A Clinical Consideration: Retinal Nerve Fiber Layer Examination and Glaucoma

Jeffrey J. Fitzmaurice
Literature Review
Senior Project
1997

INTRODUCTION

The purpose of this paper is to review and investigate how the nerve fiber layer can be useful in the diagnosis and early detection of glaucoma. Although historically, the histological changes and ophthalmoscopy findings of the nerve fiber layer in glaucoma have been considered, a definitive conclusion has never been achieved. It remains a rather controversial topic. For myself, the early detection of glaucoma is what I would refer to as a vast "gray zone". There are several parameters that need to be considered in the detection of glaucoma, and there interpretation is rather subjective and easily biased.

Although the evaluation of the retinal nerve fiber layer may not be considered by some, as the standard approach in detecting glaucoma. I would like to present an approach to evaluating the nerve fiber layer and why the information may be useful. With legislation moving in favor of optometrists using therapeutics and the nature of the disease, I feel it is an excellent position for optometry to make a contribution to the field of study. From this statement, I would like to take the opportunity to discuss the different parameters used to define glaucoma and their clinic pitfalls. I would like to emphasize the usefulness and value of the retinal nerve fiber layer evaluation as another means of data to collectively diagnosis glaucomatous change, and provide an approach to evaluating the nerve fiber layer as describe by the current and past literature. I will be referring to primary open angle glaucoma.

THE ENIGMA

Glaucoma is estimated to be the third most prevalent cause of vision loss in the world. (1) The disease's clinical picture is difficult to detect, especially because the patient is normally

asymptomatic. However, the progression of the optic neuropathy ultimately leads to loss of visual function.(1) The detection and diagnosis of glaucoma is determined by several parameters: family history and related risk factors, intraocular pressure, optic nerve head appearance, visual field findings and nerve fiber layer structure. There are several mechanisms, mechanical verses ischemic, that have been postulated to explain the etiology and the characteristics , but for the most part these studies are inconclusive, and it may be multifactorial.(2) By definition glaucoma is normally defined as an increase in the intraocular pressure in the eye which results in damage to the optic nerve.(3) Unfortunately, screening by intraocular pressure alone fails to detect half of those with glaucoma. (4) Some studies have suggested that one sixth to one half of all patients with glaucoma have an initial pressure of less then 21mmHg, whereas one tenth of patients with an increased pressure have visual field loss from glaucoma. Measurements of intraocular pressure cannot be used to accurately and consistently predict which patients will have glaucomatous damage from increased intraocular pressures. (5) In an exam setting, it is merely a snap-shot in time and cannot predict fluctuations in the intraocular pressure. In addition, the criteria that is used to define "normal" ranges in the intraocular pressure may not be representative in all populations of patients measured. What I am referring to is low or "normal" tension glaucoma patients. (4,5,6,7)

The use of automated threshold perimetry is considered to be a more definitive testing measure. However, the interpretation of visual field findings in the early diagnosis are difficult to categorize, and may be insensitive to detect early changes.(8) Most practitioners agree that the early diagnosis of glaucoma cannot be conclusive or limited to an isolated visual field finding. Some studies have shown, that glaucomatous structural changes in the optic nerve and retinal nerve fiber layer, normally proceed visual field defects; and that diffuse depression in the visual

field may be one of the early perimetric findings before scotomas occur. In addition, some researchers have suggested that the incidence of visual field defects in patients with pressure >21mmHg on a one year follow up is low, probably 1% per year.(9) Another example, with the difficulty in using visual field testing is the degree of fluctuation between testing periods. According to some studies, it is not unusual for a patient to fluctuate 20 decibels over several years in a depressed area of their visual field. This makes it difficult to monitor the stability of the disease. (4,8,9,10) Therefore, repeated fields are necessary, making the procedure laborious and costly.

The direct, objective observation of the optic nerve head is probably , by most practitioners, the most influential technique in the diagnosis of glaucoma. Yet, here again, there is controversy over the best procedure to evaluate the optic nerve and the characteristics of damage in the progression of the disease. Also, the clinical impressions are subjective and open to interpretation between professionals. Generally, optic nerve head changes occur before visual field defects. The expansion of the optic nerve cup or thinning of the neurorim tissue is a sign of diffuse loss. The value of the retinal nerve fiber layer evaluation, is that it can be used to confirm optic nerve findings when diffuse loss seems present. As the converse, when the decision is difficult to determine whether the optic nerve head is normal or abnormal, the retinal nerve fiber layer can be a critical differential. (11)

After considering separately each parameter used to define glaucoma, the practitioner then has the dilemma of correlating the data from each area and deciding if the patient has glaucoma. If we consider the progression of the disease at various stages , for most practitioners, a patient presenting with end-stage glaucoma would not be difficult to diagnosis. It is the patient in the early stages of the disease that presents with elevated intraocular pressures, healthy

appearing optic nerves with no visual field defects, that the practitioner is faced with the question: "Is this normal for this individual or early signs of glaucoma?" At this point, the practitioner must decide their approach in managing this patient.

HISTORICAL CONSIDERATIONS

Ophthalmoscopy of the retinal nerve fiber layer was first recognized by Vogt in the early turn of the century. Although at the time, its usefulness was not appreciated diagnostically but rather investigative as to the potential of the information that could be derived from investigation.. It wasn't until 1973 that Hoyt and co-workers began to recognize its usefulness in the detection of glaucoma. From Hoyt's work, Miller and Sommer began to study nerve fiber layer structure changes in ocular hypertensive patients, and were able to detect individuals who were progressing to visual field loss prior to their functional loss of vision. This stimulated and motivated other researchers to investigate techniques to evaluate the retinal nerve fiber layer in patients suspicious of glaucoma. Many longitudinal and cross-sectional studies were performed and in 1991 Quigley et al., reported their results of a 12 year study of the predictive value of the retinal nerve fiber layer examination in glaucoma suspects. Their study consisted of masked examinations of the retinal nerve fiber layer alone to detect glaucoma suspects who would later develop visual field loss, and did so five years prior to visual field loss. This study confirmed findings from their predecessors more that a decade ago. (12,13)

NORMAL ANATOMY

Function of the Ganglion Cells

When we observe a nerve fiber layer, what is actually being investigated are the retinal ganglion cells, of which there are over one million in each eye.(1,3) Light that enters the eye stimulates the photoreceptors, which conduct an electrical impulse to the bipolar cells, leading to the ganglion cells, which travel over the retinal surface, closest to the vitreous, to the optic disc and exit to the centers of the brain responsible for vision. Thus, the integrity of the retinal ganglion cells is vital to proper visual functioning.

Structural Arrangement

The structural arrangement of the retinal nerve fiber layer throughout the sphere of the eye is not the same in all locations. The retinal nerve fiber layer tends to be thinner in the peripheral retina becoming rapidly thicker as it approaches the optic disc. The fibers arch around the fovea as not to obstruct vision, also making the retinal nerve fiber layer thinner in this area. As the retinal ganglion cells converge around the optic disc, the distribution and thickness is not symmetrical in all the areas around the disc. In a normal eye, the retinal nerve fiber layer is generally thicker in the superior and inferior poles of the optic disc and thinner on the temporal and nasal sides. Furthermore, because the fibers arch over the fovea before entering the disc, the nerve fiber layer tends to be thickest at the 11:00 and 7:00 position of the right eye and the 1:00 and 5:00 in the left eye. (9,12,13)

Properties of the Retinal Nerve Fiber Layer Based on Structure

The orientation of the retinal nerve fiber layer ,as it enters at the optic disc, gives it a different thickness depending on the location. The varying degree of thickness is what gives the nerve fiber layer it's appearance of brightness and texture.

Brightness

The thicker the nerve fiber layer is in a given area the more light will reflect back to the observer and the brighter it will appear on observation. From our previous discussion the retinal nerve fiber layer will appear brighter near the optic disc and fade as you move towards the peripheral retina where the nerve fiber layer is thinner. Due to the asymmetrical arrangement of the nerve fiber layer around the disc, a pattern and the appearance of the retinal nerve fiber layer in a normal eye can be appreciated. Because it is thicker in the superior and inferior poles upon observation of the temporal macular side of the disc, a bright-dark-bright appearance is given. When evaluating the retinal nerve fiber layer it is this area that is used and will be discussed later. (9,12,13)

Texture

As the nerve fibers travel across the retinal surface to the optic disc, they travel in bundles and are supported by glia cells. Upon observation what this represents is a discontinuity in the quality of brightness. Instead of the retinal nerve fiber layer appearing smooth and white in all area, it has a striated appearance with white reflections interspaced with black lines. The white lines represent the reflectance of light from the individual bundles themselves and the black from supporting cells. Since the nerve fiber layer is thickest at the optic disc compared to the peripheral retina, it is difficult to appreciate the striated pattern. (9,12,13)

NERVE FIBER LAYER ATROPHY AND GLAUCOMA

Although the exact mechanism of glaucoma is not definitive, one of the consequences is injury to the retinal ganglion cells. The end result is ganglion cell death, and unfortunately the nerve cells are incapable of regeneration.(2,3) What can be observed by the examiner during

investigation is a decrease in the nerve fiber layer thickness. What is appreciated are changes in the retinal nerve fiber layer brightness and texture.

Change in Brightness

Since glaucoma tends to have characteristic fundus changes of the optic nerve and nerve fiber layer, the normal brightness pattern will vary in its characteristic pattern due to glaucomatous changes. As described earlier, the brightness pattern in a normal patient is typically defined as bright-dark-bright in the temporal macular region. It is typically brighter at the superior pole and inferior pole on the temporal macular region of the disc, and darker in the mid-zone due to the fovea .(11,12,13,14,15) In a glaucoma patient, depending on the stage and severity of the disease, this pattern is disrupted due to retinal nerve fiber layer atrophy. The three patterns of loss are diffuse, wedge and slit-like defects. According to Quigley, glaucoma causes a selective loss of fibers that pass throughout the upper and lower poles of the optic disc. As a result, the areas in which the retinal nerve fiber layer is normally most bright becomes dim. This thinning is normally evenly distributed over the upper, lower and mid zone and is referred to as diffuse loss.(11,12) When the retinal nerve fiber layer atrophy is more organized to a specific area, a local or specific area of brightness becomes darker and is classified as a wedge defect. A wedge defect, typically has a triangular appearance, in which it appears narrower at the disc, where the fibers converge and is wider as it extends towards the peripheral retina. These types of defects are normally associated with notch defects on the optic nerve.(11,12,14,15) An important point to know, is that a true wedge defect starts at the optic disc and extends to the periphery. Unlike pseudo- like defects, which may be normal anatomical variations, they do not start at the disc and are typically smaller than an arteriole width in size but can easily be confused with wedge or slit like defects.(11,12,14,15) Slit like defects, which are usually found in the superior and

inferior arcuate bundle zones, are different from wedge defects in the fact that they do not widen as they approach the periphery and are classified as being as wide as an arteriole. (3,11,12,14,15)

Diffuse atrophy is the most common type of atrophy, but is the hardest to detect clinically. It is also worth mentioning that it is possible to have a combination of the different types of defects. However, it is not certain if there is a characteristic or pattern to the development of retinal nerve fiber layer atrophy, or if one type of defect proceeds another or later develops into a different defect. (11,12,14,15)

Changes in Texture

If we consider the normal anatomy, as the retinal ganglion cells converge at the optic disc to exit the eye, they are organized in a layered fashion. It is unknown for certainty at this time the exact organization as they travel across the retina, but a model has been suggested that the longer peripheral fibers are closer to the vitreous and make up the outer portion of the neuro-rim tissue (further from the CRA & CRV) while the shorter fibers travel closer to the sclera and make the inner portion of the neuro-rim tissue.(9,12) Due to nerve bundles organization and supporting cells a texture is perceived upon observation. It is typically described as striated. However, where the retinal nerve fiber layer is thickest the striations are not as visible verses where the nerve fibers are thinner. This is due to the large number of nerve fibers layered onto of each other and the limitations of what the human visual system can resolve. (9,12) According to Quigley, in early to mild forms of atrophy, the texture changes from course striations to a finer, better defined set of lines or etched appearance. This is due to the thinning of the retinal nerve fiber layer and as the atrophy increases the striations become more difficult to appreciate. (12)

STEPS IN EVALUATION

During a clinical exam, probably one of the fastest and more efficient stereoscopic techniques to examine the retinal nerve fiber layer is with a slit lamp, a +78 D or +90 D lens with maximal pupillary dilatation, under red-free light. Red-free light is utilized because it is absorbed by the RPE and choroid, which creates a background that enhances the appearance of the reflection off the retinal nerve fiber layer. Typically, the more dense and heavier pigmented fundus the better the imaging, which is why the technique is easier on brown-eyed dark pigmented patients, and is more difficult on a 'blonde' fundus. The slit beam should be fairly narrow and is often best positioned at the level of the major vessels. Attention should be directed within 2DD on the temporal macular side of the disc. According to Quigley, in a normal patient, the first and second branching out of arterioles and venules are always blurred by overlying nerve fiber layers. Mild diffuse atrophy bares the first order branches of vessels, bringing their walls into sharp view. Moderate and severe atrophy uncovers the smaller vessels. Therefore, on a normal patient, it may seem difficult to bring the vasculature system into perfect focus, which should not be confused with examiner error. It may suggest a healthy nerve fiber overlying the vessels. (11,12,14,15)

Where and What to Investigate

Glaucoma causes a selective loss of fibers that pass through the upper and lower poles of the optic disc. (2) Therefore, the points of focus during the examination, should be directed at the retinal nerve fiber pattern from the superior pole to the inferior pole on the temporal macular side of the disc. In a normal patient, the pattern should be as follows: bright-dark-bright. If this pattern is not observed at first, the observer should refocus. However, in lighter pigmented patients or patients with severe ganglion loss visualization may be difficult or not present. If we theoretically consider the different clinical pictures, the patterns may appear as follows: dark-

dark-bright, bright-dark-dark, dark-bright-dark, or dark-dark-dark. Obviously there would be variations within these predicted patterns. A logical approach for the observer, would be to compare the brightness pattern above and below the midpoint of the disc on the temporal macular side. Then the observer would ask the following questions:

1. **Do I see a bright pattern and striations?**
2. **Is the pattern brighter above and below the midpoint zone on the disc (corresponding to the fovea)?**
3. **Is the brightness less than expected?**
4. **How does the brightness compare between the inferior and superior zones?**
5. **Does the brightness pattern become continually darker towards the periphery, and are the striations more visible?**
6. **If atrophy is present, what is the classification of the defect?**
7. **Are there any optic nerve changes that can support nerve fiber layer observations and findings?**

The following tables that have been provided are a grading scheme, suggested by Quigley, to record atrophic findings.

SUMMARY

In summary, we have discussed the various parameters of glaucoma and how to evaluate the retinal nerve fiber layer. The characteristic retinal nerve fiber layer defects have been discussed and a classification system has been provided. The next clinical consideration, would be to discuss the predictive power of nerve fiber layer evaluation.

According to some studies, untreated glaucoma patients demonstrated visible nerve fiber layer defects that proceeded visual field loss by as much as five years . Either local defects or diffuse atrophy were present in 84% of all eyes with field loss. This is comparable in sensitivity to using disc features to identify eyes with glaucomatous field loss. The studies also mentioned that a

small percentage of glaucoma suspects could be identified based on retinal nerve fiber layer findings alone. However, the defining characteristics and exact percentage of patients in the study was not identified. Other studies have suggested that nerve fiber layer atrophy can identify 90% of the patients with field loss. (11,16)

After reviewing the literature, in my opinion, it is difficult to determine the characteristic/s clinical picture, definitive test or technique that can differentiate between ocular hypertensive, glaucoma suspect or glaucoma patients. Even the clinical criteria used to define or categorize these patients varies among researchers and practitioners. The stages of the disease, clinical impression and retinal sensitivity at different periods of the disease, vary among patients. This makes the diagnosis difficult from a clinical and management perspective. What I have come to realize is that there is not a true standard to diagnosis glaucoma, it depends on what school of thought or training the practitioner has been disciplined under. Although a model or criteria may be constructed to help a practitioner differentiate between patients, I think it would be correct to state that there is not one single formula. The diagnosis of glaucoma is a clinic diagnosis that is open to interpretation. The purpose of this paper was to provide an argument for the usefulness of retinal nerve fiber layer evaluation as another means of data. It must be determined by the individual practitioner to decide if it will be incorporated into their own criteria. What I hope is that this paper will motivate other optometrists to consider nerve fiber layer evaluation as another means to detect patients who appear to have glaucomatous damage.

TABLE

Grading scheme for Diffuse Atrophy of the NFL

NFL Feature	Grade D0	Grade D1	Grade D2	Grade D3
Brightness	Bright	Less Bright	Minimally Bright	Dark
Texture	Coarse and fine striations	Fine striations	Barely detectable striations	No texture
Blood Vessels				
Large	Clear or blurred	Clear	Clear	Clear
Medium	Blurred	Less blurred	Clear	Clear
Small	Very Blurred	Still blurred	Clear	Clear

Grading scheme for Wedge atrophy

NFL feature within wedge	Grade W1	Grade W2
Brightness	Less bright	Dark
Texture	Fine Striations	No texture
Vessel Visibility	Small vessels covered	Small vessels bare
Equivalent diffuse grade	D1	D2

Works Cited

1. Foster A.: Patterns of blindeness. In: Duane's Clinical Ophthalmology, Vol 5. Eds: Tasman W, Jaegar EA, 1980. JP Lippencott, Philadelphia, 1990 Chapter 53: p.p. 1-7.

2. Fechtner RD, Weinreb RN: Mechanisms of Optic Nerve Damage in Primary Open Angle Glaucoma. Survey of Ophthalmology, Vol 39, No 1. July-Aug 1994. p.p. 23-41.

3. Litwak BA: Evaluation of the Optic Nerve in Glaucoma. In: Primary Care of the Glaucomas. Eds: LL Thomas, M Fingeret, 1990. Appletone Lange, Chapter 9 p.p. 137-55.

4. Sommer A, Tielich JM, Katz J, Quigley HA, Gottsch JD, Javitt J: Relationship Between Intraocular Pressure and Primary Open Angle Glaucoma Amoung White and Black Americans: The Baltimore Eye Survey. Arch. Ophthalmology, 1991. p.p. 1090-1095.

5. Sommer A: Intraocular pressure and Glaucoma. American Journel of Ophthalmology, Vol 107, No 2. Feb 1989. p.p. 186-88.

6. Sponsel WE: Tonometry in Question: Can Visual Screening Tests Play a More Decisive Role in Glaucoma Diagnosis and Management? Survey of Ophthalmology, Vol 33, Feb 1989. p.p. 291-300.

7. Anderson DR: Glaucoma: The Damage Caused by Pressure. XLVI Edward Jackson Memorial Lecture. Ophthalmology, Vol 108, No5. Nov 1989. p.p. 485-95.

8. Hyung S, Kim DM, Youn DH: Optic Disc and Early Glaucomatous Visual Field Loss. Korean Journel of Ophthalmology, Vol 4 ,1990. p.p. 82-91.

9. Caprioli J: Correlation of Visual Function with Optic Nerve and Nerve Fiber Structure in Glaucoma. Survey of Ophthalmology, Vol 33, Feb 1989. p.p. 319-30.

10. Jonas JB, Fernandez MC, Naumann G: Glaucomatous Optic Nerve Atrophy in Small Discs with Low Cup-to-Disc Ratios. Ophthalmology, Vol 97, No 9. Sept. 1990. p.p. 1211-1215.

11. Quigley HA: Nerve Fiber Layer Assessment in Managing Glaucoma. American Academy of Ophthalmolgy. Focal Points 1988: Clinical Modules for Ophthalmologists.

12. Quigley HA: Manuscript that is untitled and unpublished.

13. Jonas JB, Nguyen N, Naumann GOH: The Retinal Nerve Fiber Layer in Normal Eyes. Ophthalmology Vol 96, No 5. May 1986. p.p. 627-32.

14. Litwak AB: Evaluation of the Retinal Nerve Fiber Layer in Glaucoma. Journel of the American Optometric Association, Vol 61 No 5. May 1990. p.p. 390-97.

15. Jonas JB, Dichti A: Evaluation of the Retinal Nerve Fiber Layer. Survey of Ophthalmology, Vol 40, No 5. Mar-Apr 1996. p.p. 369-78.

16. Quigley HA, Neil R, Miller MD, George T, RBP,FBPA: Clinical Evaluation of the Nerve Fiber Layer Atrophy as an Indicator of Glaucomatous Optic Nerve Damage. Arch Opthalmology, Vol 98, 1980. p.p. 1564-71.

Supplemental Literature

17. Boeglin RJ, Caprioli: Contemporary Clinical Evaluation of the Optic Nerve in Glaucoma. Ophthalmology Clinics of North America, Vol 4 No 4. Dec 1991. p.p. 711-31.

18. Chihara E, Honda Y: Multiple Defects in the Retinal Nerve Fiber Layer in Glaucoma. Graefe's Archive Clinical and Experimental Ophthalmology, Vol 230,1992. p.p. 201-205.

19. Jonas JB,Xu L: Optic Disc Hemorrhages in Glaucoma. American Journel of Ophthalmology, Vol 118, 1994. p.p. 1-8.

20. Mikelberg FS, Drance SM, Schulzer M, Yidegiligne HM, Weis MM: The Normal Human Optic Nerve Axon Count And Axon Diameter Distribution. Ophthalmology, Vol 96, 1989. p.p. 1325-8.

21. Niesser AGJE, Van Den Berg T, Langerset LT, Grove LE: Retinal Nerve Fiber Layer Assessment by Scanning Laser Polarimetry and Standarized Photography. American Journel of Ophthalmology, Vol 121, 1996. p.p. 484-93.

22. Pugesgaard T, Autzen T, Nielsen N, Work K: Retinal Nerve Fiber Layer Photography in Glaucomatous and Normal Eyes. ACTA Ophthalmologica, Vol 68, 1990. p.p. 441-44.

23. Quigley HA, Katz J, Borick RJ, Gilbert D: An Evaluation of the Optic Disc and Nerve Fiber Layer Evaluation in Monitoring the Progression of Early Glaucoma Damage. Ophthlmology, Vol 99, 1992. p.p. 19-28.

24. Repka MX, Quigley HA: The Effect of Age on the Normal Human Optic Nerve Fiber Number and Diameter. Ophthalmology, Vol 96, 1989. p.p. 26-31.

25. Sommer A, Katz J, Quigley HA, Miller NR, Robin AL, Richter RC, Witz KA: Clinically Detectable Nerve Fiber Atrophy Precedes The Onset Of Glaucomatous Field Loss. Arch Ophthalmology Vol 109, Jan 1991. p.p.77-81.

26. Toulonen A, Atraksinen PJ: Initial Glaucomatous Optic Disc and Retinal Nerve Fiber Layer Abnormalities and there Progression. American Journel of Ophthalmology, Vol 111, Apr 1991. p.p. 485-90.

27. Weinreb RN, Shakiba S, Zangwill L: Scanning Laser Polarimetry to Measure the Nerve Fiber Layer of Normal and Glaucomatous Eyes. American Journel of Ophthalmology, Vol 119, No5. May 1995. p.p.627-36