

Presence of an Optic Disc Notch and Glaucoma

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Purpose: To assess the prevalence and associations of a notch in the optic disc neural rim.

Methods: Stereo-photographs from the Blue Mountains Eye Study were graded for the presence of a notch (defined as focal reduction in neural rim width associated with a change in the curvature of the rim for no greater than 4 clock hours).

Results: A notch was found in at least 1 eye of 205 participants (5.7%), and was bilateral in 51 (1.4%). Notch prevalence increased with age from 2.48% in participants aged < 60 years, to 4.1% for ages 60 to 69 years, 7.98% for ages 70 to 79 years and 15.3% for ages 80 years or older. No sex differences were found. Notches were more frequent in eyes with myopia (odds ratio, OR, 1.98, 95% confidence interval, CI, 1.31-2.98) or beta-peripapillary atrophy (OR 2.20, CI 1.52-3.22). No associations were found with intraocular pressure, optic disc hemorrhage, or migraine history. After adjusting for other risk factors, a neural rim notch was strongly associated with glaucoma diagnosis (OR 21.2, CI 8.8-50.8). The sensitivity and specificity for glaucoma with visual field loss of finding a notch in either eye was 90.3% and 96.8%, respectively. The positive predictive value of a notch was 45.4% and negative predictive value 99.7%.

Conclusions: A notch in the neural rim is a relatively infrequent sign in normal eyes but is very frequent in glaucoma. This sign has both good sensitivity and a positive predictive value for glaucoma.

Key Words: optic disc, glaucoma, population-based study, diagnosis, Sydney, University, diagnosis, notch

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Structural abnormality of the optic disc neural rim is a particular feature of glaucoma that helps to distinguish it from other causes of optic neuropathy. Although quantitative optic nerve head imaging now plays an increasingly important role, the presence of structural abnormality on clinical examination when combined with a spatially corresponding defect in the visual field indicates the presence of glaucoma for most ophthalmologists.

Localized glaucomatous damage causes a focal loss of tissue from the neural rim of the optic disc. This tissue loss manifests clinically as a notch in the neural rim. It can be distinguished from more generalized thinning of the neural rim by its limited circumferential extent and the relatively large change in the curvature of the inner rim surface at the

edge of a notch. Notches can be subclassified by their radial extent as being wholly within the rim tissue or extending to the margin of the optic disc. Notches, particularly those extending to the disc margin have been regarded as pathognomonic of glaucoma for many years.^{1,2} However, this information has been derived primarily from clinical studies of patients with glaucoma³⁻¹⁰ with few papers making a comparison with normal optic discs.¹¹

Focal neural rim signs of glaucoma have not previously been reported in population-based samples, making it difficult to confirm their true value in glaucoma detection. The aims of this study were to describe the prevalence and associations of these signs in a well-defined population and assess their diagnostic value for glaucoma with manifest visual field loss.

METHODS

Participants were drawn from the Blue Mountains Eye Study, a population-based survey of eye disease and visual impairment among individuals aged 49 years or older, living the Blue Mountains region, west of Sydney, Australia. Detailed methodology has been described earlier.¹² Briefly, 3654 people participated in the Eye Study (82.4% of those eligible). Examination included ETDRS subjective refraction, Goldmann intraocular pressure (IOP) measurement, Zeiss 30° color stereo optic disc photography and Humphrey visual field testing. Ethics committee approval was provided by the Western Sydney Area Human Research Ethics Committee and written informed consent was obtained from each participant.

Open angle glaucoma (OAG) cases were diagnosed by consensus of an expert panel who examined a subset of Humphrey 30-2 visual fields printouts and stereo-photographs in a masked fashion, without reference to earlier history or treatment, or to other examination findings such as IOP. Glaucomatous visual field loss was defined as an abnormal Humphrey Glaucoma Hemifield Test (GHT) plus 1 or more of the following visual field defects which could not be explained on the basis of nonglaucomatous ocular, or neurological, causes: (1) arcuate or paracentral scotoma at least 4 contiguous points on pattern deviation plot depressed at $P < 0.5\%$ level; (2) a nasal scotoma at least 2 contiguous points horizontally on pattern deviation plot depressed at $P < 0.5\%$ level; (3) advanced glaucomatous field loss (hemispheric or severe generalized field loss, with residual temporal or central islands). No particular optic disc criteria were specified other than that the disc appearance should explain the visual field defect. The very small number of glaucoma cases due to angle-closure, rubeosis, or secondary glaucoma, other than pseudoexfoliation syndrome were excluded from this study.¹²

Stereo-optic disc photographs were subsequently independently graded and measured in a masked fashion by a trained (non-clinician) grader. Repeat testing on a

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subset of photographs showed excellent intraobserver agreement.¹³ The optic cup was determined by its contour, rather than its pallor. The outer margin of the cup was taken to be the point in which its wall met the plane of the retinal surface. The path of the vessels (particularly the smaller veins) frequently helped to define the contour of the neural rim. The definition of a notch was based on earlier clinical descriptions and studies.³⁻¹⁰ To maintain reliability in this large study, all optic disc features were strictly defined for purposes of grading. A notch within the neural rim was defined as a focal reduction in neural rim width associated with a change in the curvature of the rim for no greater than 4 clock hours, in which the outer border was neural rim tissue. A notch extending to the disc margin was defined as a notch within the rim, except that the outer border of at least part of the notch was the optic disc margin (the inner edge of the peripapillary scleral ring). These definitions were based on the contour of the inner edge of the neuroretinal rim and restricted to 4 clock hours to differentiate this sign from generalized neuroretinal rim loss. The basis for defining 2 separate notch types based on radial extent was that a notch that extends to the disc margin is easier to discern clinically and might also be expected to signify more advanced tissue loss. The location of the sign was not restricted. As a focal change in curvature was specified, the normal shallowness or thinning of the temporal neuroretinal rim did not confound its assessment. Other specific signs graded included the presence of optic disc hemorrhage and β -peripapillary atrophy (β -PPA).

For linear optic disc and cup measurements, the longest diameter in a range between clock hours 11 to 1 and 5 to 7 was measured using a template of small circles (Pickett small circles no.1203). These were used to calculate vertical cup-disc ratio. Optic disc, cup, and rim measurements were corrected for magnification using the spherical equivalent refraction for each eye.¹⁴ Queries and adjudications were addressed by 1 of the investigators (PH) who also verified the presence of all notches.

Low-pressure glaucoma (LPG) was defined as OAG with IOP in each eye ≤ 21 mm Hg, both at screening and on a subsequent visit. These participants were not receiving ocular hypotensive treatment and had no history of earlier glaucoma surgery. Other OAG cases were defined as high-pressure glaucoma (HPG). Ocular hypertension was defined as IOP > 21 mm Hg without evidence of glaucoma. Participants were classified as having presumed ocular hypertension (presumed OH) if they were not diagnosed as having glaucoma within the BMES criteria, had IOPs within the normal range but were taking ocular hypotensive agents. Pseudoexfoliation was diagnosed on clinical examination.

A multivariate model of factors associated with the presence of a notch was developed using logistic regression with SAS software V9 (SAS Institute, Cary NC). Odds ratios (OR) and 95% confidence intervals (CI) are presented.

RESULTS

Of the 3654 participants, 3582 (98%) had retinal photographs of at least 1 eye, 72 (2.0%) had no retinal photographs taken and 14 (0.4%) had photographs of 1 eye only. A notch within the neural rim or a notch extending to the disc margin was found in at least 1 eye of 205 participants (5.7%). This number comprised 127 right eyes and 129 left eyes. In 51 participants (1.4%), the sign was bilateral.

A total of 108 participants (3.0%) had open-angle glaucoma (OAG). OAG prevalence increased exponentially with age from 0.4% of persons aged < 60 years to 11.5% of persons aged 80 years or older and was higher in women than in men.¹² Ocular hypertension (OH) was found in 135 participants (3.7%). A further 55 participants without glaucoma (1.5%) were classified as having “presumed ocular hypertension” (presumed OH) as they were using glaucoma medications but did not have elevated IOP at the time of examination.¹² Gratable optic disc photos were available from 103 participants with OAG, 132 with OH, and 52 with presumed OH.

Associations

There was a strong age-related increase in the prevalence of a notch, from 2.5% in participants aged < 60 years, to 4.1% of participants 60 to 69 years, 8.0% of participants 70 to 79 years and 15.3% of those aged 80 years or older ($P < 0.001$ as a continuous variable in the multivariate model) (Fig. 1). No sex difference was found. Eyes with a notch had a larger vertical cup-disc ratio than those without. A notch was more frequent in eyes with myopia (OR 1.98, CI 1.31-2.98, multivariate model by subject adjusted for age, cup-disc ratio and β -PPA) or β -PPA (OR 2.20, CI 1.52-3.22 multivariate model by subject adjusted for age, cup-disc ratio and myopia). The relationship with myopia was present across all levels of myopic refraction. No associations were found between the presence of a notch and IOP, optic disc hemorrhage, or typical migraine.

Associations With Glaucoma

The presence of a notch was very strongly associated with OAG. OAG prevalence was greatly increased in participants with a notch in one or both eyes across all age groups (Fig. 2). The prevalence of a notch in eyes of participants with perimetric OAG in at least one eye was 86.1% compared with a prevalence of only 3.2% in eyes of participants without OAG. No difference was found between participants classified as having high versus low-pressure glaucoma. After adjusting for other glaucoma risk factors, a notch in either eye was associated with a 21-fold increase in the odds of a diagnosis of OAG (OR 21.2, CI 8.8-50.8 after adjusting for age, presence of IOP > 21 mm Hg in either eye, the largest vertical cup-disc ratio in either eye or an optic disc hemorrhage in either eye).

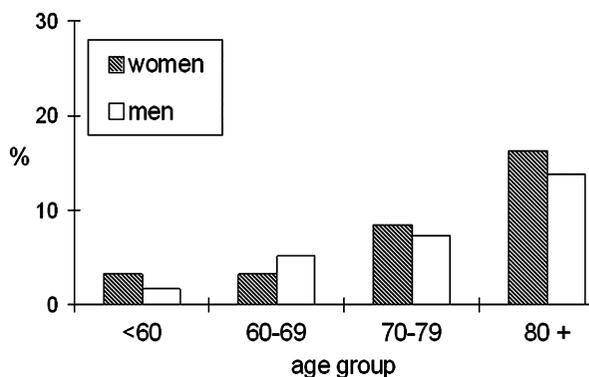


FIGURE 1. Prevalence of an optic disc rim notch among Blue Mountains Eye Study participants by age and sex.

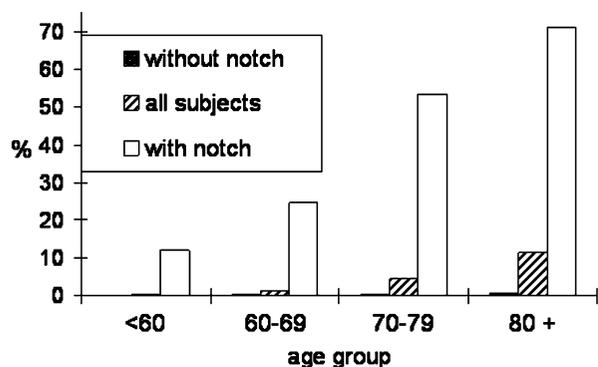


FIGURE 2. Prevalence of open-angle glaucoma among Blue Mountains Eye Study participants with or without a notch in the optic disc rim, in one or both eyes.

Notch Extending to the Disc Margin

A notch to the disc margin was the most frequent sign, occurring in either eye of 138 participants (3.8%); 85 (78.7%) of whom had OAG and 53 (1.5%) who did not (Table 1). Of the 53 eyes with a notch to the disc margin among participants without glaucoma, 22 (41.5%) had myopia (OR 3.8, CI 2.19-6.63).

Notches Within the Neural Rim

A notch within the neural rim (ie, the outer border of which was neural rim tissue) was found in either eye of 30 (27.7%) participants with OAG and 59 (1.7%) participants without OAG, or an overall prevalence of 2.4% (Table 1). Of those without OAG, 14 eyes with a notch (23.7%) had myopia (OR 1.6, CI 0.89-3.00, NS). The presence of a notch was not associated with ocular hypertension. But a notch within the neural rim was more frequent among participants with presumed ocular hypertension than in normal participants (OR 3.27, CI 1.17-9.11, adjusting for age and cup-disc ratio).

Notch Within the Rim and Disc Margin in the Same Eye

The combination of a notch within the neural rim and to the disc margin in the same eye was found in 22 participants (20.4%) with OAG, but not in any normal participants.

Predictive Value for Glaucomatous Visual Field Loss

The sensitivity of the presence of a notch in either eye for perimetric OAG was 90.3% and the specificity 96.8%.

TABLE 1. Prevalence of an Optic Disc Rim Notch in one or Both Eyes of Blue Mountains Eye Study Participants by Age Group and Notch Extent

Age Group	% of Participants (Number) With Open-angle Glaucoma		% of Participants (Number) Without Glaucoma	
	To Disc Margin	Within Rim	To Disc Margin	Within Rim
49-59 y	50 (2)	50 (2)	0.7 (7)	1.5 (15)
60-69 y	70 (12)	35 (17)	1.41 (18)	1.72 (22)
70-79 y	88 (38)	28 (12)	2.01 (18)	1.90 (17)
≥ 80 y	85 (33)	26 (10)	3.31 (10)	1.66 (5)
Total	83 (85)	30 (29)	1.52 (53)	1.7 (59)

The positive predictive value of a notch was 45.4% and the negative predictive value 99.7%. For comparison, the positive predictive values for a notch within the neural rim and a notch extending to the disc margin, were 33.7% and 61.1%, respectively. Using stricter diagnostic criteria by including participants in whom disc photos could not be taken or graded reduced the sensitivity to 86.1% but had no impact on the other diagnostic measures.

DISCUSSION

The loss of tissue from the neural rim of the optic disc characterizes glaucomatous optic neuropathy. However, this is often a very slow process, and observation of the consequent structural change can take many years.^{15,16} Recognition of characteristic signs of structural abnormality on or around the optic disc allows the clinician to make a provisional diagnosis of glaucoma without observing structural change. Reported signs include: an abnormally large ratio of the diameter of the cup to the disc (cup-disc ratio),¹⁷ focal notching,^{5,6} “bean-pot cupping” in which the edges of the rim seems undermined,⁶ visibility of lamina cribrosa pores⁵ and pit-like changes within the optic disc.¹⁸

Reports of the population prevalence of optic disc signs thought to be predictive of glaucoma are scarce. We have earlier examined the visibility of lamina cribrosa pores and found that this sign predicted cup size rather than glaucoma.¹⁹ Optic disc pits, while strongly related to glaucoma when at the lower or upper poles, are very infrequent.²⁰ Optic disc hemorrhages have the strongest association of any sign we have reported to date, with an OR of 9.0 (age-sex adjusted).²¹ Although the specificity (98.96%) of this sign was high, its sensitivity (12.9%) was found to be very low.

A notch in the neural rim has been reported to occur relatively frequently in glaucoma and to correspond well with reproducible visual field defects.⁵ This sign may also occur in the morphological group with the highest risk of a threat to fixation.⁹ Thus, the identification of glaucoma based on a notch may be more likely to diagnose a patient with clinically important visual field loss. We earlier reported that 50% of subjects with glaucoma who had manifest field loss remained undiagnosed in the community.¹² Participants from this group would have been more likely to be detected if the presence of a notch was used as a diagnostic indicator.

Our data suggest that the finding of a notch is indeed an important sign of glaucoma, although like many signs in medicine, one that does sometimes also occur in eyes without glaucomatous visual field loss. With the OR of 21 in this study, the presence of a notch was even more strongly associated with glaucoma than the presence of an optic disc hemorrhage.²¹ Like disc hemorrhages, a notch was numerically more frequent among normal participants than those with OAG. Our data suggest, however, that the presence of more than 1 notch, within the neural rim and extending to the disc margin in the same eye, may be pathognomic for OAG.

The relationship between presence of a notch and vertical cup-disc ratio is confounded by measurement bias. When a notch occurred between 5 to 7 or 11 to 1 o'clock, this was included in the measurement of cup size, thereby increasing the measured vertical cup-disc ratio. Nevertheless, the relationship with OAG remained strong, even after adjustment for the relationship with cup-disc ratio.

An association between the presence of a notch and β -PPA in glaucomatous eyes has been reported in clinic-based studies.^{22–24} The association between a notch and myopia has not been previously reported. The strength of these 2 associations was not merely due to a strong association in glaucomatous eyes, as the relationship remained after excluding the glaucoma cases. Although myopia and β -PPA are associated with each other, both remained significantly associated with a notch after adjusting for the other factor. This suggests there is a real relationship between a notch and both myopia and β -PPA, and not one due to confounding.

The association between presence of a notch in eyes with myopia or β -PPA, but without glaucoma, may be due to optic disc shape. Myopia is 6 times and β -PPA 4.5 times more frequent in eyes with tilted optic discs.²⁵ Non-glaucomatous tilted optic discs often also have an atypical distribution of neural rim tissue, in places appearing as a notch. As both myopia and β -PPA are also associated with glaucoma,^{24,26–31} the presence of these features cannot be used to exclude glaucoma in a disc with a notch.

Contrary to earlier reports,^{8,32,33} we did not find any association between the presence of a notch and migraine, younger age, low IOP or disc hemorrhage, either in our glaucoma or nonglaucoma subgroups. This is consistent with other data from the Blue Mountains Eye Study which suggest that population-based samples of subjects with glaucoma and low IOP may not be representative of those found in clinic-based NTG studies.^{20,34}

Optic disc assessment is particularly important in glaucoma screening, given the high-false positive rate of many visual field screening tests.^{12,35} The performance of optic disc assessment in glaucoma screening depends on the morphological parameters assessed. Clinical studies have mostly focused on cup-disc ratio, a clinically measurable surrogate for neural rim area. Vertical cup-disc ratio is linearly related to vertical disc diameter¹³ making it useful to adjust cut-off values for disc diameter in glaucoma assessment.^{36,37} This is perhaps part of the reason why cup-disc ratio does relatively poorly as a diagnostic criterion for glaucoma.³⁸ In contrast, the performance of a notch for predicting glaucoma was quite good, with relatively high sensitivity and specificity.

Limitations of this study include the relatively small number of glaucoma cases and its cross-sectional nature. It is likely that among the eyes with a notch but without visual field defects that satisfied our glaucoma definition, there were a number of early glaucoma cases misclassified as normal. Conversely, using the 30-2 program of the Humphrey perimeter to define glaucomatous visual loss may bias toward glaucomatous discs with focal polar damage.^{9,39} It is thus also likely that a number of perimetrically equivocal glaucoma cases existed in the population without a notch which, if included, would reduce the strength of the association with glaucoma and the performance of a notch as a diagnostic indicator. A caution in attempting to generalize the results of this study is that the accuracy and reliability of photographic grading is not necessarily transferable to other grading methods, such as slit lamp biomicroscopy.

The strength of the study is clearly its population-base, which has been well-defined in both place and time and is highly generalizable to the older caucasian population. The quality and completeness of data acquisition was very high. The glaucoma cases represent moderate to advanced disease as they all had visual loss on standard automated

perimetry. This provides the advantage that they are cases with sufficient visual morbidity with a commensurately high risk of further vision loss to make their detection in the community a priority. Another advantage was that a non-clinical technician performed the notch grading accurately and reliably. This suggests that the reliable recognition of a notch may be taught to non-ophthalmic eye-care professionals. This may be useful in the context of a glaucoma screening program.^{40,41}

In conclusion, this study provides the first estimate of the population-prevalence of a notch in the neural rim. It suggests that this sign is relatively frequent in moderate to advanced open angle glaucoma and is not restricted to rarer glaucoma subtypes. This suggests that the presence of a notch does well as an initial criterion for the glaucomatous diagnostic process. Lastly, the study highlights the importance of qualitative optic disc signs in the diagnosis of open-angle glaucoma.

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