Glaucoma Diagnosis – The Role of Optic Nerve Examination

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Glaucoma is a chronic progressive disease that, left untreated, can lead to blindness. Glaucoma represents a range of conditions in which the flow of aqueous humour in the eye is blocked, causing an increase in intraocular pressure (IOP). An impaired blood flow to the optic disc may also cause glaucoma, even without an abnormally high IOP. Even with careful monitoring and lowering of IOP, approximately 25% of patients lose their sight. Consequently, glaucoma is the second most common cause of blindness worldwide.

The global prevalence of glaucoma was estimated to be 67 million in 2001. Approximately 13% of these were estimated to be in Europe, of which half were undiagnosed and untreated. The most prevalent type of glaucoma, primary open-angle glaucoma (POAG), has subtle symptoms early in its course and, consequently, often remains undetected. Late diagnosis of glaucoma significantly increases the cost of treatment and raises the risk of visual impairment. Historically, an increased level of IOP was presumed to be the most accurate means of diagnosis; however, it is now recognised that high IOP is a risk factor for glaucoma, but is not an accurate diagnostic. Therefore, there is a need for an accurate diagnosis system.

Glaucoma Diagnosis – The ‘Gold Standard’ Tests

In glaucoma, structural changes usually occur first and are followed by functional deficits. There are three well-established ‘gold standard’ tests used by ophthalmologists to diagnose glaucoma: IOP measurements, visual field tests and (stereoscopic) assessments of the optic nerve. Together, these methods provide information on both structural and functional defects.

Intraocular Pressure

A gradual increase in IOP has long been recognised as the major risk factor for glaucoma, and the lowering of IOP serves to impede progression of optic nerve damage. Therefore, IOP measurements are usually documented over time. The Goldmann applanation tonometer is the standard device used by physicians to detect alterations in IOP. Although the device is fairly accurate, the measurement of IOP is not always a precise indication of glaucoma. Individually, IOP is highly variable, and even low IOP cannot be ruled out for risk of glaucoma. Additionally, IOP does not indicate the extent of damage or, indeed, that damage has actually been done to the optic nerve. Thus, in the diagnosis of glaucoma this variable can be used only alongside other evidence for a positive outcome.

Perimetry

Peripheral vision is usually the first to deteriorate in glaucoma; hence, tests of the visual field have been used to diagnose the disease. Perimetry is a systematic measurement of light sensitivity in the visual field by the detection of targets presented on a defined background. The standard diagnostic tool for visual field examination is the computerised field analyser. Responses are statistically analysed and compared with a database of normal responses. Even with this comparison it is challenging to state definitively whether a patient has glaucoma. Previously, for detecting any progression the test results were judged by comparing print-outs from visual field tests, which was time-consuming and often inaccurate. Today, new software provides ophthalmologists with automated visual-field-progression analysis; however, it may take three examinations before an accurate baseline is obtained. Also, long-term fluctuations in the field tests can often occur, thus the accuracy of this method of diagnosis is still in question.

Stereoscopic Optic Nerve Photographs

Glaucam leads to alterations in the size and shape of the optic disc, the neuroretinal rim and the size ratio between the optic disc and cup. By means of photographs of the optical nerve head (ONH), morphological changes in glaucoma are qualitatively monitored. In addition, significant thinning of the retinal nerve fibre layer (NFL) demonstrates early-stage glaucoma. Thus, evaluation of the ONH is the mainstay of the three components of making a diagnosis. However, the appearance of the ONH differs widely between individuals, which can make it difficult to detect glaucomatous eyes.

Limitations of the Traditional Methods

The standard diagnostic techniques have several limitations, the most important of which is insensitivity. It is generally recognised that IOP measurement is a particularly insensitive and non-specific way of making a diagnosis of glaucoma. Visual field testing is a fairly insensitive method for early diagnosis, and stereoscopic evaluation of the ONH is very subjective and open to misinterpretation.

A recent study found that the clinical assessment of stereoscopic ONH photographs for diagnosing glaucoma varied greatly and was dependent on the level of training. In the study, stereoscopic ONH photographs were obtained from one eye each of 40 healthy subjects,
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48 glaucoma patients and six patients with ocular hypertension. Four glaucoma specialists, four general ophthalmologists, four residents in ophthalmology and four optometrists classified the ONH photographs as normal or glaucomatous. The study found that glaucoma specialists and general ophthalmologists had the greatest diagnostic accuracy, with residents classifying the fewest eyes correctly. The intra- and inter-observer agreement for ONH analysis was only moderate to good.

An ongoing pan-European study is assessing the consistency of stereoscopic ONH analysis in 300 general ophthalmologists from 11 European countries. The European Optic Disc Assessment Trial (EODAT) has a similar design to the investigation conducted by Reus et al.\(^7\) Stereoscopic optic disc photographs of one eye each of 40 healthy subjects, 48 glaucoma patients and six patients with ocular hypertension were assessed by the participating ophthalmologists. Preliminary data from 136 general ophthalmologists from nine European countries showed that the accuracy of European ophthalmologists for classifying optic disc photographs in glaucoma varied considerably. The study even found it to vary between countries. The intra-observer agreement from the preliminary data was moderate to very good.\(^7\) Worryingly, some participants even approached the 50% chance level.

**Beyond the Current Standard Tests**

Structural assessment is fundamental for early glaucoma diagnosis and in the management of the disease. Alterations of the ONH and the NFL are the first signs of glaucoma, commonly appearing ahead of any functional

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An increase in diagnostic accuracy was noted in glaucoma detection between the GDx-VCC device and previous devices with a fixed corneal compensation.\(^12\) The GDx-VCC device has a sensitivity of 84% for a given specificity of 94% when examining the NFL in glaucoma patients.\(^13\) An even greater corneal compensation – so-called enhanced corneal compensation (ECC) – will be released shortly. It has been shown to offer an even greater diagnostic accuracy than VCC. There are still limited data on the improvements offered by the device in glaucoma progression detection, and further studies need to be performed to discover its full potential.

**Confocal Scanning Laser Ophthalmoscopy**

The principle of light reflection is employed in CSLO. In this technique a laser is projected through a pinhole towards the area of interest.\(^14\) The reflections are picked up through another pinhole in front of a light detector. The pinholes ensure that only light reflected from a defined focal plane will reach the detector. A series of scans is undertaken and reconstructed to produce a 3D image.

The main drawback of CSLO is the generation of topographical parameters using a moderately reproducible reference plane. It is unclear to what extent blood vessels in the ONH affect the measurements. Furthermore, the operator must also outline the disc margin, which is a time-consuming and subjective task. More recent software eliminates the need for operator-dependent margin demarcation. An automated classifier – the glaucoma probability score (GPS) – quite accurately classifies healthy and glaucomatous discs. In the clinic, the most commonly used CSLO device is the Heidelberg retina tomograph (HRT). The device includes an internal fixation target, improving its reproducibility. Glaucomatous progression has been demonstrated with the HRT, although it agreed only moderately with visual field progression.\(^15\)

**Optical Coherence Tomography**

OCT, based upon interferometry, is a relatively new technique for optical imaging. It is a non-invasive, non-contact method of producing...
The importance of ONH and NFL assessment in the diagnosis of glaucoma cannot be understated. The new imaging devices can be used to evaluate patients in whom there is suspected glaucomatous ONH and NFL damage, but who have yet to show visual field defects on standard perimetry. Several studies have evaluated these devices in clinical applications. Newer perimetric tests may detect glaucomatous damage earlier than standard visual field tests, although their role is still uncertain.

A recent study compared the accuracy of HRT, GDx-VCC and OCT in the diagnosis of glaucoma, and concluded that there was no significant difference between the diagnostic capabilities for glaucoma between the three devices using the best parameters for each.22 Another study examining the devices showed that subjective assessment of the ONH provided the best diagnostic efficacy for glaucoma.21 However, recent studies have shown that automated analysis of measurements with GDx-VCC and HRT had a diagnostic accuracy for glaucoma either equal to or higher than the classification of stereoscopic ONH photographs by glaucoma specialists.7

It is also important when following up patients that the ONH and NFL be well documented. The beauty of the recent imaging devices is that they provide an objective means of documenting glaucoma, facilitating the detection of any progression. In the past photographs were used, but these have their limitations. Frequency-domain OCT may well become the gold standard for imaging glaucoma, for both its detection and the follow-up of any progression.

Summary and Conclusions

Glaucoma is a chronic progressive disease in which approximately 50% of sufferers are undiagnosed. The early stages of the disease show structural changes to the ONH and NFL, and are difficult to detect using current visual field tests or IOP measurements. Judging the ONH is currently the most common test for early diagnosis of glaucoma. However, these old mainstays are quite inadequate and, in addition, they provide very little documentation for follow-up. Promising devices such as SLP, CSLO and OCT have proved to give comparable reproducibility and accuracy in the evaluation of glaucomatous and normal eyes, and may assist clinicians in diagnosing glaucoma. Their role in detecting progression is currently being explored by several research groups. The latest-generation OCT holds great promise for both detecting and following glaucoma, although its future role is still unclear. Moreover, there is a need to improve education and training in examining the ONH; in turn, this will improve earlier glaucoma detection and thus treatment.