The Impact of Intraocular Pressure on Retinal Nerve Fiber Layer Thickness: A Comprehensive Review.

Abstract

Glaucoma, a major cause of blindness globally, is often treated by controlling and reducing eye pressure (IOP). This research examines the importance of IOP in the loss of thickness in the retinal nerve fiber layer RNFL. This review began with a search of the PubMed and Google Scholar databases. Peer-reviewed journal publications of clinical trials assessing the impact of IOP management on RNFL thickness were a prerequisite for inclusion. When no peer-reviewed articles were available, other publications from the conference proceeded. Elevated IOP is a major risk factor for injury to the RNFL. Both long-term and sudden IOP fluctuations contribute to RNFL loss. Studies have demonstrated that managing IOP helps preserve RNFL thickness and reduces glaucoma progression. For the prevention of vision loss and permanent damage, clinicians emphasize IOP control as the foundation of glaucoma management.

Keywords: Glaucoma, intraocular pressure (IOP), retinal nerve fiber layer (RNFL), Optical coherence tomography(OCT).

1. INTRODUCTION

Elevated intraocular pressure is a key risk factor for the development of glaucoma, which is one of the main causes of irreversible visual loss all around the globe. However, not everyone with high IOP develops glaucoma, and some people with normal IOP can still develop the disease. This suggests that other factors, such as IOP fluctuations, may play a role in glaucoma progression. It is estimated that over 3.5% of adults aged 40 to 80 years old have glaucoma. This number is expected to increase to 111.8 million by 2040, due to the aging population.[(1)] Glaucoma is a type of optic neuropathy that harms the optic nerve and leads to a gradual decline in vision. There are no symptoms in the early stages, so it is important to have regular eye exams to detect glaucoma early. Treatment for glaucoma can help to slow or prevent vision loss.[2]Current therapies cannot cure glaucomatous damage to the optic nerve, the retina, and the visual field. Early diagnosis and treatment can slow the progression of the disease and preserve vision. Glaucoma is a chronic illness requiring lifelong treatment.[1]Even though intraocular pressure (IOP) can cause glaucomatous optic neuropathy at any level, patients benefit from a considerable, long-term IOP drop. This finding, together with data from other research, suggests that biomechanical factors play a significant role in RNFL loss; in fact, the goal of all current treatment strategies is to lower IOP. Unfortunately, 25–45% of patients still have progression after receiving therapy, despite the availability of several IOP control options (drugs, devices, and surgical procedures. This suggests that variables other than IOP play a significant role in the disease process.[3]

2. METHODOLOGY

Articles were searched in PubMed& Google Scholar and keywords were selected for this review 1. Glaucoma, 2. Intraocular pressure, 3. RNFL thickness, 4. Optical coherence tomography from 2013-2023 years. Only peer-reviewed articles measuring IOP with tonometry and RNFL thickness by OCT and studies that investigate the association between changes in IOP and RNFL thickness were selected. A total of 20 articles were retrieved and after reading the full article 17 were included for review and 3 were excluded due to insufficient data for IOP and RNFL. Data points extracted from each article were "IOP measurement", "RNFL measurement", "the effect of IOP fluctuations on RNFL", "IOP's Effect on RNFL".

3. IMPACTS OF IOP FLUCTUATIONS

A recent study conducted by Kim and Caprioli suggests that fluctuations in intraocular pressure (IOP) could pose a significant independent risk factor for the progression of retinal nerve fiber layer (RNFL) loss. Their research indicates that the variability in IOP levels is a more accurate predictor of visual field (VF) progression compared to the average IOP levels, especially in eyes with low average IOPs. The researchers suggest that long-term fluctuations in IOP could disrupt the body's natural balance mechanisms, and sudden and irregular variations in IOP could put mechanical strain on the optic nerve, potentially causing damage. Moreover, they point out that IOP fluctuations are more likely to contribute to RNFL loss progression in eyes with average or low IOP levels.[4]The article by Brusini P, Salvetat ML, and Zeppieri M., discusses how intraocular pressure (IOP) is not a constant value but rather changes throughout the day and night. These changes can be affected by different factors such as position, level of activity, and medication. Although some variation in IOP is normal, excessive fluctuations can increase the risk of glaucoma progression. Research has shown that eyes with greater IOP fluctuations are more likely to sustain damage from glaucoma (RNFL loss) compared to eyes with smaller fluctuations. Additionally, studies have found that fluctuations in IOP are linked to a higher rate of visual field deterioration in individuals with glaucoma.[5]

4. ROLE OF IOP IN RNFL DAMAGE

A study by Alasi R and Trehan HS provides insights into IOP's influence on RNFL damage. The study revealed that RNFL thickness diminishes with age in both men and women. This age-related decline is a natural occurrence and not necessarily indicative of glaucoma. However, glaucoma is also a risk factor for RNFL damage, and the age-related decline can make early glaucoma detection more challenging. The study also found that women have thinner RNFLs than men at all ages. This difference is likely attributed to hormonal factors. It is important to note that RNFL thickness is a continuous variable, and there is a wide range of normal RNFL thickness values for both men and women. The study's findings highlight the importance of considering age and sex when interpreting RNFL thickness measurements. However, IOP remains a critical factor in RNFL damage, with elevated IOP being a major risk factor for glaucoma.[6]

According to a study by Diniz-Filho et al, the rate of retinal nerve fiber layer (RNFL) loss is closely related to intraocular pressure (IOP). The research showed that for every 1 mmHg rise in average IOP, there was a 0.051 μm/year increase in the speed of RNFL loss, and for every 1 mmHg increase in peak IOP, there was a 0.038 μm/year acceleration in the rate of RNFL loss. These findings suggest that lowering

IOP is an important part of glaucoma management, as it can help to slow or prevent RNFL loss and preserve vision. The study also found that the relationship between IOP and RNFL loss was strongest in eyes with moderate to severe glaucoma. This suggests that IOP control is particularly important for patients with more advanced disease. the study provides strong evidence that IOP is a major risk factor for RNFL loss in glaucoma. Lowering IOP is an essential part of glaucoma treatment and can help to preserve vision.[(7)]In a study by Werner and Shen, OCT angiography was used to image the RNFL in patients with glaucoma. The results showed that patients with glaucoma had thinner RNFLs than healthy controls.[(8)]Diniz-Filho et al. also found an association between IOP and RNFL loss. In their study, patients with higher IOP had faster rates of RNFL loss.[(7)]Marshall et al. found that macular ganglion cell inner plexiform layer (GCIPL) loss precedes peripapillary RNFL loss in glaucoma with lower IOP. This indicates that the damage to the RNFL in glaucoma may start in the macula.[(9)]The exact mechanisms by which IOP affects RNFL thickness are not fully understood, but it is thought to be due to a combination of factors, including Ischemic damage: Increased IOP can reduce blood flow to the optic nerve, which can lead to ischemic damage to the retinal nerve fibers. Mechanical stress: Increased IOP can also put mechanical stress on the retinal nerve fibers, which can damage them. Axonal transport: Raised intraocular pressure (IOP) can interfere with axonal transport, which is the mechanism through which nutrients and crucial molecules are carried along the retinal nerve fibersRaised intraocular pressure (IOP) can interfere with axonal transport, which is the mechanism through which nutrients and crucial molecules are carried along the retinal nerve fibers(**figure 1**).(16)

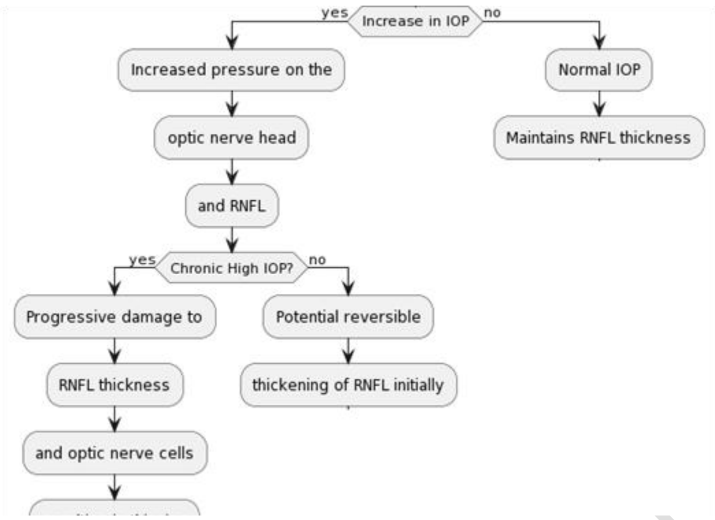

Figure 1 ILLUSTRATION OF HOW IOP CAN AFFECT RNFL THEICKNESS

According to Cronemberger et al., hypothesize that IOP variation may cause mechanical stress on the optic nerve, which could lead to RNFL damage. They also suggest that IOP variation may disrupt the normal blood flow to the optic nerve, which could also lead to RNFL damage[10]. The study by Tu et al. provides evidence that chronic ocular hypertension can lead to RNFL thickness loss in monkeys. The authors induced chronic ocular hypertension (COH) in monkeysby injecting saline solution into the episcleral space around the optic nerve.

The IOP of the monkeys was then measured weekly for 6 months. The RNFL thickness of the monkeys was also measured at the beginning and end of the study using optical coherence tomography (OCT). The authors found that monkeys with higher IOP had greater RNFL thickness loss.[11]The study by de Vries et al. found a strong negative correlation between IOP change and RNFL change (r=-0.9903), meaning that increases in IOP were associated with decreases in RNFL thickness. This suggests that elevated IOP can have a detrimental effect on the health of the retinal nerve fiber layer(**table 1**).

Table 1 According to Vries et.al. RNFL thickness loss with level of IOP[12]

IOP [mmhg]	RNFL Thickness loss [mm]
20	0.2
25	0.3
30	0.4

35	0.5
40	0.6

5. IOP CONTROL AND RNFL PRESERVATION

A study conducted by Jammal et al. found that rates of retinal nerve fiber layer (RNFL) loss in a large clinical population are connected to how well intraocular pressure (IOP) is managed. The researchers observed that eyes with stricter IOP control during follow-up visits experienced lower rates of RNFL loss compared to eyes with less strict control. They also noted that for every 1 mmHg increase in mean IOP, there was a connection to a 0.05 µm/year faster rate of RNFL loss(**figure 2**).[13]

Research conducted by Liu et al. suggests that glaucoma patients with progression in one eye also experience a similar rate of retinal nerve fiber layer (RNFL) loss in the other, non-affected eye. This highlights the importance of managing intraocular pressure (IOP) to prevent RNFL loss in both eyes of glaucoma patients, even when only one eye is showing progression. The study found that the average rate of RNFL loss in eyes that progressed conventionally was 0.89 µm/year. Interestingly, the contralateral eyes of these patients also showed a significant decline in RNFL thickness over time, at a rate of 1.00 µm/year(**table 2**).[14]

Table 2. RNFL thickness with IOP at different time durations[14]

Mean RNFL thickness [µm]	Baseline	2 years	4 years	6 years
Average	92.5 [18.3]	90.3 [19.2]	88.1 [19.8]	85.9 [20.5]
Normal	95.3 [14.7]	93.7 [15.9]	92.1 [16.4]	90.9 [17.1]
Glaucomatous	87.9 [23.2]	85.2 [23.9]	82.5 [24.4]	79.8 [25.2]

The study by Koenig and Hirneiss found that patients who had IOP control of less than 18 mmHg had a mean RNFL thickness of 87 microns, while patients who had IOP control of greater than 22 mmHg had a mean RNFL thickness of 63 microns. This difference was statistically significant, meaning that it was likely due to the difference in IOP control rather than chance. The study also found that the rate of RNFL loss was slower in patients who had better IOP control. Patients who had IOP control of less than 18 mmHg lost an average of 1.2 microns of RNFL thickness per year, while patients who had IOP control of greater than 22 mmHg lost an average of 2.4 microns of RNFL thickness per year(**table 3**).[15]

Table 3 postoperative and preoperative RNFL thickness [15]

Mean RNFL Thickness [µm]	Preoperative	Postoperative
Superior	88.2	85.8
Nasal	79.8	77.4
Inferior	77.4	75
Temporal	82.8	80.4
Mean	84.6	82.2

The study by Hou et al found that patients with lower IOP had slower rates of RNFL thinning compared to patients with higher IOP. This suggests that IOP control can help to reserve RNFL. The study found that patients with an IOP of less than 18 mmHg had a mean RNFL thickness of 92.2 µm at baseline, which was similar to the mean RNFL thickness of patients with normal IOP (93.1 µm). However, patients with an IOP of 21 mmHg or higher had a mean RNFL thickness of 86.3 µm at baseline, which was significantly lower than the mean RNFL thickness of patients with normal IOP(**table 4**).

Table 4 correlation of IOP with RNFL thickness[16]

Mean RNFL thickness [µm]	Baseline	2 years	4 years
Average	93.0 [11.4]	91.8 [12.2]	90.5 [12.8]
Normal	95.2 [10.1]	94.0 [10.8]	92.8 [11.4]

Glaucomatous	89.5 [13.5]	88.3 [14.2]	87.0 [14.9]

6. CLINICAL INTERVENTION OF STUDY

The close connection between intraocular pressure (IOP) and retinal nerve fiber layer (RNFL) thickness illustrates the significance of careful IOP regulation in the treatment of glaucoma. Consistent monitoring of IOP and timely adjustments to treatment plans are essential for preserving eyesight and avoiding permanent harm.

7. CONCLUSION

IOP elevation is a major risk factor for RNFL damage, a hallmark of glaucoma. Chronic IOP elevation and acute IOP fluctuations both contribute to RNFL loss. Evidence from numerous studies highlights the effectiveness of IOP control in preserving RNFL thickness and slowing glaucoma progression. Clinicians should prioritize IOP control as the cornerstone of glaucoma management to safeguard vision and prevent irreversible visual loss and close IOP monitoring is essential for all glaucoma patients

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Regarding this paper, there was no pertinent conflict of interest.

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Not applicable

12. DATA AVAILABILITY

All data generated and analyzed have been included in this article.

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