Optic disc morphology and interocular symmetry in children

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Abstract:

PURPOSE: The purpose of the study was to obtain a pediatric reference database for optic disc parameters and interocular symmetry. To ascertain factors that modify these parameters (age, spherical equivalent [SE], and sex).

METHODS: This was a cross-sectional study. 90 patients aged 5–17 years fulfilled all the inclusion criteria. After a full examination including cycloplegic refraction, all patients underwent optical coherence tomography (OCT) of the papilla using the three-dimensional (3D) scan protocol of the Topcon 3D 2000 OCT device. We provide reference values for optic disc parameters in the pediatric population. We also retrieved interocular symmetry reference values for these parameters.

RESULTS: The multivariate regression analysis did not reveal variations in any of the optic disc parameters associated with age, sex, or SE (all $P \geq 0.126$). The 95th percentile limit for absolute interocular differences for the cup-to-disc area ratio was 0.24. The multivariate regression analysis revealed the absence of a correlation between asymmetry of the optic disc parameters and age, sex, and the interocular difference in SE (all $P \geq 0.105$).

CONCLUSION: Pediatric reference databases for optic disc parameters and ranges of normality for interocular symmetry provide key diagnostic support in diseases that affect the optic nerve.

Keywords:

Optic disc, optic nerve, optical coherence tomography

Introduction

Optic disc parameters can vary in children as a result of disease, potentially leading to loss of vision and even blindness.[1] Furthermore, the detection of interocular asymmetry with optical coherence tomography (OCT) in optic nerve parameters could provide added value in the evaluation of measurements taken in each eye individually.[2]

No currently marketed OCT devices have reference values for patients aged <18 years, thus limiting its application in children.[3]

This study aims to provide reference values for optic disc parameters and interocular symmetry to help ophthalmologists detect ocular disease in pediatric patients.

Methods

We performed a prospective cross-sectional study in which we analyzed optic disc parameters in healthy children aged 5–17 years.

The study participants were recruited from a tertiary hospital and a primary care center. The parents or guardians of children aged 12 years or older signed the relevant informed consent documents before the examinations. The study was approved by our local Clinical Research Committee.

The exclusion criteria were as follows: birth at <37 weeks of gestational age or bodyweight of under 2500 g, best-corrected visual acuity (BCVA) lower than 0.1 logMAR or a difference in BCVA of more than 1 line between both eyes, abnormalities of ocular motility or strabismus, absence of stereopsis with the TNO test, fundus abnormalities,

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previous ophthalmological surgery, orbital abnormalities, spherical equivalent (SE) greater than ± 5.5 diopters (D), and astigmatism greater than three-dimensional (3D). Other exclusion criteria were inability to cooperate in the examinations and poor-quality testing (i.e., a test with a quality lower than 40, blinking, movement, or misalignment) and the presence of known systemic diseases, ocular diseases that can cause structural damage, and family history (first-degree) of retinal or neuroophthalmological disease.

All patients underwent a complete ophthalmological examination including BCVA, refraction with and without cycloplegia (3 drops of cyclopentolate 1% every 10 min, 3 times), stereopsis with the TNO test, color vision with the Ishihara test, the examination of intrinsic and extrinsic ocular motility, anterior segment examination with a slit lamp, and funduscopy with indirect ophthalmoscopy. Finally, after pharmacological mydriasis, the patient underwent OCT of the optic disc using the 3D scan protocol of the Topcon 3D 2000OCT device (Topcon Corporation, Tokyo, Japan), in which the area examined is 6 mm^2, with a scanner density of 512 (vertical) × 128 (horizontal).[4] This approach yielded itemized thicknesses for the various optic disc parameters. Both the examinations and the image capture were performed by four ophthalmologists who had been trained in image capture with this device. The reproducibility of the Topcon 3D 2000 device in children has been verified elsewhere.[5]

Data analysis

Data were analyzed using an Excel spreadsheet and SAS 9.3 (SAS Institute Inc., Cary, North Carolina, USA).

The reference database of the optic disc parameters was analyzed using only right-eye measurements since using data from both eyes in the same patient could yield less reliable results.[6,7] In the case of interocular symmetry, both eyes were assessed.

All measurements are expressed as the mean and standard deviation (SD), median, range, and percentiles. Univariate and multivariate analyses were performed taking into account three independent variables (age, sex, and SE). The tables generated with the reference values took these factors into account.

Symmetry was calculated, first, by analyzing the means for the parameters in both eyes and subtracting the measurement for the left eye from that of the right (positive values when the right eye value is greater and negative when that of the left eye is greater), and second, by obtaining the interocular difference in absolute values (only positive values). The interocular difference values considered to be within the normal range were established with the p95 of the absolute interocular difference. The intraclass correlation coefficient (ICC) was calculated to measure the interocular correlation or level of agreement.

Univariate and multivariate analyses were performed to ascertain the effect of age, sex, and the interocular difference in SE on the symmetry of the different parameters. The regression coefficient and P value were extracted. Statistical significance was set at $P < 0.05$.

Results

For the statistical analysis of the reference database for optic disc parameters, we eventually obtained reliable measurements for 90 of the 140 patients evaluated at baseline: 14 children did not fulfill the inclusion criteria, and of the remaining 126, 36 were not sufficiently cooperative to enable us to obtain images of sufficient quality to be included in the study. Of these, 48 (53.3%) were girls and 69 (76.7%) were European. The mean SE was 0.78 (SD 1.52) D, and the cylinder value was–0.43 (0.55) D.

The descriptive values for the different papillary parameters in the pediatric population are shown in Table 1.

The univariate analysis revealed a statistically significant positive correlation between SE and disc area (0.214 [SD 0.031], $P = 0.043$). However, no statistically significant correlations were found in the multivariate analysis for SE ($P \geq 0.087$), age ($P \geq 0.126$), or sex ($P \geq 0.179$). Table 2 shows the variation in papillary parameters by the SE group.

The analysis of interocular symmetry was based on values from 78 children since, in 12, an image of suitable quality was only achieved for the right eye.

The results of the global analysis of interocular symmetry for the papillary parameters are shown in Table 3. The ICCs for all interocular symmetry parameters were high (≥0.65), except for ring area and vertical disc diameter, in which we found an ICC of 0.60 and 0.58, respectively.

We measured the impact of age and the interocular difference in SE on the symmetry of the optic disc parameters. The multivariate regression analysis revealed a lack of correlation between asymmetry in the optic disc parameters and age, sex, and the difference in interocular SE ($P \geq 0.105$ for all values).

Discussion

The reference ranges for optic nerve parameters have been evaluated by several authors. However, to the best of our knowledge, the present study is the first to provide reference values for optic disc parameters in the pediatric population using OCT with the Topcon 3D 2000 protocol.[8] We also provide interocular symmetry values for these parameters.

A reduction in ring area or volume could indicate a loss of pRNFL. Therefore, the availability of pediatric reference databases such as the present could prove highly relevant when making the differential diagnosis with conditions such as glaucoma in patients with suspect papillae. This is particularly important in children, in whom difficulties arising from lack of cooperation often prevent reliable visual fields from being obtained, and thus, diagnostic conclusions from being reached.

Table 4 includes information about previous studies of optic disc parameters in children.

Table 1: Optic disc parameters in healthy children aged 5–17 years (n=90)

	Mean (SD)	Range	Percentiles						
			p1	p5	p25	p50	p75	p95	p99
Disc area (mm²)	2.58 (0.46)	1.79–3.98	1.79	1.86	2.24	2.58	2.82	3.36	3.97
Cup area (mm²)	0.65 (0.48)	0.02–2.58	0.02	0.13	0.29	0.53	0.90	1.80	2.57
Rim area (mm²)	1.94 (0.43)	1.17–3.08	1.17	2.32	1.58	1.91	2.21	2.72	3.05
Cup-to-disc area ratio	0.24 (0.15)	0.01–0.69	0.01	0.05	0.12	0.23	0.33	0.55	0.68
Linear cup-to-disc-ratio	0.47 (0.15)	0.10–0.83	0.10	0.23	0.34	0.48	0.58	0.74	0.80
Vertical cup-to-disc ratio	0.47 (0.15)	0.11–0.89	0.11	0.23	0.35	0.47	0.57	0.74	0.85
Cup volume (mm³)	0.12 (0.13)	0.00–0.76	0.00	0.00	0.02	0.09	0.16	0.37	0.70
Rim volume (mm³)	0.61 (0.37)	0.04–1.43	0.04	0.12	0.27	0.60	0.85	1.04	1.37
Horizontal disc diameter (mm)	1.71 (0.17)	1.32–2.06	1.32	1.45	1.59	1.72	1.79	2.02	2.04
Vertical disc diameter (mm)	1.91 (0.19)	1.55–2.63	1.55	1.63	1.78	1.92	2.02	2.22	2.39

p: percentile, SD: Standard deviation

Table 2: Papillary parameters in healthy children aged 5–17 years (n=90) by spherical equivalent group

	SE (D)					
	−5.5–−1 D (n=13)		−1–+2 D (n=62)		+2–+5.5 D (n=15)	
	Mean (SD)	Percentiles 5 and 95	Mean (SD)	Percentiles 5 and 95	Mean (SD)	Percentiles 5 and 95
Disc area (mm²)	2.28 (0.28)	1.97 2.75	2.65 (0.46)	1.85 3.40	2.55 (0.48)	1.79–3.50
Cup area (mm²)	0.55 (0.29)	0.02 0.90	0.68 (0.51)	0.15 1.85	0.59 (0.51)	0.08–2.00
Rim area (mm²)	1.73 (0.29)	1.33 2.08	1.98 (0.45)	1.26 2.74	1.96 (0.39)	1.39–2.30
Cup-to-disc area ratio	0.24 (0.12)	0.01 0.38	0.25 (0.15)	0.06 0.59	0.22 (0.15)	0.04–0.55
Linear cup-to-disc-ratio	0.46 (0.16)	0.10 0.62	0.47 (0.16)	0.24 0.76	0.44 (0.15)	0.20–0.75
Vertical cup-to-disc ratio	0.47 (0.15)	0.11 0.61	0.47 (0.15)	0.24 0.74	0.46 (0.17)	0.23–0.87
Cup volume (mm3)	0.11 (0.10)	0.00 0.28	0.12 (0.14)	0.00 0.43	0.09 (0.10)	0.00–0.35
Rim volume (mm3)	0.58 (0.37)	0.04 1.20	0.62 (0.36)	0.14 1.34	0.60 (0.43)	0.06–0.85
Horizontal disc diameter (mm)	1.61 (0.12)	1.47 1.75	1.73 (0.17)	1.42 2.03	1.71 (0.17)	1.42–1.91
Vertical disc diameter (mm)	1.79 (0.12)	1.62 1.95	1.94 (0.18)	1.66 2.22	1.88 (0.21)	1.55–2.20

D: Diopters, SD: Standard deviation, SE: Spherical equivalent

Table 3: Interocular symmetry of optic disc parameters based on optical coherence tomography in healthy children aged 5-17 years (n=78)

	Right eye, mean (SD)	Left eye, mean (SD)	Interocular difference (right eye–left eye)					Absolute interocular difference	
			Mean (SD)	p2.5	p5	p95	p97.5	p90	p95
Disc area (mm²)	2.57 (0.47)	2.61 (0.52)	−0.04 (0.35)	−0.86	−0.64	0.44	0.60	0.50	0.65
Cup area (mm²)	0.66 (0.49)	0.63 (0.44)	0.04 (0.36)	−0.65	−0.46	0.52	1.26	0.49	0.79
Rim area (mm²)	1.91 (0.42)	1.99 (0.50)	−0.08 (0.43)	−1.47	−0.77	0.53	0.98	0.62	1.12
Cup-to-disc area ratio	0.25 (0.15)	0.23 (0.14)	0.01 (0.11)	−0.24	−0.16	0.21	0.36	0.17	0.24
Linear cup-to-disc-ratio	0.48 (0.15)	0.46 (0.15)	0.02 (0.11)	−0.21	−0.17	0.24	0.30	0.18	0.25
Vertical cup-to-disc ratio	0.48 (0.15)	0.46 (0.14)	0.02 (0.12)	−0.26	−0.23	0.23	0.30	0.23	0.26
Cup volume (mm³)	0.12 (0.13)	0.11 (0.13)	0.01 (0.07)	−0.11	−0.09	0.11	0.18	0.09	0.14
Rim volume (mm³)	0.61 (0.34)	0.66 (0.36)	−0.05 (0.25)	−0.62	−0.52	0.53	0.62	0.52	0.61
Horizontal disc diameter (mm)	1.71 (0.16)	1.72 (0.21)	−0.01 (0.14)	−0.33	−0.29	0.22	0.23	0.22	0.29
Vertical disc diameter (mm)	1.91 (0.20)	1.93 (0.19)	−0.02 (0.18)	−0.39	−0.34	0.25	0.44	0.32	0.39

SD: Standard deviation, p: Percentile

Table 4: Main studies about optic disc parameters in children

Authors	Device	Differences with sex	Differences with age	Differences with spherical equivalent	Limit of normal interocular symmetry in the cup-to-disc ratio
Patel *et al* [9]	Portable OCT device	-	Increase in the size of the papilla with age	-	-
Kiziloglu *et al* [10]	iVue 100 SD-OCT	No	Small differences with adults	-	-
Bhoiwala *et al* [12]	SD-OCT RTVue	-	Small differences with adults	-	-
Huynh *et al* [20]	StratusOCT, software v. 4.0.4	Mild	-	Mild	<0.25
Pang *et al* [21]	HRT II	Mild	No	No	-
He *et al* [22]	HRT 3	Mild	Mild	Mild	-
Altemir *et al*.[25]	Cirrus HD-OCT	No	-	-	<0.25
Pawar *et al* [23]	Cirrus HD-OCT	No	No	-	<0.22
Al-Haddad *et al* [30]	Cirrus HD-OCT	No	No	No	<0.20
Current study (Muñoz-Gallego *et al*)	OCT Topcon 3D-2000	No	No	No	<0.24

OCT: Optical coherence tomography, HRT: Heidelberg retinal tomography, SD: Standard deviation, HD: High definition

Patel *et al*.[9] used a portable OCT device to measure the development of the optic disc from the first day of life up to 13 years and found high ICCs for the diameter of the disc and the cup-to-disc ratio, as well as a progressive increase in the size of the papilla with age. Yabas Kiziloglu *et al*.[10] studied optic disc parameters in Turkish children using the OCT iVue 100 SD-OCT device, and as in our study, did not find significant differences in these parameters between boys and girls. The authors compared their results with the adult database for the same device and observed that in children, the optic disc and ring area were larger than in adults and that the vertical cup-to-disc ratio was lower in children than in adults.[10] These results are similar to those reported by Larsson *et al*.[11] with the Heidelberg Retina Tomograph (HRT) and Bhoiwala *et al*.[12] with SD-OCT RTVue. In their study of adults based on stereoscopic images of the optic disc, Varma *et al*.[13] found no differences in the various parameters with age or SE, although they did find that the papilla was 2%–3% larger in males than in females. Nevertheless, numerous studies found no differences in optic disc parameters according to sex.[10,11,14-18] Similarly, Huynh *et al*.[19] did not find differences with sex, except in horizontal and vertical diameter, which were slightly higher in males. In a study of adolescents, the same authors found that optic disc diameter, disc area, and ring area were greater in females, whereas the cup-to-disc ratio was greater in males; however, these differences were very small.[20] Similarly, in a study of African American children, Pang *et al*.[21] did not find differences between the sexes, except for the cup-to-disc ratio, which was higher in boys. He *et al*.[22] also found that this ratio was 0.03 units lower in girls. Pawar *et al*.[23] and other authors[24,25] did not find differences in optical disc parameters according to sex. Therefore, we can conclude that even though there may be small differences between the sexes, the clinical relevance of these differences is minimal or almost nonexistent, owing to the small ratio. Wenner *et al*.[26] found that the optic disc in the eyes of children with high hypermetropia was smaller than in those with emmetropia. In the present study, the multivariate analysis revealed no statistically significant correlation with age, SE, or sex.

As for interocular symmetry, we found that the highest correlation was for cup volume, disc area, ring volume, horizontal diameter, and cup area. Huynh *et al*.[24] found that the mean interocular differences were ≤0.02 mm for the diameter of the optic disc and of the cup, and ≤0.04 mm^2 for optic disc area, cup, and ring area. In this case, the cup-to-disc ratio was the most symmetrical parameter, with minimal interocular differences; therefore, asymmetry was lower than 0.25 in 95% of children.[24] Altemir *et al*.[25] also found the cup-to-disc ratio to be the most symmetrical. Larsson *et al*.[11] found greater intraocular differences for the cup-to-disc and ring-to-disc ratios and lower differences for disc and ring areas in a study performed with HRT. Yabas Kiziloglu *et al*.[10] studied the interocular symmetry of optic disc parameters in Turkish children using the OCT iVue 100 SD-OCT device and found an interocular correlation of more than 0.75 for all the parameters, although they did not set limits of normality. In our study, the most symmetrical parameter was cup volume, followed by disc area and ring volume. The ICC of the cup-to-disc ratio was 0.682. Studies performed in adults also revealed a high correlation between both eyes for disc area but a low correlation for depth and cup volume, as in the Blue Mountains Eye Study, which was performed with HRT3.[27]

In the case of suspected glaucoma, interocular symmetry in the cup-to-disc ratio is known to be a predictor of future axonal damage in patients with ocular hypertension.[28,29] Altemir *et al*.[25] suggested considering an interocular difference in the cup-to-disc ratio of 0.25 as pathological, thus reflecting the wide degrees of symmetry they found in the proportions of this ratio. Pawar *et al*.[23] set this limit at 0.22 and Al-Haddad *et al*.[30] at 0.20. In our study, a normal value for papillary asymmetry in the cup-to-disc ratio would be 0.17 if we take into account p90, and 0.24 if we take into account p95. Therefore, our values are similar to those of the abovementioned studies. In fact, in the Blue Mountains Eye Study (adult sample), the authors concluded that 24% of patients with glaucoma had interocular asymmetry ≥0.2 in this ratio compared with 6% of healthy patients.[31]

Few studies evaluate the potential influence of factors that modify the interocular symmetry of optic disc parameters. As in our study, Al-Haddad *et al*.[30] did not find a correlation between the asymmetry of papillary parameters and age or sex. Furthermore, we found no correlation with the interocular difference in SE.

Our study is subject to a series of limitations. Axial length (AL) was not assessed, although the correlation between AL and SE in healthy children has previously been reported to be negative.[32] We were unable to analyze the relationship between geographical origin and optic disc parameters, as most of the children were from Europe.

Conclusion

Having pediatric reference values for the optic disc and interocular symmetry could prove to be a very valuable tool in cases of suspected diseases of the optic nerve.

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Conflicts of interest

There are no conflicts of interest.

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