The Relationship between Glaucoma and Myopia

The Blue Mountains Eye Study

Paul Mitchell, MD, FRCOphth, Fleur Hourihan, BSc, MPH, Jen Sandbach, MB, FRACO, Jie Jin Wang, MB, MMed (ClinEpi)

Objective: To quantify the relationship between myopia and open-angle glaucoma, ocular hypertension (OH), and intraocular pressure (IOP) in a representative older population.

Design: Cross-sectional population-based study of 3654 Australians 49 to 97 years of age.

Methods: Subjects with any myopia (≥-1.0 diopter [D]) were identified by a standardized subjective refraction and categorized into low myopia (≥-1.0 D to < -3.0 D) or moderate-to-high myopia (≥-3.0 D). Glaucoma was diagnosed from characteristic visual field loss, combined with optic disc cupping and rim thinning, without reference to IOP. Ocular hypertension was diagnosed when applanation IOP was greater than 21 mmHg in either eye in the absence of glaucomatous visual field and optic disc changes.

Main Outcome Measure: General estimating equation models were used to assess associations between eyes with myopia and either glaucoma or OH.

Results: Glaucoma was present in 4.2% of eyes with low myopia and 4.4% of eyes with moderate-to-high myopia compared to 1.5% of eyes without myopia. The relationship between glaucoma and myopia was maintained after adjusting for known glaucoma risk factors, odds ratio (OR) of 2.3, and 95% confidence intervals (CI) of 1.3 to 4.1 for low myopia. It was stronger for eyes with moderate-to-high myopia (OR, 3.3; CI, 1.7–6.4). Only a borderline relationship was found with OH, OR of 1.8 (CI, 1.2–2.9) for low myopia, and OR of 0.9 (CI, 0.4–2.0) for moderate-to-high myopia. Mean IOP was approximately 0.5 mmHg higher in myopic eyes compared to nonmyopic eyes.

Conclusions: This study has confirmed a strong relationship between myopia and glaucoma. Myopic subjects had a twofold to threefold increased risk of glaucoma compared with that of nonmyopic subjects. The risk was independent of other glaucoma risk factors and IOP.

An association between myopia and primary open-angle glaucoma has been recognized for decades and documented in numerous case series and in most, but not all, case–control studies. Other reports have highlighted the high frequency of myopia in young adults presenting with open-angle glaucoma. Some studies have found the relationship only in patients with high myopia. Myopia has also been found to have an influence on intraocular pressure (IOP). In a large case–control study, myopic refractive error was found to be strongly associated with ocular hypertension (OH). An Israeli study of 2403 subjects documented a significant relationship between myopia and increasing IOP, particularly in persons of North African or Asian origin. Other studies have reported higher applanation pressures in myopic subjects, including children, or in subjects with increased axial length. However, no relationship with IOP was found in a United Kingdom study or in myopic anisometropia, whereas one study reported an association between myopia and low-tension glaucoma. Selection bias could account for some of the reported association between glaucoma and myopia in case series and case–control studies, as myopic subjects are likely to seek ophthalmic care more frequently and glaucoma is a relatively underdiagnosed condition in the community. This bias may be lessened in population studies, in which the diagnosis of disease is based on a masked assessment of diagnostic characteristics.

To date, however, no large population-based studies have examined the role and relative strength of myopia as a risk factor for glaucoma. The “use of eyeglasses for reading” was assessed in the Barbados Eye Study, but the relationship between open-angle glaucoma and myopia was not assessed. We therefore aimed to investigate associations between myopia and open-angle glaucoma, OH, and IOP in a well-defined older population, in which both re-
fractive error\textsuperscript{26} and glaucoma prevalence\textsuperscript{24} were assessed and other glaucoma risk factor data were collected.

Methods

The Blue Mountains Eye Study is a population-based survey of age-related eye diseases in residents of an urban population in the Blue Mountains region, west of Sydney, Australia. Survey methods were described previously.\textsuperscript{24,26,27} All permanent noninstitutionalized residents 49 years of age or older were identified in a door-to-door census. Of 4433 eligible residents, 3654 (82.4\%) were examined from 1992 to 1994. After excluding persons who died or left the area during the survey and could not be examined, the response rate was 87.9\%. The study was approved by the Western Sydney Area Human Ethics Committee, and written, informed consent was obtained from all participants.

An interviewer-administered questionnaire included demographic characteristics, medication use, visual function, and medical history including diabetes, hypertension, and migraine. Subjects underwent a detailed eye examination, which included applanation tonometry, Humphrey automated perimeter, stereoscopic optic disc photography, slit-lamp examination, and subjective refraction.\textsuperscript{24,26} The Humphrey 76-point suprathreshold visual field test (Allergan Humphrey, San Leandro, CA) was performed in 3241 (89\%) participants, of whom 352 persons (9.6\%) were classified as glaucoma suspects, either from defects on the 76-point test or because optic disc signs suggested glaucoma. All were asked to return for Humphrey full-threshold 30–2 Visual Fields, of whom 336 (9.2\% of the population) completed the test. Stereo optic disc photographs of both eyes (30\°) were performed in 98\% of subjects.

Open-angle glaucoma (here termed glaucoma) was diagnosed by the presence of matching optic disc cupping with rim thinning (cup–disc ratio $\geq$ 0.7 or cup–disc asymmetry $\geq$ 0.3) and characteristic visual field loss on automated perimeter, after excluding rubeotic, secondary, or angle-closure glaucoma with gonioscopy. The diagnosis of glaucoma was made without reference to IOP.\textsuperscript{24} Characteristic glaucomatous field loss was defined as an abnormal Humphrey 30–2 Glaucoma Hemifield Test with one or more of the following defects not explained by ocular or neurologic causes: (1) arcuate or paracentral scotoma, at least four contiguous points on the pattern deviation plot depressed at $P < 0.5\%$ level; (2) nasal step at least two horizontal points in width (10\°) on the pattern deviation plot depressed at $P < 0.5\%$ level; or (3) advanced glaucomatous field loss. The OH was defined as an IOP greater than 21 mmHg in either eye, but without diagnostic visual field and optic disc signs, after excluding persons with open-angle or other forms of glaucoma.

A Humphrey autorefractor (Model 530) was used to obtain an objective refraction. Subjective refraction was then performed using the Beaver Dam Eye Study modification of the Early Treatment Diabetic Retinopathy Study protocol with a logarithm of the minimum angle of resolution (LogMAR) chart.\textsuperscript{26} Spherical equivalent refractive error was calculated as (sphere $+$ cylinder/2) measured in diopters (D). Myopia was defined when myopic spherical equivalent of the eye (SEQ) was -1.0 D or greater, hyperopia if SEQ was greater than +1.0 D, and emmetropia when SEQ was in the range from -0.99 to +1.0 D. Low myopia was defined in eyes with a myopic SEQ of -1.0 D or greater to less than -3.0 D. Moderate-to-high myopia was defined in eyes with a myopic SEQ of -3.0 D or greater. For analyses involving persons, SEQ was calculated as the mean value of the two eyes.

Diabetes was diagnosed from history or an elevated fasting blood glucose of 7.8 mmol/l or greater (140 mg %).\textsuperscript{27} Hypertension was defined as a history of hypertension with current use of antihypertensive medication or elevated blood pressure (systolic $\geq$ 160 mmHg or diastolic $\geq$ 95 mmHg). The questionnaire assessed family history of glaucoma, history of typical migraine,\textsuperscript{28} and history of inhaled or systemic steroid use.\textsuperscript{29} Pseudoexfoliation was assessed from the slit-lamp examination.

Statistical Analysis System (SAS; SAS Institute, Cary, NC) was used for statistical analyses, including Mantel–Haenszel chi-square test for trend and generalized linear models. Associations between glaucoma and myopia were assessed for individual eyes, because of the asymmetry of refractive error, glaucomatous damage, or IOP in some subjects. The Liang and Zeger general estimating equation method,\textsuperscript{30} which takes into account the correlation between eyes, was used to assess relationships between these variables. Analyses by subject were also performed using logistic regression. Age and IOP were used as continuous variables. Odds ratios (OR) and 95\% confidence intervals (CI) are presented.

Results

Definite or probable glaucoma was diagnosed in 108 persons (3\%); the prevalence increased exponentially with age.\textsuperscript{24} Among persons diagnosed with glaucoma, 72 (66.7\%) had typical glaucomatous field loss in the right eye and 88 (81.5\%) had field loss in the left eye (total, 160 eyes). After nonphakic eyes were excluded, a total of 126 eyes had diagnostic glaucomatous field loss and could be used for analysis. The OH was found in 135 participants, a prevalence of 3.7\% (CI, 3.1–4.3) but with no significant age-related increase in prevalence.\textsuperscript{24} Among persons with OH, 124 (91.9\%) had elevated IOP in the right eye and 109 (80.7\%) had elevated IOP in the left eye (total, 233 eyes). After excluding nonphakic eyes, a total of 211 eyes had OH and were available for analysis.

After nonphakic eyes were excluded, 866 eyes (12.5\%) with any myopia (SEQ $\geq$ -1.0 D) were available for analysis (Table 1). Low myopia ($\geq$ -1.0 D to $< -3.0$ D) was present in 524 eyes (7.6\%), and moderate-to-high myopia (SEQ $\geq$ -3.00 D) was found in 342 eyes (4.9\%). A higher age-adjusted prevalence of myopia was found in women than in men (OR, 1.4; CI, 1.0–2.0), and the prevalence decreased significantly with increasing age ($0_2$ trend $= 10.73, 1$ degree of freedom, $P < 0.001$).

A strong association was found between low myopia and glaucoma, as shown in Table 2. Glaucomatous damage to the optic disc and visual field was more than twice as frequent in eyes with low myopia (4.2\%) than in eyes without myopia (1.5\%) (OR, 2.1; CI, 1.2–3.8) after adjusting for age and gender. This relationship remained after simultaneously adjusting for other known glaucoma risk factors as well (e.g., glaucoma family history, diabetes, hypertension, history of typical migraine, steroid use, and presence of pseudoexfoliation) (OR, 2.3; CI, 1.3–4.1). It was also consistently present across the age groups examined, apart from the youngest age group, which had inadequate statistical power because of small numbers.

A stronger association was found between moderate-to-high myopia and glaucoma, also shown in Table 2. Glaucoma was almost threefold as frequent in eyes with moderate-to-high myopia (4.4\%) than in eyes without myopia (1.5\%) (OR, 3.3; CI, 1.7–6.4) after adjusting for other known glaucoma risk factors. Again, it was consistently present across the age groups.

A weaker association was found between low myopia and OH, as shown in Table 3. The OH was more frequent in eyes with low myopia (4.8\%) than in eyes without myopia (2.9\%) (OR, 1.7; CI, 1.1–2.7) after adjusting for age and gender. This relationship remained after simultaneously adjusting for other known glaucoma risk factors as well (OR, 1.8; CI, 1.2–2.9). The magnitude of this
relationship, however, varied across the age groups examined, ranging from OR 0.5 to 3.9. No association was found between moderate-to-high myopia and OH. Similar prevalence rates for OH were found in eyes with moderate-to-high myopia (3.5%) to eyes without myopia (2.9%) (OR, 0.9; CI, 0.4–2.0) after adjusting for other known glaucoma risk factors.

Associations between myopia and glaucoma or OH were also assessed in subjects in the multivariate model using mean refractive error of the two eyes and the presence of glaucomatous damage or elevated IOP in either eye. For glaucoma, a similar magnitude of association was found for subjects with any myopia (SEQ ≥ -1.0 D) (OR, 2.4; CI, 1.5–4.0). Age-specific prevalence rates for glaucoma in subjects with and without myopia are compared with overall glaucoma prevalence rates, as shown in Figure 1. Myopia was associated with a substantially increased risk of glaucoma at all except the youngest age group.

Table 2. Associations between Glaucoma and Low Myopia (spherical equivalent ≥ -1.0 to < -3.0 diopters) or Moderate to High Myopia (spherical equivalent ≥ -3.0 diopters), Stratified by Age and Adjusted for Confounders

<table>
<thead>
<tr>
<th>Age Group (yrs)</th>
<th>Glaucoma in Eyes with Low Myopia (No. [%])</th>
<th>Glaucoma in Eyes without Myopia (No. [%])</th>
<th>Sex-adjusted OR (95% CI)</th>
<th>Multivariate-adjusted OR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;60</td>
<td>1 (0.3)</td>
<td>4 (0.2)</td>
<td>1.7 (0.2–13.9)</td>
<td>Insufficient data</td>
</tr>
<tr>
<td>60–69</td>
<td>5 (4.0)</td>
<td>16 (0.7)</td>
<td>2.5 (0.8–7.5)</td>
<td>2.6 (0.9–7.7)</td>
</tr>
<tr>
<td>70–79</td>
<td>7 (5.9)</td>
<td>41 (2.6)</td>
<td>2.1 (0.8–5.9)</td>
<td>2.1 (0.8–5.7)</td>
</tr>
<tr>
<td>80+</td>
<td>9 (16.7)</td>
<td>28 (5.7)</td>
<td>2.4 (1.0–5.4)</td>
<td>2.6 (1.1–6.2)</td>
</tr>
<tr>
<td>All ages</td>
<td>22 (4.2)</td>
<td>89 (1.5)</td>
<td>2.1 (1.2–3.8)†</td>
<td>2.3 (1.3–4.1)†</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Glaucoma in Eyes with Moderate to High Myopia (No. [%])</th>
<th>Glaucoma in Eyes without Myopia (No. [%])</th>
<th>Sex-adjusted OR (95% CI)</th>
<th>Multivariate-adjusted OR (95% CI)*</th>
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<td>2.7 (1.0–7.4)</td>
</tr>
<tr>
<td>80+</td>
<td>6 (19.4)</td>
<td>28 (5.7)</td>
<td>4.1 (1.4–12.1)</td>
</tr>
<tr>
<td>All ages</td>
<td>15 (4.4)</td>
<td>89 (1.5)</td>
<td>3.7 (2.0–6.9)†</td>
</tr>
</tbody>
</table>

OR = odds ratio; CI = confidence interval.

* Adjusted for sex, family history of glaucoma, diabetes, hypertension, typical migraine history, steroid use, and presence of pseudoexfoliation.

† Adjusted also for age.
This population-based study of an Australian white community has found a strong relationship between open-angle glaucoma and myopia, after taking into account the effects of other known glaucoma risk factors. This association was present for eyes with low myopia (OR, 2.3) and was stronger (OR, 3.3) for eyes with moderate-to-high myopia, suggesting a dose response. The consistency of these findings provides support for the hypothesis of a true relationship between the two conditions.

It may be deceptive to describe people with normal discs and fields but elevated IOP by a different term (OH), as IOP elevation may have been present for too short a period and the visual field test may be too insensitive to detect early damage. The likelihood that some people with OH have an early stage of glaucoma is consistent with our finding of a relatively weak association between OH and myopia, which was only found with low myopia. This weak association probably is reflected by the slightly higher (half millimeter) IOPs of myopes.

Although many clinic-based and case–control studies have suggested a relationship between glaucoma and myopia, no previous population-based studies have examined the association in detail while taking into account the effects of other known glaucoma risk factors. Our findings are relevant, as the population-based design is likely to have minimized the possibility of selection bias affecting the results. Confirmation that myopia is a frequent risk factor for glaucoma (one in four glaucoma cases in this age group) should help to identify this group, whose participants need earlier and regular ophthalmic screening and closer follow-up.

Could our findings of a strong association between glaucoma and myopia be confounded by measurement error or misclassification of either the glaucoma or myopia status of persons in this older population? Such misclassification could bias the findings and lead to an overestimation of any relationship between the two conditions.

The overall glaucoma prevalence reported from our study (3.0%) is higher than in some other recent population-based prevalence studies, including Beaver Dam and Rotterdam. However, these two studies examined either a younger age range or had a lower proportion of subjects in the oldest age group. Given the exponential increase in glaucoma prevalence with age found in our study, such age differences could have a marked effect on the overall prevalence.

More likely sources of misclassification are the documented changes in the appearance of the optic disc in myopia. These could either result in the overclassification

![Graph](image-url)
of nonglaucomatous field defects resulting from tilted discs as glaucomatous or underclassification of glaucoma because of the difficulties in grading the cup–disc ratio and neuroretinal rim in some myopic eyes. Tilted discs may cause visual field defects, but these are predominantly temporal and often cross the vertical meridian. Patients with myopia may also develop enlarged blind spots, supertemporal defects, and irregular defects from myopic retinopathy. Great care was taken in the adjudication of field defects to include only those defects that were typically glaucomatous. Patients with myopia also tend to have larger optic discs and cups. The stereo optic disc photographs from all myopic eyes classified as having glaucomatous field defects were also carefully reviewed. Disc cupping, which matched the field defects, was confirmed in these glaucoma cases, although rim thinning was occasionally more difficult to evaluate, because of the flatter nature of some myopic discs.

Care was taken in the assessment of myopia to include only phakic eyes, as cataract surgery would affect measurement of the underlying refractive state. Although the myopia prevalence rates in this study are slightly lower than in comparable United States studies, these differences may be due in part to small differences in myopia definition.

The 0.45-mmHg IOP difference found in our study between myopic and emmetropic eyes is slightly lower than in some previous reports, which have reported differences ranging from 0.75 to more than 1.0 mmHg. We were also unable to confirm a trend with increasing levels of myopia, which has been demonstrated previously. The small difference found between myopic and nonmyopic eyes, although statistically significant, is unlikely to be important clinically.

A number of mechanisms have been postulated to explain the link found between glaucoma and myopia. The optic nerve head in myopic eyes may be structurally more susceptible to glaucomatous damage from elevated or normal IOPs than in nonmyopic eyes. Quigley has proposed that shearing forces exerted by scleral tension across the lamina cribrosa may be important in the pathogenesis of glaucomatous damage. Cahane and Bartov calculated that myopic eyes have higher scleral tension across the lamina than in eyes with shorter axial length, even when IOP is the same, with the difference even more marked in eyes with thinner sclera. Similar connective tissue changes may also occur in glaucoma and myopia.

Both glaucoma and myopia have a strong familial basis and may share a common genetic link. An early report indicated that people with high myopia are more likely to be steroid responders than those in the general community. Recently, the gene coding for a trabecular meshwork-induced glucocorticoid response protein in the GLC1A locus on chromosome 1q21-q31 was identified and found in 3.9% of a glaucoma population compared to 0.3% of a general population. It is possible that this and other glaucoma genes may be represented more frequently in persons with myopia.

In summary, these data from the Blue Mountains Eye Study have confirmed the strong relationship between glaucoma and myopia in an older white population sample. Subjects with myopia had a twofold to threefold increased risk of glaucoma compared with that of nonmyopic subjects. This risk was independent of other glaucoma risk factors and IOP. Myopic eyes had slightly higher IOPs than emmetropic or hyperopic eyes, and we found only a borderline association between myopia and OH.

### References


