CLINICAL AND EXPERIMENTAL
OPTOMETRY

COMMENTARY

When is glaucoma really glaucoma?

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The approach to the diagnosis and management of glaucoma has undergone considerable changes in recent years. Current concepts of glaucoma diagnosis focus on structural assessment and structure–function correlation, and relies less on the finding of visual field abnormalities. In turn, contemporary approaches to management have also changed and revolve around earlier initiation of pressure lowering medication based on pre-perimetric findings. This article presents an approach to the assessment of the patient with suspected glaucoma, highlighting those structural and ancillary diagnostic investigations that will aid in the correct diagnosis. It also discusses the differentiation of glaucoma from other, non-glaucomatous disease processes.

Key words: GDx, glaucoma, HRT, nerve fibre layer defects, notching, OCT, optic nerve, peripapillary atrophy, visual fields

The diagnosis and management of glaucoma has undergone dramatic changes in recent years. This article will discuss current concepts relating to the diagnosis of glaucoma and differentiating glaucoma from non-glaucomatous disease processes affecting the optic disc and from physiological variants of normal.

In recent years, there has been a progressive shift in the approach to the diagnosis of glaucoma. Reliance on the identification of visual field loss has yielded more to the assessment of structural changes prior to visual field loss, heralding the era of pre-perimetric glaucoma detection. Traditionally, the diagnosis of glaucoma has been based largely on the finding of raised intraocular pressure, perhaps in combination with the finding of increased cup size and visual field loss. Indeed, in many cases, treatment was instituted on the sole basis of raised intraocular pressure, while in cases of borderline raised intraocular pressure, treatment was often withheld until an increase in cup disc ratio or visual field loss could be demonstrated. Once the decision was made that the patient had glaucoma, treatment consisted of lowering pressure to within normal range. Follow-up visits in many cases rarely went beyond measuring intraocular pressure and sometimes performing visual field testing. Until the advent of recent glaucoma clinical trials, there was little evidence that lowering intraocular pressure had any proven benefit in preventing visual field loss.

Modern glaucoma management recognises that raised intraocular pressure is only a risk factor and that by the time a visual field loss becomes apparent, the patient already has advanced glaucoma. Indeed, visual field loss can occur in the absence of raised intraocular pressure in normal pressure glaucoma and conversely raised intraocular pressure can be present in the absence of visual field loss in ocular hypertension. Thus, the focus of assessment has moved more to optic disc and retinal nerve fibre layer evaluation, both clinically and by use of new technologies such as the confocal scanning laser ophthalmoscope (HRT), scanning laser polarimeter (GDx) and optical coherence tomograph (OCT). Additionally there are now technologies such as short wavelength automated perimetry (SWAP), frequency doubling technology (FDT), flicker perimetry and multifocal visual evoked potentials (VEP) perimetry, which may detect functional loss earlier.

Despite a plethora of new technologies, the basis of diagnosis is optic disc assessment. In some cases, this is made more difficult due to the wide variation in the optic disc appearance among the normal

population, which overlaps with the findings in patients with glaucoma. Furthermore, difficulties arise as other non-glaucomatous processes, some of which can be vision or life threatening, may result in abnormal optic disc appearances similar to those found in glaucoma.

DIAGNOSIS OF GLAUCOMA

The process of identifying the glaucomatous patient is a step-wise process, which begins by taking a history. This is followed by examination with emphasis on the optic disc and is completed by investigations such as field-testing and other imaging.

History

When taking the history, it is important to consider the patient's family history in addition to any past or present medical problems. Certain risk factors have been identified as having an association with the development of glaucoma and these should be sought prior to examining the patient, as they will stratify the patient into a high or low risk for glaucoma. A family history of glaucoma, specifically an affected first-degree relative, and advancing age are the strongest risk factors associated with glaucoma. Family history is important, as certain forms of glaucoma have been linked to genetic markers.[1–3] As many as eight gene locations including the MYOC and OPTN genes have been linked to open angle glaucoma and the CYP1B1 has been linked to congenital glaucoma. Other regions of the genome have also been identified as possibly predicting risk of glaucoma development. Other risk factors include hypertension,[4,5] diabetes[6,7] and vasospastic diseases such as migraine[8] or Raynaud's phenomenon.[9] More recently, sleep apnoea has been identified as a risk factor for normal tension glaucoma.[10]

General ophthalmic examination

Anterior segment examination is critical and should seek to identify the presence or absence of ocular clues to the presence of disease. High intraocular pressure, thin central corneas, large cup-disc ratio or cup-disc ratio asymmetry, disc haemorrhages, peripapillary atrophy, nerve fibre layer defects or high myopia are all risk factors for glaucoma and should be looked for. Conditions such as pseudoexfoliation, pigment dispersion, Axenfeld-Reigers anomaly, phacomorphic and phacolytic glaucoma may also be missed if not specifically sought. A Krukenberg spindle along with iris transillumination can sometimes be seen in the case of pigment dispersion and if present, may alert the clinician to this possibility. Gonioscopy should be part of the evaluation to differentiate between the open angle glaucomas and the less common angle-closure glaucoma. It will allow the identification of angle recession and cyclodialysis clefts, as well as the relatively uncommon plateau iris configuration. Patients with pigmentary glaucoma and to a lesser degree, pseudoexfoliation glaucoma, will tend to have a heavily pigmented trabecular meshwork and this finding may help to make the diagnosis. Pachymetry is now considered a routine part of the anterior segment examination for glaucoma and will help to classify the patient into a risk group as well as guide management.[11]

Optic disc assessment

Assessing the optic disc for glaucoma in the primary care setting is difficult for a variety of reasons. First, most practitioners tend not to perform dilated examinations; second, there is a wide variety of experience in examining for disease and finally, there is considerable inter-observer variability in detecting disease.[12] Even among experienced ophthalmologists using direct ophthalmoscopy only, up to 50 per cent of abnormal discs may be missed.[13] The accuracy of detection is improved by the use of dilating agents, examination of the optic disc at the slitlamp and by use of disc photography.

Traditionally, optic disc assessment was largely performed by estimating a cup-disc ratio and monitoring for an increase over time. Now, it is recognised that on its own, this is inadequate and that many other factors can aid in detecting the abnormal disc. The optic disc size, appearance of the neuroretinal rim, peripapillary atrophy, rim haemorrhages and nerve fibre layer abnormalities among others, are useful parameters in the assessment of the optic disc head and will be discussed.

OPTIC DISC SIZE

The optic disc size is the major determinant of its other features. The rim area, disc area, cup size and volume and thus cup-disc ratio are all dependent on the optic disc size.

Disc diameters range from 0.95 to 2.90 mm with an average in the range of 1.85 to 1.95 mm.[14–16] There is considerable racial variation in disc diameter[17] with larger disc diameters in the Aboriginal and Chinese population.[18] Disc area can vary from 0.8 to 6.0 mm^2.

The optic disc is the point at which 1.2 million ganglion cell axons exit the eye.[19] Thus, if the opening is large then the morphology of the disc will be quite different from one in which the same number of fibres is crowded through a smaller opening. Therefore, larger discs have larger cups, thinner rims and larger cup-disc ratios than smaller discs, which may have no cup at all. This is a very important point, as a cup-disc ratio of 0.8 may be normal in an individual with a large disc, whereas a cup-disc ratio of 0.4 may be glaucomatous in an individual with a small disc. Failure to account for disc size can result in inappropriate management of the patient. Treatment on the basis of a large cup-disc ratio or asymmetry may be unnecessary in patients with large discs, while apparently normal cup-disc ratios in the setting of small discs may go untreated.

Accurate measurement of optic disc size is made difficult by the effects of ammetropia, the position of the fundus lens from the eye and the magnification effect of the fundus lens itself. An estimation of the optic disc size is possible with a Welch Allyn ophthalmoscope. The smallest white round spot of the Welch Allyn ophthalmoscope usually illuminates a cone angle of five degrees and casts a light of 1.5 mm in diameter on the retina.[20] This retinal spot size remains constant in phakic eyes with refractive errors between -5.00 D and +4.00 D. A more precise method is the use

of a slit beam, the size of which can be altered. The slit is superimposed over the optic disc and then the size is read from the vernier scale on the slitlamp. A fixed multiplication factor can be applied depending on the lens used.[20] With this method a 60 D lens will give close to a one to one correction, whereas a Superfield lens will need a multiplication factor of 1.5. For ammetropia between -5 D to +5 D, there is little error in this method, however, beyond -8 D or +5 D, there can be considerable error. A more precise method using a mathematical formula to correct for ammetropia can be used[21,22] but for clinical practice, this is probably not required.

CUP-DISC RATIO

Cup-disc ratio is a very useful parameter to both diagnose and monitor progression in patients with glaucoma. As noted above, it is important to view it in the context of the optic disc size. The range of normal cup disc ratios varies from 0.0 to around 0.8.

Less than five per cent of the population has a cup-disc ratio of greater that 0.65[23] and cup-disc ratio asymmetry of greater than 0.2 is found in less than four per cent of the normal population.[24] Therefore, findings significantly outside these ranges are likely to indicate disease. As an increasing cup size is a reflection of a thinning neuroretinal rim, it is a useful parameter for detecting progressive disease. It is not very instructive to merely document the cup-disc ratio, as a large cup-disc ratio with an otherwise healthy neuroretinal rim indicates a less serious clinical status than a similar cup-disc ratio in which the cup is enlarged inferiorly due to rim thinning. It is useful to follow optic disc appearance using serial photography, where an enlarging cup can be more readily detected.

NEURORETINAL RIM

Normal optic discs tend to be oval vertically with a horizontally oval cup. The cup tends to be located supero-temporaly. Therefore, the neuroretinal rim is thickest inferiorly followed by superiorly, nasally and finally it is thinnest temporally. This is known as the ISNT rule.[24]

In glaucomatous neuropathy, selective loss of neuroretinal rim tissue occurs primarily in the infero-temporal region of the optic disc and, to a lesser extent, in the supero-temporal sector in the early stages of damage. With time, there tends to be loss temporally and finally nasally with the disruption of the usual pattern of the ISNT rule.

This tends to result in an alteration of the usual configuration of the horizontally oval cup to a more vertical orientation.

Damage to the optic disc can occur in an asymmetrical manner. This will result in focal areas of damage resembling a notch or 'bite' out of the rim. In particular, the laminar dot sign has been attributed to glaucomatous disc damage and consists of focally visible laminar pores adjacent to an area of neuroretinal rim thinning.[25] Recently, it has been suggested that increasing visibility of laminar pores may imply progressive glaucoma, it tends to be a feature of eyes with large cups and thus may be found in normal eyes. In general, it can be said that notching, per se, represents focal areas of ischaemia resulting in localised loss of neuroretinal rim.[26]

DISC HAEMORRHAGES

A disc haemorrhage is localised at the disc margin or in the immediate peripapillary area extending to the disc margin[27] (Figure 1). These are quite specific for glaucomatous damage, rarely occurring in other conditions.[27,28] The majority of disc haemorrhages tend to occur infero-temporally, followed by supero-temporally. The finding of a disc haemorrhage indicates that there is a high risk of further progression and is an indication that treatment should target a lower intraocular pressure.[29] In normal tension glaucoma in particular, disc haemorrhages are the most strongly associated finding with the progression of visual field loss.[30] Recurrent disc haemorrhages are associated with a greater rate of visual field loss.[31] The subsequent field loss is thought to correspond to the location of the haemorrhage, however, not all studies agree with this.[32]

The mechanism of a disc haemorrhage is unclear but many investigators believe that there is a link between haemorrhages, ischaemic insult and subsequent rim notching.[33] These haemorrhages are usually visible for up to nine months and are commonly followed by a nerve fibre layer defect.

Not all disc haemorrhages are due to glaucoma. Vein occlusions, hypertension, trauma and diabetic retinopathy are also capable of producing haemorrhages. Therefore, it is important to view these haemorrhages in context with the patient's other medical history and other ophthalmic findings.

PERIPAPILLARY ATROPHY

Peripapillary chorioretinal atrophy is another morphologic finding that can aid with the diagnosis of glaucoma and in differentiating various forms of glaucoma. This finding is considered to be less specific than neuroretinal rim changes for the diagnosis of glaucoma.

Peripapillary atrophy constitutes defects in the retina[33] and can be divided into a central beta zone and a peripheral alpha zone[34,35] (Figure 2). Alpha zone atrophy is more common and frequently occurs in normal individuals. It consists of focal areas of both hyper- and hypopigmentation. Histologically, there is thinning of the adjacent chorioretinal layers. Beta zone atrophy occurs inner to the alpha zone and outer to the peripapillary scleral ring. It represents total loss of the retinal pigment epithelium and a markedly diminished layer of photoreceptors. Bruch's membrane and the adjacent choriocapillaris remain. The choroidal vessels are clearly visible as is the underlying sclera. Beta zone atrophy differs histologically from both myopic scleral crescent and the inferior scleral crescent found in a tilted disc. In myopic scleral crescents, only the inner limiting membrane and remnants of the nerve fibre layer are seen histologically. In the inferior scleral crescents the retinal pigment epithelium is retracted from the disc margin and the choroid may be thinned, exposing some of the underlying sclera.

Beta zone atrophy corresponds psychophysically to an absolute field defect,[36] whereas alpha zone atrophy corresponds to a relative field defect.[37] Beta zone

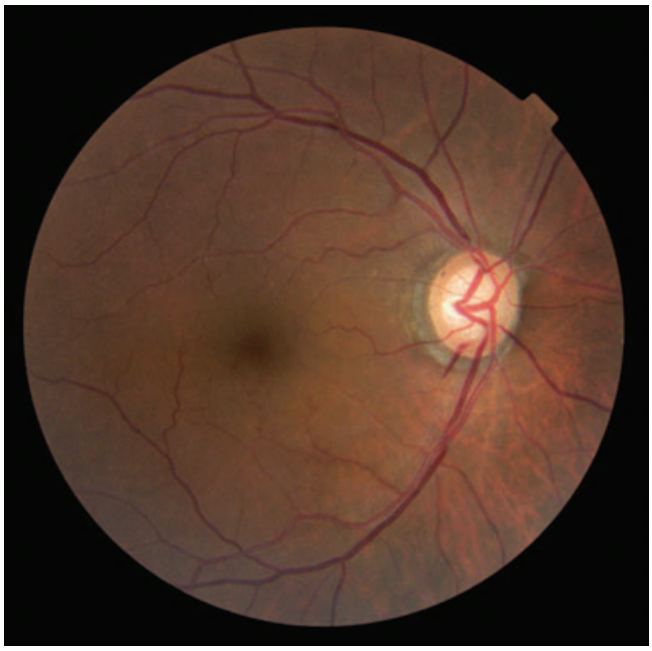

Figure 1. Drance haemorrhage and peripapillary atrophy

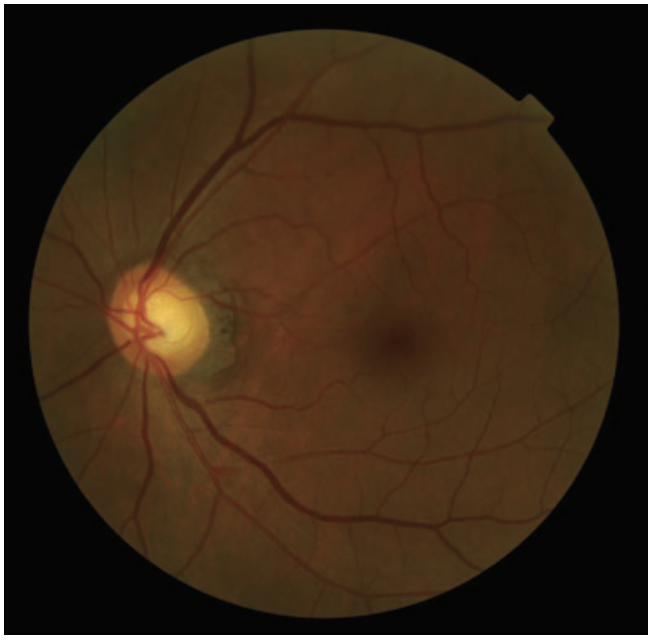

Figure 2. Peripapillary atrophy

atrophy is mostly temporal followed by the infero-temporal and supero-temporal regions. It is least common nasally.[38] It is more specific for glaucomatous damage and tends to be larger than alpha zone atrophy. Additionally, it is significantly associated with other factors such as rim loss, neuroretinal rim haemorrhages and field defects. There is a correlation between increasing beta zone atrophy and progression of glaucoma.[39] In anomalous eyes where disc assessment is often difficult, peripapillary atrophy can be used to assess progression.

Beta zone atrophy is more prominent in normal tension glaucoma than primary open angle glaucoma and least prominent in the secondary open angle glaucomas, such as pseudoexfoliation.[40,41] It can also be found in non-glaucomatous processes such as senile changes, autosomal dominant optic atrophy, anterior ischaemic optic neuropathy, tilted optic disc and myopic scleral crescent. Patients with anterior ischaemic optic neuropathy tend not to show enlargement of beta zone atrophy over time.[42]

NERVE FIBRE LAYER DEFECTS

The nerve fibre layer is constant in its morphology with little variation between individuals. This constancy is exploited in nerve fibre layer analysers and defects are often a marker of disease. A nerve fibre layer defect is a localised loss of ganglion cells, which allows light reflected from the relatively more exposed retinal pigment epithelium to be seen. The pathogenesis of these defects is not well understood. These defects are best seen with a red-free light and often there is a corresponding field defect. A true defect terminates at the disc margin unlike pseudo-defects or slit defects, which do not. The appearance of these defects can differ, appearing larger and closer to the fovea in normal tension glaucoma, while in primary open angle glaucoma they tend to be smaller and located further from the fovea (Figure 3).

Nerve fibre layer defects are often the earliest markers of disease.[43,44] They can be present at a time when the optic disc and visual fields may be normal or borderline. It has been estimated that 20 per cent of the retinal nerve fibre layer needs to be lost to produce five decibel loss on visual field testing and that 40 per cent loss will result in a 10 dB loss.[45] Nerve fibre layer defects can sometimes be seen following a rim haemorrhage. Similar defects can be seen in other conditions, for example following optic neuritis. Thus taken alone, they are not diagnostic.

Intraocular pressure

Recently, the importance of lowering intraocular pressure in the management of glaucoma has been demonstrated by studies such as the Advanced Glaucoma Intervention Study,[46] the Normal Tension Glaucoma Study,[47] the Ocular Hypertension Study,[48] the Collaborative Initial Glaucoma Treatment Study[49] and the Early Manifest Glaucoma Study.[50] Thus, although the precise role of intraocular pressure in the pathogenesis of glaucoma is not well understood; what is known is that lowering intraocular pressure in patients with normal tension glaucoma by 30 per cent or in patients with primary open angle glaucoma to less than

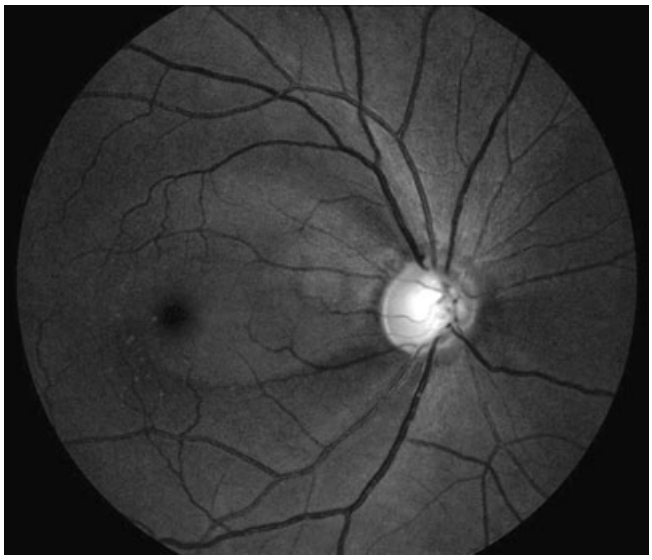

Figure 3. Nerve fibre layer defect

18 mmHg will slow or even halt progression.[50] In patients with ocular hypertension, reduction of pressure by 20 per cent will reduce the risk of progression to primary open angle glaucoma by 55 per cent.[48]

Intraocular pressure has a non-Gaussian distribution in the population with the distribution curve being skewed to the right. Historically, an upper limit of 21 mmHg has been accepted as the upper limit of normal pressure. Patients with intraocular pressure greater than this are nearly nine times more likely to develop glaucoma.[51]

Until recently, raised intraocular pressure was the basis on which the diagnosis of glaucoma was made but now it is viewed as a risk factor rather than a causal factor. Alone, it is a poor indicator of glaucoma. If based solely on intraocular pressure, screening will tend to miss those patients with normal tension glaucoma and misclassify patients with ocular hypertension or increased central corneal thickness as glaucoma.

Intraocular pressure measurement has a low sensitivity and specificity of 65 per cent for detecting glaucoma, if a cut-off pressure of 18 mmHg is used. Although raising the cut-off to 21 mmHg improved the sensitivity to 92 per cent, it lowered the specificity to 44 per cent.[51] There is no intraocular pressure cut-off at which reasonable sensitivity and specificity are obtained for the diagnosis of glaucoma.

Various factors affect the accuracy of intraocular pressure measurement, including physiologic variables in the patient. Central corneal thickness is known to affect intraocular pressure measurement, such that thicker corneas result in an overestimation of the true pressure and thinner corneas in an underestimation. Intraocular pressure tends to exhibit a diurnal fluctuation with peaks occurring in the early morning hours. It is also increased by recumbent position. Random intraocular pressure measurement has been estimated to miss up to 50 per cent of patients with a confirmed diagnosis of glaucoma.[51] Due to this variability in intraocular pressure, it is important to develop a pressure profile for each patient measuring at different times of the day, not only to determine whether disease exits but also to determine what type of glaucoma the patient has and whether treatment has achieved target pressure. The choice of tonometer is also known to influence accuracy of intraocular pressure measurement. Non-contact tonometry has good agreement with Goldmann applanation tonometry, the gold standard manometric method.[52] The mean difference between these ranges between -1.0 mmHg and +0.9 mmHg. Although most studies show a constant difference across the range of intraocular pressures,[53–57] some have shown non-contact tonometry to overestimate Goldmann applanation tonometry at high intraocular pressure and to underestimate the Goldmann applanation tonometry at low intraocular pressure.[58,59]

Central corneal thickness

Recently, central corneal thickness has been shown to be an important consideration in the diagnosis and management of glaucoma.[60] It influences the measurement of intraocular pressure, and may in itself be an independent risk factor for the progression of glaucoma. The Ocular Hypertension Treatment Study[61] showed that central corneal thickness is a predictor of the subsequent development of glaucoma in patients with ocular hypertension. Patients with thin central corneas, defined in the study as less than 555 microns, had a threefold greater risk of developing glaucoma than those with a central corneal thickness of greater than 588 microns.

The accuracy of all tonometric methods is affected by central corneal thickness. A study using a manometric cannulation technique of the human anterior chamber, showed the relation between measured intraocular pressure and central corneal thickness to be linear.[62] This study demonstrated the need for a 0.40 mmHg adjustment for every 10 µm of deviation in thickness of the central cornea from 550 µm as measured by ultrasonic pachymetry. Measurement of intraocular pressure by Goldmann applanation tonometry is less affected by central corneal thickness than non-contact tonometry.[63–65] The average intraocular pressure measurement error is 0.27 mmHg per 10 µm with Goldmann applanation tonometry and 0.46 mmHg per 10 µm with non-contact tonometry. Newer methods such as dynamic contour tonometry are less

affected by measurements of central corneal thickness, however, these methods tend to overestimate intraocular pressure as compared to Goldmann applanation tonometry.

Faced with this information, central corneal thickness should be taken into account when assessing a patient for glaucoma. However rather than attempting to use nomograms to adjust for intraocular pressure, clinically, it is more useful to categorise the patient as having a thick, normal or thin central cornea, which aids in overall risk assessment. In this manner, an estimate of patient risk can be made. Further, patients with elevated intraocular pressure and thick central corneas but absolutely no other risk factors can be safely labelled as having ocular hypertension and observed rather than subjected to a lifetime of treatment.

Perimetry

Visual field testing is an important tool for detecting and monitoring progression of glaucoma, as visual loss is the end point of glaucoma. Currently, standard threshold automated perimetry (SAP) is the cornerstone of visual field testing. However, it is estimated that as many as 40 per cent of ganglion cells may have been lost by the time a defect is manifest.[66,67] Further, visual field testing suffers from a high level of variability in its ability to detect disease and that variability increases as the disease advances.

Newer technologies have attempted to address these shortcomings, including short wavelength automated perimetry (SWAP), frequency doubling technology (FDT), flicker perimetry, Rarebit perimetry and high pass resolution perimetry (HRP). SWAP and FDT in particular are technologies that were thought to work by targeting a subset of ganglion cells, which are presumed to be damaged earliest in the natural history of glaucoma. These are the larger M and K neurons, which project through the magnocellular pathway. More recently, it has been shown that all classes of neurons are damaged at similar rates[68,69] and that these technologies probably work by reducing redundancy in the pathway allowing for earlier detection.[70]

SWAP is a modification of SAP using the same perimeter and programs. It uses a 440 nm, 1.8 degree target at 200 milliseconds duration on a 100 candelas/m^2 yellow background to test selectively the short wavelength sensitive cones and their connections. Most likely, the test is processed by the small bistratified blue-yellow ganglion cells, which encompass approximately nine per cent of the total population of retinal ganglion cells.[71]

Until recently, the test duration of more than 15 minutes made use of this test impractical, however, with the availability of SITA-SWAP, test duration is reduced to three minutes, making this test more useable. One of its limitations is that it is affected by significant cataract.[72] Therefore, its use is mainly in younger patients with early disease.

Frequency doubling technology (FDT) has also been shown to detect functional visual loss earlier than SAP[73] and therefore, is potentially a good method of screening.

There is a number of issues relating to the accuracy of field testing. First, there is the inherent variability in the test results. Indeed in the Ocular Hypertension Treatment Study,[74] it has been estimated that as many as 85 per cent of visual field defects detected on initial testing will not be apparent on repeat testing. This variability relates to patient factors including patient concentration, use of sedating medication or alcohol and distractions such as noise in the test room. This may result in unnecessary further investigations or referral for the exclusion of disease. A good strategy in this situation is to retest any patient who has an isolated field abnormality without other corroborating findings. Even if there are other associated findings, repeat field testing should be undertaken to confirm the defect.

Another problem with field testing is the inter-test variability that tends to be greater in pathological conditions such as glaucoma. As glaucoma progresses and the depth of the defects increase, the variability of threshold sensitivity also tends to increase.[75] It has been suggested that this increase in variability is due, in part, to increasing ganglion cell loss and the subsequent decrease in sampling of the test area with a given stimulus size.[76]

Finally, standard field tests examine only the central 24 degrees or sometimes 30 degrees of the visual field. This will result in some patients with early glaucoma being missed. Indeed the Ocular Hypertension Treatment Study[77] found that of all patients with field loss, only 59 per cent lie within the central 24 degrees, leaving more than 41 per cent that would be missed. Thus, for detection of functional loss in glaucoma, SAP is not the optimal method. While it is generally held that optic neuropathy is detected best by optic nerve examination[78] and that changes here will develop before any detectable changes in SAP, this is not always true. This does not mean that there are no alterations to visual function in patients with detectable neuropathy and normal SAP, rather it reflects the relatively poor sensitivity of SAP to detect this decrease in function. There are situations in which functional loss detected by various techniques will precede structural change. Hence, a combination of techniques, such as SWAP or FDT, plus structural assessment are best employed for early detection.[79,80]

Ancillary testing

It is generally accepted that structural optic disc and retinal nerve fibre layer changes precede functional lost.[81] This is not wholly supported by the available literature with some studies demonstrating that functional loss can precede structural changes. This suggests that the temporal relationship between structure and function is less well defined than previously thought.[82] Despite this, recent years have seen the development of a number of computer-based imaging instruments, which provide quantitative information on the optic disc and retinal nerve fibre layer, aimed at earlier (structural) diagnosis. Three commercially available diagnostic imaging instruments—the confocal scanning laser ophthalmoscope (HRT), the scanning laser polarimeter (GDx) and an optical coherence tomograph (OCT)—provide quantitative assessment of the optic disc and retinal nerve fibre

layer for the diagnosis of glaucomatous optic neuropathy. Each instrument includes an age-adjustment normative database so that measurements can be identified as borderline or outside normal limits.

HEIDELBERG RETINAL TOMOGRAPHER

The Heidelberg retinal tomographer (HRT III; Heidelberg Engineering, Dossenheim, Germany) consists of a scanning laser that produces a topographic map of the optic disc. The disc is divided into sectors and each is labelled as normal, suspect or abnormal. The HRT has been used primarily to measure and characterise optic disc topography but it also assesses retinal nerve fibre layer information indirectly. Most studies report that HRT linear discriminant functions, Moorfields regression analysis, rim measurements or cup measurements have better diagnostic accuracy than retinal nerve fibre layer measurement.[83–86] The ability of the HRT to discriminate between normal and glaucomatous eyes[87] and its measurement precision[89] make the HRT a good candidate for the detection of glaucomatous progression. Characteristic baseline HRT changes have been associated with the development of glaucomatous changes in ocular hypertensive eyes without detectable optic disc or visual field changes[90] and in glaucoma suspect eyes.[91] Development of glaucoma is strongly and independently associated with HRT mean-height contour, more so than retinal nerve fibre layer measurement.[90]

Diagnosis of glaucoma

Scanning laser polarimetry can be used to assess structural losses of the retinal nerve fibre layer with instruments such as the GDx VCC nerve fibre analyser (Carl Zeiss Meditec, Inc). A correlation has been demonstrated between standard automated perimetry and GDx VCC measurements in patients with glaucoma, suggesting that GDx VCC measurements relate well with functional loss in glaucoma however, no correlation was found in healthy patients between perimetry and GDx VCC measurements.[92]

Reproducibility of retinal nerve fibre layer thickness measurements on GDx VCC is high in both healthy and glaucomatous eyes. The variation between repeat measurements may be greater than 10 per cent, so distinguishing between physiological variability and real retinal nerve fibre layer thickness changes may sometimes be difficult.[93]

Studies using the GDx NFA have shown baseline retinal nerve fibre layer measurements to be independently predictive of glaucomatous visual field loss in glaucoma suspect eyes.[94,95] There appears to be no information on the predictive value of GDx VCC retinal nerve fibre layer measurements for the development of glaucoma or for monitoring its progression.

OPTICAL COHERENCE TOMOGRAPHY

Optical coherence tomography (StratusOCT; Carl Zeiss Meditec, Inc, Dublin, CA) can image retinal structures and differentiate between the layers of retina to provide retinal nerve fibre layer measurements. Its principle use is in the detection of retinal pathology but when set for glaucoma, it can detect nerve fibre layer thinning, given that ganglion cells are lost in the glaucomatous process. Several studies have demonstrated that retinal nerve fibre layer inferior thickness and average thickness have the best diagnostic accuracy in distinguishing glaucomatous eyes.[84,87–89,96–98] Little information has been published regarding the ability of the OCT to predict or determine progression of glaucomatous changes.

Use of these devices is not intended to substitute for a clinical examination. None of these technologies will provide a diagnosis. Their role is to augment the information obtained from history taking and examination. Serial disc photography remains the gold standard for following glaucoma.

NON-GLAUCOMATOUS DISEASE AND ANATOMICAL VARIANTS

One of the difficulties with optic disc assessment is determining when an abnormal disc is due to some other, non-glaucomatous process. Compressive optic neuropathy, Leber's optic neuropathy, anterior ischaemic optic neuropathy and anomalous optic discs can be challenging and difficult to differentiate from glaucoma. There are some basic principles that if followed will help to differentiate glaucomatous from non-glaucomatous disease processes.

Visual acuity

Glaucoma does not usually lead to a decrease in visual acuity. While this can occur if central fixation is involved, it is uncommon. Thus, any unexplained visual loss needs to be further investigated and not attributed to glaucoma until all other causes are excluded.

Colour vision

Dyschromatopsias are not caused by glaucoma but are commonly found in neurological disease. Compressive lesions of the optic disc and demyelinating disease in particular can frequently lead to colour vision abnormalities. Therefore, any patient who demonstrates abnormal colour perception needs further neurological evaluation.

Optic disc pallor

Although pallor of the optic disc may be present in end-stage disease, is also an uncommon finding in glaucoma. A pale optic disc should immediately raise suspicion and requires investigations. Disc pallor is found more commonly in conditions such anterior ischaemic optic neuropathy, optic nerve compression or Leber's optic neuropathy. A prior ischaemic event, such as a significant hypotensive episode, perhaps in the setting of trauma or following surgery, can lead to optic disc ischaemia with field defects and an abnormal appearance of the optic disc. Here again, the field defect will remain stationary with time differentiating it from glaucoma.

Disc swelling

Shunt or new vessels at the disc or disc swelling is never seen in glaucoma and suggests other pathology, such as an old central retinal vein occlusion, retinal ischaemia or compressive lesions of the optic disc.

Optic disc drusen

Disc drusen can give the impression of disc swelling and can produce arcuate field defects, which can mimic glaucomatous defects. Disc drusen exhibits the phenomenon of autofluorescence, which can help identify it.

Tilted and anomalous discs

Tilted discs may produce field defects, which together with other findings such as positive family history or borderline high intraocular pressure, may lead to the suspicion of glaucoma. They can be challenging to differentiate from glaucomatous discs. In this situation, observation will show a stationary defect, which requires no treatment.

Similarly, optic disc pits and optic disc colobomata can be difficult to assess. An optic disc pit can be difficult to differentiate from a notch, however, pits are most commonly found on the temporal side of an optic disc, whereas more frequently disc notches tend to be superotemporal or inferotemporal. A disc coloboma may be associated with an adjacent retinal or iris coloboma. These tend not to produce field defects and again close observation will reveal no progression over time.

Any of these findings requires further investigation with imaging of the brain using either CT or MRI. A careful history may elicit the presence or symptoms of diabetes, hypertension or vein occlusion, Similarly, symptoms such as headache or other neurological phenomena suggest compressive disease. Sleep studies may need to be considered in patients with a history suggestive of sleep apnoea.

CONCLUSION

The detection and diagnosis of diseases of the optic disc are best achieved by examining the optic disc. Intraocular pressure measurement, visual field testing and imaging technologies are sources of additional information. When viewed in context with the examination and history, these will help to stratify the patient in terms of risk for glaucoma.

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