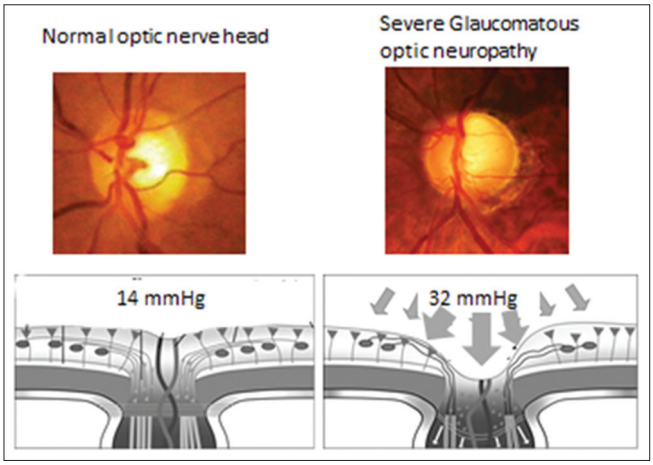

Figure 1: A normal optic nerve head functions at an average intraocular pressure of 14–17 mmHg (left), while an eye having glaucomatous optic neuropathy is damaged by high intraocular pressures, which need to be lowered so that the remaining nerve fibers can function as best as possible (right)

3. Parameters that influence progression and hence target IOP
4. Suggested methods to determine "target" IOP
5. Limitations of using "target" IOP
6. Clinical determination and management to attain "target" IOP
7. Reassessing "target" IOP over time.

What is "Normal" Intraocular Pressure?

It is important to know the IOP in people without glaucoma in a population, both for better diagnosis and also better management of glaucoma patients from that population, as there are racial differences. Hollows and Graham conducted a survey in the UK in 1966, where they found the mean applanation IOP to be 15.9 mmHg in males and 16.6 mmHg in females. Two standard deviations above the mean, which is the 97.5th percentile, was calculated to be 21 mmHg and hence the commonly held belief is that an IOP >21 mmHg should be considered as abnormal and that <21 mmHg as normal. Hollows and Graham themselves noted that >21 mmHg "should not be construed as meaning clinical abnormality, as the distribution is skewed and physiological variables need not necessarily follow a Gaussian distribution."[12] It is therefore to be understood that the so-called cutoff of an IOP of 21 mmHg is not clinical or evidence-based evidence of "normal," but a statistical construct.

There are known racial differences in measured IOP, and as clearly stated, a statistical construct cannot reflect a physiological parameter, with its inherent variability. Therefore, an IOP of < 21 mmHg should not be taken an appropriate "target" IOP or as normal.

Some population-based normal IO*P* values from literature are given in Table 1.

The Concept of "Target" Intraocular Pressure

In 1977, Chandler reviewed patients seen by him over the years and noted that patients with increasing severity of glaucomatous neuropathy did better with IOPs in the mid-teens or lower.[1] In the last few decades, many randomized studies have provided evidence-based data for the management of different stages and types of POAG, and the American Academy of Ophthalmology introduced the term "target" IOP for appropriate management. Palmberg analyzed Advanced Glaucoma Intervention Study (AGIS), data, and later surgical data to suggest the practice of "target" IOPs that would prevent progression.[13,14] There are also some long-term studies on PACG looking at long-term prognosis with different severity of damage.[15-19]

Definitions of target intraocular pressure

1. The European Glaucoma Society guidelines define target IOP as "an estimate of the mean IOP obtained with treatment that is expected to prevent further glaucomatous damage"[20]
2. The American Academy of Ophthalmology defines target IOP as "a range of IOP adequate to stop progressive pressure-induced injury"[21]
3. The World Glaucoma Association defines it as "an estimate of the mean IOP at which the risk of decreased vision-related quality of life due to glaucoma exceeds the risk of the treatment."[22]

The concept of "Target: IOP" is, therefore, that of an IOP that prevent further progression of glaucomatous visual field (VF) loss, without compromising a patient's quality of life. Quality of life would be significantly and permanently affected by progression of VF loss and stabilization of the VF is therefore the major goal.[23,24]

Parameters that Influence Progression and Hence Target Intraocular Pressure

VF loss due to glaucoma is irreversible and therefore needs to be prevented or slowed down so that the patient can continue his daily activities without a problem. Over the years, many risk factors for progression have been studied and highlighted.

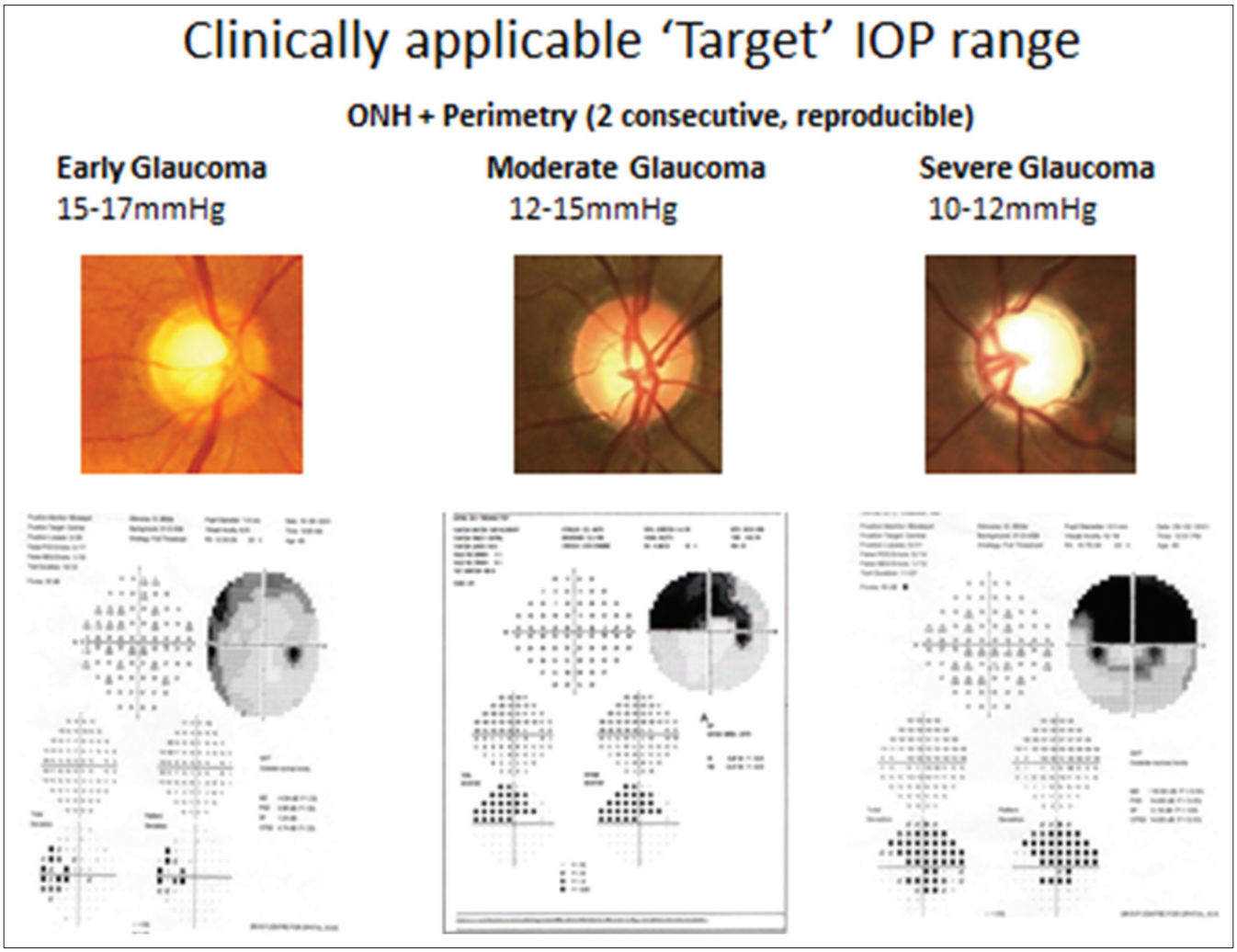

Figure 2: Suggested "target" range of intraocular pressures at three stages of glaucomatous damage as determined by optic nerve head and perimetric evaluation

Certain important risk factors need to be assessed before an objective plan to prevent/stabilize glaucoma progression in POAG and PACG can be formulated.

1. Examination of the optic nerve head, looking especially at the inferior and superior poles as pointed out by Chandler, helps identify thinning/notching/pallor of the neuroretinal rim and associated retinal nerve fiber layer defects. This provides a measure of the amount of structural damage to the nerve
2. IOP – At least three IOP measurements, taken at different times of the day, ideally with an applanation tonometer, help determine baseline IOP, the pressure at which optic nerve damage can be taken to have occurred. Any single IOP measurement taken between 7 am and 9 pm has a > 75% chance of missing the highest point of a diurnal curve.[25] Therefore, IOP should be measured at different times, to have the best chance of observing the maximal value. In PACG, it is important that the baseline IOP be recorded after iridotomy. On review, the IOP should be rechecked at the point of peak baseline IOP, if available
3. Perimetry – Reliable perimetry with reproducible VF defects on at least two consecutive fields allows staging of the functional visual loss in each patient. The speed of progression of VF loss over time; rate of progression on glaucoma progression analysis of Humphrey field analyzer should also be noted, as it will indicate the need for a more or less aggressive therapy
4. Age – Collaborative Initial Glaucoma Treatment Study (CIGTS) found that patients who were a decade older had a 40% risk of perimetric loss.[26] Early Manifest Glaucoma Trial (EMGT) reported that those > 68 years old were more likely to progress.[27] On analysis, AGIS also noted that an older patient was more likely to progress.[28] Similar association with age has been seen in PACG eyes as well[15]
5. Additional risk factors such as a family history of glaucoma, thinner central pachymetry, pseudoexfoliation, history of an acute PACG attack,[17] cardiovascular disease, patient's life expectancy, steroid use, transient ischemic attacks (TIAs), and other systemic problems should be recorded.[27,29]

Staging of Glaucomatous Damage

The extent of existing glaucomatous damage appears to significantly influence likely progression at a given IOP and therefore is extremely important in determining "target" IOP. Staging of glaucomatous damage can be done on the

basis of either or both – structural optic nerve head damage or functional loss on perimetry. Unfortunately, there is no universally accepted staging of either optic nerve head abnormalities or VF changes, with regard to their relevance to progression [Fig. 3].

Optic Nerve Head Examination

Chandler observed that "eyes with advanced cupping at both ends of the disc worsened, if IOP was not consistently < 15 mmHg… and require pressures below the average of the population." However, "eyes with limited cupping, confined to one pole of the disc, appear to withstand tension better, mid to high teens." Finally, "eyes with a normal disc appear to withstand pressure < 30 mmHg well" for years.[3] Interindividual variability in disc size and shape make evaluation difficult; however, the extent of thinning of the neuroretinal rim needs to be recorded.

Cup: disc (C: D) ratio is more commonly employed in clinical practice and recommended as a means of staging glaucomatous damage into – mild with a C: D of < 0.65, moderate 0.7–0.85, and severe > 0.9 [Table 2]. This is best assessed by a 90/78 D examination for accurate delineation of the neuroretinal rim. Ocular Hypertension Treatment Study (OHTS) found baseline C: D ratio to be a predictor of further damage in Ocular hypertensives. However, in patients with early POAG, EMGT did not find baseline C: D ratio to be a significant risk factor for glaucomatous progression. In advanced POAG, AGIS reported that patients with more severe glaucomatous damage, as measured by larger C: D ratio, 0.81 + 0.13, were at the great risk of progression. Sihota *et al*. found baseline linear C: D on Heidelberg retina tomography (HRT) to be a significant risk factor for progression at all stages of glaucomatous neuropathy in both POAG and PACG eyes.[15,16]

For example, a significant narrowing or loss of neuroretinal rim at both poles, with a C: D ratio of 0.8, would need a "target" IOP below the population average, which in Indians would mean <14 mmHg.

Spaeth *et al*. described a disc damage likelihood score, DDLS, based on the radial width of the narrowest neuroretinal rim, and divided into 10 stages, with stages 6–10 requiring aggressive therapy.[31]

Perimetric Staging

There are many suggested classifications of the severity of glaucomatous damage –Hodapp Parrish Anderson,[32] Glaucoma Severity Staging system (GSS),[33] enhanced GSS,[34] etc. They are based on the extent of damage and proximity to fixation, using global indices and number/percentage of significantly depressed loci, with multiple and varied stages. These need time and effort to analyze and stage a patient's perimetric loss, are

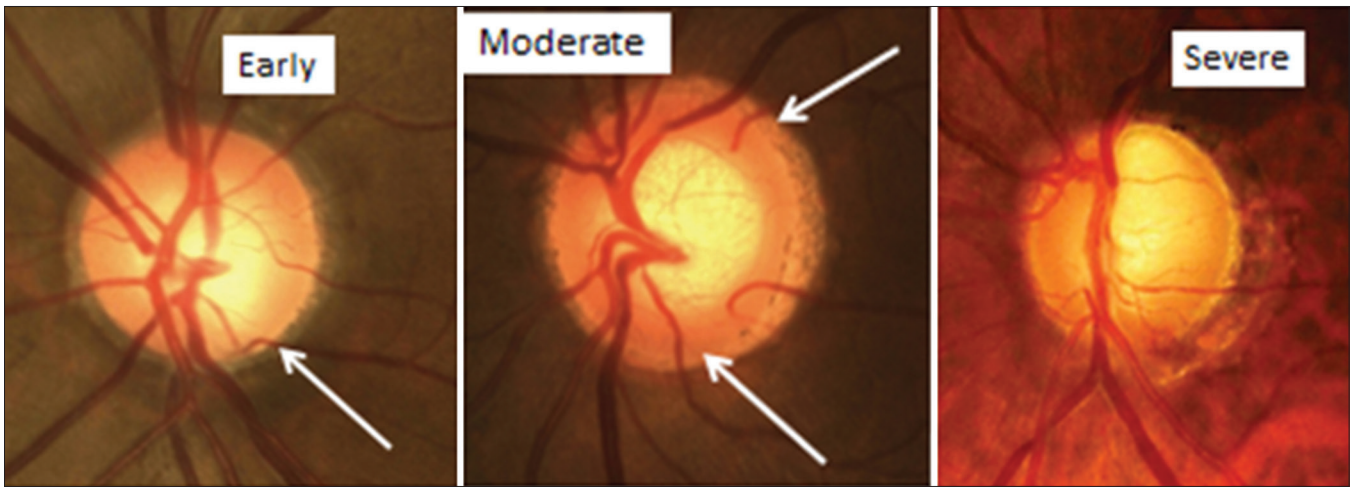

Figure 3: Staging glaucoma by a careful examination of the neuroretinal rim. Rim loss generally starts inferiorly, and then superiorly, finally extending around the disc. The inner edge of the neuroretinal rim should be identified by the bending of the blood vessels onto the surface of the neuroretinal rim, as shown by the arrows

Table 2: Some simpler Glaucoma staging methods

	Mild	Moderate	Severe
AAO[21]	Optic disc cupping but no visual field loss	Glaucomatous neuropathy with visual field loss not within 5° of fixation	Visual field loss in both hemispheres or within 5° of fixation
Canadian guidelines[30]	C: D ratio <0.65 or mild visual field defect not within 10° of fixation	C: D ratio 0.7-0.85 or visual field defect not within 10° of fixation or both	C: D ratio >0.9 or visual field defect within 10° of fixation or both
International Classification of Diseases 10	Optic nerve abnormalities consistent with glaucoma + normal fields	Optic nerve abnormalities consistent with glaucoma + one hemifield abnormality, not within 5°	Optic nerve abnormalities consistent with glaucoma + both hemifield abnormality or within 5°

AAO: American Academy of Ophthalmology

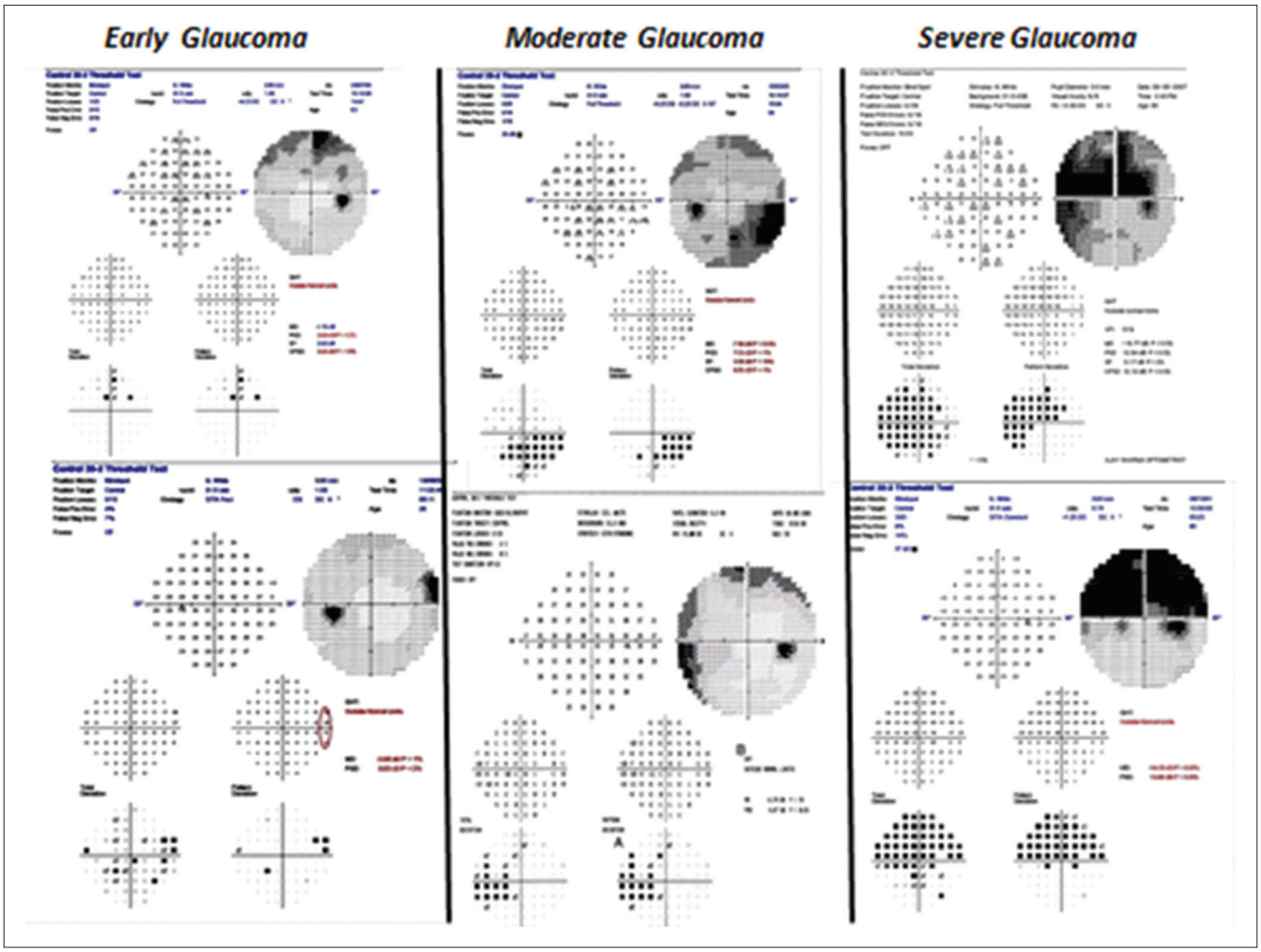

Figure 4: Representative visual field defects that could be classified as early, moderate, or severe glaucoma

largely used for research purposes at present, and are difficult to apply clinically, by most ophthalmologists.

EMGT found that a greater mean deviation (MD) loss at baseline was a risk factor for greater progression.[27] CIGTS reported that a unit increase in their baseline VF score was associated with a 0.74-unit progression.[26] In the AGIS, patients with greater baseline damage, as evidenced by perimetric MD values of − 11.4 ± 5.5, were more likely to progress rapidly.[20] The odds of VF progression increased by 11% for every 1-dB worsening in baseline MD.[18] Baseline functional damage determination requires any defect to be reproduced on at least two occasions, to obviate a learning curve, perimetric noise, etc.

There is therefore a felt need for simple glaucoma staging guidelines so that appropriate management algorithms can be developed and validated. All perimeters with normative data provide global indices and contain a plot highlighting localized loss in the VF that is definitive of glaucoma, similar to the pattern deviation plot on HFA. These can be easily used to ascertain the pattern of loss and stage glaucoma in each eye [Table 2 and Fig. 4].

Some simpler glaucoma staging methods are detailed in Table 2.

Methods of Determining Target Intraocular Pressure

Having ascertained the degree of VF damage, baseline IOP, and risk factors, an IOP that would prevent further damage needs to be set. There needs to be a balance, between setting an appropriate target to prevent optic nerve damage and being over aggressive in IOP lowering, to avoid side effects and an economic burden.

Various approaches for setting a target IOP include as follows:

- Threshold/absolute cut off value
- Percentage reduction
- Formula-based values.

An absolute/threshold target range is easiest for clinicians and is now most often used. Setting a 'target" IOP by percentage reduction or a threshold value has been used in many randomized control trials and studies. Formula-based "target" IOP setting is more time-consuming but appears to address risk factors in an individual patient.

Absolute/threshold values as "target" intraocular pressure

Threshold or absolute values of target IOP are those that are relatively fixed and can be applied to a large number if not all patients having a similar degree of glaucomatous damage.

Target IOP in AGIS was <18 mmHg and eyes with a mean MD of −10.5 dB had no average progression in 8 years of follow-up at pressures consistently reduced to <18 mmHg. However, a *post hoc* analysis showed that in these eyes, the average IOP was 12.3 mmHg. Eyes that had a mean IOP in the mid-teens showed progression by 2.5 dB, and those with a mean of 20 mmHg had a progression by 3.5 dB. Palmberg on analysis found a 30% chance of progression if the IOP remained in the mid-teens and 70% at 20 mmHg. Therefore, a target IOP of low teens should be set.[13]

A multicenter study in Japan reported that age and standard deviation of IOP were related to progression; however, in eyes with an average IOP below 15 and also 13 mmHg, only age and baseline VF total deviation were related to the progression rate.[35]

Many recent studies, especially surgical, have used designated "success" IOP levels as <18, <15, or even <12 mmHg, as the importance of lower IOPs, especially in moderate-to-advanced glaucoma where surgery is often performed, has become apparent. The World Glaucoma Association consensus on surgical success in glaucoma stated that IOP success should be reported with a number of alternative upper limits (i.e., ≤21, 18, 15, and 12 mmHg) and one lower limit (i.e., 6 mmHg).[22]

Two-hundred and forty-five POAG and PACG eyes were studied over 5 years in India, with a "target" IOP of < 18 mmHg in all eyes, except severe glaucoma where the "target" was 12–14 mmHg.[15] 12.1% and 15.5% of POAG and PACG eyes showed progression over 5 years, respectively. Moderate glaucomas commonly progressed, 32/31.5% and 26.6/25%, and hence, a target IOP of < 18 mmHg was not low enough in these eyes. Eyes with severe glaucoma rarely progressed, 0% and 5% in POAG and PACG, respectively, with an IOP of 10–12 mmHg. After that analysis, "target" IOPs in the same population were revised to < 15 mmHg, and a later evaluation of moderate POAG and PACG eyes over 10 years showed a progression in only 11% of eyes, over double the duration of review.[36]

Quek *et al*. reported that a higher mean IOP and a history of an acute attack in Chines eyes having PACG lead to poorer visual outcomes at 10 years. The mean IOP in eyes that progressed was 17.7 ± 2.6, as against 15.8 ± 2.1 mmHg in the eye that did not progress.[17]

In general, for mild-moderate-severe stage glaucoma, the initial target for absolute IOP cutoffs could be kept as IOP equal to or below 18 mmHg-15 mmHg-12 mmHg.

Percentage reduction in intraocular pressure

The large RCTs aimed for either percentage reduction in IOP or absolute values of IOP to gather information about long-term results in different severities of POAG and have generally presented reviews with both evaluations.

The OHTS found that an IOP reduction of 20% or to an IOP of 24 mmHg leads to progression in 19% of high-risk eyes over 8–10 years, suggesting that a greater reduction was necessary.

Patients having early glaucoma, an MD < 5 dB, were studied in EMGT, with a 72% progression off treatment, as compared to 45% on therapy, when IOP was lowered by a mean of 5.1 mmHg or 25%. In CIGTS, similar patients had a calculated lowering of IOP based on damage, with a mean IOP around 17 mmHg a reduction by 38% and 46% in medical or surgically treated eyes, respectively. Fifteen percent of eyes were seen to progress and 15% improve. Lichter *et al*. reported that those with a peak IOP of 13 mmHg had more frequent improvement than worsening of the VF.[37] With an IOP in the mid-teens, there was little improvement or progression; however, when

Table 3: Literature regarding mean intraocular pressure, percentage reduction in intraocular pressure and progression in different stages of primary open-angle glaucoma and primary angle-closure glaucoma

Study	Type of glaucoma	Baseline IOP	Percentage IOP reduction	Progression	Mean IOP level
Ocular Hypertension Treatment Study[29]	Open angle	24.9	20%	4.4/9.5%	19.3
Early Manifest Glaucoma Trial[27]	POAG	20.6	25%	45/62%	Mean fall 5.2 mmHg
Collaborative Normal Tension Glaucoma Study[38]	NTG		30%	12/35%	
Collaborative Initial Glaucoma Treatment Study Medical[26]	POAG	27	38%	15% progressed and 15% improved	17-18 mmHg
Surgical[26]		27	46%		14-15 mmHg
Advanced Glaucoma Intervention Study[28]	POAG	23.7-24.8	IOP mean 12.3 mmHg	Did not progress	
Stewart *et al*.[39]	POAG	19.5±3.8		0% 6% 26%	<12 mmHg<17 mmHg ≥ 18 mmHg
Sihota *et al*.[15]					
Early	POAG and PACG	24.9±8	32%-43%	18.7%	<18 mmHg
Moderate		28.3±5	44%	21.3%	<18 mmHg
Advanced		27.7±9	50%	2.3%	12 mmHg

IOP: Intraocular pressure, POAG: Primary open-angle glaucoma, PACG: Primary angle-closure glaucoma

peak IOP was > 16 mm Hg, progression was significant. Early glaucoma therefore appears to need an IOP in the mid-teens.

An Indian study[15] found perimetric progression in 21.3% of POAG and PACG eyes with moderate glaucomatous damage over 5 years when the target IOP was <18 mmHg. For a patient with moderate glaucomatous optic neuropathy, it appears that lower IOPs, with an upper limit of 15 mmHg, would be required to stabilize VFs.

The AGIS had an average reduction in IOP of 40% with significant rates of progression.[28] An Indian study recorded progression in just 2.3% of POAG and PACG eyes with advanced glaucoma over 5 years when the target IOP was 12–14 mmHg.[15]

Collaborative Normal-Tension Glaucoma Study aimed to lower IOP by 30% and found a 5-year progression in 12% of treated patients as against 35% in untreated eyes.

Literature regarding mean IOP, percentage reduction in IOP, and progression in different stages of POAG and PACG are collated in Table 3.

Formulas for setting a "target" intraocular pressure

Formulas attempt to incorporate baseline and risk factors into determining "target" IOP. Jampel first calculated target IOP by taking into account several attributes of the patient – initial pretreatment IOP, Z score (an indicator of disease severity), and Y factor (burden of therapy).[40]

Target IOP = (Initial IOP × [1 – initial pressure/100] – Z + Y ± 1 mmHg)

Modified equations increased the range of Z score, 0–7.[41,42] The CIGTS formula for target IOP was based on a patient's baseline IOP (mean of six IOP measurements taken over two visits) and their reference VF score (the mean of VF scores from at least two Humphrey 24-2 VF tests).[18]

Recent studies can be seen to have predetermined target/success IOPs as shown in Table 4.

Clinical Recommendations of Absolute/Threshold "Target" Intraocular Pressure Range in Different Stages of Primary Open-Angle Glaucoma and Primary Angle-Closure Glaucoma

Setting and achieving a "target" IOP range provide an algorithm for management. Quality of life may be affected by the medications used, but how much more is it affected by progressive glaucomatous optic neuropathy because it is not VF defects only, but contrast sensitivity, mobility, night vision, driving, etc., that are significantly affected. After an iridotomy, PACD eyes appear to respond similarly to IOP control, as in POAG.[15]

In ocular hypertension or primary angle closure with ocular hypertension, the decision to treat should depend on high-risk factors such as – a family history, high baseline C: D ratio, high baseline IOP, low central corneal thickness (CCT), and older age. The suggested upper limit of the initial IOP range should be less than 18 mmHg in patients at high risk of progression, older age, thinner CCT, males, cardiovascular disease, greater baseline C: D ratio, IOP, and pattern standard deviation.[29]

For a patient with early POAG/PACG, an IOP in the mid-teens, with a possible upper limit of 17 mmHg, should be initially aimed for and modified after a review with at least 6 monthly perimetric evaluations.

In POAG and PACG eyes with moderate glaucomatous damage, it appears that lower IOPs, with an upper limit <15 mmHg, would be required to stabilize VFs in the long term.[15]

In advanced POAG, there is an apparent correlation between peak IOP, IOP recorded over time, and progression.[28] Similarly, in advanced PACG, an IOP in the low teens was found to reduce progression to 5%.[15] Advanced glaucomas appear to need an IOP of <14 mmHg and preferably a mean of 12 mmHg with minimal fluctuations over time.

For normal tension glaucoma, a fall in IOP of 30% from baseline has been shown to significantly reduce progression.

After acute PACG, 15% of patients developed PACG among Caucasians, when the IOP was high after resolution of the

Table 4: IOP recording in recent studies

Study group	Type of study	IOP criteria (mmHg)
AVB[43]	Multicenter, randomized trial	Primary : 5-18 Secondary : 5-21 and 5-15
ABC Ahmed Baerveldt Comparison Study[44,45]	Multicenter, randomized trial	Primary: 6-21 Secondary: 6-18, 6-15
Cillino *et al*.[46]	Collagen implant-RCT	IOP ≤21,17,15
Lopes *et al*.[47]	Prostaglandin efficacy open-label	IOP ≤18
Sugimoto *et al*.[48]	Surgery - observational	IOP <22,19,16,13
Pakravan *et al*.[49]	AGV - RCT	IOP ≤15
Akkan and Cilsim[50]	Trabectome - RCT	IOP <21,18,15,12
Miki *et al*.[51]	Trabeculectomy - retrospective	IOP ≤15
Al-Mugheiry *et al*.[52]	MIGS -observational cohort	IOP ≤18, 15
Perez *et al*.[53]	Trabeculectomy - retrospective	IOP ≤18
Khandelwal *et al*.[54]	Trabeculectomy - retrospective	IOP ≤18,15,12
Nguyen *et al*.[55]	Trabeculectomy - retrospective case-control study	IOP ≤18,15,12
Takihara *et al*.[56]	Trabeculectomy - prospective cohort	IOP <21,18,15
Ahuja *et al*.[57]	Trabectome - retrospective	IOP <21,18
Sihota *et al*.[15,58]	POAG/PACG	IOP <18, <14
Sihota *et al*.[15,58]	POAG/PACG	IOP <16, <14, <12

AVB: Ahmed Versus Baerveldt, RCT: Randomized control trials, AGV: Ahmed glaucoma valve, MIGS: Microinvasive glaucoma stent, POAG: Primary open-angle glaucoma, PACG: Primary angle-closure glaucoma

attack. About 11%–16% were blind or visually impaired.[18,59] It is therefore apparent that patients with acute angle-closure glaucoma need a long-term control of IOP, to at least the population normal.

Determination of a target IOP is an important step in the management of glaucoma, but it cannot be determined with any certainty, and achieving the set target IOP does not give complete assurance that disease progression will be prevented, as many other factors also play a part in glaucoma progression.

EMGT concluded that mean elevated IOP is a major risk factor for progression in POAG, while fluctuations are not. A change of IOP by 1 mmHg resulted in about a 10% change in risk of progression.[60] De Moraes *et al.* found mean IOP, peak IOP, and IOP fluctuation to be significant risk factors for progression in POAG. Sihota *et al*. found that an intervisit fluctuation in IOP of > 4 mmHg over a median of three visits was associated with progression in POAG and chronic PACG eyes.[15]

Achieving "Target" Intraocular Pressure

Lowering an IOP to such levels may need medications, lasers, and even surgery in some patients. In a cross-sectional study from India, 92.2% POAG and 98.4% CPACG eyes were on ≤ 2 glaucoma medications at 5 years. 15.5% POAG eyes underwent trabeculectomy and 14.6% argon laser trabeculoplasty, while among CPACG eyes, 16.3% underwent trabeculectomy to achieve target pressure.[15] Thus, achieving target IOP in glaucoma patients is not difficult but requires the use of all therapeutic modalities. Liang *et al*. reported the initial use of trabeculectomy in PACG and an iridotomy and medications in PAC eyes.[58] Trabeculectomy is effective in significantly reducing IOP in the long term in both POAG and PACG eyes.[61-63]

The question frequently raised is whether such low IOPs should be aimed for as soon as therapy is instituted or whether a graded lowering of IOP should be done. van Gestel *et al*. studied a mathematical model of stepped reduction of IOP 21–18 mmHg, then further to 15 mmHg, or directly < 15 mmHg, and found that an initially low target IOP gave better-quality adjusted life years (QALYs), as compared to a gradual reduction over time.[64] A low initial target pressure (15 mmHg) resulted in 0.115 QALYs gained and €1550 (approximately Indian Rupees 116,777/-) saved compared to a gradual decrease from 21 to 15 mmHg upon progression. These lower target IOPs, however, required more medications, laser trabeculoplasty, trabeculectomies, and drainage implants. From a cost-effectiveness and quality-of-life point of view, it seems advantageous to aim for a low IOP in all glaucoma patients [Fig. 5].

Limitations of target intraocular pressure

IOP recording, even by applanation, is imprecise, with known diurnal and physiological variations, which could confound IOP measurements on long-term review. Corneal thickness and hysteresis changes can influence IOP measurements so that a baseline IOP and later IOPs should be evaluated keeping these fallacies in mind. For example, a review IOP of 16 mmHg in a patient with moderate damage and a

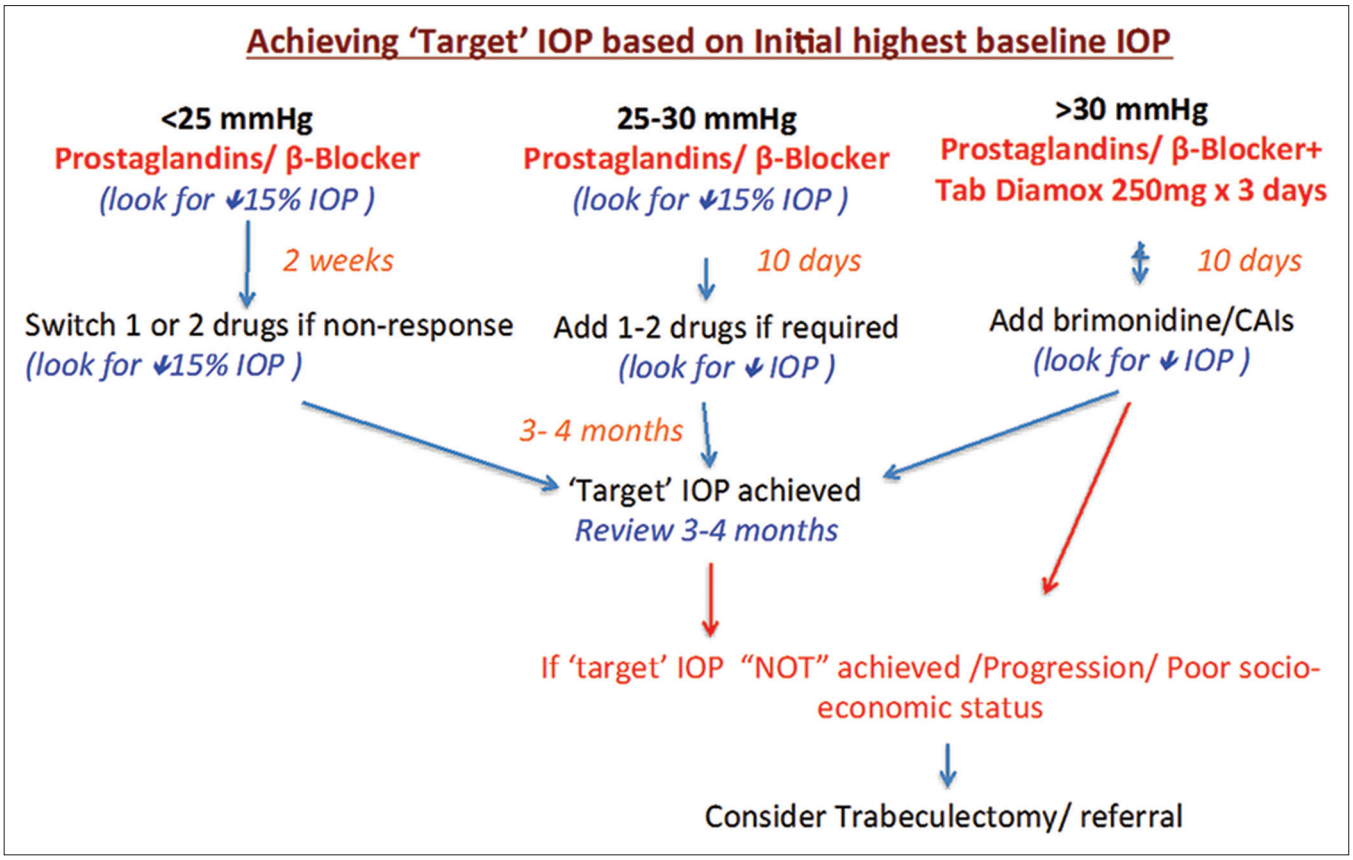

Figure 5: Achieving target intraocular pressure based on initial baseline intraocular pressure

CCT of 420 μ would have a higher corrected IOP that is not appropriate for this eye.

Aiming for low IOPs in all glaucoma patients needs aggressive IOP reduction and may lead to a reduction in quality of life due to the medications necessary to achieve this or the risks of glaucoma surgery. Adherence to therapy is difficult to ascertain on review and may lead to unnecessary increases in therapy when an IOP appears to be above the target. In addition, once a "target" IOP is set, patients could be stressed and unhappy if it is not achieved at every visit. There may be possible medicolegal consequences if "target" IOP is considered the standard of care and progression continues.

To date, there are inadequate data available to show that if an individual patient exceeds this target, he/she will progress, and there are not enough evidence-based studies to determine absolute IOP levels in each individual. It is also difficult to definitively diagnose early progression by perimetry or objective monitoring so that resetting target IOP may be delayed, allowing some loss of VF.

However, "target" IOP range has been shown to help prevent progression and should be discussed thoroughly with the patient.

Reassessing "Target" Intraocular Pressure over Time

Due to the inherently ill-defined assessment of target IOP, therapy must be tailored to the individual patient with re-evaluation periodically. There is no single, safe level of IOP that is appropriate for all patients at all times, and in spite of achieving target IOP, a few patients show progression of the disease, probably because of other pathological factors. "Target" IOP requires further lowering when the patient continues to progress or develops systemic diseases such as a TIA. Conversely, in the event of a very elderly or sick patient with stable nerve and VF over time, the target IOP could be raised and medications reduced.

The change of MD over 5 years in POAG and CPACG eyes that progressed was 4.9 ± 3.7 and − 7.04 ± 4.7 dB, respectively, as against − 0.36 ± 3.8 and − 0.37 ± 3.4 dB in stable POAG and CPACG eyes, respectively, i.e., a rate of change of MD by 0.06 dB/year in each group.[15] The EMGT found a decrease in MD of 1.93 dB in eyes that progressed. A change of in MD of more than 1 dB/year, any reproducible change in 2–3 loci on perimetry or in known risk factors, should alert the treating ophthalmologist to the possibility of progression and hence a closer review for perimetry and a change in medications.

Imaging of the optic nerve may help pick up progression earlier than perimetry in certain patients. HRT predated VF changes in 57.1% of POAG and 40% of CPACG.[15,16] Artes *et al*. have shown that POAG patients with perimetric progression were three times more likely to have prior HRT changes.[29] Therefore, patients with progression on imaging need to be reviewed more closely and target IOP revised so that there is no significant loss of VF.

Conclusion

Target IOP is a useful concept to formulate broad guidelines in the treatment of POAG and PACG patients; however, it should not be "written in stone." Long-term serial objective recording of the optic disc and retinal nerve fiber layer and VFs can highlight early progression and therefore modification of glaucoma therapy when required. There is significant individual variability in anatomical and physiological parameters and numerous other coexisting systemic diseases and medications. However, it is apparent that with an appropriate target IOP range and continuous reassessment, glaucoma progression can be considerably slowed down so that at most, only a few loci show a change.

For both POAG and PACG after an iridotomy, in mild glaucoma, the initial target IOP range could be kept as 15–17 mmHg, for moderate glaucoma 12–15 mmHg, and in the severe stage of glaucomatous damage 10–12 mmHg.

Appropriate use of medications/laser/surgery to achieve such a "target" IOP range in POAG or PACG can maintain VFs and quality of life, preventing glaucoma blindness.

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Conflicts of interest

There are no conflicts of interest.

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