TARGET IOP: TO SET OR NOT TO SET?

Ophthalmologists weigh the pros and cons of setting a numeric goal.

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A NECESSITY IN CLINICAL PRACTICE

BY ARTHUR J. SIT, MD

Glaucoma is a multifactorial disease, but reduction of IOP remains the only proven treatment. Setting a target IOP has long been a mainstay of glaucoma management, and its use is currently recommended in the AAO’s Preferred Practice Pattern for Primary Open-Angle Glaucoma. However, since IOP is only one of many risk factors, it is reasonable to question whether or not the concept of a target IOP is an outdated paradigm that should be discarded, similar to the notion that glaucoma is simply an IOP greater than 21 mm Hg.

WHY NOT HAVING A TARGET IS INADEQUATE

One potential alternative to target IOP is the application of a standard treatment regimen for all patients. This approach was utilized by the Early Manifest Glaucoma Trial (EMGT), which used a standard protocol of argon laser trabeculoplasty and betaxolol versus observation and no therapy for newly diagnosed glaucoma patients. The study found that treatment, which resulted in a mean IOP reduction of 25%, was associated with a 45% rate of progression over 5 years as compared with a 62% rate of progression (Continued on page 44)

NO ONE MAGIC NUMBER

BY HARRY A. QUIGLEY, MD

A patient with an untreated IOP of 20 mm Hg has visual field (VF) loss and begins taking drops. On two subsequent visits, the patient’s IOP measures 19 mm Hg. Does the ophthalmologist tell the patient, “The drop is working; come back in 6 months”? Of course not, as the patient’s IOP must decrease by some amount in the short term. But what is that amount, and how do we calculate this target IOP? Some ophthalmologists argue against using any target, calling it a cookbook method of care. These individuals believe that one must instead consider the patient’s overall disease and general health and adjust his or her therapy accordingly. Naturally, it is advisable to do both: We should keep the patient’s IOP within a set range while monitoring structure, function, and quality of life.

The AAO’s Preferred Practice Pattern for Primary Open-Angle Glaucoma tells us to “maintain the IOP in a range at which VF loss is unlikely to significantly reduce a patient’s health-related quality of life.” However, for the first 2 to 3 years of care, we do not truly know whether the patient’s VF or OCT is stable or getting worse, so we use an IOP (Continued on page 43)
reduction goal that is individualized for each patient.

PEARLS FOR SETTING IOP TARGET

Several pearls for effectively using IOP to set a target pressure are as follows.

Measure the baseline IOP. It is important to measure the patient’s baseline IOP more than once without treatment. The Preferred Practice Pattern assumes that “the measured pretreatment pressure range contributed to optic nerve damage and is likely to cause additional damage in the future.” To determine the baseline IOP, take the patient briefly off any drop treatment that he or she may have been prescribed for a couple of visits, reassuring the patient that damage will not progress in a week’s washout.

Remember that the magic number 21 is meaningless. “Normalizing” IOP to less than the mythical 21 mm Hg is insufficient. More than 50% of patients with open-angle glaucoma incur damage despite having so-called normal pressures, but lowering IOP further in these patients has been shown to be beneficial. Ganglion cell susceptibility to pressure differs among patients and between right and left eyes. Damage is most often asymmetric, and therefore IOP targets can vary between eyes.

Incorporate degree of injury. Clinical trial data suggest a minimum IOP lowering of 20% from baseline. Data from the Collaborative Initial Glaucoma Treatment Study (CIGTS) and Advanced Glaucoma Intervention Study (AGIS) were recently used to create a predictive model for estimating the likelihood of glaucomatous damage worsening at different IOP levels. Although this is only a guide, it suggests that the range of lowering should be between 20% for low-risk eyes and 50% for high-risk or badly damaged eyes. Because it is impossible to tell how likely a patient is to worsen or to recover lost function, the degree of injury present must be part of the target IOP selection: Worse damage, lower target.

Refute the notion of a rigid, single number. Instead, the targeted IOP should lie in a tight range. Because applanation tonometry varies by ±1 mm Hg and diurnal variation is somewhat greater than that, some flexibility is key. However, intervisit IOP variability is itself an independent risk factor for progressive VF loss. If the patient’s target IOP is 30% lower than the baseline measurement, a variability of ±5% is acceptable, but it should remain within that range.

Assess adherence. If the patient’s target IOP is 15 mm Hg and IOP at this visit is 18 mm Hg, should one change the target or add more drops? Neither. Instead, try to assess whether the patient is adherent with the prescribed treatment. At least half the time, with improved adherence the patient regains the target. For a patient who is achieving his or her target IOP and yet having confirmed worse VF, improved adherence is still a likely solution. If it is not, a lower target and closer OCT and VF followup are needed. Targets are not unchangeable, and they can increase after years of stability.

For eyes without VF loss, perform a risk assessment before starting treatment. One formula for determining target IOP has been improved in an online calculator (https://ohts.wustl.edu/risk/) that incorporates data from the Ocular Hypertension Treatment Study (OHTS) and a study by members of the European Glaucoma Society. This risk calculator can help ophthalmologists predict the likelihood that damage will occur without treatment within 5 years.

Calculate the threshold to treat. An ophthalmologist following a glaucoma suspect with no prescribed IOP lowering may want to estimate how high the patient’s IOP should be allowed to go. The threshold to treat can be calculated by using the OHTS risk data and examining the risk level
for various IOP levels (http://oil.wilmer.jhu.edu/threshold).10

Record the target IOP in the patient’s chart. It is impossible to remember the target IOP of 40 patients seen in a daily clinic. Therefore, this information should be recorded in each patient’s chart. Will you get sued if you record a target and it isn’t achieved? No, but you are not following standard of care if you don’t have a target IOP. If the target is not achieved, you can document what you did to try to achieve it, which shows good care.

Do not worry about central corneal thickness. Central corneal thickness is not important when setting a target IOP for eyes with VF loss; instead, it is necessary to know only the patient’s baseline IOP and the degree to which his or her IOP should be lowered. Thus, because it does not matter whether the measured IOP is 25 mm Hg or 20 mm Hg, one does not have to adjust for central corneal thickness.

WHEN NOT TO HAVE A TARGETED IOP RANGE

There are four scenarios in which it is acceptable not to have a targeted IOP range:

• No. 1: In an acute glaucoma, high IOP crisis;
• No. 2: For a blind eye, when the goal is comfort;
• No. 3: In a 95-year-old patient with minimal damage; and
• No. 4: When achieving the target could cause more damage than the glaucoma itself.

In all other scenarios, setting a customized targeted IOP range for each patient is a necessity. Taking into consideration the points outlined above can help glaucoma specialists to obtain a macroscopic view of each patient’s care, rather than a narrow focus on one arbitrary number.

This suggests that a more nuanced approach to treatment is required to prevent further symptomatic visual impairment, and the selection of at target IOP can help.

SELECTING AND ADJUSTING THE TARGET IOP

There are two basic methods by which a target pressure can be selected. The first is selection of a percentage reduction from baseline. The second is the use of fixed levels based on disease severity. The OHTS used the first method, with a standard IOP target of 20% reduction from baseline or an IOP less than 24 mm Hg, whichever was lower.4 Although the rate of progression to glaucoma at 5 years was reduced in the treatment group compared with the observation group (from 9.5% to 4.5%), a significant proportion of patients still developed glaucomatous optic neuropathy.5 This suggests that a uniform target based on percentage reduction may be sub-optimal for many patients.

Simply adopting a more aggressive percentage IOP reduction is an option, but there may be diminishing returns, at least in early-stage glaucoma. In the CIGTS trial, newly diagnosed glaucoma patients were randomly assigned to medical treatment or trabeculectomy.6 After initiating treatment, the mean IOP was 17 to 18 mm Hg (roughly 35% reduction) in the medical group and 14 to 15 mm Hg (roughly 40% reduction) in the surgical group. Overall, though, there was no significant difference in the progression rates between the medically and surgically treated groups. This suggests that initial IOP reductions greater than 35% may have a limited benefit in this patient population.

However, in patients with advanced disease, more aggressive IOP reduction may be required to prevent further progression. In a classic paper, Grant and Burke7 stated, “The worse
the initial condition of the eye, the lower the tension needs to be to prevent further loss or blindness.” This has been supported by the results of several large clinical trials in glaucoma. A subgroup analysis of the CIGTS demonstrated that patients who presented with advanced disease, defined as a mean deviation < -10 dB, had slower VF progression than medically treated patients who had a higher mean IOP after treatment. A similar benefit of aggressive IOP reduction was reported by the AGIS trial: In patients with advanced disease, lower IOP was associated with a lower rate of progression over a 6- to 18-month period after argon laser trabeculectomy or trabeculectomy.

Based on this information, initial selection of target IOP should address the needs of patients at different stages of disease. Additionally, instead of a specific number, use of a target pressure range is helpful for coping with the variability in IOP. As a starting point, I use a target of low teens for advanced disease, mid-teens for moderate disease, and high teens to low 20s mm Hg for early-stage disease, with a minimum starting IOP reduction of approximately 30%. Once a target IOP is selected, it should not be considered fixed. Instead, it may need to be lowered if further progression is detected despite IOP at target.

Determination of the target IOP must also take into account other risk factors. Some types of glaucoma may have elevated risk of progression and warrant more aggressive target IOPs. For example, in the EMGT, ocular hypertensive patients (IOP 24–31 mm Hg) with pseudoxfoliation were more likely than age-, sex-, and IOP-matched patients without pseudoxfoliation to develop glaucoma (55% vs 28% at a mean of 8.7 years). Other risk factors that should be considered in determining the target IOP include decreased central corneal thickness, older age, African ancestry, family history of glaucoma, and low corneal hysteresis, among others. The presence or absence of these risk factors would warrant modifying the target IOP.

LIMITATIONS OF TARGET IOP

One of the limitations of setting a target IOP is that our phenotyping of any particular patient is inevitably incomplete. As a result, different patients who seemingly have similar risk profiles may have different thresholds for further glaucoma progression. However, this is no reason to abandon target IOP completely. Instead, it must simply be viewed as a first, best guess at a therapeutic target—one that will need adjustment in many patients. To not have a target at all is to ignore the knowledge that has been gained from the major glaucoma clinical trials.

Another limitation is that our clinical measurements simply do not reflect the true dynamic nature of IOP. There is a significant body of literature suggesting that IOP variability may be an independent risk factor for glaucoma. However, this does not negate the utility of target IOP. Instead, the potential risk of IOP variability suggests the need for better IOP measurement tools, including continuous IOP monitoring, allowing a more robust characterization of this parameter. The way that we determine target IOP will change with new technology, but the concept will continue to remain useful.

CONCLUSION

Although not perfect, target IOP remains a useful tool in managing glaucoma patients. It is an acknowledgment that every patient is unique and that a management plan needs to be tailored to the needs of the individual. With every patient, a balance must be achieved between the benefits of IOP reduction and the burdens of therapy. Setting a target IOP can help codify our best estimate for where this balance lies, but it requires evaluation of multiple factors in addition to IOP and the recognition that the target may have to be adjusted based on the clinical course of each patient.