行政院國家科學委員會專題研究計劃成果報告

計畫名稱：	中國人原發性隅角開放性青光眼與近視及其它風險因素之長期研究
（中、英文）	Long-term study of myopia and other risk factors in primary open angle glaucoma among Chinese

計畫類別：個別型計畫

計畫編號：NSC 88-2314-B002-369

執行期間：87 年 8 月 1 日至 88 年 7 月 31 日

個別型計畫： 計畫主持人：洪伯廷

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處理方式：一年後可對外提供

執行單位：台灣大學醫學院眼科

中華民國 88 年 12 月 10 日

摘　　要

近視與原發性青光眼之關係，最近引起近視與青光眼兩組學者之廣泛興趣。因此，本研究試從其重要性、近視流行病學，以及近視特有之眼軸長度、網膜視神經變化等因素，觀察兩者之共同點，檢討其關係。

(1) 重要性：近年來的研究顯示，近視為原發性隅角開放性青光眼之危險因子，反之亦是。因此從研究青光眼之立場，澄清兩者之關係甚為重要。

(2) 流行病學上研究台灣學童之眼屈折，顯示近視近年來逐漸增加其盛行率以及近視之度數。兩者與近視發生之年齡有關。

(3) 初步眼軸長度之研究，顯示青光眼與近視眼之眼軸都較正常人為長，為兩者重要之共同點。

關鍵詞：原發性隅角開放性青光眼，近視，軸長，台大醫院

ABSTRACT

(1) Myopia as a possible risk factor of glaucoma was proposed from the observation of high prevalence of myopia among primary open angle glaucoma (POAG) and high prevalence of glaucoma among myopia. The evaluation of myopia as risk factor for POAG is therefore important as it may provide an alternative approach to study POAG.

(2) In order to understand and update the prevalence of myopia in Taiwan, a nationwide survey was performed in 1995. The prevalence of myopia in Taiwan increased year by year. The increase in severity and prevalence of high myopia may be due to earlier onset.

(3) In the preliminary study of axial length, the primary open angle glaucoma have higher rate of myopia and association of longer axial length than controls.

Key words: POAG, Myopia, Axial length, NTUH

Axial Length and Refractive Error in Primary Open Angle Glaucoma

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Supported in party by the National Science Council Executive Yuan, Republic of China.
NSC 88-2314-B-002-369

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Key words: myopia, axial length, primary open angle glaucoma, refractive error

Abstract

Purpose: To investigate the differences in axial length and refractive error between primary open angle glaucoma (POAG) patients and healthy subjects, and those between the younger and older population.

Methods: This was a prospective case-control study. Eighty POAG patients were enrolled from the Glaucoma Clinic of Ophthalmology Out-patient Department of the National Taiwan University Hospital from 1998 through 1999. Another eighty age and sex-matched healthy subjects were recruited from the Health Examination Department of the Hospital as the control group. Routine eye examination, A-scan ultrasonography, and cycloplegic refraction were performed on both eyes of each patient. The correlation between refractive error or axial length and primary open angle glaucoma was evaluated.

Results: All subjects were subdivided into the young-age group (< 40 years old) and old-age group (≥ 40 years old). The mean axial length was significantly longer in the POAG group than in the control group ($P < 0.01$, Student's t test). This difference was evident in both the young and the old-age groups. The mean cycloplegic spherical equivalent refractive error was significantly more myopic in the POAG group than in the control group ($P < 0.01$, Student's t test). This difference was also evident in both the young and the old-age groups. The prevalence rate of myopia was higher in the POAG subjects than healthy ones, especially that of sever myopia (≥ -6.0 D).

Conclusion: Our results suggest that POAG patients have a more myopic refractive status and a longer axial length than people without glaucoma. Thus it seems to be the "axial myopia" which contributes to the higher prevalence rate of myopia in POAG patients. Further study is important to show if the myopes are more suspectible to develop primary open angle glaucoma.

Introduction

The relationship between myopia and glaucoma is an important but still controversial issue worldwide today even though most of the reports indicated the close relationship between both of them in the past decades.(1) (2) (3) The prevalence of glaucoma was reported to be higher among the myopic eyes than in both hypermetropes and emmetropes.(1) An accelerated progression of visual field loss in myopic patients relative to that in emmetropic or hypermetropic patients was also showed in previous study.(4,5) Furthermore, the relative risk of open angle glaucoma was found to increase incrementally as the refractive error shifted from hypermetropia to myopia, becoming three times greater for myopes of more than -5.0 sphere diopters as compared with hypermetropes.(6) Thus myopia may be a risk factor and a poor prognostic factor for the development and progression of glaucoma.

The frequency of myopia has been increasing in association with high myopia rate in Taiwan for the past decades, especially in the younger population.(7) The same tendency also observed in Japan and other regions. A nationwide survey revealed that the prevalence of myopia among senior high school students was about 84%, and over 10% had myopia more than 6 D.(8) It has been reported that the association between myopia and intraocular pressure was stronger in persons born in Asia or Africa than those born in Europe or North America.(9) Thus, as a potential complication or an associated condition, the relationship of glaucoma and myopia is an issue of great concern in Taiwan as well as other parts of the worlds. Myopia can result from axial myopia, corneal myopia, lenticular myopia, or a combination of these components. In this study, we tried to investigate the relationship between myopia and glaucoma by analyzing the cycloplegic refraction and axial length in primary open angle glaucoma (POAG) patients as compared with age and sex matched control in healthy subjects. We also studied such association between the young-age and old-age population.

Methods

We enrolled eighty patients with the definite diagnosis of POAG (mean age 42.3 ± 15.5 yr, range 16-82) from the Glaucoma Clinic of Ophthalmology Outpatient Department of the National Taiwan University Hospital from 1998 through 1999. There were 45 men and 35 women. For the control group, 48 men and 32 women from the Health Examination Department of the Hospital were recruited (mean age 42.4 ± 15.3 yr, range 15-75), excluding those who had ocular diseases other than refractive errors. In both groups, those who had received any kind of ophthalmic surgery such as cataract surgery, glaucoma filtering surgery, or vitreoretinal surgery etc were excluded. The POAG and the healthy subjects were both age and sex matched.

After routine eye examinations, each subject underwent biometry by A-scan ultrasonography (Sonomed, A-1500, Lake Success, NY. USA). Tissue recognition of anatomic structures allowed automatic measurement of the tested variables, which was also confirmed by examiners with the check of interface spikes corresponding to anatomic structures. Three consecutive measurements of each feature were recorded when an acceptable A-scan pattern was observed, and the mean of the three recordings was used as the final value. Measurements were recorded in both eyes. Then we instilled one drop of 0.5% Tropicamide + 0.5% Phenylephrine HCl (Mydrin-P Ophthalmic solution) into both eyes of each subject every five minutes for three times. Cycloplegic refraction was measured thirty minutes later by autorefraction (Auto Kerato-refractometer, KR-7000, Topcon, USA). The mean of three consecutive measurements was used as the final value and the cycloplegic spherical equivalent refractive error was calculated.

Student's *t*-test and Chi-square test were used for statistical analysis and statistical significance was defined as a p value less than 0.05.

Results

All of the POAG patients and the healthy subjects were subdivided into a young-age group (< 40 years old) and a old-age group (≥ 40 years old) while undergoing statistical analysis. For the young-age group, the mean age in the POAG group was 28.85 ± 7.12 years old (range 15-38), and that in the control group was 29.08 ± 6.49 years old (range 16-39). For the old-age group, the mean age in the POAG group was 55.70 ± 8.47 years old (range 42-76), and that in the control group was 55.75 ± 8.53 years old (range 42-82). The POAG and the control group were sex and age matched (Table 1).

For the young-age subjects, the mean axial length was 25.84 ± 1.35 mm (range 23.75-28.59) of the right eye and 25.80 ± 1.37 mm (range 23.76-28.78) of the left eye in the POAG group, which was significantly longer than that in the control group: 24.81 ± 1.28 mm (range 22.10-27.47) and 24.81 ± 1.23 mm (range 22.44-27.55) respectively. The P value was 0.0008 and 0.001 respectively. The mean cycloplegic spherical equivalent refractive error was -5.19 ± 2.69 D (range 0.25 ~ -10.25) of the right eye and -5.19 ± 2.75 D (range 0 ~ -10.25) of the left eye in the POAG group, which was significantly more myopic than that in the control group: -3.61 ± 2.45 D (range 0.25 ~ -10.88) and -3.58 ± 2.28 D (range 0.25 ~ -10.88) respectively. The P value was 0.0082 and 0.006 respectively. The other two measurements of A-scan biometry, the anterior chamber depth and the lens thickness, showed no significant differences between the POAG and the control group (Table 2).

For the old-age subjects, the mean axial length was 24.42 ± 1.28 mm (range 22.10-27.60) of the right eye and 24.39 ± 1.30 mm (range 22.12-27.52) of the left eye in the POAG group, which was significantly longer than that in the control group: 23.30 ± 0.92 mm (range 21.87-25.71) and 23.27 ± 0.91 mm (range 21.84-26.03) respectively. The P value was 2.9E-05 and 3.5E-05 respectively. The mean cycloplegic spherical equivalent refractive error was -1.73 ± 2.85 D (range +2.00 ~ -9.13) of the right eye and -1.68 ± 2.78 D (range +1.00 ~ -9.75) of the left eye in the POAG group, which was significantly more myopic than that in the control group: +0.19 ± 1.47 D (range +2.75 ~ -5.25) and +0.11 ± 1.51 D (range +3.00 ~ -4.75) respectively. The P value was 0.0004 and 0.0007 respectively. The anterior chamber depth was significantly deeper for both eyes in the POAG group than that in the control group. However, the lens thickness showed no significant differences between the POAG and the control group (Table 3).

The distribution of axial lengths of the right eyes in the POAG and healthy subjects was illustrated on Fig 1. It demostrated that the axial length tended to be longer in the POAG eyes than in the healthy ones. There were 51% POAG eyes having their axial lengths longer than 25 mm, but only 23% healthy eyes having their axial length longer than this. The same tendency was well-demostrated on their left eyes. 48% of POAG eyes had an axial length longer than 25 mm, but only 24% of healthy eyes had such a long axial length (Fig 2).

Since most people considered an axial length longer than 26 mm to be pathological myopia and thus to have greater risk to develop glaucoma, the number of subjects who had an axial length longer than 26 mm was calculated. For the young-age subjects, there were more than 38% of POAG eyes having axial lengths longer than 26 mm, but less than 20% of healthy eyes having such long axial lengths (Table 4). The difference was significant by Chi-square test in both eyes. For the old-age subjects, there was only one in eighty healthy eyes having an axial length longer than 26 mm, but there were eleven (14%) in eighty POAG eyes having axial lengths longer than this. (Table 5)

The distribution of cycloplegic spherical equivalent refractive errors of the right eyes in the POAG and healthy subjects was illustrated on Fig 3. It demostrated that the refractive status tended to be more myopic in the POAG eyes than in the healthy ones. The same

tendency was well-demostrated on their left eyes (Fig 4).

Most people considered myopia more than -6.0 D to be high myopia or pathological myopia who had a greater risk to develop glaucoma, myopia between -2 to -6 D as moderate myopia, and that less than -2.0 D as mild myopia and emmetropia. The number of subjects with moderate to high myopia was calculated (Table 6). There were 85% of POAG eyes having moderate to high myopia, among which alomost half belonged to the high myopia group. There were only 65-75% of healthy eyes having moderate to high myopia. In addition, most of them were moderate myopia. (Table 7)

Discussion

The mean axial length was significantly longer and the mean cycloplegic spherical equivalent refractive status was significantly more myopic in the youn-age group than in the old-age ones. The results indicated that there were much more axial myopic eyes in the young-age subjects of our study. Although there might be a selection bias with the possibility that those young subjects who visited the hospital were in a great proportion because of refractive error-related blurred vision, this finding corresponded with the previous study showing that the frequency of myopia is increasing in school-aged children in Taiwan.(8)

The mean axial length was significantly longer and the mean cycloplegic spherical equivalent refractive status was significantly more myopic in the POAG patients than in the controls. This tendency was obvious in both the young and the old-age groups. Our study showed a positive correlation between axial length and POAG, and also between myopic refractive error and POAG. The prevalence rate of moderate to severe myopia was much higher in POAG eyes than in the controls, especially high myopia more than –6.0 D. It seemed to be the "axial myopia" which contributed to the refractive errors.

Our previous study (12) demostrated that glaucoma patients had a longer axial length than people without glaucoma, and the visual field defects were more pronounced in patients with long axial length than in those with short axial length. However, another case-controlled study found no relationship between refraction error and intraocular pressure, with relative risk = 1 (6). We did measure the intraocular pressure (IOP) of each subject in our study. The reason of not including the IOP data for statistical analysis was that most of the POAG patients had received medication for IOP control for a period of time before measuring A-scan biometry and autorefraction. Thus it would be unappropriate either to correlate the IOP under medication with refractive errors or axial lengths, or to elucidate any conclusion from this to state the relationship between these parameters.

In conclusion, the mean axial length is significantly more longer and the mean cycloplegic refraction was significantly more myopic in the POAG eyes than in the controls in either the young-age or the old-age groups. The prevalence rate of myopia, especially that of high myopia, was higher in the POAG eyes, and it might be due to the "axial myopia". We must pay more attention to those moderate to high myopic patients, regarding to the positive correlation between myopia and glaucoma. Further population-based cohort study is important to show if the myopes are more susceptible to develop POAG.

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Table 1. the age and sex distribution in POAG patients and healthy subjects

	man (persons)	woman (persons)	total (persons)
Young-age group (< 40 years old)			
POAG subjects (persons)	22	18	40
Healthy subjects (persons)	25	15	40
Old-age group (> 40 years old)			
POAG subjects (persons)	23	17	40
Healthy subjects (persons)	23	17	40

Table 2. A-scan ultrasonographic biometry in the young-age group

	Axial length (mm)	Anterior chamber depth (mm)	Lens thickness (mm)	Spherical equivalent refractive error (diopter)
Right eye				
Healthy	24.81 ± 1.28	3.58 ± 0.33	3.82 ± 0.28	-3.61 ± 2.45
POAG	25.84 ± 1.35	3.64 ± 0.31	3.81 ± 0.34	-5.19 ± 2.69
p value	*0.0008*	*0.3810*	*0.8780*	*0.0082*
Left eye				
Healthy	24.81 ± 1.23	3.58 ± 0.29	3.81 ± 0.27	-3.58 ± 2.28
POAG	25.80 ± 1.37	3.61 ± 0.33	3.78 ± 0.35	-5.19 ± 2.75
p value	*0.0010*	*0.6700*	*0.6660*	*0.0060*

Table 3. A-scan ultrasonographic biometry in the old-age group

	Axial length (mm)	Anterior chamber depth (mm)	Lens thickness (mm)	Spherical equivalent refractive error (diopter)
Right eye				
Healthy	23.30 ± 0.92	3.06 ± 0.33	4.57 ± 0.35	0.19 ± 1.47
POAG	24.42 ± 1.28	3.22 ± 0.33	4.56 ± 0.38	-1.73 ± 2.85
p value	*2.9E-05*	*0.0351*	*0.9112*	*0.0004*
Left eye				
Healthy	23.27 ± 0.91	3.03 ± 0.32	4.53 ± 0.40	0.11 ± 1.51
POAG	24.39 ± 1.30	3.20 ± 0.33	4.53 ± 0.39	-1.68 ± 2.78
p value	*3.5E-05*	*0.0259*	*0.9623*	*0.0007*

Table 4. Axial length in young-age subjects

	Axial length		*p* value
	< 26 mm	≥ 26 mm	
Right eye			
Healthy	32	8	0.08378
POAG	25	15	
Left eye			
Healthy	34	6	0.0066
POAG	23	17	

* *p* value : by " Chi-square test "

Table 5. Axial length in old-age subjects

	Axial length		*p* value
	< 26 mm	≥ 26 mm	
Right eye			
Healthy	40	0	0.0209
POAG	35	5	
Left eye			
Healthy	39	1	0.0479
POAG	34	6	

* *p* value : by " Chi-square test "

Table 6. Cycloplegic refraction (spherical equivalence) in young-age subjects

	Spherical equivalen: refractive error			*p* value
	< -2.0 D	-2.0 ~ -6.0 D	≥ -6.0 D	
Right eye				
Healthy	14	18	8	0.06865
POAG	6	19	15	
Left eye				
Healthy	10	23	7	0.07686
POAG	6	18	16	

* *p* value : by " Chi-square test " ; □ D : diopter

Table 7. Cycloplegic refraction (spherical equivalence) in old-age subjects

	Spherical equivalent refractive error			*p* value
	< -2.0 D	-2.0 ~ -6.0 D	≥ -6.0 D	
Right eye				
Healthy	37	3	0	0.04695
POAG	25	12	3	
Left eye				
Healthy	37	3	0	0.04695
POAG	25	12	3	

* *p* value : by " Chi-square test " ; □ D : diopter

Table 8. A-scan ultrasonographic biometry in healthy subjects

	Axial length (mm)	Anterior chamber depth (mm)	Lens thickness (mm)	Spherical equivalent refractive error (diopter)
Right eye				
Young-age	24.81 ± 1.28	3.58 ± 0.33	3.82 ± 0.28	-3.61 ± 2.45
Old-age	23.30 ± 0.92	3.06 ± 0.33	4.57 ± 0.35	0.19 ± 1.47
p value	*7.9E-08*	*1.3E-09*	*1.8E-16*	*1.1E-11*
Left eye				
Young-age	24.81 ± 1.23	3.58 ± 0 29	3.81 ± 0.27	-3.58 ± 2.28
Old-age	23.27 ± 0.91	3.03 ± 0.32	4.53 ± 0.40	0.11 ± 1.51
p value	*2.3E-08*	*2.0E-11*	*1.2E-13*	*3.5E-12*

* *p* value : by " Student's *t*-test "

Table 9. A-scan ultrasonographic biometry in POAG subjects

	Axial length (mm)	Anterior chamber depth (mm)	Lens thickness (mm)	Spherical equivalent refractive error (diopter)
Right eye				
Young-age	25.84 ± 1.35	3.64 ± 0.31	3.81 ± 0.34	-5.19 ± 2.69
Old-age	24.42 ± 1.28	3.22 ± 0.33	4.56 ± 0.38	-1.73 ± 2.85
p value	*8.7E-06*	*1.4E-07*	*3.1E-14*	*4.4E-07*
Left eye				
Young-age	25.80 ± 1.37	3.61 ± 0.33	3.78 ± 0.35	-5.19 ± 2.75
Old-age	24.39 ± 1.30	3.20 ± 0.33	4.53 ± 0.39	-1.68 ± 2.78
p value	*1.3E-05*	*7.7E-07*	*1.1E-13*	*3.1E-07*

* *p* value : by " Student's *t*-test "

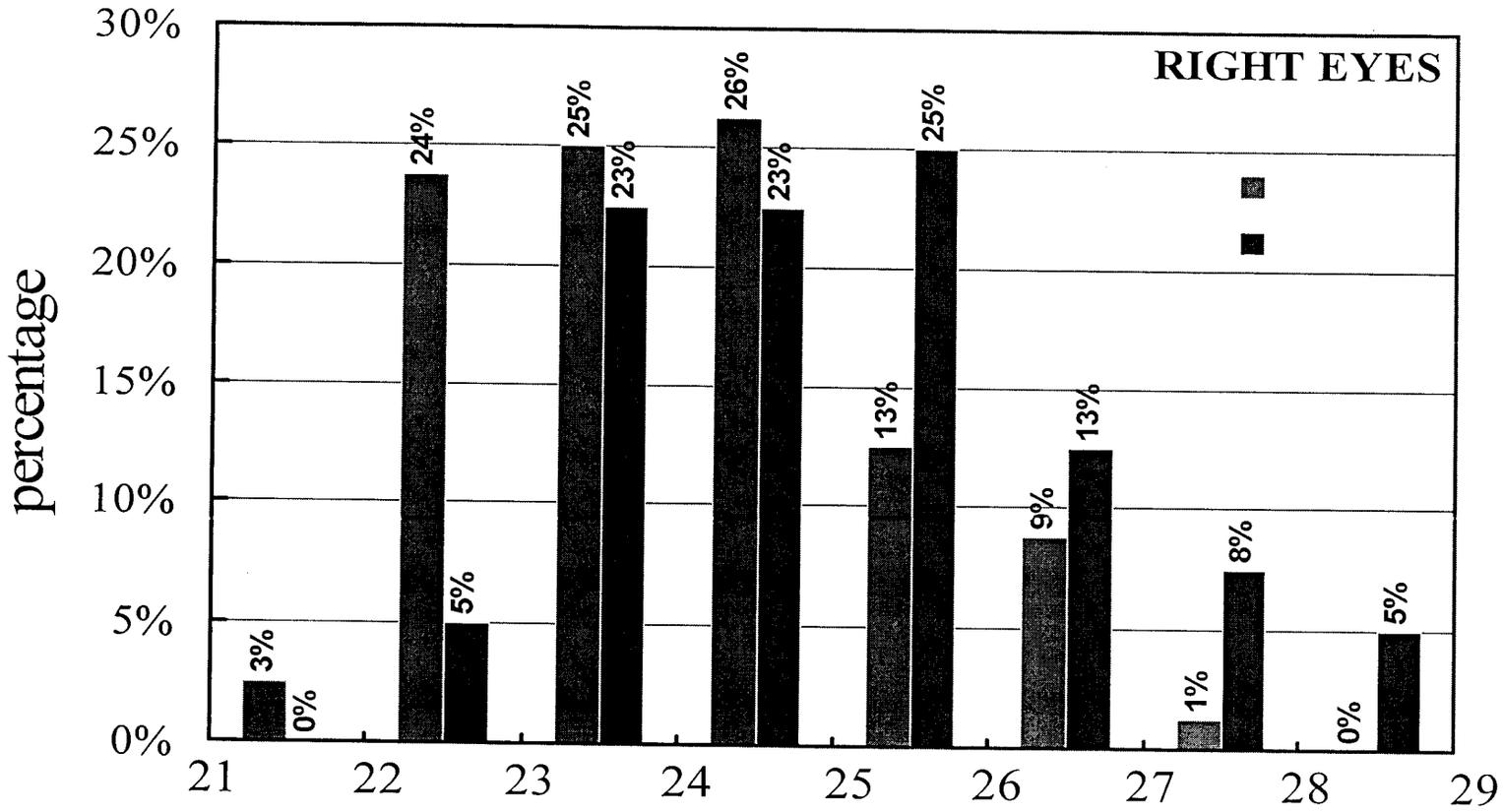

Figure 1. distribution of axial lengths in healthy and POAG subjects

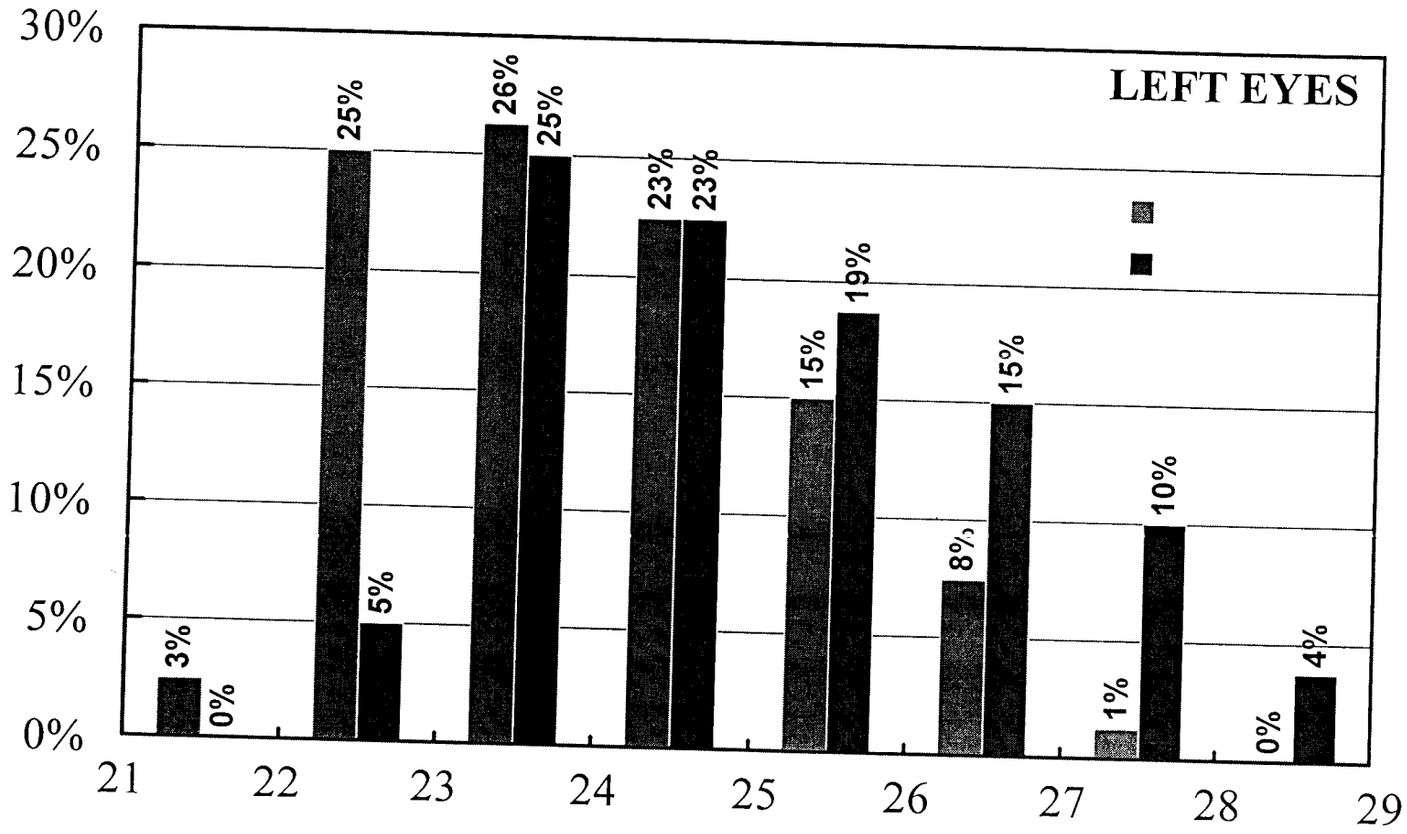

Figure 2. distribution of axial lengths in healthy and POAG subjects

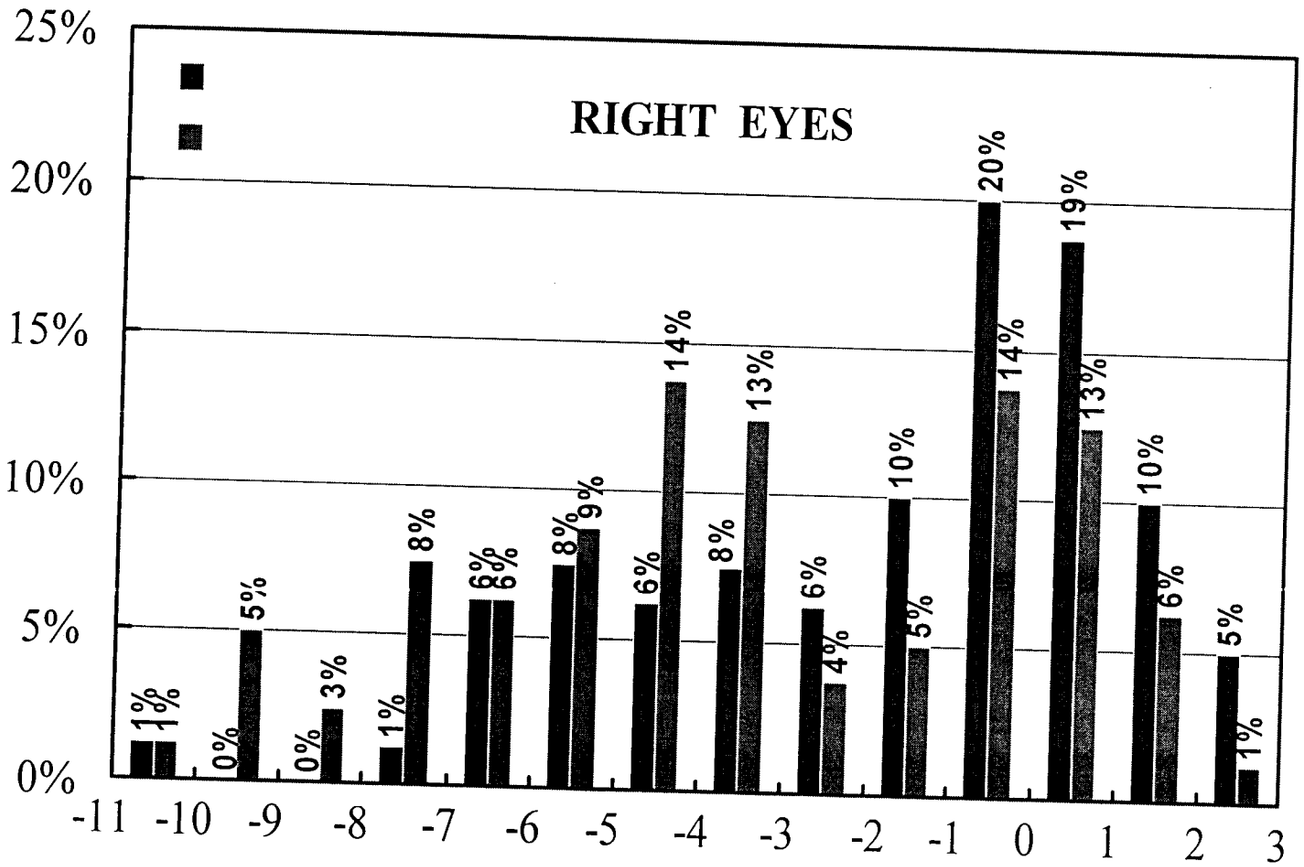

Figure 3. distribution of refractive errors in healthy and POAG subjects

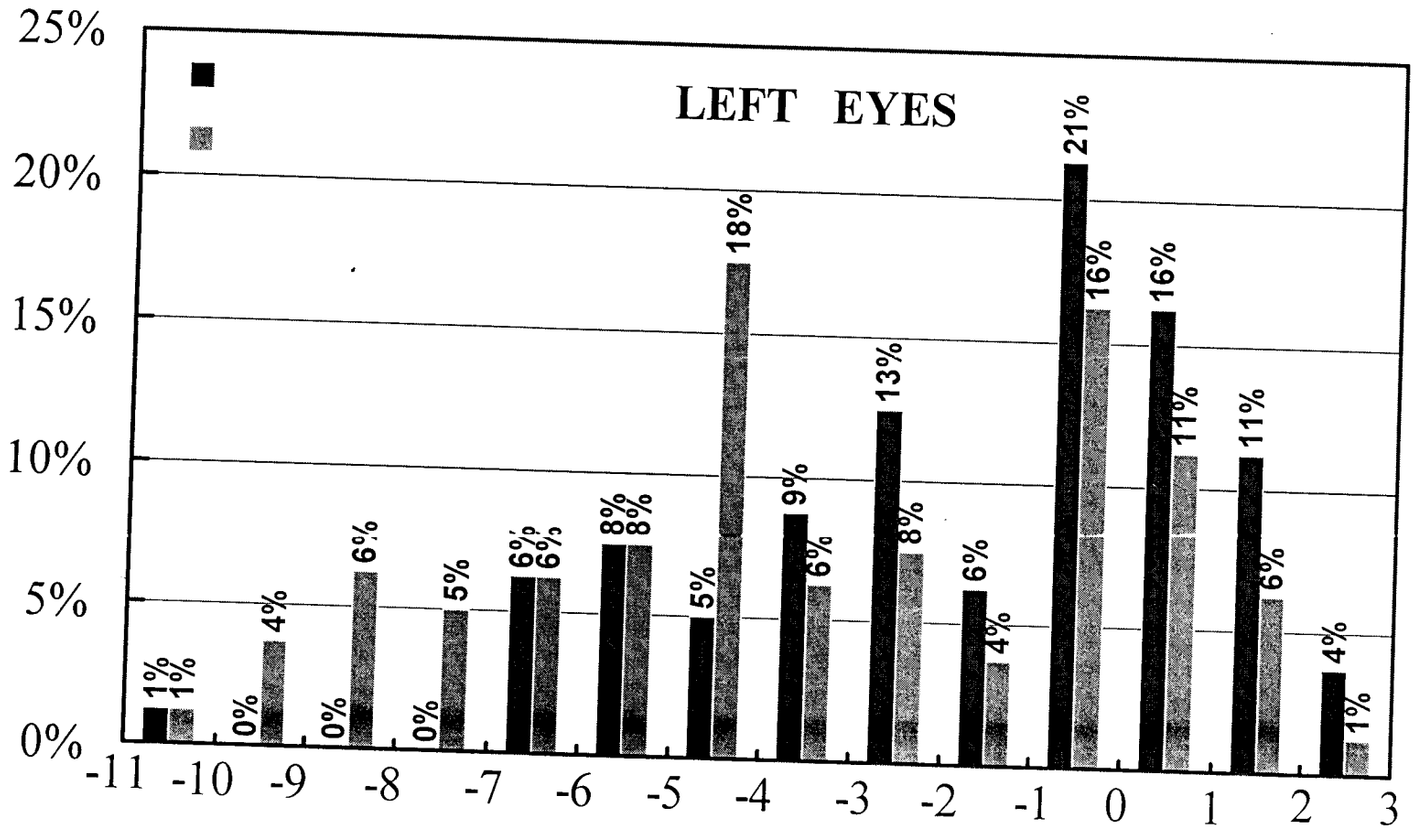

Figure 4. distribution of refractive errors in healthy and POAG subjects