

THEORY AND METHODS

Primary open angle glaucoma. The need for a consensus case definition

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Primary open angle glaucoma is an important cause of visual impairment and blindness in the United Kingdom. This paper gives a brief overview of the condition and its management. It presents evidence of the continued absence of a consensus case definition for this condition. This has resulted in considerable uncertainty about what is diagnosed and treated as primary open angle glaucoma. The important negative effects of this situation are outlined. These include the impact on the person wrongly diagnosed with the condition, the uncertainties both for commissioning and provision of clinical healthcare services, and the lack of a firm basis for research into the condition. It is argued that there is an urgent need to resolve this problem to improve the health of the population.

It was while carrying out a study to establish the local prevalence of primary open angle glaucoma (POAG)¹ that the authors encountered the subject of the case definition for this condition.

THE CONDITION

The development of epidemiological research in this area of ophthalmology over the past 20 years has led to greater understanding of the condition.

Glaucoma is generally defined as "a progressive optic neuropathy involving characteristic structural damage to the optic nerve and characteristic visual field defects".² Glaucoma can be classified into primary, secondary, and developmental glaucomas. Primary glaucomas are those in which there is no associated ocular disorder or associated diseases. POAG is differentiated from primary angle closure glaucoma by the presence in POAG of a normal (open) anterior chamber angle.

POAG is the commonest type of glaucoma in the United Kingdom. No recent general population survey data are available from the United Kingdom to estimate the proportion of glaucoma cases that is attributable to POAG. However, a population survey from Ireland showed that about 80% of definite cases of glaucoma identified was attributable to POAG.³

There is an estimated prevalence for the age group 40–89 years in the white population of the United Kingdom of 1.2%.⁴ One author estimates that there are nearly 300 000 people with POAG in England and Wales.⁴ From the results of large population surveys it is predicted that about half

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of this group are undiagnosed.^{3 5–9} As a cause of blindness certification, glaucoma is the second most common cause at 11.7% of all certifications for 1990–1991 in England and Wales.¹⁰

POAG usually affects both eyes and has no noticeable symptoms in most patients until the later stages of the disease, when patients lose their central vision. The blindness caused by glaucoma is irreversible.

There is uncertainty about the aetiology of POAG. Risk factors that have been identified for POAG include:

- 1 Age: older age groups affected
- 2 Family history
- 3 Race: African origin
- 4 Raised intraocular pressure
- 5 Myopia

The evidence for sex as a risk factor is inconsistent. Diabetes and hypertension have been proposed as risk factors but the evidence is contradictory.¹¹ No environmental, infectious, or social risk factors have been identified.

There is debate about the exact diagnostic criteria for this condition among ophthalmologists. Diagnosis usually includes tonometry (measurement of the intraocular pressure), gonioscopy (measurement of the anterior chamber angle), examination of the optic disc and nerve fibre layer, and visual field testing.¹² In practice, ophthalmologists have to make subjective decisions about the quantitative and qualitative results from a particular patient including any changes over time and decide whether they fulfil the general criteria for POAG.

Optometrists carry out tests for the detection of POAG during routine eye assessments. It is thought that optometrists account for at least 75% of all referrals of POAG to hospital clinics.¹³

Raised intraocular pressure was considered a diagnostic feature but it has now been shown to be only a risk factor, with 25%–50% of POAG cases having normal intraocular pressure.¹² These cases are classified as normal tension glaucoma (NTG). NTG is considered to be within the diagnostic group POAG. An association has been identified between NTG and evidence of vascular spasm, such as Raynaud's Syndrome or migraine.¹¹

Raised intraocular pressure remains a strong risk factor and it has been shown that the higher the intraocular pressure at presentation, the greater the risk of developing POAG.^{14 15} However,

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Abbreviations: POAG, primary open angle glaucoma; NTG, normal tension glaucoma

Table 1 Summary of general diagnostic criteria

Condition	Diagnostic criteria
Primary open angle glaucoma (POAG)	Open anterior chamber angle, glaucomatous visual field and/or optic disc defects.
Normal tension glaucoma (NTG)	Open anterior chamber angle, glaucomatous visual field and/or optic disc defects and intraocular pressure less than 21 mm Hg.

Table 2 Summary of the features of the major population surveys

Surveys	Ferndale (UK) 1966 ²⁷	Framingham (USA) 1977 ²⁸	Baltimore (USA) 1991 ²⁹	Beaver Dam (USA) 1992 ³⁰	Roscommon (Eire) 1993 ³	Rotterdam (Netherlands) 1994 ⁴	Casteldaccia (Sicily) 1995 ⁶	Blue Mountains (Aust.) 1996 ⁷
Main diagnostic tests	F + D	F ³¹	F + D	F + D or IOP >21 mm Hg + F or D	F + D or IOP >30 mm Hg + F or D + V	F + D or IOP >21 mm Hg + F	F	F + D
Total population examined	4608	2352	2913	4926	2186	3062	1062	3654
Prevalence—all ages in survey (95% CI)	0.43%	1.15%	1.1% (0.75 to 1.55)	2.1%	1.88% (1.35 to 2.53)	1.1% (1.09 to 1.11)	1.2%	2.4%

F, glaucomatous visual field defect as defined by individual authors; D, optic disc defect as defined by individual authors; V, visual acuity less than or equal to 6/60; IOP, intraocular pressure.

there is no single level of intraocular pressure above which POAG can be said to always develop and there is no lower level below which POAG never develops.¹⁴ The most common level defined as the upper limit of normal is 21 mm Hg. This has been derived statistically, as two standard deviations from the population mean of 16 mm Hg (European population).¹¹ There is diurnal variation in intraocular pressure with a peak in the morning hours. Intraocular pressure also increases with age.¹⁶ Table 1 summarises the different diagnostic criteria for POAG.

There is no one test for POAG that is sufficiently specific and sensitive. For example, colour photography of the optic disc with an estimate of the vertical cup:disc ratio set at greater or equal to 0.5 resulted in a sensitivity of 39% and a specificity of 93% for an eventual clinical diagnosis. The combination of tonometry and colour photography of the optic disc resulted in a sensitivity of 61% and a specificity of 84%.¹⁷ If the prevalence of the condition is taken to be 1.2% for a white population aged 40–89 years, this results in a positive predictive value of 4.4% for both tests combined. This means that for every 1000 people aged 40–89 years assessed with the two tests combined, 158 people will test positive for the disease but not have the condition, five people will have the disease and test negative and seven people with the disease will test positive.

The overall assessment by the ophthalmologist including any test results remains the essential part of the diagnostic process. This assessment is not standardised and therefore there is likely to be considerable observer variability.

When a patient is diagnosed with POAG then he/she is advised to attend for regular follow up at the ophthalmology department. Follow up is usually life long. The aim of treatment for POAG is to prevent further loss of vision. Treatment includes both medical and surgical interventions.

Medical treatment is usually the first line of treatment and includes the use of several classes of topical agents. They all act by reducing intraocular pressure. Topical β blockers are the commonest drug treatment. Other agents include α agonists, prostaglandin analogues, and carbonic anhydrase inhibitors. A carbonic anhydrase inhibitor is also used for systemic treatment. The combination of two topical drug agents can be used if one agent is ineffective. General side effects of topical medical treatment include dryness and itching of eyes. Changes in iris colour, darkening of the eyelids, and growth of eyelashes can occur in those prescribed prostaglandin analogue treatment for greater than six months.¹⁸ Topical β blockers have been reported to have caused deaths through the exacerbation of chronic obstructive airway disease, bradycardia, or other cardiovascular side effects.¹⁹

Surgical treatment is considered in cases of unsuccessful intraocular pressure control. The most common procedure is trabeculectomy. This procedure produces a permanent channel for the drainage of aqueous humour from the anterior chamber to the sub-conjunctival space and thereby permits the reduction of intraocular pressure. Other procedures for POAG include argon laser trabeculoplasty and YAG laser iridotomy.²⁰

There is evidence to show that the treatment of intraocular pressure has a beneficial effect on the progress of POAG and increases the time period before the onset of blindness.^{15 18 21–24} It has also been found that lowering the intraocular pressure is not uniformly effective in preventing progression.²⁴

A study in the United States showed that the 20 year cumulative probability of blindness for POAG cases receiving treatment was 9% in both eyes and 26% in at least one eye.²²

The treatment for NTG is the same as outlined for POAG. There is evidence to show that despite a “normal” intraocular pressure, a reduction in the intraocular pressure in this group of patients is beneficial in terms of disease progression.²⁵

CASE DEFINITION

There is a lack of consistency in how POAG is defined. This is illustrated by one published literature review. It reviewed all articles on open angle glaucoma published in the years 1980, 1985, 1990, and 1995 in the journals *Ophthalmology*, *American Journal of Ophthalmology*, and *Archives of Ophthalmology*. One hundred and eighty two papers were identified. One of the findings of this review was that in the 1990s 34% of articles provided specific descriptions of the optic disc and 61% provided specific visual field criteria. However, many papers used qualitative findings such as “characteristic glaucomatous changes”. Nearly 20% of the papers from the 1990s still used intraocular pressure as the sole criterion for defining glaucoma.²⁶

Table 2 summarises the major population surveys establishing the prevalence of POAG and also it shows the lack of consistency in the criteria used to define a case of POAG.

One of the major surveys looked at the effect of applying different commonly used criteria for the diagnosis of open angle glaucoma. This resulted in prevalence figures ranging from 0.1% to 1.2% in the same population.³² When this range of prevalence estimates is applied to the population of the United Kingdom over the age of 55 years as for the study age group, it results in a range of prevalence for POAG of 15 560 to

186 713 persons.³³ This example confirms that the use of study specific case definitions makes the interpretation and comparison of research results very difficult.^{18, 34}

A definition and classification system for glaucoma including POAG for use in prevalence studies has recently been published.³⁵ This consensus case definition was the result of a large consultation exercise involving leading glaucoma specialists and ophthalmic epidemiologists. It remains to be seen whether this is accepted by the wider ophthalmology research community and is introduced into practice by ophthalmologists in the form of guidelines for the referral and treatment of POAG.

CONCLUSION

POAG is an important cause of disability and handicap. We believe that the lack of a consensus case definition for POAG is a serious public health problem for the following reasons.

The absence of an agreed detailed case definition for POAG that can be applied in clinical practice results in considerable uncertainty about the diagnosis of this condition. This means that there will be people who are diagnosed as having this incurable condition and it will be recommended that they have lifelong treatment and hospital follow up when they do not have the condition. This may have a negative impact on the health of the person in terms of mental health, worrying about the possible loss of vision and perhaps blindness, and the possible physical side effects of treatment. The cost to the person of having to attend ophthalmology outpatients on a regular basis for the rest of their life could also be considerable. It is unknown what proportion of cases are false positives. We suspect that the proportion could be large based on the positive predictive value of some of the tests used in the diagnosis of POAG.

The impact on healthcare services is likely to be considerable. The large number of people attending ophthalmology outpatients for regular review is a great demand on general ophthalmology services in the NHS. The uncertainty about whether this is an effective use of limited resources should be a cause of concern. This uncertainty would be magnified further if the cases of POAG presently unknown to healthcare services, possibly as many again as those who have been diagnosed, were identified. There has been little discussion or investigation of this situation in the NHS.

The absence of a consensus case definition is a fundamental weakness of research into POAG. It prevents the accurate estimation of the burden of illness in a population, the use of generalisable results and the accumulation of valid information about the condition, and the effectiveness of treatment.

We hope that by bringing this serious problem to the attention of public health specialists, we will encourage urgent further work in this area in partnership with ophthalmologists and optometrists. In particular further investigations into the size and nature of the healthcare impacts of the diagnostic uncertainty for POAG and in the development and implementation of a consensus case definition in research and general ophthalmic practice.

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