EDITORIAL

Screening for chronic glaucoma

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Glaucoma is an acquired chronic optic neuropathy which causes progressive loss of peripheral vision and is a common cause of blindness. While the precise pathophysiology of glaucoma is unknown, the end result is retinal ganglion cell death with loss of nerve fibres. Most individuals with glaucoma have raised intraocular pressure (IOP) secondary to reduced aqueous outflow through the trabecular meshwork. Two major prospective studies and a recent meta-analysis of randomized controlled trials have shown conclusively that treatment to reduce IOP can prevent visual disability and blindness in this condition.[1–3]

The prevalence of chronic open-angle glaucoma in people aged over 40 years is 1–2% for whites and 5–7% for blacks.[4–6] Population-based studies show that the most important risk factor for developing glaucoma is increasing age. In the Beaver Dam Survey a prevalence of 0.9% was reported in people aged 43–54 years of age, rising to 4.7% in those aged 75 years or older.[5] In the Barbados Eye Study, the prevalence in blacks rose from 1.4% for those over 40 years old to 14.8% for those over 70 years old.[6] A positive family history of glaucoma puts an individual at increased risk of glaucoma. The Baltimore Eye Survey reported an odds ratio of having glaucoma for those with siblings or parents with the disease of 3.69 and 2.17, respectively.[4]

Glaucoma is frequently described as the ideal disorder for screening in that it is an asymptomatic condition with an extended course before impairment occurs, and effective therapy exists. Throughout the world, however, the detection of glaucoma creates great difficulties. Approximately 50% of those with glaucoma in developed countries are undiagnosed and more than 90% in developing countries are outside care.[7,8] Even in the UK, glaucoma screening outside a hospital ophthalmology setting is often ineffective, and the problem is compounded by the fact that the ageing of the population means that the number of cases of glaucoma is expected to increase by 30% in the next 20 years.[9,10] Detection of the disease in the early stages is not easy, as patients are usually asymptomatic. Extensive optic nerve damage and visual field loss have often occurred by the time of diagnosis.[11] Since effective treatment is available, finding individuals with glaucoma before they are visually disabled should be a public health imperative.

The diagnosis of glaucoma is based on the measurement of IOP, the characteristic appearance of the optic nerve head and typical visual field defects. Evaluation of the retinal nerve fibre layer may also facilitate and support the clinical diagnosis of glaucoma.[12] There are advantages and disadvantages associated with the measurement of these parameters, ranging from the discriminating power of the measure to more practical considerations, such as how easy it is to obtain high-quality, reproducible results. Subjective tests (visual function) frequently have high variability and a level of expertise is required to accurately interpret the results.[13] Objective methods of detection are preferable to subjective methods, but the instruments needed are expensive and are not readily available in clinical practice.

IOP is the most important risk factor for glaucoma: the higher the IOP the greater the risk (Table 1). The mean IOP in individuals over the age of 40 years is 16 mmHg, with a normal range of 11–21 mmHg. Most patients with glaucoma have raised IOP (>21 mmHg) and the treatment for glaucoma is to reduce the IOP using medication (usually in the form of eye drops) or surgery. The measurement of IOP (tonometry) is simple, fast and inexpensive, and is one of the most heavily relied-on measures for glaucoma diagnosis. For screening purposes a one-off value of 21 mmHg is often used, but this is neither sensitive nor specific.[14] Conversely, 32–53% of individuals with glaucoma have an IOP on first presentation that is within the normal range (IOP <21 mmHg); these patients have so-called 'normal tension' glaucoma.[5,14,15] The limitations of IOP as a screening tool are evident on analysis of the findings of the Baltimore Eye Survey: a screening IOP of >21 mmHg detected only 47% of individuals with glaucoma, while an IOP of <21 mmHg correctly identified 92% of individuals without glaucoma.[14]

The visual field is generally assessed using automated perimetry. Many clinicians consider this to be the gold standard for glaucoma diagnosis. The main weakness of screening using the visual fields is the subjective nature of the test and the high variability of the results.[13] There is also good evidence to suggest that by the time there is a visual field defect present on perimetry, structural abnormalities in the optic nerve and ganglion cell layer are already present.[16] The sensitivity and specificity of perimetry have been reported to be 70% and 67%, respectively.[17] Visual fields should therefore not be interpreted in isolation, but in conjunction with other clinical findings such as the level of IOP and the appearance of the optic disc and retinal fibre layer.

Optic nerve head assessment has traditionally involved ophthalmoscopy and biomicroscopy (using a slit lamp). Stereophotography has emerged as a potential tool to detect glaucoma, as a high-resolution image of the optic disc is produced which creates a permanent record for close evaluation and future comparison.[18] Digital technology provides immediate results which can be electronically accessed. The limitation of this technique is the expense of the equipment and the need for clear media and a dilated pupil. It can be difficult to differentiate physiological variation from damage due to glaucoma (normal eyes with large optic discs will tend to have large cups, which can be inaccurately diagnosed as glaucoma; and eyes with small optic discs will tend to have small cups, which can be misinterpreted as normal). Optic nerve head changes can be difficult to detect in early glaucoma: in a study of ocular hypertensives who converted to glaucoma, only 19% exhibited optic nerve head changes.[19] The Early Manifest Glaucoma Treatment Study found that only 7% of all patients showed progressive changes in their optic disc during the entire six years of follow-up, whereas 53% were shown to progress using visual field analysis.[20] In general, the sensitivity and specificity values based on optic nerve

Table 1 The prevalence of chronic glaucoma and the relative risk at different intraocular pressure levels (from The Baltimore Eye Survey)[14]

Presenting IOP (mmHg)	Prevalence (%)	Relative risk
<15	0.65	1
16–18	1.3	2
19–21	1.8	3
22–24	8.3	13
25–28	8.3	13
30–34	25.4	39
⩾35	26.1	40

head assessment are higher than with IOP assessment alone. The diagnostic accuracy varies depending on the level of glaucomatous damage, but most studies report sensitivity and specificity values in the 70–80% range.[18] In a clinical setting, the actual sensitivity and specificity values are probably lower than these figures.

Retinal nerve fibre layer defects have been shown to be the earliest sign of glaucoma and can be found up to six years before the visual field changes.[21] There is evidence that retinal nerve fibre layer changes can occur even before optic nerve head changes can be detected.[19] The sensitivity and specificity for red-free retinal nerve fibre layer photography has been reported to be in the range of 70–80%.[22] New methods of assessing the retinal nerve fibre layer include scanning laser polarimetry and ocular coherence tomography. Reproducibility is good and these devices have excellent diagnostic power.[23] A recent study using the GDx VCC scanning laser polarimetry instrument revealed a sensitivity of 89% and a specificity of 96%.[12] Unfortunately, these instruments are expensive and are not normally available outside a hospital setting. A need exists for guidelines for the use of these objective tests, so that those involved in screening for glaucoma can use the most effective, efficient and economical methods for detection.[24]

A new psychophysiological test of visual function based on frequency doubling technology (FDT) has been devised. It is now commercially available and relatively inexpensive (Zeiss Humphrey systems, Welch Allyn FDT). This technology has been extensively investigated in the past seven years and the results are extremely encouraging.[25–27] The frequency doubling contrast test targets the visual function of magnocellular ganglion cells with relatively large diameter nerve fibres, as these cells are susceptible to glaucomatous damage and appear to be preferentially lost in early glaucoma. The loss of a small number of these cells can have a significant effect on visual function. Patients find the test easy to undertake and the testing time is short. There is a good correlation between clinical examinations of the optic disc and nerve fibre layer and FDT results.[26] When screening for early glaucoma, FDT appears to be better than scanning laser polarimetry (GDx).[27] Receiver operating curves have shown 100% sensitivity for detecting advanced glaucomatous visual field loss, 96% sensitivity and specificity for detecting moderate loss, and 85% sensitivity with 90% specificity for early loss.[25] Despite its promise, FDT should not be used as the sole test for glaucoma screening, particularly in developing countries.[28] A number of studies have shown that the best sensitivity and specificity is achieved by using a combination of tests that include FDT as one of the options.[27,29] Ideally, the test should be undertaken every two years in individuals over the age of 60 years and every year in individuals over the age of 50 years with a family history of glaucoma.

In the UK, the government envisages a significant proportion of clinical glaucoma management being transferred from hospital to primary care in the next few years.[30] Central to the new system will be the development of a cadre of specialist optometrists who, it is proposed, will assume much of the work of screening and initial management of referrals for suspected glaucoma currently carried out by ophthalmologists. Screening for the disease should be aimed at those at greatest risk: all individuals over the age of 60 years, those with a family history of glaucoma and individuals of African/Afro-Caribbean racial background. Breaking down barriers to access, targeted screening and a campaign to inform people about the need for regular eye examinations are as important as using sensitive technology to diagnose this condition at an early stage.[31] Because current diagnostic tools still have inadequate sensitivity and specificity when used alone, the key to the diagnosis of glaucoma is to undertake a careful examination and to use more than one parameter to reach a conclusion.[29]

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