European Review for Medical and Pharmacological Sciences 2023; 27: 3580-3589

Corneal biomechanical properties in myopic and emmetropic children

M. MARINESCU[1,2], D. DASCALESCU[1,2], M. CONSTANTIN[3], V. COVILTIR[1,2], M. BURCEL[3], D. DARABUS[4,5], R. CIULUVICA[6], D. STANILA[7], L. VOINEA[1], V. POTOP[1,2]

[1]Department of Ophthalmology, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
[2]Department of Ophthalmology, Clinical Hospital for Ophthalmological Emergencies, Bucharest, Romania
[3]Department of Ophthalmology, City Hospital Videle, Videle, Romania
[4]Department of Ophthalmology, Oftaclinic, Bucharest, Romania
[5]Department of Ophthalmology, Victor Babeș University of Medicine and Pharmacy, Timișoara, Romania
[6]Department of Anatomy, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
[7]Department of Ophthalmology, Faculty of Medicine, Lucian Blaga University, Sibiu, Romania

Abstract. – OBJECTIVE: The purpose of this study was to investigate the relationship between corneal biomechanics and ocular morphology in myopic children and adolescents.

PATIENTS AND METHODS: The study included 170 right eyes, from 170 patients under the age of 18 years, who underwent a complete ophthalmologic examination, gathering the following data: spherical equivalent (SE) (under pharmacological cycloplegia), biomechanical parameters – corneal hysteresis (CH) and corneal resistance factor (CRF), structural parameters – axial length (AL) and central corneal thickness (CCT).

RESULTS: The average age of the patients was 15.26 years old (55.29% girls, 44.70% boys). Out of the 170 eyes, 111 were myopic eyes and 59 were emmetropic. Myopic eyes had a significantly lower CH (p=0.001), CRF (p=0.002) and CCT (p=0.009), and higher AL (p<0.001) than emmetropic eyes. The AL and CCT were significantly higher in myopic males, compared to myopic females (p<0.001 and 0.001). In myopes, we found statistically significant negative correlations between AL and CH (Pearson's r=-0.218), CRF (r=-0.226) and also SE (r=-0.539), and positive between SE and either CH (r=0.193) or CRF (r=0.201).

CONCLUSIONS: Corneal biomechanical properties are significantly related to myopia parameters in children.

Key Words:
Myopia, Emmetropia, Corneal biomechanics, Axial length, Corneal thickness.

Introduction

Myopia is a frequent ophthalmological pathology, with an important impact on the patients' quality of life and daily activities. Recent epidemiological studies[1] in European populations report a prevalence of the disease of up to 24.4%, and an ascending trend for the following decades. According to the World Health Organization[2], 52% of the world's population is projected to be myopic by 2050.

In children, the disease is particularly concerning, both for the parents and for the medical practitioners, including ophthalmologists and pediatricians. An increase in the number of myopic children has been reported[3] in several populations: in eastern Asia, the prevalence increased by 23% over a decade, while in Caucasian populations, the time trends are smaller. Raising parents' awareness on myopia and means of prevention is important in clinical practice and has been proven[4] to decrease myopic shift and cumulative incidence rate in primary school children. However, even in children who receive myopia treatments, such as topical atropine, there is a proportion of patients who still progress[5], and may need more intensive monitoring and treatment.

The disease associates a significant risk of ocular complications, such as macular degeneration or retinal detachment, even at low refractive values. Studies[6] show that a myopic eye with a refractive error of -3.00 diopters (D) has 4 times the

Corresponding Author: Dana Dascalescu, MD; e-mail: dana.dascalescu@umfcd.ro

risk of macular degeneration and 3 times the risk of retinal detachment of a myopic eye of -1.00 D. Myopia accounts for a large proportion of visual loss worldwide, with several studies[7,8] citing myopic macular degeneration as a leading cause of blindness in these patients.

Myopic eyes are significantly different compared to emmetropic ones, both structurally and biomechanically[9]. Myopia may be characterized by a mismatch between the optical power and the higher axial length (AL) of the eye[10], and therefore, myopic eyes are significantly longer than emmetropic eyes. The pathogenesis of myopia is complex and includes an interaction between the genetic and the environmental factors of each individual. Peripheral retinal defocus plays an important role, triggering a series of cellular and biochemical transformations in the retina, choroid, and sclera, ultimately leading to axial elongation[11]. In addition to these risk factors, physiological states, such as puberty and menstruation, have a certain impact on refractive values in myopic eyes. It has been reported[12] that, during puberty, axial length and spherical equivalent increase faster in children that have an earlier height growth – thus, there is a myopic progression during these growth spurts.

Several behavioral risk factors have been associated[9] with the development of myopia, including low amounts of time spent outdoors and continuous near work (reading, writing, and computer work). Recently, especially due to the COVID-19 pandemic, many individuals have experienced lifestyle changes resulting in increased digital screen time in both children and adults and a low amount of time spent outdoors[13]. Studies[14] have shown a higher rate of myopia progression during strict home confinements compared to pre-pandemic rates.

Several parameters appear to differ between myopic and emmetropic eyes, including peripapillary retinal nerve fiber layer (RNFL) thickness, peripapillary retinal vessel density[15] or even the intraocular inflammatory profile[16]. Furthermore, the blood flow area in the choriocapillaris is lower in higher degrees of myopia, while the macular vascular density is lower in all four quadrants in these patients[17]. In relation to axial length and refractive equivalent, other ocular characteristics are hypothesized to differ in the myopic eye, including the biomechanical properties of the cornea[18].

Corneal biomechanical properties can be easily measured in almost every individual, including children and adolescents[18]. A continuous interest in their research has been shown due to their role in diseases such as glaucoma[18,19], keratoconus[20], and in the field of refractive surgery[21]. Regarding myopia, both the morphological and biomechanical properties of the cornea are of importance, and may help identify children with a higher risk of myopia progression[16,18].

A recent meta-analysis[22], which included one pediatric cohort, confirms that CH and CRF are significantly higher in low myopes, compared to high myopes, and more studies are needed to determine whether modulation of corneal biomechanical parameters may influence myopia progression, especially in pediatric populations. More recently, data[23] have been published that demonstrate an association between a low baseline CH and axial elongation in spectacle-wearing myopic patients, which might reveal CH as a predictive factor of myopia progression. This link between the biomechanical state of the myopic cornea and the evolution of myopia could aid in the identification of children with a high risk of faster evolution, in which frequent monitoring and treatment are necessary.

Taking all these into account, the objective of our study was to explore the relationship between corneal biomechanics and ocular morphology in a pediatric myopic population, compared to a pediatric emmetropic population.

Patients and Methods

The study was designed as a prospective, non-randomized, non-interventional cross-sectional study. We screened all patients under the age of 18, who consecutively presented to a private clinic (Oftaclinic) in Bucharest, Romania, between January 2021 and April 2022 (Figure 1). The research related to human use complies with all the relevant national regulations, institutional policies, and is in accordance with the tenets of the Helsinki Declaration. Informed consent was obtained from all participants/legal guardians of the patients included in this study. The study was approved by the Oftaclinic Ethics Committee.

The inclusion criteria were the diagnosis of low-moderate myopia [spherical equivalent (SE) between -0.50 D and -6.00 D][24] and emmetropia (SE between -0.50 D and +0.50 D)[25]. Included patients were divided in the study and control groups according to the value of the spherical equivalent calculated after pharmacological cycloplegia (cyclopentolate 10 mg/ml, instilled 3 times, at 5-minute intervals, in each eye). The study group included eyes with low to moderate myopia, while the control group included emmetropic eyes.

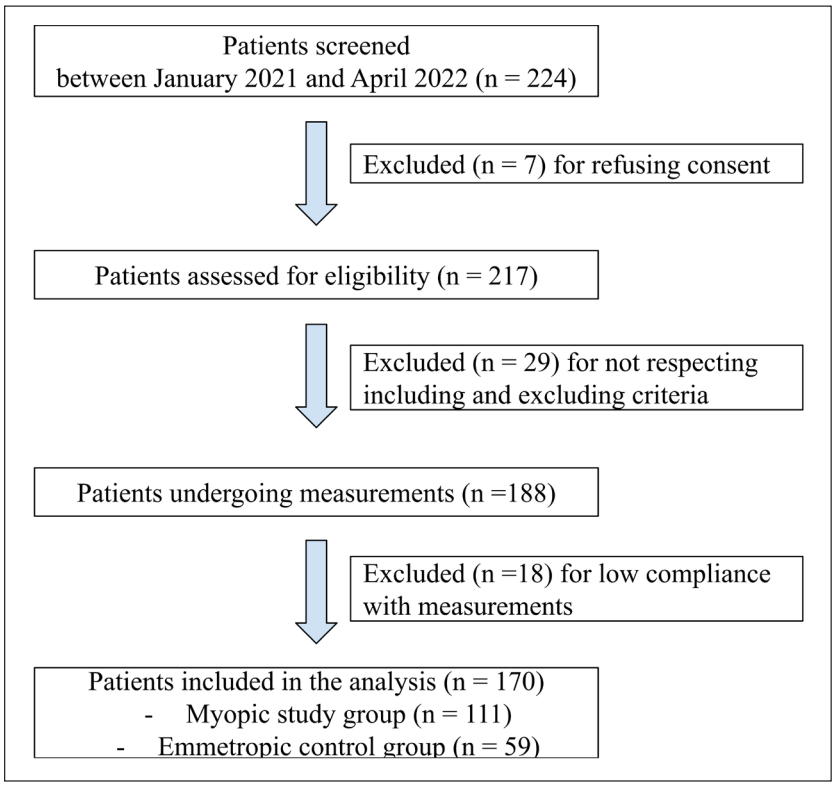

Figure 1. Flow diagram detailing the selection of the study cohort.

The exclusion criteria were represented by a history of refractive surgery and ocular pathology, other than myopia (hyperopia, glaucoma, cataract, keratoconus, vitreoretinal pathology). Patients were also excluded if not compliant with testing, e.g., low waveform in Ocular Response Analyzer (ORA) testing. Randomly, only the right eye of each patient was included in the analysis.

Data Sources/Measurements

The ophthalmological evaluation of the patients included autorefractometry, before and after pharmacological cycloplegia, using Topcon KR800 (Topcon, Tokyo, Japan) to assess spherical error and equivalent (spherical error + ½ cylindrical error), slit lamp examination, fundus examination, Goldmann applanation tonometry, biomechanical analysis using Ocular Response Analyzer (Reichert Ophthalmic Instruments Inc., Depew, NY, USA) to determine corneal hysteresis (CH), corneal resistance factor (CRF), Goldmann-correlated intraocular pressure IOP (IOPg) and measurement of axial length and central corneal thickness (CCT) using Aladdin biometer (Topcon, Tokyo, Japan).

The Ocular Response Analyzer is a device, based on non-contact tonometry, that applies an air pulse on the corneal surface and follows the corneal deformation and its return to the initial state using infrared light, thus recording 2 applanation pressures. ORA measures intraocular pressure (IOPg, equivalent to the IOP measured using Goldmann Applanation Tonometry) and two estimates of corneal viscoelastic behavior: corneal hysteresis, which represents corneal ability to absorb and dissipate energy (CH is the pressure difference between the first and second applanation) and the corneal resistance factor, which is a factor of the global corneal resistance (similar to CH, with the second applanation multiplied with a constant)[26]. Autorefractometry is an electronic method for measuring refractive errors, based on the principle of retinoscopy (following the movement of the retinal reflection of a light, projected towards the patient's eye)[27]. The Aladdin is an optical low-coherence interferometer accurately measuring ocular parameters, including the anteroposterior length of the globe (axial length) and the thickness of the cornea[28].

Quantitative Variables and Statistical Methods

The study included categorical data (gender and refractive status - myopic or emmetropic) and numerical, continuous data (SE, CH, CRF, IOPg, AL, CCT). Statistical analysis of the data was performed using SPSS Statistics v. 26 (IBM Corp., Armonk, NY, USA).

Categorical data were described using absolute and relative frequency. To identify significant differences between the groups, the Independent Samples *t*-test was used, preceded by Levene's test for equality of variances. In order to identify correlations between variables reported in the study, Pearson's correlation coefficient (Pearson's r) was calculated. A Pearson's r between 0.3 and -0.3 reveals a weak correlation, between 0.3 and 0.5 and between -0.3 and -0.5 reveals a moderate correlation, and a Pearson's r of over 0.5 or under -0.5 signifies that the correlation is strong. All correlations have been calculated controlling for IOPg, which acts as a confounding variable. A *p*-value of under 0.05 is considered a threshold for statistical significance.

Results

Descriptive Data

Referring to the 170 patients included in the study, 94 (55.29%) were female, and 76 (44.70%) were male. The mean age was 15.26 [standard deviation (SD) 2.686].

Of the 170 right eyes from 170 patients who met the inclusion criteria, 111 (65.29%) were myopic and 59 (34.70%) were emmetropic, after pharmacological cycloplegia. The gender distribution was balanced in both the study and the control group, with 61 (54.95%) females and 50 (45.05%) males in the myopic group; 33 (55.93%) females and 26 (44.07%) males in the emmetropic control group.

Main Results

Myopic eyes had a significantly lower SE, CH, CRF, CCT and higher AL, compared to emmetropic eyes (Table I). Male eyes had a significantly higher AL and CCT than female eyes in the myopic group, while in emmetropes the difference is significant only regarding AL. In the myopia group CRF was significantly higher in males compared to females (Table II).

There were significant correlations between the morphological and biomechanical properties of the eye in myopic patients, accounting for IOPg

Table I. Mean and standard deviation of the age, SE (spherical equivalent), AL (axial length), CCT (central corneal thickness), CH (corneal hysteresis) and CRF (corneal resistance factor) in the whole cohort and in the myopic and emmetropic groups, with mean difference, standard error and *p*-value of independent samples *t*-test.

	Mean (Standard deviation)				*p*-value
	Entire cohort (N=170)	Myopic study group (N=111)	Emmetropic control group (N=59)	Mean difference (Standard error)	
Age (years)	15.26 (2.69)	15.4 (2.50)	15.02 (3.003)	0.38 (0.46)	0.409
SE (D)	-1.73 (1.77)	-2.64 (1.54)	-0.04 (0.33)	-2.60 (0.15)	<0.001
AL (mm)	24.21 (1.08)	24.56 (1.00)	23.55 (0.88)	1.01 (0.15)	<0.001
CCT (mm)	0.558 (0.038)	0.552 (0.037)	0.569 (0.040)	-0.016 (0.006)	0.009
CH (mmHg)	11.79 (1.98)	11.43 (1.73)	12.47 (2.30)	-1.03 (0.31)	0.001
CRF (mmHg)	11.98 (2.17)	11.64 (1.99)	12.70 (2.31)	-1.06 (0.34)	0.002

Table II. Mean, standard deviation and *p*-value of the independent samples *t*-test, regarding the age, SE (spherical equivalent), AL (axial length), CCT (central corneal thickness), CH (Corneal hysteresis) and CRF (corneal resistance factor) in male and female subjects, in the myopia and emmetropia groups.

	Myopic study group (N=111)			Emmetropic control group (N=59)		
	Males (n = 50)	Females (n = 61)	*p*-value	Males (n = 26)	Females (n = 33)	*p*-value
Age (years)	15.22 (2.68)	15.54 (2.36)	0.504	15.54 (2.64)	14.61 (3.24)	0.240
SE (D)	-2.59 (1.59)	-2.68 (1.50)	0.762	-0.058 (0.29)	-0.026 (0.36)	0.720
AL (mm)	24.94 (0.90)	24.25 (0.97)	<0.001	23.97 (0.86)	23.22 (0.76)	0.001
CCT (mm)	0.565 (0.04)	0.541 (0.03)	0.001	0.571 (0.04)	0.567 (0.04)	0.682
CH (mmHg)	11.73 (1.65)	11.20 (1.76)	0.110	11.89 (2.30)	12.93 (2.23)	0.083
CRF (mmHg)	12.10 (2.22)	11.26 (1.70)	0.027	12.30 (2.08)	13.03 (2.46)	0.232

Table III. Correlations in the myopic group and in the emmetropic group, between SE (spherical equivalent), AL (axial length), CCT (central corneal thickness), CH (corneal hysteresis) and CRF (corneal resistance factor).

	Pearson's correlation coefficients	
	Myopic study group	Emmetropic control group
AL-CH	-0.218*	-0.162
AL-CRF	-0.226*	-0.171
CCT-CH	0.412†	0.625†
CCT-CRF	0.384†	0.612†
SE-CH	0.193*	-0.097
SE-CRF	0.201*	-0.079
CCT-SE	0.229*	-0.102
AL-SE	-0.539†	0.046
CCT-AL	-0.009	0.031

*$p<0.05$; †$p<0.001$.

as a confounding variable. In the emmetropic subgroup, there were strong positive correlations between CCT-CH and between CCT-CRF (Table III). In the myopic subgroup, there were moderate positive correlations between CCT-CH and CCT-CRF (Figure 2), strong negative correlation between AL-SE, weak positive correlations between SE-CH, SE-CRF and CCT-SE, and weak negative correlations between AL-CH and AL-CRF (Figure 3). There were moderate, negative, statistically significant correlations between age and both CH and CRF, in the myopic group and in the emmetropic group (Table IV).

Discussion

Consistent with other studies in literature, the results of our study indicate that, in children and adolescents, myopic and emmetropic eyes are significantly different in terms of AL, CH and CRF.

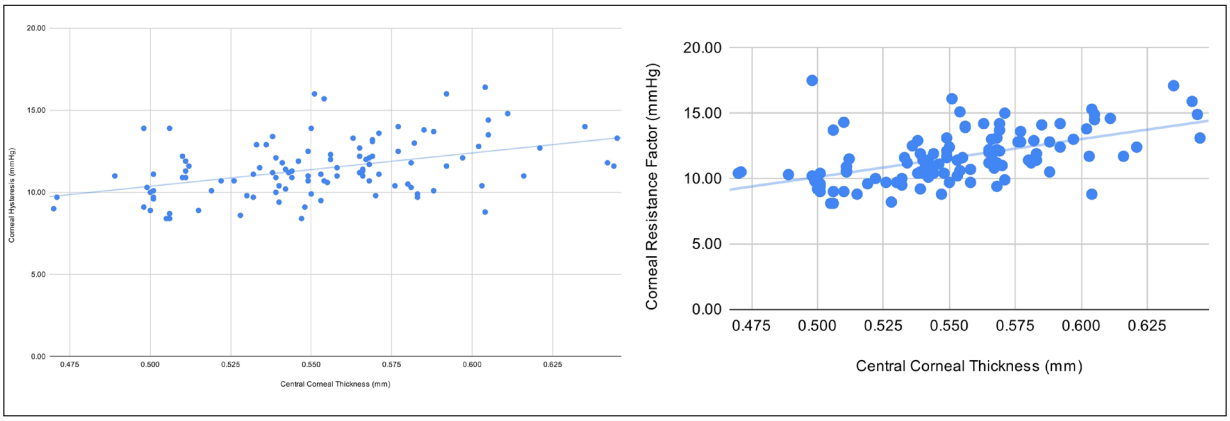

Figure 2. Correlation between central corneal thickness and corneal hysteresis (first scatter plot) and corneal resistance factor (second scatter plot) in the myopic study group.

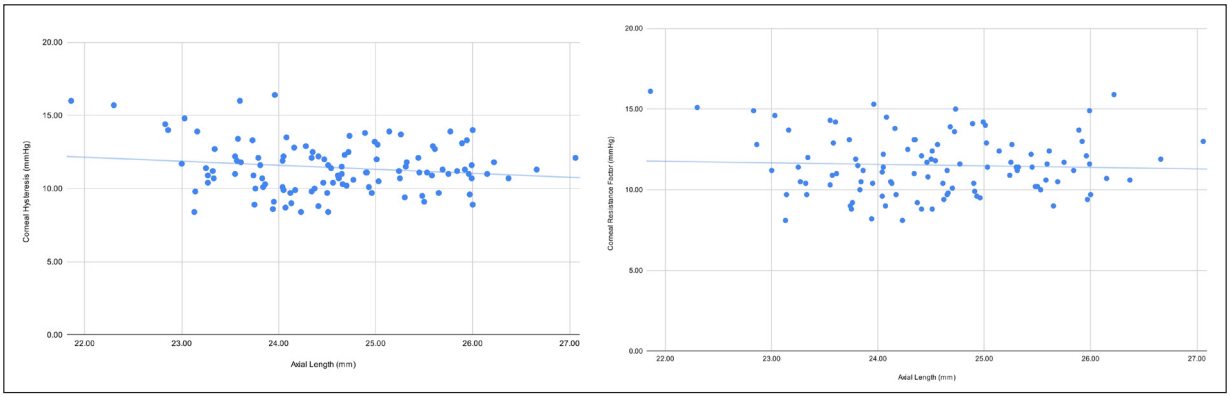

Figure 3. Correlation between axial length and corneal hysteresis (first scatter plot) and corneal resistance factor (second scatter plot) in the myopic study group.

Table IV. Correlations in the myopic group and in the emmetropic group, between age and AL (axial length), CH (corneal hysteresis) and CRF (corneal resistance factor), CCT (central corneal thickness), SE (spherical equivalent).

	Pearson's correlation coefficients	
	Myopic study group	Emmetropic control group
Age-AL	0.097	0.209
Age-CH	-0.311*	-0.436*
Age-CRF	-0.304*	-0.458†
Age-CCT	-0.059	-0.194
Age-SE	-0.033	-0.037

*$p<0.01$; †$p<0.001$.

Furthermore, in our myopic pediatric cohort there were statistically significant correlations between CCT and both CH and CRF, between AL and CH or CRF, and between SE and CH, CRF, AL and CCT.

An important finding of this study relates to the biomechanical properties of the cornea: in myopes, CH and CRF were significantly lower than in emmetropes, and were inversely correlated with AL. Our results are generally similar to those obtained in previous studies in literature. In a pediatric cohort[29] of 293 eyes, both CH and CRF were correlated with AL and CCT, and were significantly lower in myopes, compared to emmetropes.

Moreover, the data from the literature show that central corneal thickness is lower in myopia[30], while not influenced by the degree of myopia[31]. This suggests that in myopic eyes changes appear mostly in other structures, such as the sclera[32], choroid, and even retinal pigment epithelium[33].

In our study, the correlations between CCT and either CH or CRF were positive and moderate or strong, both in myopes and in emmetropes. Regression models in myopes revealed that the variation of CH and CRF is highly dependent on CCT, far more than on refraction values[34]. These complex interrelations may be explained by a flattening and thinning effect that axial elongation may have on the cornea[35], a lower rigidity in myopic eyes[36], or an alteration in collagen fibers in myopia, which impacts biomechanical properties[37].

Furthermore, there seems to be a certain relationship between CCT and SE: a diverse cohort of children revealed that a decrease of 1 micrometer in CCT is associated with a decrease of 1.00 D of SE[38]. However, since regression analysis revealed a large proportion of CCT variability unaccounted for SE, more data are needed to accurately describe the relationship between CCT, SE and other myopic components, such as AL and corneal curvature.

Our study revealed the interplay between AL, CH, and SE, with significant correlations between each two of these parameters. The relationship between spherical equivalent and corneal biomechanics was proved to be complex. There are correlations between CH or CRF and SE in myopia study group, with no correlation in emmetropes. This may be due to the fact that myopia has both an axial component (that is, long AL) and a refractive component (high optical power of the eye). Therefore, AL cannot be fully correlated with SE, as the refractive component is unaccounted in this relation. For this reason, we decided to include both AL and SE in the study. Similar studies[39] have found varying levels of correlations between CH and either SE or AL. CH has a comparable level of correlation with AL and SE, suggesting that in the myopic eye, a low corneal hysteresis reflects both a higher axial length and a greater refractive power of the cornea and lens.

Gender accounted for the differences in AL and CCT in our study. However, similar studies[40] have found no differences between genders in terms of AL and CCT, and an extensive study[41] in an Italian population revealed significant differences between genders in terms of CH and CRF, while CCT did not differ. Several studies in literature have revealed that gender plays a role in the evolution of myopia. Annual myopia progression has been proven[42] to be faster in girls. Studies[43] have shown that in children, the prevalence of myopia is higher in girls (5.96% in boys and 10.37% in girls, between the ages of 13 and 16), a difference appearing from the age of nine[3]. The fact that myopic males had a significantly longer AL in our study, and no differences in SE, compounded by the varying results in the literature, suggests that the underlying mechanism is unclear; however, it might involve a heightened corneal rigidity in men. Interestingly, in terms of biomechanics, only the CRF in myopic boys was significantly higher than in girls, in our study. More research is needed to identify the factors that lead to certain biomechanical or morphological differences between genders, in different populations.

Our study confirms an inverse correlation between CH or CRF and age, both in myopes and in emmetropes. In a recent genome-wide association study[44] of corneal biomechanical properties, both CH and CRF are associated with age, and on average, men had lower CH and CRF than wom-

en. Although both AL and CCT are expected to evolve during childhood, the literature[45] reports a steep increase during early childhood, with no statistically significant AL growth over the age of 15 years, and no substantial variability in CCT between the ages of 12 and 17[38]. The age bracket of our cohort may explain why no significant age differences have been identified.

It is of note that in our study the age was not correlated with the structural parameters. Similarly, a large study[46] that included both myopes and emmetropes has found that CCT does not vary significantly between the ages of 6 and 18. In a Japanese population, it has been reported[47] that CCT reaches values similar to adult ones around the age of 5, which would explain the lack of variance across age groups.

Ocular development during childhood ensures a reduction in refractive errors, tending toward emmetropia, a process called emmetropization. At birth, the eye is hyperopic, and this refractive error gradually decreases, until the age of 5-7 years old, when children approach emmetropia and usually measure between plano and +2.00 D spherical error[48]. Starting from this age, the rate of myopia starts increasing, reflecting the abnormal continuation of this process, through mechanisms not yet entirely understood[48]. Therefore, during childhood there is a trend of AL growth, which has been correlated with anthropometric measurements, such as height. Studies[49,12] confirm the correlation between AL and height values and growth rates, in different populations, and even between height evolution before puberty and SE at age 15. Importantly, an earlier peak of AL and SE growth has been correlated[12] with an earlier peak of height growth, and earlier puberty onset has been associated with earlier myopia onset.

Notably, our myopia cohort has not included eyes with high myopia (refraction equivalent of under -6.00 D). In terms of corneal biomechanics, high myopia associates with certain characteristics, different from low-moderate myopia, such as our cohort. CH is significantly lower in high myopes, compared to low myopia controls (without significant differences in CCT and CRF)[50]. The study[51] of several biomechanical parameters suggests that in higher myopia, there is a decrease in corneal rigidity, independent of corneal thickness. In high myopes, both CH and CRF correlate with the thickness of the stromal corneal layer[52]. Further studies are needed to a better understanding of the biomechanical behavior of highly myopic eyes.

Limitations

One limitation of our study is the small sample size, considering the relative frequency of myopia and emmetropia in the general population. Our study is cross-sectional; therefore, we cannot follow the temporal evolution of the patients, in relation to the variables discussed. One important aspect is whether corneal biomechanics are altered following the axial length increase, or the low biomechanical parameters act as risk factors for globe elongation and, subsequently, myopia progression. We are planning a prospective follow-up of this cohort, in order to test the assumption that the corneal biomechanical status at this point in time relates to the evolution of myopia in the future, if a low corneal hysteresis may predict further axial elongation.

Conclusions

To summarize, our study brings to light the complex interactions between corneal biomechanics, ocular morphology, and refractive status in myopic children. In myopic eyes, the axial length was significantly higher and the central corneal thickness, corneal hysteresis, and corneal resistance factor were significantly lower compared to emmetropic eyes. AL and CCT were significantly higher in male myopes, compared to female myopes. There were significant correlations between CH and AL, CCT and CH or CRF, SE and AL, CH or CRF in myopic eyes, and between CCT and CH or CRF in emmetropes.

Acknowledgments

We would like to thank Cristiana Vlagali for support in data management, analysis, and graphic design.

Funding

The publication of this paper was supported by the University of Medicine and Pharmacy Carol Davila, through the institutional program "Publish not Perish".

Authors' Contributions

All authors had equal contribution.

ORCID ID

Maria Marinescu: 0000-0001-8242-8809
Dana Dascalescu: 0000-0001-6421-9675
Valeria Coviltir: 0000-0002-0552-2479
Miruna Burcel: 0000-0002-9701-4104
Radu Ciuluvica: 0000-0002-1922-515X
Vasile Potop: 0000-0002-2049-6694

Conflicts of Interest
The authors declare that they have no conflict of interest to declare.

Availability of Data and Materials
The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Informed Consent
Informed consent was obtained from all participants/legal guardians of the patients included in this study.

Ethics Approval
The study was conducted according to the declaration of Helsinki. The study is approved by the Oftaclinic Ethics Committee (Ethics approval 2/15.12.2020).

References

1) Xiang ZY, Zou HD. Recent Epidemiology Study Data of Myopia. J Ophthalmol 2020; 4: 4395278.
2) World Health Organization-Brien Holden Vision Institute. The impact of myopia and high myopia. 2015; 1-29. Available at: Myopia_report_020517.pdf (myopiainstitute.org).
3) Rudnicka AR, Kapetanakis VV, Wathern AK, Logan NS, Gilmartin B, Whincup PH, Cook DG, Owen CG. Global variations and time trends in the prevalence of childhood myopia, a systematic review and quantitative meta-analysis: implications for aetiology and early prevention. Br J Ophthalmol 2016; 100: 882-890.
4) Li Q, Guo L, Zhang J, Zhao F, Hu Y, Guo Y, Du X, Zhang S, Yang X, Lu C. Effect of School-Based Family Health Education via Social Media on Children's Myopia and Parents' Awareness: A Randomized Clinical Trial. JAMA Ophthalmol 2021; 139: 1165-1172.
5) Wildsoet CF, Chia A, Cho P, Guggenheim JA, Polling JR, Read S, Sankaridurg P, Saw SM, Trier K, Walline JJ, Wu PC, Wolffsohn JS. IMI - Interventions Myopia Institute: Interventions for Controlling Myopia Onset and Progression Report. Invest Ophthalmol Vis Sci 2019; 60: M106-M131.
6) Cooper J, Tkatchenko AV. A Review of Current Concepts of the Etiology and Treatment of Myopia. Eye Contact Lens 2018; 44: 231-247.
7) Holden B, Sankaridurg P, Smith E, Aller T, Jong M, He M. Myopia, an underrated global challenge to vision: where the current data takes us on myopia control. Eye 2014; 28: 142-146.
8) Buch H, Vinding T, La Cour M, Appleyard M, Jensen GB, Nielsen NV. Prevalence and causes of visual impairment and blindness among 9980 Scandinavian adults: the Copenhagen City Eye Study. Ophthalmology 2004; 111: 53-61.
9) Czepita M, Czepita D, Lubiński W. The Influence of Environmental Factors on the Prevalence of Myopia in Poland. J Ophthalmol 2017; 2017: 5983406.
10) Harb EN, Wildsoet CF. Origins of Refractive Errors: Environmental and Genetic Factors. Annu Rev Vis Sci 2019; 5: 47-72.
11) Németh J, Tapasztó B, Aclimandos WA, Kestelyn P, Jonas JB, De Faber JHN, Januleviciene I, Grzybowski A, Nagy ZZ, Pärssinen O, Guggenheim JA, Allen PM, Baraas RC, Saunders KJ, Flitcroft DI, Gray LS, Polling JR, Haarman AE, Tideman JWL, Wolffsohn JS, Wahl S, Mulder JA, Smirnova IY, Formenti M, Radhakrishnan H, Resnikoff S. Update and guidance on management of myopia. European Society of Ophthalmology in cooperation with International Myopia Institute. Eur J Ophthalmol 2021; 31: 853-883.
12) Yip VC, Pan CW, Lin XY, Lee YS, Gazzard G, Wong TY, Saw SM. The relationship between growth spurts and myopia in Singapore children. Invest Ophthalmol Vis Sci 2012; 53: 79617966.
13) Wang J, Li Y, Musch DC, Wei N, Qi X, Ding G, Li X, Li J, Song L, Zhang Y, Ning Y, Zeng X, Hua N, Li S, Qian X. Progression of Myopia in School-Aged Children After COVID-19 Home Confinement. JAMA Ophthalmol 2021; 139: 293-300.
14) Picotti C, Sanchez V, Fernandez Irigaray L, Iurescia A, Iribarren R. Rapid progression of myopia at onset during home confinement. J AAPOS 2022; 26: 65.e1-65.e4.
15) Li Y, Miara H, Ouyang P, Jiang B. The Comparison of Regional RNFL and Fundus Vasculature by OCTA in Chinese Myopia Population. J Ophthalmol 2018; 2018: 3490962.
16) Coviltir V, Burcel M, Cherecheanu AP, Ionescu C, Dascalescu D, Potop V, Burcea M. Update on Myopia Risk Factors and Microenvironmental Changes. J Ophthalmol 2019; 2019: 4960852.
17) Meng Y, Yi ZH, Xu YS, He L, Li L, Chen CZ. Changes in macular vascular density and retinal thickness in young myopic adults without pathological changes: an OCTA study. Eur Rev Med Pharmacol Sci 2022; 26: 5736-5744.
18) Potop V, Coviltir V, Corbu C, Burcel MG, Ionescu CI, Dascalescu DMC. Corneal Hysteresis, A Glaucoma Risk Factor Independent of The Intraocular Pressure. Rev Roum Sci Techn- Electrotechn et Energ 2019; 64: 297-300.
19) Potop V, Coviltir V, Schmitzer S, Corbu C, Ionescu CI, Burcel M, Dăscălescu D. The Relationship Between Corneal Hysteresis and Retinal Ganglion Cells - A Step Forward in Early Glaucoma Diagnosis. Med Sci Monit 2020; 26: e924672.
20) Mas Tur V, MacGregor C, Jayaswal R, O'Brart D, Maycock N. A review of keratoconus: Diagnosis, pathophysiology, and genetics. Surv Ophthalmol 2017; 62: 770-783.
21) Jin SX, Dackowski E, Chuck RS. Risk factors for postlaser refractive surgery corneal ectasia. Curr Opin Ophthalmol 2020; 31: 288-292.

22) Wu W, Dou R, Wang Y. Comparison of Corneal Biomechanics Between Low and High Myopic Eyes—A Meta-analysis. Am J Ophthalmol 2019; 207: 419-425.

23) Wan K, Cheung SW, Wolffsohn JS, Orr JB, Cho P. Role of corneal biomechanical properties in predicting of speed of myopic progression in children wearing orthokeratology lenses or single-vision spectacles. BMJ Open Ophthalmol 2018; 3: e000204.

24) Chuck RS, Jacobs DS, Lee JK, Afshari NA, Vitale S, Shen TT, Keenan JD, American Academy of Ophthalmology Preferred Practice Pattern Refractive Management/Intervention Panel. Refractive Errors & Refractive Surgery Preferred Practice Pattern. Ophthalmology 2018; 125: P1-P104.

25) Hagen LA, Gilson SJ, Akram MN, Baraas RC. Emmetropia Is Maintained Despite Continued Eye Growth From 16 to 18 Years of Age. Invest Ophthalmol Vis Sci 2019; 60: 4178-4186.

26) Roberts CJ, Liu J. Corneal Biomechanics: From Theory to Practice. Kugler Publications, 2017.

27) Bhattacharyya B. Textbook of Visual Science and Clinical Optometry. Jaypee Brothers Medical Publishers, 2009.

28) Mandal P, Berrow EJ, Naroo SA, Wolffsohn JS, Uthoff D, Holland D, Shah S. Validity and repeatability of the Aladdin ocular biometer. Br J Ophthalmol 2014; 98: 256-258.

29) Bueno-Gimeno I, Martínez-Albert N, Gené-Sampedro A, España-Gregori E. Anterior Segment Biometry and Their Correlation with Corneal Biomechanics in Caucasian Children. Curr Eye Res 2019; 44: 118-124.

30) Elijah CN, Pedro ECN, Ejimadu CS. Association between myopia and central corneal thickness among patients in a tertiary hospital in south-south Nigeria. Adv Ophthalmol Vis Syst 2016; 5: 221-223.

31) Fam HB, How ACS, Baskaran M, Lim KL, Chan YH, Aung T. Central corneal thickness and its relationship to myopia in Chinese adults. Br J Ophthalmol 2006; 90: 1451-1453.

32) Metlapally R, Wildsoet CF. Scleral Mechanisms Underlying Ocular Growth and Myopia. Prog Mol Biol Transl Sci 2015; 134: 241-248.

33) Zhang Y, Wildsoet CF. RPE and Choroid Mechanisms Underlying Ocular Growth and Myopia. Prog Mol Biol Transl Sci 2015; 134: 221-240.

34) Jiang Z, Shen M, Mao G, Chen D, Wang J, Qu J, Lu F. Association between corneal biomechanical properties and myopia in Chinese subjects. Eye (Lond) 2011; 25: 1083-1089.

35) Chang SW. The cornea in young myopic adults. Br J Ophthalmol 2001; 85: 916-920.

36) Alkhaldi SA. The Association of Ocular Rigidity with Axial Length and Intraocular Pressure in Healthy Myopic Adults. Am J Biomed Sci & Res 2021; 14: 324-330.

37) Spaide RF. The Sclera and Induced Abnormalities in Myopia. Pathologic Myopia. Springer International Publishing, 2016.

38) Pediatric Eye Disease Investigator Group, Bradfield YS, Melia BM, Repka MX, Kaminski BM, Davitt BV, Johnson DA, Kraker RT, Manny RE, Matta NS, Weise KK, Schloff S. Central corneal thickness in children. Arch Ophthalmol 2011; 129: 1132-1138.

39) Huang Y, Huang C, Li L, Qiu K, Gong W, Wang Z, Wu X, Du Y, Chen B, Lam DS, Zhang M, Congdon N. Corneal biomechanics, refractive error, and axial length in Chinese primary school children. Invest Ophthalmol Vis Sci 2011; 52: 4923-4928.

40) Hashmani N, Hashmani S, Murad A, Asghar N, Islam M. Effect of Demographic Variables on the Regional Corneal Pachymetry. Asia Pac J Ophthalmol (Phila) 2019; 8: 324-329.

41) Strobbe E, Cellini M, Barbaresi U, Campos EC. Influence of age and gender on corneal biomechanical properties in a healthy Italian population. Cornea 2014; 33: 968-972.

42) Jones-Jordan LA, Sinnott LT, Chu RH, Cotter SA, Kleinstein RN, Manny RE, Mutti DO, Twelker JD, Zadnik K, CLEERE Study Group. Myopia Progression as a Function of Sex, Age, and Ethnicity. Invest Ophthalmol Vis Sci 2021; 62: 36.

43) Czepita M, Czepita D, Safranow K. Role of Gender in the Prevalence of Myopia among Polish Schoolchildren. J Ophthalmol 2019; 2019: 1-4.

44) Simcoe MJ, Khawaja AP, Hysi PG, Hammond CJ, UK Biobank Eye and Vision Consortium. Genome-wide association study of corneal biomechanical properties identifies over 200 loci providing insight into the genetic etiology of ocular diseases. Hum Mol Genet 2020; 29: 3154-3164.

45) Bach A, Villegas VM, Gold AS, Shi W, Murray TG. Axial length development in children. Int J Ophthalmol 2019; 12: 815-819.

46) Zhou Q, Gao TY, Fan SJ, Peng Y, Li L, Lin Z, Han W, Lin HS, Wang NL, Liang YB. Intraocular Pressure, Age, and Central Corneal Thickness in a Healthy Chinese Children Population: The Handan Offspring Myopia Study. Ophthalmic Epidemiol 2022; 29: 499-506.

47) Hikoya A, Sato M, Tsuzuki K, Koide YM, Asaoka R, Hotta Y. Central corneal thickness in Japanese children. Jpn J Ophthalmol 2009; 53: 7-11.

48) Wolffsohn JS, Flitcroft DI, Gifford KL, Jong M, Jones L, Klaver CCW, Logan NS, Naidoo K, Resnikoff S, Sankaridurg P, Smith EL 3rd, Troilo D, Wildsoet CF. IMI - Myopia Control Reports Overview and Introduction. Invest Ophthalmol Vis Sci 2019; 60: M1-M19.

49) Tao L, Wang C, Peng Y, Xu M, Wan M, Lou J, Yu X. Correlation Between Increase of Axial Length and Height Growth in Chinese School-Age Children. Front Public Health 2022; 9: 817882.

50) Shen M, Fan F, Xue A, Wang J, Zhou X, Lu F. Biomechanical properties of the cornea in high myopia. Vision Res 2008; 48: 2167-2171.

51) Sedaghat MR, Momeni-Moghaddam H, Azimi A, Fakhimi Z, Ziaei M, Danesh Z, Roberts CJ, Monfared N, Jamali A. Corneal Biomechanical Properties in Varying Severities of Myopia. Front Bioeng Biotechnol 2021; 8: 595330.

52) Wong YZ, Lam AKC. The roles of cornea and axial length in corneal hysteresis among emmetropes and high myopes: a pilot study. Curr Eye Res 2015; 40: 282-289.