THE PREDICTION OF GLAUCOMA FROM OCULAR BIOMETRIC DATA

Part 2
An Evaluation

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ABSTRACT

A method of glaucoma prediction from ocular biometric data has been described previously. A study was undertaken to evaluate the performance of tie existing multiple regression equations (prediction systems) on data obtained from an independent sample consisting of 22 angle-closure glaucoma, 29 open angle glaucoma and 44 normal subjects. This performance, found by comparing the predicted and actual classification for this sample, was such that between 2 and 7% false positives and 12 and 27% false negatives were found on the equations differentiating glaucoma from normal subjects; and between 14 and 27% false positives, with 10 to 14% false negatives on the equations classifying the glaucoma subjects as angle-closure or open angle. From these results the efficiency of glaucoma prediction from ocular biometric data would appear to be equal to that of the combined tonography and provocative tests, provocation with corticosteroids and visual field screening.

Certain dimensions of the eye show characteristic departures from the normal in patients with angle-closure and simple (open angle) glaucoma. [1,2] In an attempt to obtain a method for predicting the presence or absence of either form of glaucoma, Tomlinson and French (Part 1) derived two sets of multiple regression equations by the analysis of biometric data from the eyes of normal and glaucomatous subjects. One set, the 'Glaucoma Equations* were designed to discriminate between glaucomatous and normal subjects and another set, the 'Classification Equations,' to segregate the former into angle-closure and open angle categories. The discrimination in both sets of equations was achieved by the comparison of the score obtained for an individual with a cut-off (discriminant) score. The equations performed well on the sample from which they were derived, but in order to assess their true worth and validity it was necessary to apply them to data obtained from

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another sample.[3] The intention of this study was to assess the performance of these equations on such a sample and the data were obtained by one of us[4] independent of the previous data.

MATERIAL

Subjects:
The data analysed in this study were obtained from 22 patients with angle-closure glaucoma and 29 patients with open angle glaucoma who attended the University Unit of the Manchester Royal Eye Hospital. The other 44 subjects were 'normal' in that they had no demonstrable ocular pathology or family history of glaucoma. This latter group of subjects consisted of University staff, students and patients attending the refraction clinic.

METHOD

Ocular Biometry:
Ten ocular dimensions had been recorded for the sample considered, with their method of measurement these were:

(i) CR – vertical corneal radius, measured by Javal Shiotz Keratometry,

(ii) CD – horizontal corneal diameter from a colour photograph of the anterior surface of the eye,

(iii) CH – corneal height calculated from the formula,

$$\text{height} = \text{corneal radius} - \sqrt{(\text{cor. radius})^2 - \frac{(\text{cor. diameter})^2}{4}}$$

(iv) ACD – Axial depth of the anterior chamber measured with the type II attachment for the Haag-Streit slit lamp.

(v) LTH – Thickness of crystalline lens; (vi) VL – Length of vitreous body — from anterio-posterior axis trace of the eye obtained by A-Scan ultrasonography.

(vii) AL – Axial length of the eyeball – found from the addition of (iv), (v) and (vi).

(viii) RLP – Relative lens position calculated from the formula,

$$\frac{\text{ant. chamber dp.} + \tfrac{1}{2}\text{ lens thick.}}{\text{axial length}}$$

(ix) IOP – The highest intra-ocular pressure recorded at any time with the applanation tonometer attached to the Haag-Streit slit lamp,

(x) BSR — Best sphere refraction i.e. sphere + V4 power of the cylinder, obtained by objective and subjective refraction.

To these dimensions were added the age and sex of the subject, and the laterality of the eye measured.

A score was obtained for each subject, feeding the values of the above dimensions into five of the eight 'Glaucoma Equations' derived by Tomlinson and French (Part 1). It was not possible to employ all eight equations as corneal thickness, a factor in three equations, had not been recorded. The resultant score for each subject was compared with the discriminant score for the equation reported by Tomlinson and French. If the value was greater than, or equal to the discriminant score, the subject was classified as 'glaucomatous' and if it was below as 'normal.[1] Fifty-two subjects were classified as glaucomatous by one or more of the 'Glaucoma Equations.' The recorded dimensions of these subjects were then fed into three of the eight Classification Equations[1] derived previously; the absence of corneal thickness precluding the use of the other five. The scores for the glaucoma subjects were compared with the reported discriminant scores for each equation and the subjects categorized as angle-closure glaucoma if their scores were equal to or greater than this value and as open angle, if below.

RESULTS

The performance of the 'Glaucoma Equations' in segregation of glaucomatous from the normal • subjects in this sample can be seen in Table I. The incidence of false positives, i.e. the incorrect classification of normals as glaucomatous, was generally low varying between 2 and 7%. But the incidence of false negatives, i.e. the incorrect classification of glaucoma as normal, was higher, varying between 12 and 27%.

The subjects defined as glaucomatous by this first stage analysis were now grouped into angle-closure and open angle glaucoma categories by the appropriate 'Classification Equation;' the appropriate equation being the one which contained a similar number of variables to the original Glaucoma Equation. The results of this may be seen in Table II. The incidence

TABLE I: The table shows the effectiveness of the 'Glaucoma Equations' (Tomlinson and French) when applied to the present data with the discriminant score for glaucoma as indicated.

Regression Equation	Variables in Equation	Discriminant Score	False Positives Number (%)	False Negatives Number (%)
Ab	10 – CD,CH,ACD,LTH,VL, AL,RLP,IOP,BSR and SEX	⩾0.37	2 (5)	14 (27)
Ac	4 – CH,ACD,IOP and BSR	⩾0.39	2 (5)	14 (27)
Ad	2 – ACD and IOP	⩾0.41	1 (2)	6 (12)
Ae	1 – IOP	⩾0.30	3 (7)	10 (20)
Bc	3 – ACD, IOP and BSR	⩾0.42	2 (5)	7 (14)

False positive, is the classification of a normal subject incorrectly in the glaucoma category.
False negative, is the classification of a glaucoma incorrectly as a normal.

TABLE II: The table shows the effectiveness of the 'Classification Equations' (Tomlinson and French) when applied to the present data for subjects defined as glaucomatous by the 'Glaucoma Equations,* with the discriminant score for angle-closure glaucoma as indicated.

Regression Equations					
'Glaucoma' Equation	'Classification' Equation	Variables in Classification Equation	Discriminant Score for Classification Equation	False Posit. Number (%)	False Negat. Number (%)
Ac	Ac	5 – ACD,LTH,VL, AL and BSR	1.49	4 (16)	3 (10)
Ae	Ad	1 – ACD	1.54	3 (14)	4 (14)
Bc	Bc	1 – ACD,BSR	1.47	6 (27)	3 (10)

False positive, is the incorrect classification of an actual open angle glaucoma subject as an angle-closure case.
False negative, is the classification of an actual angle-closure glaucoma subject incorrectly as a case of open angle glaucoma.

TABLE III: The table shows the results of Tables I and II presented together by a more descriptive method than that of false positives and negatives.

		Angle-Closure Glaucoma Subjects (Actual tot. 22)			Open-Angle Glaucoma Subjects (Actual total 29)			Normals (Actual total 44)	
'Glaucoma' Equation applied to data	'Classification' Equation applied to data	Misclassified as Normal	Misclassified as Open-Angle	Correctly Classified	Misclassified as Normal	Misclassified as Angle-Closure	Correctly Classified	Misclassified as Glauco.	Correctly Classified
Ac	Ac	3	3	16	11	4	14	2	42
Ae	Ad	7	4	11	3	3	23	3	41
Bc	Bc	1	3	18	6	6	17	2	42

of false positives, i.e. the incorrect classification of open-angle as angle-closure glaucoma, varied between 14 and 27% and false negatives, i.e. the incorrect classification of angle-closure as open-angle glaucoma, between 10 and 14%.

As it is difficult to picture the actual performance of the two sets of equations represented in terms of false positives and negatives, Table III was compiled from the results of Tables I and II. Table III lists under descriptive headings the numbers of subjects glaucoma or normal, correctly and incorrectly classified. Although the results vary dependent on the equations applied to the data it may be said that for this sample the normal subjects are well defined; and of the glaucoma groups, which are not as well defined, the angle-closure subjects are better described than those with open angle glaucoma.

DISCUSSION

This evaluation of the method of prediction of glaucoma from ocular biometric data has presented some interesting results. As anticipated the performance of the 'Glaucoma' and 'Classification Equations[1] on the sample considered here is not as good overall, as it was on the data from which the equations were derived. A comparison of the performance of the 'Glaucoma Equations' shows that although the number of false positives reported for this sample is smaller than that for the original sample, the number of false negatives is considerably greater. The performance of the 'Classification Equations' for this sample compares unfavourably, in both the number of false positives and negatives, with the very good results obtained for the previous sample.

It would appear from a consideration of the results of the two studies that the performance of the two sets of equations on the second sample would have been improved if the discriminant scores were reduced for the Glaucoma Equations. As an illustration let us consider the application of 'Glaucoma' and 'Classification Equations' Ac to the data. The results obtained with discriminant scores of 0.39 for Glaucoma and 1.49 for angle-closure can be seen in Tables I to III. If the discriminant score for glaucoma was reduced to 0.25 the results from the Glaucoma Equation Ac would be 5% false positives and 12% false negatives. This would mean that with a discriminant score for angle-closure glaucoma unchanged at 1.49, the results of each groups would read: angle-closure glaucoma — misclassified as normal 1, misclassified as open angle 4, correctly classified 17; open angle glaucoma — misclassified as normal 5, misclassified as angle-closure glaucoma 4, correctly classified 20; normals — misclassified as glaucoma 2, correctly classified 42. The original choice of 0.39 as the discriminant score for glaucoma was made by Tomlinson and French (Part 1) to minimize the number of false negatives obtained *on the original data.* It is possible that even with no statistical differences between the two samples considered, i.e. they belong to the same general population, that the best discriminant score for each sample differs. This is a strong argument for the derivation of the discriminant score from as large a sample as possible, so that the best score can be derived for general application.

Where characteristic differences in ocular dimensions arise between normal and glaucomatous eyes, the values obtained for open angle glaucoma usually lie between those recorded for angle-closure glaucoma and the normal. This is reflected in the results of Table III for equations Ac and Be where the segregation of open angle glaucoma from the normal and angle closure glaucoma categories on the basis of ocular biometric data is seen to be the most difficult task faced by these systems of glaucoma prediction. It may be possible by the introduction of new variables such as volume of eyeball, and/or equatorial diameter of the lens to improve the efficiency of the predictions made by these regression equations, but for the-present the methods of measurement of such variables are difficult. The single variable equations, Ac for glaucoma and Ad, for classification which appear to favour the more accurate prediction of open angle glaucoma are deficient in the selection of angle closure glaucoma; mainly due to the failure to select on the Glaucoma Equation Ac the angle-closure glaucoma subject from the normal on the basis of the highest recorded intra-ocular pressure alone. Perhaps this is not surprising in a condition in which the intra-ocular pressure may be raised occasionally but not constantly to a high level. In considering the efficiency of any new system of prediction of glaucoma it is necessary to compare its performance with that of exist-

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