Medical University of Varna

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Faculty of Medicine

Department of Eye Diseases and Vision Sciences

Control of Myopia

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ABSTRACT ON A DISSERTATION PAPER FOR OBTAINING AN EDUCATIONAL AND SCIENTIFIC DEGREE "DOCTOR OF SCIENTIFIC SPECIALTY "OPHTHALMOLOGY", CODE 03.01.36

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The dissertation contains 225 pages, including 49 tables and 34 figures, with 256 cited literary sources, 4 of which in cyrilic and 252 in latin. Five chapters are presented, corresponding to the aim and tasks and meeting the requirements for the layout of the thesis. The dissertation work was discussed and proposed for defense to the departmental council of the Department of Eye Diseases and Visual Sciences at the MU "Prof. Dr. Paraskev Stoyanov" - Varna on 03/04/2026.

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The official defense of the dissertation work will take place at a meeting of the Scientific Jury on 02/07/2026 at 8:30 at the Department of Eye Diseases and Visual Sciences of the University of Varna. The defense materials are available at the Scientific Department of the Medical University - Varna and are published on the website of the Medical University - Varna.

CONTENTS

Note: The numbering of the figures and tables in the abstract does not correspond to the numbering in the dissertation work.

Note: The team and principal investigator declare that they have no financial interest or affiliation with any of the mentioned trademarks of the products used in the study, devices or sites cited.

ABBREVIATIONS

VR-QoL Vision related quality of life

QoL Quality of life

VFQ Visual Function Questionnaire

NEI-VFQ National Eye Institute - Visual Function Questionnaire

NEI-RQL 42 National Eye Institute - Refractive Quality of Life (42 questions)

PREP Pediatric Refractive Error Profile

SCARED Screening for Emotional Disorders Associated with Childhood Anxiety

S-PPCGS-W Child Global Self-Perception Profile

PSQI Pittsburgh Sleep Quality Index

SHS Subjective Happiness Scale

HADS Hospital Anxiety and Depression Scale

OSDI Ocular Surface Disease Index

RSVP Refractive Status and Vision Profile questionnaire

QIRC Quality of Life Impact Refractive Correction questionnaire

CLIQ Contact Lens Impact on Quality of Life questionnaire

DEQ−5 Dry Eye Questionaire

NIBUT Noninvasive break-up time

SCL, CL, MCL Soft Contact Lenses

GP, RGP Gas Permeable Contact Lenses

OrthoK, Ortho-K Orthokeratology

WHO World Health Organization

D Diopter

IQ intelligence quotient

IOL Intraocular lens

AD, AL axial length

SE, SER spherical equivalent

MDM, MMD myopic macular degeneration

OAG open-angle glaucoma

OR odds ratio

CNV choroidal neovascularization

CNS Central nervous system

BHVI Brien Holden Vision Institute

IMI International Myopia Institute

ARVO Association for the Research of Vision and Ophthalmology

ROVS Research Ophthalmology and Visual Sciences

IMC International Conference on Myopia

WSPOS World Society for Pediatric Ophthalmology and Strabismus

ESO European Society of Ophthalmology

NHANES National Health and Nutrition Examination Survey

COMET The Correction of Myopia Evaluation Trial

CLEERE Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error

CCT Central Cochlear Thickness cornea

ACD Anterior Chamber Depth

CC Corneal Curvature

CR Corneal Radius of Curvature

AL/CR Axial Length to Corneal Radius Ratio

UDVA Uncorrected Distance Visual Acuity

BCVA Best Corrected Visual Acuity

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CHAPTER I. INTRODUCTION

Myopia is a type of ametropia characterized by more refractive eye medias and/or a longer axial length of the eyeball (1). As a result, the rays coming from infinity are focused in front of the retina, which leads to reduced visual acuity at a distance (1). Due to its high prevalence globally, the World Health Organization (WHO) classifies it among the most common causes of reversible blindness – uncorrected refractive errors occur in 123.7 million people (2). According to the WHO, high myopia is a degree of myopia of -5 diopters (D) or more, connected with an increased risk of vision loss, due to its association with certain eye diseases' complications, including degenerative changes in the macula, optic nerve and peripheral retina, retinal detachment, myopic choroidal neovascularization, glaucoma and cataract (3). Holden et al. estimate that the incidence of myopia will continue to increase worldwide, affecting 5 billion people by 2050, leading to a so-called myopic pandemic (4). The onset of myopia at an earlier age is a particularly worrying aspect of its epidemiology and a significant risk factor for progression and high-grade myopia in the future (5). The rapid increase in its prevalence globally, especially in urban areas, and its association with various ocular complications are of public health importance. As a result, the control of this ametropia has become an area of extensive research and clinical focus in recent years. The average incidence of myopia in the European population is already at 30.6% and is continuously growing, which in turn reinforces the need for effective intervention strategies (5).

Factors that play a role in the pathophysiology of myopia include time spent outdoors, prolonged hours of near work activities, prenatal factors and heredity, socioeconomic status and urbanization, and probably account for its increased incidence more than the genetic factors alone (5). Over the past few decades, research into methods for myopia control has increased significantly, leading to the development of various options for preventing its progression. Atropine is an effective pharmacological agent, achieving 50%–90% control, depending on its concentration. Although low concentrations (0.01%; 0.05%) have been identified as effective with minimal side effects, all are still associated with significant subjective symptoms such as dry mouth, photophobia, poor near vision, glare and allergic conjunctivitis (6). Orthokeratology is another effective optical agent that reduces axial progression by about 50% per year (6) (7).

The literature indicates that at least 6 months of Ortho-K lenses wear is required for effective treatment and that they carry a risk of complications such as corneal staining, papillary conjunctivitis and microbial keratitis (6) (7). The cost, the intensity of follow-up and the additional skills required by eye care professionals and patients also pose some barriers (7). Progressive, bi- and multifocal lenses and soft multifocal contact lenses are also prescribed as optical correction devices, but do not appear to have a significant effect on controlling the underlying progression of myopia (6) (8). Spectacles or contact lenses with a defocusing design may represent an alternative for individuals who cannot physiologically or financially tolerate other control devices (6). Another emerging trend is related to outdoor activities for children, as the literature suggests that natural light may have a protective effect against myopia progression (5). This approach, although simple, has attracted considerable attention in public health initiatives aimed at reducing the incidence of myopia in children.

Studies of various control and correction devices have shown that more and more children and parents are trying to find an alternative to glasses that is both aesthetically acceptable and provides better myopia control (9) (10) (11). Others suggest that contact lens wearers tend to be perceived better and are more socially accepted (12). Often, eye care professionals focus on patients' visual acuity, subjective symptoms and objective signs, without paying attention to their self-esteem, levels of anxiety, peer relationships, performance in school, sports, hobbies, and extracurricular activities. The latter are also of great importance in achieving optimal patient cooperation, strengthening the doctor-patient relationship and improving the quality of life of people with myopia.

In addition to individual health, myopia also carries significant societal and economic costs. The burden of treatment, the potential for visual impairment and the healthcare resources required to manage the condition’s complications, the inability to cope with daily tasks, education and pursuing certain careers, contribute to the increasing financial strain on healthcare systems worldwide. Thanks to new trends, clinical trials, advances in medical technology and innovation, it is likely that the knowledge of specialists in the control of myopia will develop furthermore, providing even more effective tools for eye health professionals to manage the condition.

Regular large-scale epidemiological studies are lacking in Bulgaria and we often refer to European and global data on the incidence of various diseases (13). In a study by Kirilova from 2015, screening 1,437 children of preschool and school age, in 95% of the children the examination performed at the screening was the child's first examination by an ophthalmologist (13). Isolated studies by Oscar and colleagues in the period 2013-2015 in North-East Bulgaria among children in the same age group found that 90% of them were not examined by a specialist ophthalmologist (13). A study by Dragomirova from 2016 of 1227 students, shows that 56.7% of children have never had an eye examination, 35% have vision disorders (myopia, hyperopia or astigmatism), only 15% have prescribed glasses and half of them declare that they do not wear them (13). All known studies for Bulgaria show that a very large proportion of children do not undergo the recommended examinations by an ophthalmologist, and unfortunately, there is no effective state policy for timely detection of vision problems in children (13). That is why this socially significant and present-day problem became the subject of the present study.

CHAPTER II. AIM AND TASKS

2.1. AIM

The main objective of this dissertation paper is to prospectively study and analyze the demographic characteristics and degree of myopia, as well as to assess the clinical efficacy of the applied methods for myopia control for a period of 5 years in patients aged between 6 and 16 years from the city of Varna, who underwent follow-up at USBOBAL-Varna.

2.2. TASKS

To meet our aim, the following tasks were set:

1. To review the publications in the literature on modern methods for myopia control and their efficacy on a global scale.

2. To determine the course of progression rates and the degree of myopia of the patients included in the study, who underwent follow-up at USBOBAL - Varna.

3. To analyze the changes in the axial length of the eyeball, monitored by performing optical biometry (IOL Master 500, Carl Zeiss Meditec, Inc) and keratometric values using corneal topography (Pentacam®, Oculus Optikgeräte GmbH).

4. To compare the results of the efficacy of the applied approaches for myopia control among the studied group of patients.

5. To assess the subjective symptoms, quality of life and visual function of the patients included in the study before starting and during the implementation of the respective method for myopia control.

6. To create a questionnaire for children and parents regarding the subjective symptoms of the patients, which will be of assistance to eye health specialists.

CHAPTER III. METHODOLOGY OF THE DISSERTATION

The present study was conducted at the Department of Eye Diseases and Visual Sciences of the Medical University - Varna on the territory of the University Specialized Hospital for Eye Diseases for Active Treatment USBOBAL - Varna for a period of 5 years from 01/09/2020 to 01/09/2025. The study examined a total of 93 patients who underwent follow-up on the territory of the aforementioned medical institution. The selection of patients was based on precisely defined criteria - patients from the city of Varna, with myopia and refractive error ≤-2.00D, cylindrical refraction no more than 1.00D and anisometropia no more than 1.50D, aged between 6 and 16 years, with no history of ophthalmic surgeries, traumas or systemic diseases that could affect the quality of vision, without reported mental disorders; verbal patients, with parents/guardians who signed a declaration of informed consent.

The methodology of the study includes a documentary method through research and analysis of the published scientific literature on the types of approaches for myopia control and their efficacy, analysis of the progression of axial length and refractive error in patients with myopia, their mechanism of action, indications for application and the impact of the various methods for myopia control and modern approaches applied to control myopia and new proposals for preventing its progression. The sociological method consisted of preparing questionnaires that met the objectives of the study and conducting a survey of patients. Clinical methods included autorefractometry (HRK-1, Huvitz (HUVITZ Co., Ltd., Republic of Korea), skiascopy with a Heine Beta® 200 retinoscope (HEINE Ophthoecnic, Herrsching, Germany), optical biometry (ZEISS IOLMaster 700 with SWEPT Source Biometry®), corneal topography (Pentacam®, Oculus (OCULUS, Optikgeräte GmbH), history taking and visual acuity testing. The collected data from the study were statistically processed using the following methods - analysis of variance (ANOVA, MANOVA), variation, correlation, regression and comparative analysis and risk assessment analysis (OR, RR). In all analyses, an acceptable level of significance of $p<0.05$, $p<0.01$, $p<0.001$ at a standard confidence interval of 95% was assumed. The data was statistically processed using SPSS v.20, using descriptive indicators for quantitative and qualitative variables, presented in tabular and graphical form.

CHAPTER IV. RESULTS

4.1 Research and analysis of the socio-demographic characteristics of patients with myopia.

Over a period of 5 years (2020-2025), 92 patients with myopia underwent follow-up examination on the territory of USBOBAL-Varna. Of these, 40 were male (43.48%) and 52 were female (56.52%) in a ratio of 10:13. The average age of myopic patients was 11.57, with the lowest being 8 years old and the highest being 17 years old. In terms of spherical equivalent (SE) for right eye (OD), 20 patients had high-grade myopia (SE ≤ -6.00 D) and 72 had low-grade, 67 had astigmatism, and the average values of SE and |Cyl| were -4.13 D and -0.83 D, respectively. The spherical equivalent (SE) for the left eye (OS) displayed, that 21 patients had high myopia, again about 73% had astigmatism and the mean values of SE and |Cyl| were -4.19 D and -0.84 D, separately. Combined for OD and OS, 78% of the patients in the study had low-degree myopia, nearly 82% had astigmatism and the mean values of SE and |Cyl| were -4.27 D and -0.82 D, individually. Regarding the distribution of patients by gender and degree of myopia, we observed more patients with low-grade myopia to be male (35:22). More female patients in the study had high myopia (21:14). Concerning the questions about the time spent daily working at close distance or by doing outdoor activities, we observed the following data.

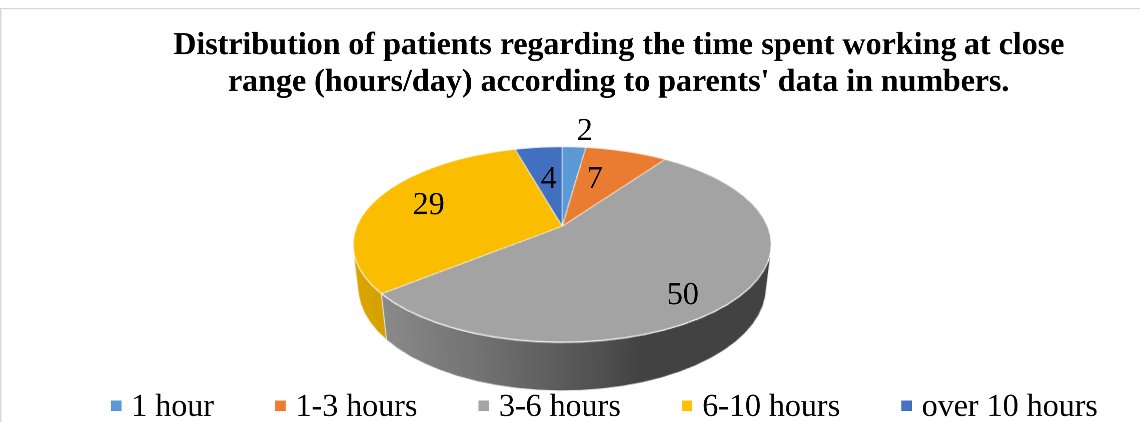

Figure 1. Distribution of patients regarding the time spent working at close range (hours/day) according to parents' data in numbers.

The largest number of patients included in the study spent between 3 and 6 hours a day working at close range (n=50), followed by those who strained their visual analyzer between 6 and 10 hours (n=29). Interestingly, twice as many patients spent more than 10 hours (n=4) in front of a mobile device or reading than the group of patients who did so for only an hour a day (n=2).

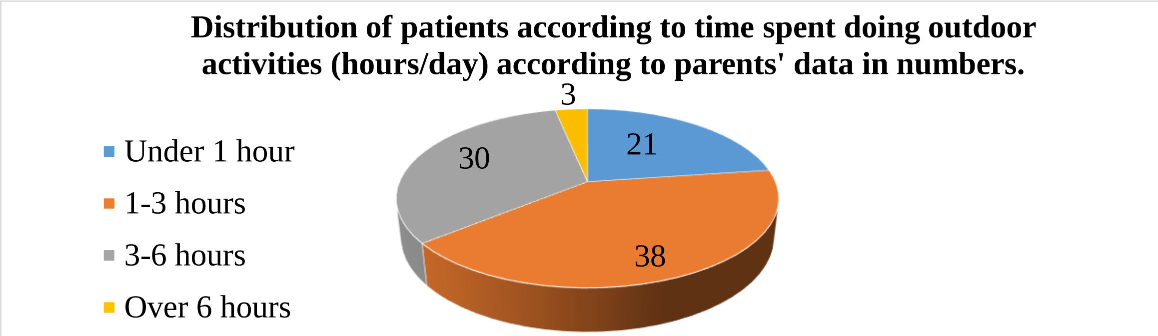

Figure 2. Distribution of patients according to time spent doing outdoor activities (hours/day) according to parents' data in numbers.

The studied population of patients most often spends between 1-3 hours outdoors (n=38) or between 3-6 hours per day (n=30). However, the trend remains alarming, especially that a much higher number of patients spend less than 1 hour per day outdoors – 21 of them. Only three patients spend more than 6 hours per day doing outdoor activities. We did not find a statistically significant difference in terms of time spent working/reading at close range or spent outdoors at the beginning and the end of the study (p>0.05). Regarding other family members with myopia, 56 of all studies have data on myopia in the family, or nearly 61% of all. Of these, 31 have two myopic parents, 12 – one myopic parent, 10 – a brother or sister with myopia, and only 3 – a grandmother or grandfather with myopia. In terms of age, the patients were divided into 2 groups – aged between 8 and 12 years and aged between 13 and 16 years. The number of patients in both groups was similar – 44 patients in the 13-16 group and 48 – 8-12 years.

In terms of the prevalence of moderate and high-grade myopia, we observed a higher frequency among the group of patients aged between 13-16 years – 25 children and adolescents had high-grade myopia compared to 10 in the younger group. Nineteen patients in the 13-16 group had low-grade myopia, compared to 38 in the other group.

Sample – power calculation and justification

A total of 92 patients with myopia participated in the study, divided into four therapeutic groups. The average age of the participants was 11.57 ± 2.52 years, with no statistically significant difference between the groups (p>0.05). The groups were also balanced by myopia degree and gender, which reduced the risk of systematic bias in the analysis of the results. The distribution of participants by group was approximately equal in each treatment category.

The sample size was pre-calculated using a power analysis performed using G*Power 3.1. With the set values of $\alpha=0.05$, power $(1-\beta) = 0.80$ and expected mean effect (f) = 0.30 (medium to moderate Cohen effect size), we calculated that the minimum number of participants required for a one-way ANOVA with 4 groups was 88 to detect a statistically significant difference between them. The current study included 92 participants, which provided sufficient statistical power and minimized the risk of type II error. This allowed us to perform a reliable comparative analysis between treatment groups.

For an objective comparison between treatment groups, we used the indicator change in spherical equivalent (ΔSE) in diopters. The mean ΔSE for each group was calculated as the arithmetic mean of the values for the right (OD) and left (OS) eyes. The results showed the following mean values: Ortho-K -7.25 D, monofocal glasses (control group) -5.50 D, multifocal contact lenses -4.50 D and atropine drops -5.94 D. The values indicate that the groups are comparable in myopia severity, with the differences between them being within the clinically acceptable range for an interventional comparison. This balancing of the degree of refractive error between the groups is important for the reliability of subsequent analyses. The mean age of the participants by group ranged between 10.48 and 13.08 years, with the lowest mean age being in the atropine drops group and the highest - in the multifocal contact lens group. The difference is within 2.6 years, which is considered acceptable in the study of children and adolescents. This ensures balance between the groups and minimizes the risk that the age factor will significantly affect the results.

4.2 Assessment of quality of life in patients with myopia before and after the introduction of a control device.

The quality of life of the patients included in the study was assessed using questionnaires specially designed for the purposes of this scientific work. The main parameters of the study were the attitude towards the respective myopia control device, the ease of handling and management by the patients, their overall vision, as well as vision for near and far distance separately, the perception of their peers and relatives, their subjective symptoms and the impact on their appearance, school activities, hobbies and extracurricular activities.

The Cronbach's alpha of the questionnaire for all 10 factors is higher than 0.6, which indicates acceptable internal consistency. Significantly higher scores were reported for overall, near and distance vision, appearance, attitude, activities and hobbies, handling and perception for soft contact and ortho-K lens wearers than for spectacle wearers (p-value<0.05). No significant difference was found between the groups of ortho-K and soft contact lens wearers for any factor (p>0.05). Regarding attitude, handling, overall vision, symptoms and school environment, we did not observe statistically significant differences between the control group and the atropine drops group (p>0.05).

Table 1. Reliability of the factors included in the PREP questionnaires (Cronbach's alpha), distributed according to the control method.

Category	**Cronbach's alpha**			
	Monofocal glasses (n=19)	Atropine drops (n=20)	Multifocal CL (n=29)	Ortho-K lenses (n=24)
Attitude	0.802	0.712	0.623	0.625
Handling	0.723	0.722	0.719	0.725
Overall vision	0.815	0.819	0.713	0.747
Perception	0.892	0.709	0.612	0.632
Symptoms	0.840	0.826	0.731	0.724
Near distance vision	0.722	0.842	0.743	0.765
Appearance	0.889	0.612	0.602	0.603
Far distance vision	0.856	0.656	0.612	0.628
School environment	0.898	0.821	0.621	0.619
Activities and hobbies	0.893	0.778	0.611	0.613

The worst results, especially in terms of handling, overall vision, symptoms and appearance, were observed in the atropine drops group and the control group, as well as in terms of performance in a school environment and regarding extracurricular activities and hobbies. The best results were reported in the groups corrected with MCL and ortho-K lenses in all parameters, without exception. We did not find a statistically significant difference between these two methods of myopia control (p>0.05).

Table 2. Statistical significance of the PREP results of the participants with myopia in the study, categorized according to their myopia control means - p-value.

*Glasses – Monofocal glasses; MCL – Multifocal contact lenses

Category	P-value					
	Glasses vs. MCL	Ortho-K vs. Glasses	Ortho-K vs. Atropine drops	Ortho-K vs. MCL	Glasses vs. Atropine drops	Atropine drops vs. MCL
Attitude	<0.001	<0.001	0.89	0.90	0.75	<0.001
Handling	0.001	0.08	0.07	0.88	0.88	0.001
Overall vision	0.05	0.01	0.78	0.45	0.89	0.01
Perception	<0.001	<0.001	0.06	0.39	0.03	<0.001
Symptoms	0.03	0.81	0.08	0.06	0.92	<0.001
Near distance vision	0.06	0.05	0.05	0.06	0.03	0.03
Appearance	<0.001	0.001	0.43	0.40	0.04	<0.001
Far distance vision	<0.001	<0.001	0.65	0.75	0.03	<0.001

School environment	0.32	0.65	0.68	0.87	0.88	0.92
Activities and hobbies	<0.001	<0.001	0.64	0.73	0.78	0.01

The Cronbach's alpha of the SCARED questionnaire for all factors was between 0.623-0.992, indicating acceptable internal consistency. Significantly worse scores on the anxiety questionnaire were given by monofocal spectacle wearers for symptoms, shyness and performance than in comparison with contact lens wearers in all groups, including the atropine drops group (p-value < 0.05).

Table 3. Reliability of the factors included in the questionnaires (Cronbach's alpha), distributed according to the correction factor (SCARED questionnaire).

Category	**Cronbach's alpha**			
	Monofocal glasses (n=19)	Atropine drops (n=20)	Multifocal CL (n=29)	Ortho-K lenses (n=24)
Symptoms (headache, stomachache, sweating, dizziness in school.)	**0.992**	**0.768**	**0.753**	**0.743**
Shyness (having troubles when in contact to new people or places, feeling tense and etc.)	**0.848**	**0.683**	**0.623**	**0.713**
Performance (worrying over other people's opinion, achievements and presentation, doing any activities in front of other people and etc.)	**0.891**	**0.633**	**0.751**	**0.753**

The following figure displays the results of the SCARED questionnaires, which indicate various mood or mental health disorders among the participants in this study. Monofocal spectacle wearers had the highest anxiety scores among all other participants – median=26 ($p<0.05$), followed by the atropine drops group – median=15. No statistically significant difference was observed between multifocal contact lens wearers and Ortho-k wearers – median=2 for both groups ($p>0.05$). Students with spectacles showed higher levels of anxiety than multifocal CL wearers (26 (2, 28) vs. 2 (2, 8), p=0.001), the atropine drops group (26 (2, 28) vs. 15 (2, 20), p=0.020) and Ortho-k wearers (26 (2, 28) vs. 2 (2, 10), p=0.003).

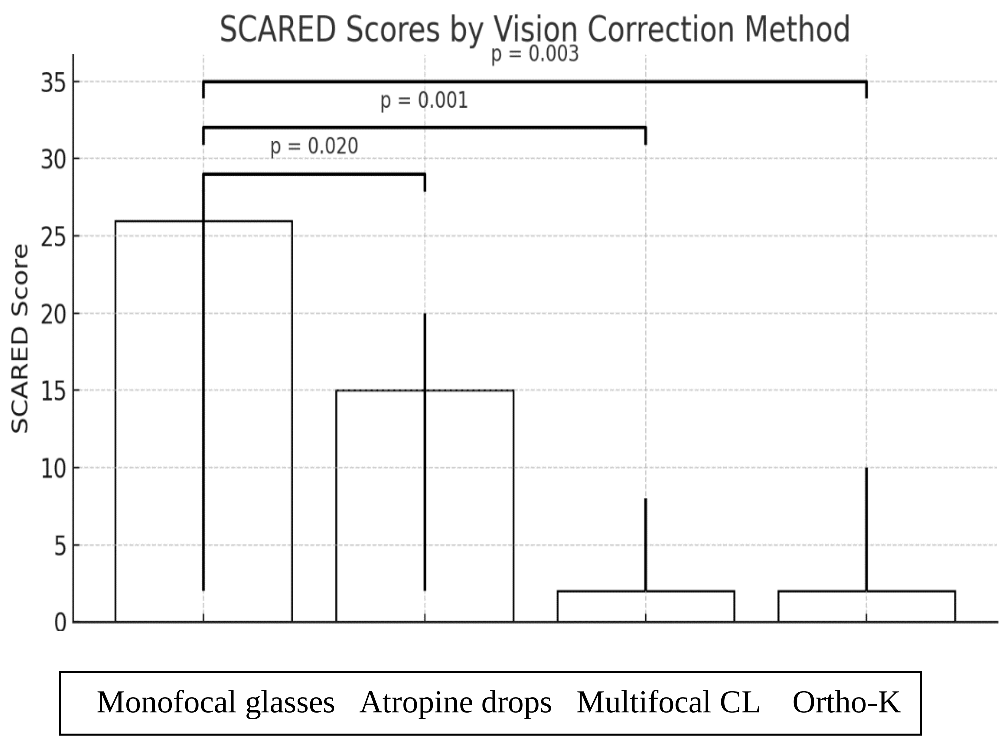

Figure 3. SCARED scores (median) of the participants in this study, distributed by the mean for myopia contol.

On the following table, we present the results of the completed questionnaires, distributed by category according to the choice of myopia control aid (Table 4). Quantitatively, we can once again observe that the monofocal glasses group showed worse results overall compared to all other patient groups.

Table 4. Results of the completed questionnaires distributed by categories.

0-164	Median			
Randomized groups	Monofocal glasses (n=19)	Atropine drops (n=20)	Multifocal CL (n=29)	Ortho-K lenses (n=24)
Attitude	3,5	3	1	1
Handling	12	10	3	4
Overall vision	10	10	3	3
Perception	7	1	1	0
Symptoms	13	12	3	4
Near distance vision	4	5	1	1
Appearance	10	1	1	1
Far distance vision	5	4	1	1
School environment	4	5	0	0
Activities and hobbies	6	4	2	1

The distribution of patients in terms of the corrective device and the results obtained from the anxiety questions arrays the worst results in the groups of patients with glasses (median - 26) and atropine drops (median - 15), and the best - in the group of children and adolescents fitted with contact lenses - MCL (median - 2) and ortho-K (median - 2) separately. According to the dispersal in terms of the lowest quality of life, represented by the worst results of the questionnaire for quality of vision and mood disorders and anxiety levels, we noted a significantly higher percentage of participants (total n = 34) from the control group - 61.77% of 34 patients, who had the lowest results in terms of quality of vision and anxiety score. The results of participants with lower quality of life, based on the results of the questionnaire, were calculated for each group separately and represents 36.96% of all participants (34 out of 92 patients). Fifteen of these patients were from the monofocal glasses group – 44.12%; 12 from the atropine drops group – 35.29%, 3 from the Ortho-K group – 8.83% and 4 from the multifocal CL wearers – 11.76%. We did not report a significant difference between the multifocal and Ortho-K lens wearers ($p>0.05$). Patients with myopia above -6.00 D had the highest anxiety scores and lower visual quality among all participants with myopia – myopia of -6.00 D represented 76.47% of the total score in the patients with the lowest scores (n=26/34), and -4.50 D for the remaining 23.53% (n=8/34). We did not find a statistically significant difference between the scores obtained by the parents and those provided by the children ($p>0.05$).

4.3 Assessment of subjective symptoms of myopic patients included in the study.

When examining patients with myopia, the following indicators were used to assess subjective symptoms: blurred vision, headache and pain. They were monitored before the appointment of the respective control method and every 6 months for a period of 2 years.

The results reveal that 19.56% of patients experienced pain before the appointment of a certain method for myopia control, 57.61% had blurred vision, 26.09% - headache. A significant positive impact on the pain syndrome, followed by blurred vision, was observed already at the sixth month after randomization in a certain group, with only 4.35% reporting pain, 14.13% - for blurred vision and 9.78% - for headache. A statistically significant difference was found regarding the perceptions of pain and blurred vision in patients with different degrees of myopia, regardless of the method of myopia control before treatment and at the sixth month after randomization to a specific group ($p<0.001$), at the first year of application of a control method ($p<0.001$) and at the second year ($p<0.001$). It is striking that a large proportion of patients in the atropine drops group continued to report blurred vision and headache, which is probably due to the side effects of the drop therapy - in terms of blurred vision at the sixth month - 69.23% of all reported were patients using atropine drops (n=9), and in terms of headache - 77.77% (n=7). In the first year of the study, 3.26% had pain, 10.87% had blurred vision (atropine drops group: n=6), and 7.61% had headaches, with the highest proportion again being in the atropine group (n=5). In the second year, patients reported no pain, 7.61% had blurred vision, and 4.35% had headaches, with the highest rates again being in the pharmacological agent group (n=4 and n=2, respectively) ($p<0.001$).

In summary, we found a statistically significant difference in the perceptions of blurred vision and pain in patients with different degrees of myopia ($p<0.001$). The most prominent subjective symptoms before randomization in a certain group was observed in patients with high-grade myopia – 83.33% of all patients with myopia ≥-6.00 diopters reported pain at the beginning of the study (n=15 out of 18), 37.74% - blurred vision (n=20 out of 53) and 79.16% - headache (n=19 out of 24).

4.4 Evaluation and analysis of the efficacy of the introduced approach to control myopia.

Knowledgeable from the literature review, the values of the spherical equivalent and axial length are objective signs of progression and are also used as criteria for the efficacy of the applied method for myopia control and for its progression rates.

Table 5. Mean values of the axial length and visual acuity of the patients included in the study, before the introduction of a method for myopia control.

Parameter	Count	Mean value	Standard deviation	Min	25%	50% (Median)	75%	Max
Age	92	11.57	2.52	8	9	12	13	16
OD Axial lenght	92	24.59	1.28	22.11	23.58	24.45	25.57	27.61
OS Axial lenght	92	24.76	1.22	22.10	23.75	24.78	25.73	27.86
Visual acuity (OD/OS)	92	0.92	0.15	0.5	0.8	1.0	1.0	1.0

We did not observe any significant differences in the values of axial length and visual acuity between the individual groups before the introduction of the respective myopia control method.

Concerning the axial length, the average values for the left and right eyes at baseline and 2 years after the application of a certain control method look as follows.

Table 6. Progression in the mean value of the axial length of the right and left eyes before applying a myopia control method and on the second year of the study, divided into groups with different applied methods and a control group with monofocal glasses.

Timeframe	Method	Mean axial length OD (mm)
Baseline	OrthoK	25.73
Baseline	Atropine	24.37
Baseline	MCL	24.22
Baseline	Spectacles	23.92
2 year	OrthoK	26.13
2 year	Atropine	24.88
2 year	MCL	24.85
2 year	Spectacles	24.66
Timeframe	**Method**	**Mean axial length OS (mm)**
Baseline	OrthoK	25.21
Baseline	Atropine	23.45
Baseline	MCL	24.50
Baseline	Spectacles	24.71
2 year	OrthoK	25.61
2 year	Atropine	24.09
2 year	MCL	25.02
2 year	Spectacles	25.57

As for the visual acuity, we obtained the following data.

Table 7. Progression in the mean value of visual acuity of the right and left eyes before the introduction of a myopia control method and on the second year of the study, divided into groups with different applied methods and a control group with monofocal glasses.

Timeframe	Method	Mean Visual Acuity OD	Mean Visual Acuity OS
Baseline	OrthoK	0.825	0.825
Baseline	Atropine	0.905	0.905
Baseline	MCL	0.972	0.972
Baseline	Spectacles	0.968	0.968
2 year	OrthoK	0.838	0.838
2 year	Atropine	0.915	0.915
2 year	MCL	0.979	0.979
2 year	Spectacles	0.968	0.968

Visual acuity remained almost unchanged for all groups. The changes in the mean values of the right and left eyes in axial length and spherical equivalent before application of a certain method for myopia correction and every six months for a period of two years are presented in tabular form. The smallest progression in axial length was observed in the groups with Ortho-K lenses and atropine drops, and the highest – in the control group with glasses ($p<0.001$).

Table 8. Progression in the mean value of axial length and spherical equivalent of the right and left eyes before the introduction of a myopia control method and every six months for a period of 2 years, divided into groups with different applied methods and a control group with monofocal glasses.

Parameter	Control method	Baseline	6 months	1 year	1y. 6m.	2 years
ΔAL OD (mm)	OrthoK lenses	25.73	25.83	25.92	26.04	26.13
ΔAL OS (mm)	OrthoK lenses	25.21	25.32	25.42	25.51	25.61
ΔAL OD (mm)	Monofocal spectacles	23.92	24.13	24.34	24.45	24.66
ΔAL OS (mm)	Monofocal spectacles	24.71	24.92	25.13	25.35	25.57
ΔAL OD (mm)	MCL	24.22	24.38	24.54	24.70	24.85
ΔAL OS (mm)	MCL	24.50	24.65	24.80	24.96	25.02
ΔAL OD (mm)	Atropine drops	24.37	24.52	24.67	24.72	24.88
ΔAL OS (mm)	Atropine drops	23.45	23.61	23.77	23.93	24.09
ΔSE OD (D)	OrthoK lenses	-7.25	-7.30	-7.35	-7.40	-7.45
ΔSE OS (D)	OrthoK lenses	-7.25	-7.30	-7.35	-7.40	-7.45
ΔSE OD (D)	Monofocal spectacles	-5.25	-5.50	-5.75	-6.00	-6.25
ΔSE OS (D)	Monofocal spectacles	-5.75	-6.00	-6.25	-6.50	-6.75
ΔSE OD (D)	MCL	-4.25	-4.50	-4.75	-5.00	-5.25
ΔSE OS (D)	MCL	-4.75	-4.75	-5.00	-5.25	-5.50

ΔSE OD (D)	Atropine drops	-5.88	-6.02	-6.15	-6.30	-6.45
ΔSE OS (D)	Atropine drops	-6.00	-6.14	-6.30	-6.45	-6.60

Table 9. Confidence interval of the mean values of progression of axial length and spherical equivalent, reported at the end of the study by applied method for myopia control.

Method	Mean Δ (мм)	Mean Δ (D)	Standard deviation	n
Spectacles	0.51±0.31	1.00±0.25	0.0088	19
OrthoK	0.19±0.22	0.26±0.02	0.0053	24
MCL	0.42±0.23	0.50±0.06	0.0072	29
Atropine	0.29±0.33	0.40±0.65	0.0088	20

When distributing the patients by myopia control methods, it is clear that the smallest average progression of axial length and spherical equivalent was observed in the Ortho-K lens group, followed by the atropine drops group. We recorded a larger average progression in the group corrected with MCL and the highest – in the control group of patients with monofocal spectacles.

Table 10. ANOVA analysis of the progression in axial length of the right and left eyes.

Factor	p-value	η^2 (effect size)
Method	**< 0.001**	**0.243**
Time	0.571	0.005
Method × Time	1.000	0.005

The analysis of variance revealed that the applied methods for myopia control had a statistically significant effect ($p < 0.001$). We did not observe a statistically significant difference in terms of the time of application of the specific control approaches, nor in terms of the combination of a specific method and time of action.

As of the progression in the mean values of the spherical equivalent reported in this study, we found statistically significant differences between the different applied control methods. The results are presented in tabular form.

Table 11. Post-hoc analysis (Tukey HSD) for Δ SE for the right eye (OD).

Comparison	Difference (mean)	p-value
Atropine – MCL	-0.229	0.018
Atropine – OrthoK	-0.195	0.227
Atropine – Glasses	-0.375	0.002
MCL – Glasses	-0.325	0.019
OrthoK – MCL	-0.342	0.012
OrthoK– Glasses	-0.425	0.001

As we can see from the results, the atropine therapy group showed a statistically significant smaller progression in SE values for the right eye compared to the MCL group ($p<0.05$) and the control group ($p<0.05$). Similar results were observed in the Ortho-K lens group ($p<0.05$; $p\leq0.001$).

Table 12. Post-hoc analysis (Tukey HSD) for Δ SE for the left eye (OS).

Comparison	Difference (mean)	p-value
Atropine – MCL	-0.288	0.009
Atropine – OrthoK	-0.153	0.403
Atropine – Glasses	-0.392	0.002
MCL – Glasses	-0.319	0.018
OrthoK – MCL	-0.365	0.009
OrthoK– Glasses	-0.437	0.001

The results once again display a statistically significant difference - the atropine therapy group shows a smaller progression in SE values for the left eye compared to the MCL ($p<0.05$) and the control group ($p<0.05$). Similar results can be observed in the Ortho-K lens group ($p<0.05$;$p=0.001$).

Apropos the change in the mean values of axial length of the right eye compared to the introduced method for myopia control, we have reported the following results.

Table 13. Post-hoc analysis (Tukey HSD) - for Δ AL for the right eye (OD).

Comparison	Difference	p-value
Atropine – MCL	-0.086	0.007
Atropine – Glasses	-0.203	0.001
Atropine – OrthoK	-0.170	0.001
MCL – Glasses	-0.085	0.060
OrthoK – MCL	-0.241	0.0004
OrthoK– Glasses	-0.410	0.0001

When comparing the different methods for myopia control, the data obtained stipulates that the group of patients using atropine drops had a statistically significant difference in the mean values of progression in the axial length of the right eye compared to the group with MCL ($p<0.05$) and the control group ($p=0.001$). The same results were observed for the group with Ortho-K lenses ($p=0.001$; $p=0.001$). We did not find a statistically significant difference in the progression of the axial length for the right eye between the control group and the MCL group and between the atropine – Ortho-K lens groups.

Table 14. Post-hoc analysis (Tukey HSD) – for Δ AL for the left eye (OS).

Comparison	Difference	p-value
Atropine – MCL	-0.074	0.007
Atropine – Glasses	-0.167	0.001
Atropine – OrthoK	-0.133	0.004
MCL – Glasses	0.007	0.983
OrthoK – MCL	-0.259	0.0004
OrthoK– Glasses	-0.426	0.0001

From the obtained data, we can observe that the group of patients using atropine drops has a statistically significant difference in the mean values of progression in the axial length of the right eye compared to the group with MCL ($p<0.05$) and the control group ($p=0.001$). Similar results are observed for the group with Ortho-K lenses ($p<0.001$; $p<0.001$). There is no statistically significant difference in the progression of ΔAL for the left eye between the control group and the MCL group, as well as between the atropine – Ortho-K lens groups. The group of patients with Ortho-K lenses shows significantly the lowest progression of axial length and spherical equivalent, followed by the atropine therapy group, especially compared to the MCL and the control group.

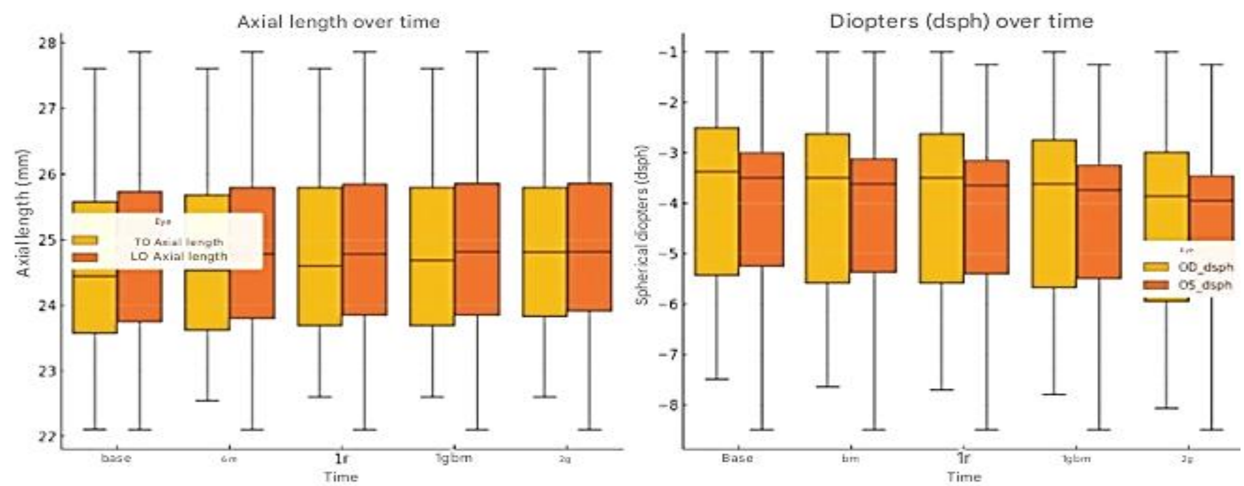

Figure 4. Box-plot graphical comparison of the change in axial length and spherical equivalent over time for the right and left eyes.

As it becomes clear from the graph, there is a visible trend for an increase in the axial length, which is more prominent after the first year of application of a myopia control method. The values of the spherical equivalent show a decrease (more negative values), which is expected with progressive myopia. We observed the greatest retention of values until the first year of application of an introduced control method.

Table 15. T-test with Holm correction for right eye (OD) and left eye (OS) between Ortho-K lenses and the other patient groups.

Comparison (OD)	p	Comparison (OS)	p
Ortho-K vs Control group	0.0011	**Ortho-K vs Control group**	0.0009
Ortho-K vs Atropine	0.117	**Ortho-K vs Atropine**	0.049
Ortho-K vs MCL	0.043	**Ortho-K vs MCL**	0.021

Table 16. Effect sizes (Cohen's d).

Comparison (OD)	d	Comparison (OS)	d
Ortho-K vs Control group	1.54	**Ortho-K vs Control group**	1.47
Ortho-K vs Atropine	0.61	**Ortho-K vs Atropine**	0.70
Atropine vs Control group	1.15	**Atropine vs Control group**	1.23

Values above 0.8 are considered to connect to a large effect, indicating that Ortho-K lenses and atropine drops have a real large effect compared to the control group. We have reported a mean effect when comparing the groups of patients with Ortho-K lenses and atropine drops of 0.61 for the right eye and 0.70 for the left eye, respectively.

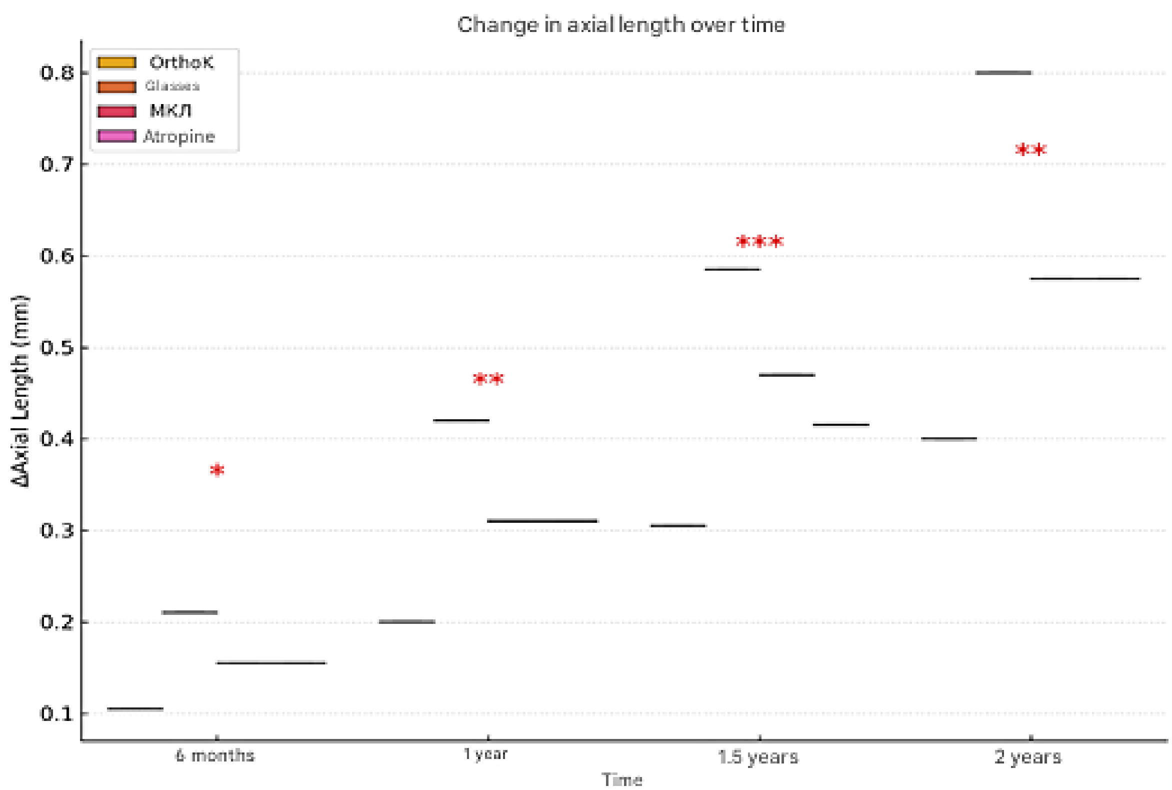

Figure 5. Box-plot depicting the change in axial length over time, depending on the method for myopia control.

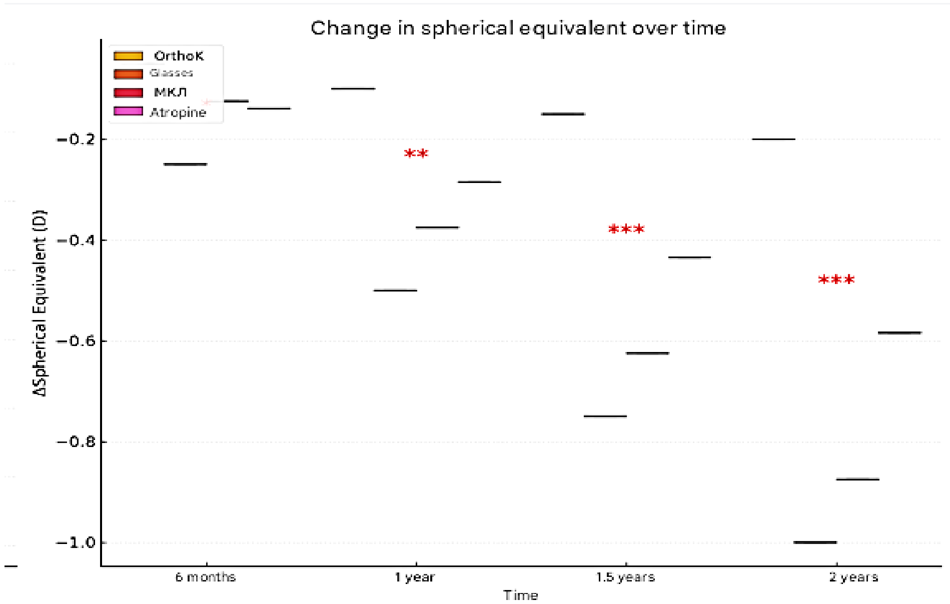

Figure 6. Box-plot depicting the change in spherical equivalent over time, depending on the myopia control method.

From Figures 5 and 6 it is clear that the group of patients with Ortho-K lenses had the smallest progression in axial length values, patients on atropine drops had relatively small increases in values, and the control group and patients with MCL showed greater axial elongation. Regarding spherical equivalent, Ortho-K and atropine drops again showed the smallest changes, suggesting the best delay in progression. Spectacles and MCL showed a greater negative progression.

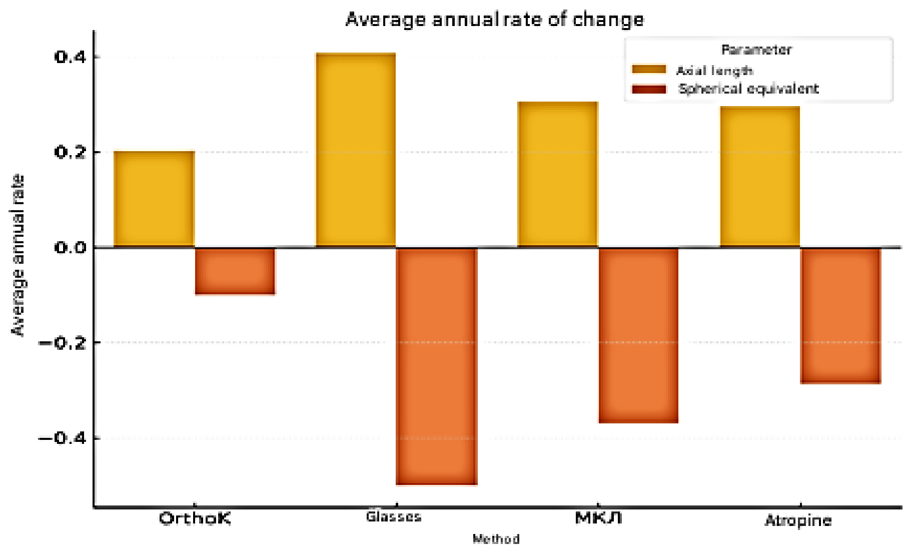

Figure 7. Average annual rate changes in AL and SE depending on the control method.

Fig. 7 displays that the Ortho-K group had the lowest rate of axial length gain, indicating that those lenses were most effective in slowing myopia progression. Spectacles showed the highest axial growth and refractive error shift, suggesting that they were the least effective in controlling progression. Atropine and MCL fell in the middle, with atropine showing better control of SE than axial length.

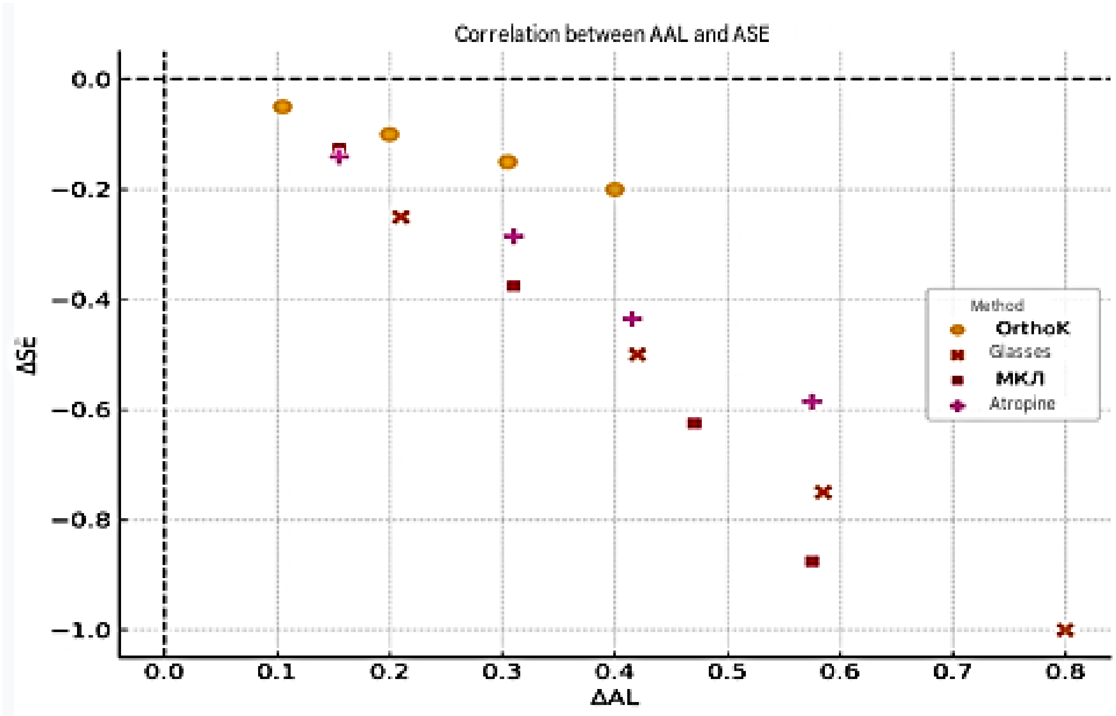

Figure 8. Correlation between the axial length and spherical equivalent values of the patients from the study by groups.

There is a positive correlation observed - as axial length increases, spherical equivalent becomes more negative. Ortho-K maintains a tight, clustered pattern, suggesting stable control. Spectacles and MCLs show a wider range, indicating greater variability and less effective control than Ortho-K lenses. This figure confirms the biological relationship between the elongation of the anterior-posterior axis of the eye and refractive error and shows that Ortho-K provides the most consistent control for both parameters.

Regarding the age of the patients included in the cohort study, we observed a faster progression in spherical equivalent and axial length values in the group of patients between 8 and 12 years of age.

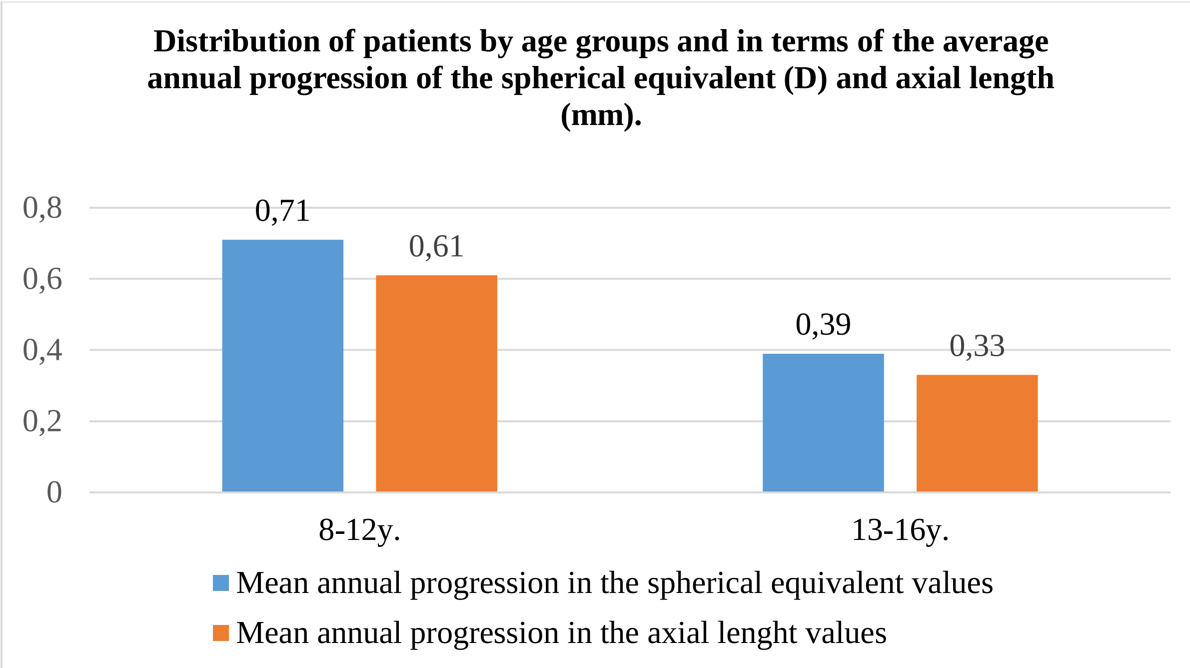

Figure 9. Distribution of patients by age groups and in terms of the average annual progression of the spherical equivalent and axial length.

As for the gender of the patients included in the study, we observed a faster progression in spherical equivalent and axial length values in the female patient group.

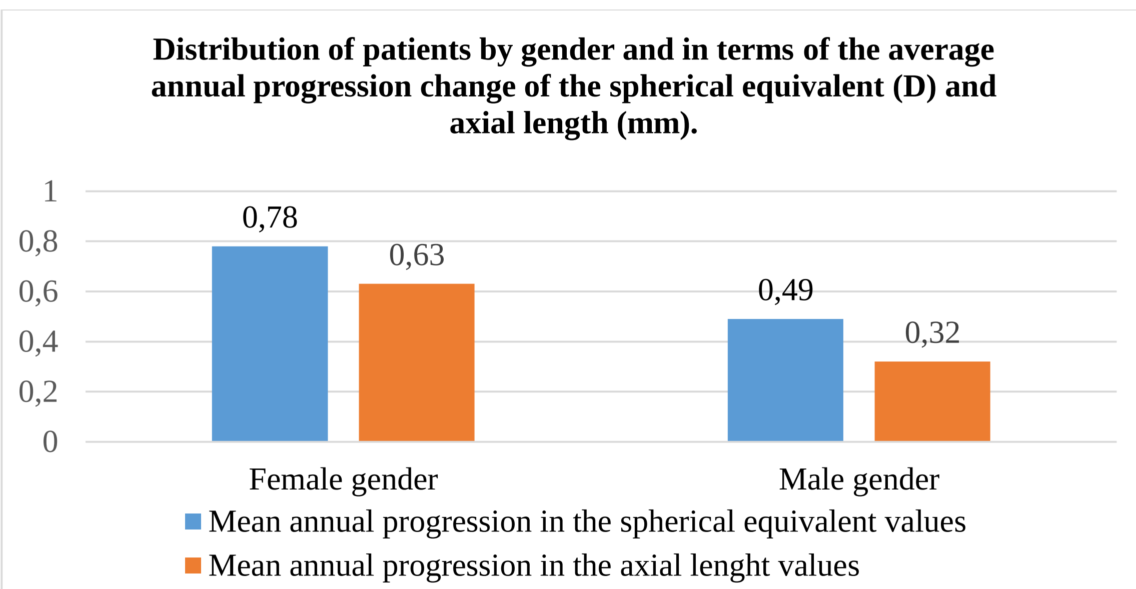

Figure 10. Distribution of patients by gender and in terms of the average annual progression change of the spherical equivalent and axial length.

4.5 Evaluation of data obtained from highly specialized studies

Using optical biometry and corneal topography, we investigated various ocular biometric parameters including axial length (AL), central corneal thickness (CCT), anterior chamber depth (ACD), corneal curvature (CC), corneal curvature radius (CR), axial length to corneal radius ratio (AL/CR ratio).

At baseline, the mean values measured for anterior chamber depth were 3.57±0.33 mm and 19.96±1.42 mm for vitreous depth. After 2 years of follow-up, a trend towards greater axial elongation was observed in all age groups. Younger participants had significantly ($p<0.001$) higher levels of myopic shift and axial elongation compared to older participants (>16 years).

The results of our study revealed a significant increase in axial length, axial length to corneal radius ratio and anterior chamber depth in both the low- and high-degree myopia groups. Corneal curvature also showed increased mean values, while central corneal thickness and corneal radius of curvature were decreased.

In the low-degree myopia group, anterior chamber depth increased together with the increasing axial length (Pearson coefficient=0.338, $p<0.01$). In the high-myopia group, we did not find a correlation with axial length (Pearson coefficient=0.057, $p=0.233$). We obtained similar values of corneal curvature for both eyes and found a correlation between refractive error and axial length (Pearson coefficient =−0.579, $p<0.001$), but not with corneal curvature.

We compared the results obtained from IOLMaster and Pentacam concerning the measured values of anterior chamber depth, keratometry and astigmatism and evaluated them by a paired t-test. The results are presented on Table 17 and Table 18, as well as on the following figure, presenting the optical biometry and corneal topography of a patient included in the study.

Table 17. Measured mean values of various anterior segment parameters by IOLMaster and Pentacam.

Parameter	Confidence interval	p-value
Axial lenght (mm)	**24.67±2.53**	**<0.001**
Anterior chamber depth (mm), **IOLMaster**	**3.56±0.31**	**<0.001**

Anterior chamber depth (mm), **Pentacam**	**3.59±0.32**	**<0.001**
K1 (D), **IOLMaster**	**42.53±1.53**	**<0.001**
K1 (D), **Pentacam**	**42.47±1.47**	**<0.001**
K2 (D), **IOLMaster**	**43.83±1.37**	**<0.001**
K2 (D), **Pentacam**	**43.71±1.24**	**<0.001**
Mean K (D), **IOLMaster**	**43.18±1.39**	**<0.001**
Mean K (D), **Pentacam**	**43.09±1.42**	**<0.001**
Astigmatism (D), **IOLMaster**	**1.33±0.15**	**<0.001**
Astigmatism (D), **Pentacam**	**1.31±0.19**	**<0.001**

Table 18. Comparison of measured mean values of anterior segment parameters measured by IOLMaster and Pentacam.

Parameter	IOLMaster	Pentacam	p-value
Anterior chamber depth (mm)	**3.56±0.31**	**3.59±0.32**	**0.270**
K1 (D)	**42.53±1.53**	**42.47±1.47**	**0.001**
K2 (D)	**43.83±1.37**	**43.71±1.24**	**0.001**
Mean K (D)	**43.18±1.39**	**43.09±1.42**	**<0.001**
Astigmatism (D)	**1.33±0.15**	**1.31±0.19**	**0.476**

Both devices did not demonstrate a statistically significant difference in determining the depth of the anterior chamber (p=0.270). With IOLMaster we observed steeper K1 values and higher mean ▲K values than Pentacam (p=0.001; p<0.001). We did not remark a statistically significant difference between the two devices when measuring patients with astigmatism (p=0.476). In the next few figures we present the examinations performed on patients included in the study.

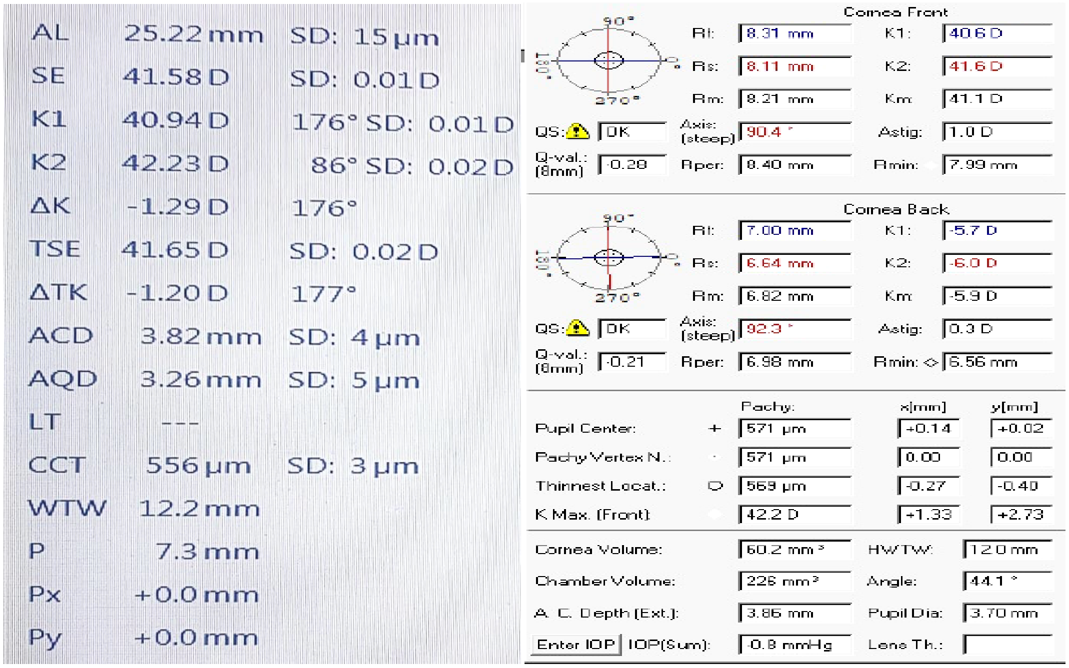

Figure 11. Results of the optical biometry (left) and corneal topography (right) of the right eye of a 9-year-old male patient included in the study.

4.6 Creating a risk profile of the studied patients with myopia and predicting the risk of progression.

High-grade myopia is socially significant and could lead to considerable structural and visual changes in the sight analyzer. Of key importance for the expected visual outcomes is its efficient control of progression, as well as a timely application of a certain approach for myopia control and its correct assessment of efficacy in individual patients. It is important for clinicians to know about the individuals at risk, as well as which factors have the strongest influence on the onset and progression of myopia.

Table 19 presents the risk profile of the patients with myopia included in the study for predicting the risk of progression.

Table 19. Risk analysis for myopia progression.

Parameter	OR	95% CI	p
SE ≤ - 6.00 D	6.43	2.03-15.36	<0.001

Age of onset ≤ 13 y.	4.19	2.57-6.08	0.001
Annual progression of SE ≤ -1.00 D	3.43	1.06-5.43	0.001
Time spent outdoors <1h on a daily basis	1.00	/	>0.05
Activities at a close range distance h/day >10h	1.27	0.79-2.05	>0.05
Parents with myopia (n=2)	2.57	1.62-3.68	<0.001
Female gender	1.83	1.02-3.28	<0.001

Throught the obtained data, we found that the risk profile for myopia progression includes female gender, two myopic parents, annual progression in SE ≤1.00 D, younger age of onset - ≤ 13 years and spherical equivalent (SE) values ≤ 6.00 D. We did not find a statistically significant difference in terms of intensive near-distance activities, nor in time spent outdoors. From the surveys conducted, the average hours per day spent working at near distance of the study patients were 6.65±3.78 hours/day and the time spent by doing outdoor activities - 2.15±1.73 hours/day. A surprising trend that we noted in our study is the high number of parents who prefer glasses as a means of correction (n=57), followed by contact lenses (n=20) and the observed low trust in the doctor's assessment (n=15) regarding the choice of correction device, after completing the survey questionnaires.

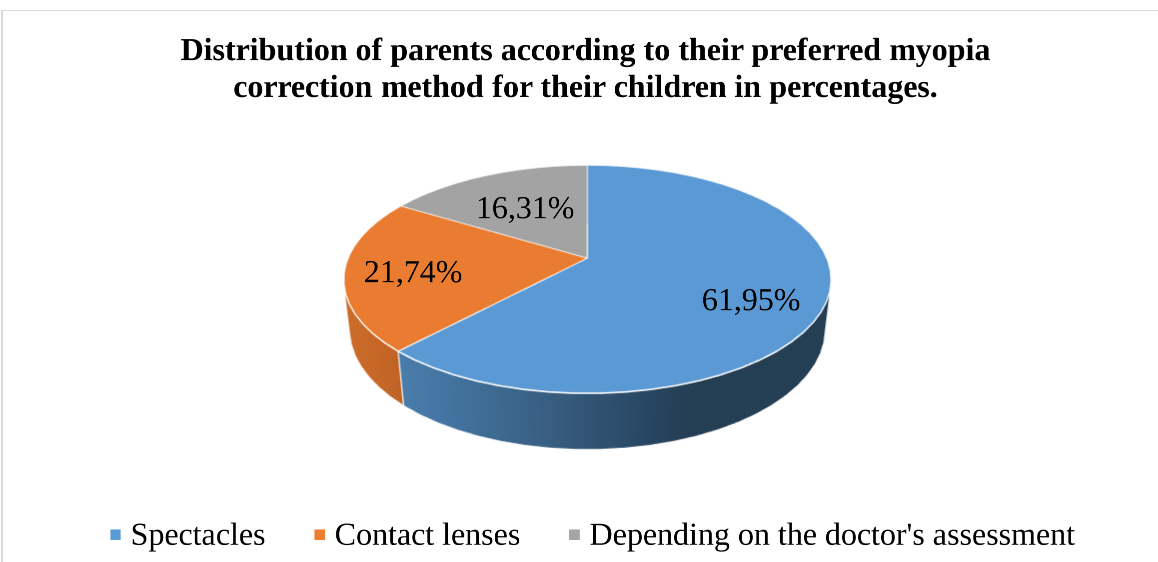

Figure 12. Distribution of parents according to their preferred myopia correction method for their children in percentages.

The highest number of parents chose soft contact lenses for myopia control (n=30), with the results for the other types of methods being similar - atropine drops (n=23), Ortho-K (n=20) and 19 parents noted that they were not sufficiently informed.

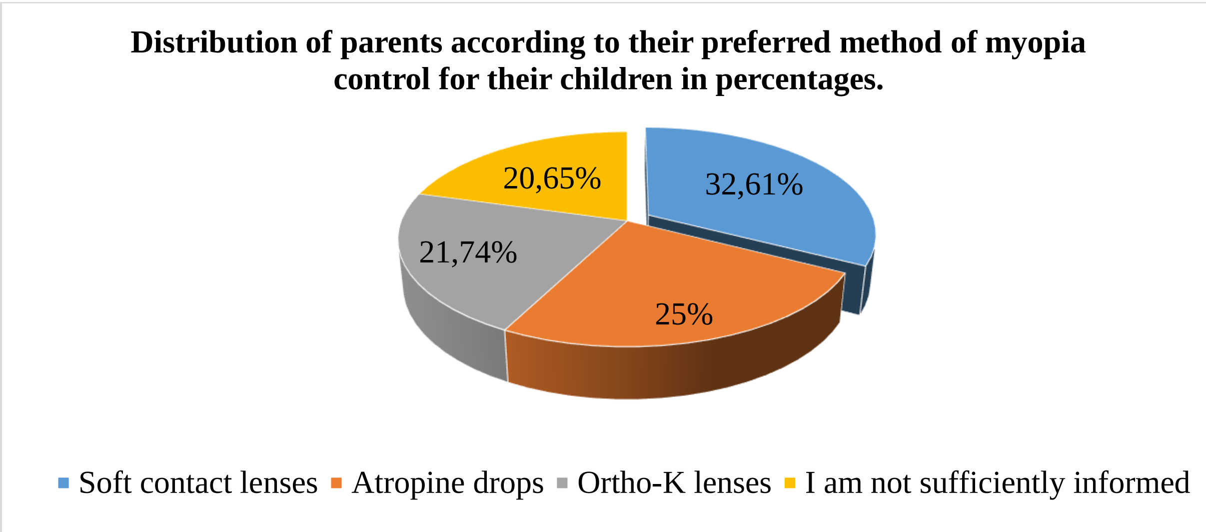

Figure 13. Distribution of parents according to their preferred method of myopia control for their children in percentages.

CHAPTER V. DISCUSSION

As we have already established from the literature review, myopia and its progressive incidence represent a global problem of high social and economic importance. The possible complications and disorders of the visual functions and ocular structures have led to international efforts to form clinical recommendations, trials of new and safer means of control, establishing the highest efficacy of such already familiar means and scientific research on hypotheses about the onset and progression of myopia, as well as the risk factors for its progression. Public attention is often focused on this very contemporary issue, preventive examinations for early diagnosis are often carried out in different countries and there are a number of campaigns to promote good eye and vision hygiene, as well as to eliminate behaviors that put individuals at risk of onset and progression. Myopia correction with glasses, contact lenses and refractive surgery has an increasingly important role in society, as uncorrected myopia leads to a decrease in visual acuity, which in turn leads to impaired visual function, as mentioned by authors of myopia studies in our country (14) (15) (16). Whether it is a question of controlling myopic progression or correcting refractive error, there are significant costs issues associated with optical and pharmacological correction, as well as with the treatment of complications related to myopia, including pathological myopia, cataracts, glaucoma, and retinal detachment (14) (16). With the increasing demand on the already limited health resources worldwide, understanding the economic costs is important for further cost-benefit analysis, decision-making, justifying the allocation of invaluable health resources and for reducing the economic burden of this type of ametropia.

The World Health Organization (WHO) considers spectacles or contact lenses as functional interventions and spectacles are also considered an assistive device, which is part of the WHO list of priority assistive products (2). Health care costs are a major concern in many countries and understanding the costs of myopia correction is of utmost importance for each country separately. Of particular urgency for developing countries or for specific populations with high prevalence of myopia and limited access to correction and control measures, as well as low per capita household income, is the analysis of treatment costs (2) (17). The latter would in turn reduce the burden of disease costs and help to allocate health system resources efficiently. There is a need for individual country considerations for integrating eye care into universal health coverage, especially for at-risk populations. Importantly, although the per capita costs are not very high, the high-rise incidence and prevalence of myopia play a role in determining the economic cost of its treatment in each country. In addition, the differentiation of costs for regular visits to an eye care provider and for devices for correction and control of refractive error also varies. When studying a pediatric population, one should also take into account the preferences and attitudes of parents regarding different types of correction and control devices. When choosing contact lenses for a patient with myopia, one should be aware of the hidden costs, namely - professional fees, care solutions and, if necessary, moisturizing or anti-inflammatory drugs. We have not found studies in the literature on the cost analysis of the use of ortho-k lenses or atropine drops, similar to the Foo et al. (17). Such studies will be needed in the future to allow a clear and definitive assessment by specialists of the benefit:cost ratio.

The literature review revealed that myopic pediatric populations often have similar underlying risk factors for the onset and progression of the condition, which is important to more easily identify individuals at risk. Therefore, we decided to examine in more detail the socio-demographic characteristics of myopic patients from pediatric groups reported in other studies. In the following table, we have summarized the socio-demographic factors proposed by other authors for the prevalence of myopia, compared with the results of our study (18) (19) (20) (21) (22) (23) (24) (25) (26) (27) (28) (29) (30) (31).

Table 20. Summary of socio-demographic factors proposed by other authors for the prevalence of myopia, compared with the results of our study.

Parameter	**Literature review data**	**Data from our study**
Age	Under 10 years of age – progression by -0.20D/year to -0.70D/year faster than older children	8-12 year olds progression by -0.32D/year faster than the 13-16 year group.
Race	Latinos > Asians > African Americans > Caucasians	N/A
Gender	Female	OR 1.83; 56.52% from everyone
Annual progression	-0.50D to -0.90D/year	-0,50D
Parents with myopia	The higher the risk with more parents with myopia	Myopic parents (n=2) OR 2.57
Incidence and prevalence	In older children – higher prevalence	In older children (13-16 years old) – higher prevalence of high-grade myopia
Gender:progression rate	Faster progression in female patients	Female patients progressed -0.29D faster than male patients

The results of our study support the literature data. Regarding age, in our study we found a faster progression of -0.32D/year in children aged 8-12 years than in those aged 13-16 years. In female patients we observed both a higher prevalence (56.52%), higher myopic progression and more frequent high-grade myopia. The annual progression reported in our control group of patients is consistent with the range reported by other authors. We found that a higher number of myopic parents carries a greater risk of myopia progression. In our study, patients were of European origin only and we cannot make a comparison regarding race. The prevalence of high-grade myopia was higher in the group of patients aged 13-16 years than in the group of patients aged 8-12 years.

Recent studies have described a number of adverse comorbidities associated with myopia, including reduced quality of life, depression and sleep problems, and prominent subjective symptoms of individuals and study cohorts as a whole. A study by Iehisa et al. assessed the mental state and sleep habits in young subjects with myopia using a questionnaire containing the Pittsburgh Sleep Quality Index (PSQI), the Subjective Happiness Scale (SHS), the Short Morning/Evening Mood Questionnaire and the Hospital Anxiety and Depression Scale (HADS). SHS and HADS scores were significantly worse in the high myopia group than in the other two groups ($p<0.05$) and patients in this group experienced more dry eye symptoms (32). The authors of another study aimed to analyze the incidence and risk factors for dry eye in children from an outpatient myopia clinic using questionnaires (33). At a mean age of 10.1 ± 2.5 years, 34 of 214 children were diagnosed with dry eye, representing 15.9% of patients (33). The researchers found a significant difference in the correlation between eye rubbing and the incidence of dry eye in children ($Z = -2.747$, $p = 0.008$) (33). In addition, the study showed that there was a statistically significant correlation between the time spent looking at electronic products and meibomian gland morphology ($Z = -2.201$, $p = 0.028$) (33). The results showed that the effects of mild and moderate myopia on noninvasive tear production time in children were statistically significant ($Z = -2.027$; $p = 0.043$) (33). The study demonstrated that in outpatient myopia clinics, a high incidence of dry eye syndrome was observed in myopic children (33). In another study with a similar aim, dry eye and anterior ocular surface condition in myopic teenagers were assessed using a questionnaire and clinical examinations (34). A total of 248 myopic subjects (aged 7–18 years) completed the Ocular Surface Disease Index (OSDI) questionnaire and were examined clinically (34). The authors found that the prevalence of dry eye in myopic teenagers was 18.95% (34). Ping et al. searched PubMed, Cochrane Library, Embase, Scopus, and Web of Science for articles assessing subjective visual quality in patients with myopia control lenses compared with single vision lenses (35). The authors found that the use of multifocal CL was associated with lower subjective visual acuity scores at different distances compared with single vision lenses ($p<0.001$), but the differences were less than one unit (35). Young adults also rated walking and/or climbing stairs and subjective comfort (35). Subjective ratings of sports were not statistically different between groups. Wearing multifocal CL was rated lower by young adults than by children for all variables (35). In both children and young adults, scores for defocus CL were significantly lower with increasing near +Add (35). It is important to note that in our study we assessed the quality of life and subjective symptoms in children, not young adults, so our results support the data presented by Ping et al. In our study, the results revealed that nearly 20% of patients experienced pain before the application of a myopia control method, almost 60% had blurred vision and 26% had headaches. A significant effect on the pain syndrome, followed by blurred vision, was observed after randomization in a certain group, regardless of the method of myopia control, before treatment and at the sixth month after randomization in a certain group ($p<0.001$), on the first year of application of the control method ($p<0.001$) and on the second year ($p<0.001$). The most pronounced subjective symptomatology before randomization in a certain group was observed in patients with high-grade myopia - 83.33% of all patients with myopia ≥-6.00 diopters reported pain at the beginning of the study (n=15 out of 18), 37.74 % - for blurred vision (n=20 out of 53) and 79.16% - for headache (n=19 out of 24). These results support the data from the literature, where, as already mentioned, other authors have found an accumulation of the symptoms with increasing myopia grade. A large proportion of patients in the atropine drops group continued to report blurred vision and headache, which is probably due to the side effects of the drop therapy - in terms of blurred vision at the sixth month - 69.23% of all reported patients using atropine drops (n=9), and in terms of headache - 77.77% (n=7). At the first year of the study, 3.26% had pain, 10.87% had blurred vision (atropine drops group: n=6), and 7.61% had headaches, with the highest proportion of patients in the atropine therapy group (n=5) again. At the second year, patients reported no pain, 7.61% had blurred vision, and 4.35% had headaches, with the highest rates again in the pharmacological agent group (n=4 and n=2, respectively) ($p<0.001$). Studies by Yam et al (36) (37) (38) between 3 groups of patients with atropine drops of different concentrations and a placebo group did not find a statistically significant difference in VRQoL between the groups, but it is important that the comparison was only between groups that applied only pharmacological control of myopia, and not optical and pharmacological, as in our study.

WHO defines quality of life as "the perception of individuals of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns (39). It is a broad concept, influenced in a complex way by a person's physical health, psychological state, level of independence, social relationships, personal beliefs and their relationship to important environmental features" (39). In ophthalmic quality of life, previous research has identified 10 relevant domains, namely activity limitation, mobility, comfort, health problems, visual symptoms, ocular comfort symptoms, general symptoms, emotional well-being and social and economic problems (39) (40). A number of instruments have been developed, which may or may not be valid in terms of specificity or sensitivity for accurately assessing the attributes in question. These questionnaires include the NEI-RQL-42, RSVP, QIRC - which covers activity limitations, symptoms, comfort, economic problems, health problems and well-being domains of quality of life, CLIQ - specifically developed for contact lens wearers but has not been validated for use in children or for assessing VR-QOL in Ortho-K lens wearers (40). The OCL-QoL has recently been developed using Rasch analysis (40).

A study by Erickson outlined a methodology for developing and validating a multidimensional quality of life scale for patients with myopia (41). Five dimensions of health-related quality of life in myopia are hypothesized to influence satisfaction with the vision correction method - frequency of visual compromise and ocular symptoms; individual tolerance of these compromises and symptoms; aesthetics; psychological attitude and personality traits (41). The team reported good internal consistency across each factor (Cronbach's alpha range, 0.76 to 0.92) (41). The relationship between the self-esteem of children with myopia and their ocular and demographic characteristics was examined in the Correction of Myopia Evaluation Trial (COMET) using the Children's Self-Perception Profile, which showed high reliability of internal consistency across the questionnaire factors (0.74 to 0.81) (42). The mean self-esteem scores of myopes in the COMET ranged from 2.72 ± 0.69 for athletic competence to 3.36 ± 0.56 for global self-esteem (42). Multiple regression analysis showed that children with fewer symptoms had higher self-esteem in all domains ($p<0.05$), except for athletic competence, and their self-esteem was also affected by age, gender, and ethnicity ($p<0.05$) (42). Zhang et al. also examined the quality of life of a myopic pediatric population using the PREP and SCARED questionnaires and the results indicated a clear benefit of CL in almost all dimensions of vision-related quality of life, especially in terms of appearance, satisfaction, activity and peer perceptions (43). The prevalence of anxiety among the monofocal group was 25.0%, the highest among all groups (43). The authors also reported that lower vision-related quality of life was associated with poorer mental health in children with myopia (43). In our study, we also revealed similar findings – our internal consistency was in the range of 0.602-0.992 for all items. However, we notice a very striking trend in the new research on the topic of quality of life in patients with myopia to include different dimensions in order to properly assess all aspects of life in which patients may exhibit deficits, discomfort or complete absence (37) (38) (44) (45) (46) (47) (48) (49) (50) (51) (52) (53) (54).

A literature review by Lipson et al evaluated the vision-related quality of life (VR-QoL) studies published to date on the most effective and most commonly prescribed interventions for slowing axial elongation and myopia progression (47). Importantly, however, for this study, there are still no instruments and questionnaires that have been validated for use with Ortho-K or multifocal CL, as well as atropine drops (47). VR-QoL is assessed with questionnaires validated for specific populations (children vs. adults) and for specific conditions (dry eye, glaucoma, etc.) (47). Based on the literature review, Lipson et al. included the following studies in their review.

Table 21. VR-QoL studies using different intervention methods.

VR-QoL studies on different modalities for myopia control (47)					
Author	Modalities	Country	Age	Questionnaire	Key findings
Optical aids					

Walline et al (48)	MCL, RGP CL, glasses	USA	18–60 y.	NEI-VFQ	NEI-VFQ is not suitable for detecting a significant difference in VRQoL between glasses, MCLs and gas-permeable CLs
Walline et al (49)	MCL vs glasses	USA	Children / Teens	PREP	Higher VRQoL score in MCL
Walline et al (50)	MCL vs glasses	USA	8–11 y.	S-PPCGS-W	Higher VRQoL score in MCL (athletic and academic performance, appearance, self-esteem)
Rah et al (51)	MCL vs glasses	USA	8–18 y.	PREP	VRQoL higher in older than younger subjects; greatest improvement in QoL for MCL – activities, appearance and satisfaction with correction
Pomeda et al (52)	MCL (MiSight) vs glasses	Canada Portugal Singapore United Kingdom	8–12 y.	PREP	Higher VRQoL score with MiSight CL (appearance, satisfaction, activities, handling, peer perception, and overall score)
Ortho-K					
Lipson et al (53)	Ortho-K vs MCL	USA	Adults	NEI-RQL 42	Higher VRQoL score with OrthoK; 68% chose to stay with OrthoK

Zhang et al (54)	Ortho-K vs glasses	China	8–12 y.	PREP	Better VRQoL with OrthoK
McAlinden et al (44)	Ortho-K, MCL, RGP CL, glasses	USA	Children and Adults	OCL-QoL	Excellent psychometric properties of the questionnaire, able to quantify VRQoL in patients with different MCL
Atropine drops					
Yam et al (37)	3 different doses of atropine and placebo	Hong Kong, China	4–12 y.	VFQ	No difference in overall VRQoL for all groups
Yam et al (38)	3 different doses of atropine and placebo	Hong Kong, China	4–12 y.	VFQ	There was no difference in overall VRQoL across groups; Photochromic glasses were required in approximately 30% of participants. More participants reported photophobia.

However, limited studies have been conducted on this topic and even fewer have focused on adolescents and especially children. The present study demonstrates a relationship between the degree of myopia, the optical correction device and the quality of life of patients. In their studies, Walline et al. reported higher VRQoL scores in soft CL wearers compared to spectacle wearers, especially in terms of physical appearance, sports competence and academic performance, self-esteem and social acceptance (48) (49). Similar findings were reported by Rah et al. for activities, appearance and satisfaction, and by Pomeda et al. for appearance, satisfaction, effect on activities, handling, peer perception and overall outcome (51) (52). Our study also showed significantly higher scores for general, near and distance vision, symptoms, appearance, attitude, activities and hobbies, handling, and perception in soft contact lens wearers than in spectacle wearers (p-value < 0.05). Regarding Ortho-K lenses, a study by Santodomingo-Rubido et al. reported higher VRQoL and acceptability with Ortho-K compared to spectacle wearers in young children in Spain (55). According to Yang et al., Ortho-K lenses improved the quality of life of participants aged 8 to 14 years in their study in terms of confidence and more time spent outdoors (56). McAlinden et al. compared the quality of life of children and adults using different optical devices, including OrthoK, soft and gas permeable contact lenses, and spectacles (44). The study showed excellent psychometric properties, able to quantify VRQoL in patients with different contact lens shapes (44). According to our study, Ortho-K lens wearers performed better than spectacle wearers in all aspects except for their pronounced symptoms (p=0.81). We did not observe a statistically significant difference between Ortho-K wearers and CL wearers for any factor (p>0.05). The negative quality of life assessment in our study was most strongly influenced by symptoms, handling, patients' perception of their appearance and that of their peers. As a result, we found that a large proportion of children who received a negative assessment in the latter two categories also showed greater anxiety about contacts with strangers and attending school. In other studies, negative assessment was also observed in the categories of symptoms, acceptance of self and others, coping, and sports performance (37) (38) (44) (45) (46) (47) (48) (49) (50) (51) (52) (53) (54) (55) (56).

In a study by Han et al. more severe myopia grade resulted in significantly reduced quality of life scores in both children and their parents (57). Zawistowska et al. used the KIDSCREEN-27 questionnaire in participants with adolescent myopia and demonstrated that high myopia can have a negative impact on health-related quality of life (HRQoL), affecting in particular the physical and psychological well-being of girls (58). The authors further considered the importance of a holistic approach in the treatment of high myopia in such a young group of patients, taking into account their HRQoL scores as part of the diagnostic process (58). In our neighboring countryTurkey, Yeter et al. reported that wearing glasses in adolescence years appears to be associated with lower self-esteem and social anxiety (59). The authors suggest an appropriate approach and in-depth psychological assessment of adolescents who wear glasses (59). In our study, children and adolescents with high myopia and/or wearing glasses had the highest anxiety scores, lower quality of life and significantly worse scores on appearance, attitude, activities and hobbies (p-value <0.05) compared to the other groups. All groups wearing lenses demonstrated better tolerance, acceptance and attitude toward their optical correction and almost no anxiety or mood disturbances regarding the refractive error correction device used. An important conclusion from our study, however, is that children with myopia control using atropine drops also showed increased levels of anxiety and difficulties in the aspects of handling, symptoms, vision and etc. We did not find any studies in the literature that evaluated the quality of life of pediatric groups of patients with optical and pharmacological control methods. Further research is needed. As a result, eye health professionals, together with parents and children, should work together to select the most effective means of optical correction or control of myopia that is safe and does not negatively affect the quality of life and mental health of children and adolescents.

Through the review, we found that different methods of myopia control lead to different subjective sensations in patients, could negatively affect the quality of life and mental health of children and adolescents and their anxiety levels. Therefore, it is of utmost importance to verify their efficacy levels so that we, as eye care professionals, can properly assess the benefit/risk ratio.

Santodomingo-Rubido et al. compared axial length growth between white myopic children wearing Ortho-K lenses and single vision spectacle wearers over a 2-year period and reported that in children aged 6 to 12 years with myopia from -0.75 to -4.00D, AL increased significantly over time, for both the Ortho-K group (0.47mm) and the spectacle group (0.69mm), with a significant time-by-group interaction ($p=0.05$) (60). Significant differences in refraction were found over time, between groups and for the time-by-group interaction for the spherical ($p<0.001$), but not for the cylindrical components of refraction ($p>0.05$) (60). Scientists have concluded that wearing Ortho-K lenses reduces axial elongation compared to single vision glasses (60). Our reported data do not differ significantly and are in support of the literature data - AL 0.19±0.22mm; SE -0.26±0.02D; -0.437mm. It is necessary to mention that in patients in groups where we applied orthokeratological or multifocal lenses, we expect a smaller degree of progression in corneal refractive power, due to temporary flattening of the cornea, and hence myopia as an absolute value. The following table presents summarized data on the efficacy of methods for controlling myopia according to data from the literature.

Table 22. Data on the efficacy of methods for myopia progression.

Study, author	Country	Results
Socio-demographic characteristics at progression		
Verkicharla et al. (2020) [61]	Asia, India	Overall mean progression -0.07±0.02D to -0.51±0.02D; maximum change in SE in children aged 6–10 years and smallest in adults aged 26–30 years; Myopia progression was greater in high myopia, followed by moderate and mild myopia, and in individuals aged ≤15 years compared to those aged >15 years.
Data from our study	Europe, Bulgaria	Maximum change in SE and faster progression in SE and AL in the group of patients aged between 8 and 12 years; greater progression with higher degrees of myopia and in individuals aged ≤13 years.
Contact lenses		
Yuval et al. (2024) [62]	Europe, Israel	AL delay by 0.11mm; SE - 0.16D; group 6-10 years, AL delay by 0.17mm and 0.31D SE; group of children with 2 myopic parents, AL delay by 0.15mm and 0.36D SE.
Peng et al. (2023) [63]	Asia, China	7 and 12y. - AL - 0.25±0.22mm; SE −0.69±0.69D in the group with multifocal CL compared to single-f CL.
Liu et al. (2024) [64]	Asia, Taiwan	Mean change in SE −0.73±0.40D in the CL group and −0.85 ± 0.51D in the control group; Mean change in AL 0.25±0.14mm in the MCL group and 0.33±0.17mm in the control group.

Walline et al. (2013) [65]	North America, USA	SE progression −1.03 ± 0.06D for those wearing single-focal lenses and −0.51±0.06 for those wearing multifocal MCLs; AL progression 0.41±0.03 for single-focal lenses and 0.29±0.03 for multifocal MCLs.
Data from our study	Europe, Bulgaria	AL 0.42±0.23mm; SE -0.50±0.06D; SE progression -0.319D
	Ortho-K lenses	
Kim et al. (2019) [66]	Asia, South Korea	mean AL 24.21±0.60mm; mean SE −2.43±0.97D.
Santodomingo-Rubido et al. (2012) [60]	Europe, Spain	AL progression for Ortho-K group 0.47mm; 0.69mm for spectacle group; significant interaction between time and group (p=0.05); significant differences in SE between groups and for the interaction between time and group for spherical (p<0.001), but not for cylindrical components of refraction (p>0.05).
Prousali et al. (2019) [67]	Europe, Greece	Ortho-K lenses (AL: 0.19 mm, [0.21 to 0.16].
Data from our study	Europe, Bulgaria	AL 0.19±0.22mm; SE -0.26±0.02D; -0.437mm
	Атропинови капки	
Zhao et al. (2020) [68]	Asia, China	Myopia progression - attenuated more strongly in the atropine-treated group than in the control group, with MD -0.80 (-0.94, -0.66). Statistical difference between 0.05, 0.5 and 1.0% atropine (p=0.004); less axial elongation with MD -0.26; 0.05% atropine probably the most optimal dose.
Huang et al. (2016) [69]	Asia, China	high-dose atropine SE: 0.68; AL: −0.21 [−0.28 to −0.16]), moderate-dose atropine (SE: 0.53 [0.28–0.77]; AL: −0.21 [−0.32 to −0.12]) and low-dose atropine (SE:

		0.53 [0.21–0.85]; AL: −0.15 [−0.25 to −0.05]) significantly slowed myopia progression.
Prousali et al. (2019) [67]	Europe, Greece	1% atropine vs. placebo SE: -0.78D, [−1.30 to −0.25], 0.025 to 0.05% atropine vs. control SE: -0.51D, [−0.60 to −0.41], 0.01% atropine vs. control SE: -0.50D, [−0.76 to −0.24] at 1 year.
Data from our study	Europe, Bulgaria	AL 0.29±0.33mm; SE -0.40±0.65D; -0.392mm
Meta-analysis		
Zhang et al. (2023) [70]	Asia, China	Ortho-K AL, 0.36; SE 0.56; 1% atropine AL 0.39; SE 0.54; 0.01% atropine + Ortho-K AL 0.47; SE 0.81; multifocal glasses SE 0.42; bifocal MCL SE 0.40; 0.5% atropine SE 0.67; 0.1% atropine SE 0.42; 0.05% atropine SE 0.57; 0.01% atropine SE 0.33; 1% Atropine + bifocal glasses SE 1.30; 1% Atropine + multifocal glasses SE 0.66; 0.01% Atropine + monofocal glasses SE 0.70; 0.01% Atropine + Ortho-K SE 0.81
Huang et al. (2016) [69]	Asia, China	Pirenzepine SE: 0.29 [0.05–0.52]; AL: 0.09 [0.17 to 0.01]), Ortho-K AL: 0.15 [0.22 to 0.08] and multifocal CL AL: 0.11 [0.20 to 0.03] showed modest effects; multifocal glasses SE: 0.14 [0.02–0.26]; AL: 0.04 [0.09 to 0.01]) - mild effects
Prousali et al. (2019) [67]	Europe, Greece	1% atropine vs. placebo SE: -0.78D, [−1.30 to −0.25], 0.025 to 0.05% atropine vs. control SE: -0.51D, [−0.60 to −0.41], 0.01% atropine vs. control SE: -0.50D, [−0.76 to −0.24]; Ortho-K lenses (AL: 0.19 mm, [0.21 to 0.16] and new multifocal MCLs (SE: -0.15D, [−0.27 to −0.03] at 1 year

Data from our study	Europe, Bulgaria	Ortho-K lenses (AL 0.19±0.22mm; SE -0.26±0.02D; -0.437mm) > atropine 0.01% (AL 0.29±0.33mm; SE -0.40±0.65D; -0.392mm) > multifocal MCL (AL 0.42±0.23mm; SE -0.50±0.06D; SE progression -0.319D) > monofocal glasses (AL 0.51±0.31mm; SE 1.00±0.25D)

The available evidence does not fully convince eye health professionals to adopt a single progression control mean, probably due to some heterogeneity, reports of side effects and lack of long-term follow-up. Further studies are needed to determine the efficacy of interventions and the benefit-risk ratio.

Changes in ocular biometric parameters in children and adolescents are closely related to refractive errors. Devices for measuring these parameters, as effective noninvasive techniques, provide objective biological markers for monitoring refractive errors such as myopia. As mentioned earlier, to follow up the patients in our study, we used optical biometry (IOLMaster) and corneal topometry (Pentacam) to examine AL, CCT, ACD, CC, CR, and AL/CR ratio. Several studies have been conducted to investigate the reported parameters of both devices in different populations with a wide range of ocular pathologies (71) (72) (73) (74) (75) (76) (77) (78) (79) (80) (81).

Dong et al compared ACD, keratometric values and astigmatism measurements made by IOLMaster and Pentacam and reported that for the group of patients with high myopia, age was reported to be positively correlated with AL but negatively correlated with ACD (74). After 2 years of follow-up in our study, we also observed a trend toward greater myopization and greater axial elongation in all age groups. Younger participants had significantly higher levels of myopic shift and axial elongation compared to older participants (>16 years) and we also observed a positive correlation between age and AL. The data from the studies with both devices reported no statistically significant difference in determining ACD ($p=0.270$). The IOLMaster demonstrated steeper K1 values and higher mean ▲K values than the Pentacam ($p=0.001$; $p<0.001$). We did not observe a statistically significant difference between the two devices when measuring patients with astigmatism ($p=0.476$). Zhu et al studied K1, K2, Km and corneal astigmatism (J0, J45) with the Pentacam and the IOL Master and their data analysis showed that there was no difference between the devices in measuring astigmatism and K2 in patients with low and moderate myopia, but they reported such differences in measuring K1 (75). However, the Pentacam and IOL Master showed good consistency (75). Mattern et al reported the best reproducibility of AL measurements between IOLMaster and Lenstar [95% limits of agreement (LoA) for reproducibility −0.06 to 0.02] (76). In another German study from Frankfurt between IOL Master 500, IOL Master 700 and Pentacam, there was no statistically significant difference between the measured AL, ACD and CC values (77). In the first study of myopia in Caucasian adults (>18 years) in a large long-term longitudinal study, Gaurisankar et al reported that the eyes of myopic patients showed a significant mean increase in axial length of 0.45 ± 0.61 mm after a mean follow-up of 144 ± 38 months ($p<0.001$) (78). The mean annual increase in AL was 0.04 ± 0.06 mm and axial elongation was associated with higher myopia ($p < 0.001$) and younger age ($p = 0.02$), as we have reported in our study. Fan et al. studied anterior segment parameters in a sample of myopic patients and found no statistically significant differences in age, gender, or intraocular pressure between three groups of myopes (80). The mean AL/CR values in the mild, moderate and high myopia groups were 3.17 ± 0.06; 3.31 ± 0.08, and 3.43 ± 0.10, respectively, with a statistically significant difference between the groups ($p < 0.001$) (80). Both AL and AL/CR were strongly negatively correlated with SE, while CR had a weak positive correlation with SE without statistically significant differences by linear regression analysis (80). For every 0.1-unit increase in AL/CR, SE increased by 1.54 D in this study (80). In the study by Tang and colleagues, the AL/CR in hyperopes, emmetropes and myopes was observed to be 2.90±0.06; 2.95±0.05, and 3.08±0.07, separately, and correlated with SE in hyperopes ($\rho=-0.54$, $p<0.001$), emmetropes ($\rho=-0.33$, $p<0.001$), and myopes ($r=-0.67$, $p<0.001$) (81). SE was more strongly correlated with AL/CR than with AL or CR alone, especially in myopes, among children aged 4–6 years (81). The results of our study revealed a significant increase in AL, AL/CR and ACD in both low- and high-myopia groups. CC also showed increased mean values, while CCT and corneal radius of curvature decreased. In the low myopia group, ACD increased with increasing AL (Pearson coefficient=0.338, $p<0.01$). In the high myopia group, we did not find a correlation with AL (Pearson coefficient=0.057, $p=0.233$). We obtained similar values of corneal curvature for both eyes and found a correlation between SE and AL (Pearson coefficient=−0.579, p<0.001), but not with corneal curvature.

Table 23. Measured mean values of various anterior segment parameters by IOLMaster and Pentacam according to data from our study and studies in the literature.

Parameter	Data from our study	Li et al (71)	Sabur et al (72)	Dong et al (Group with high degree myopia) (74)	Müller et al (73)
Axial lenght (mm)	**24.67±2.53**		**23,61±1,42 IOLMaster 23,62±1,45 Pentacam**		
Anterior chamber depth (mm), **IOLMaster**	**3.56±0.31**	**3.44±0.33**			**3.41±0.245**
Anterior chamber depth (mm), **Pentacam**	**3.59±0.32**	**3.39±0.36**			
K1 (D), **IOLMaster**	**42.53±1.53**	**43.15±2.44**	**44.59 ± 1.23**	**42.60±1.41**	
K1 (D), **Pentacam**	**42.47±1.47**	**42.98±2.47**	**44.45 ± 1.25**	**42.51±1.44**	
K2 (D), **IOLMaster**	**43.83±1.37**	**44.55±2.63**	**43.43 ± 1.29**	**43.92±1.47**	
K2 (D), **Pentacam**	**43.71±1.24**	**44.32±2.55**	**43.29 ± 1.28**	**43.81±1.44**	
Mean K (D), **IOLMaster**	**43.18±1.39**		**44.00 ± 1.19**	**43.26±1.39**	

Mean K (D), **Pentacam**	**43.09±1.42**		**43.85 ± 1.21**	**43.16±1.40**	
Astigmatism (D), **IOLMaster**	**1.33±0.15**			**1.32±0.74**	
Astigmatism (D), **Pentacam**	**1.31±0.19**			**1.29±0.70**	

The literature review suggests that the exact pathogenic mechanisms of myopia remain unclear, but recent hypotheses propose that it is likely the result of the combined and interacting effects of hereditary and environmental factors. We reviewed other research that have identified risk factors for onset and progression among the populations studied in them, including heredity (82) (83) (84) (85) (86), socioeconomic factors (87) (88) (89) (90) (91), close-up work (82) (85) (92) (93), outdoor activities as a potential protective factor (94 - 107) and others such as gender, urbanization, nutrition, Kawasaki disease and even maternal grandmother smoking during pregnancy (82) (108-115). From the data obtained from our study, we found that the risk profile for myopia progression is female gender, having two myopic parents, annual progression in SE ≤1.00 D, younger age of onset - ≤ 13 years and spherical equivalent (SE) values ≤ 6.00 D. In summary, knowledge of the various factors that influence the onset and development of adolescent myopia is beneficial for clarifying the mechanisms of onset and progression, as well as for formulating reasonable measures for prevention and control of myopia in order to protect the health of adolescents. In the following table, we have grouped the data from the literature indicating the risk factors for prevalence and progression and the data from our study.

Table 24. Risk factors for the prevalence and progression of myopia (116).

Study, author	Country	Likelihood ratio: distribution with factor vs. without factor
	Heredity	
Atowa et al. [117]	Africa, Nigeria	6.80 for one parent with myopia and 9.47 for two parents with myopia

Yang et al. [118]	North America, Canada	2.52
Harrington et al. [119]	Europe, Ireland	2.4 (paternal)
Kim et al. [120]	Asia, Korea	1.84 for myopia and 3.48 for high myopia
Loh et al. [121]	Asia, Singapore	2 myopic parents 7.70
Data from our study	Europe, Bulgaria	2.57 (for two parents with myopia)
Low outdoor activity		
Singh et al. [122]	Asia, India	19.73 (<1.5 hours per day)
Hagen et al. [123]	Europe, Norway	1.96 (less outdoor sports) and 0.67 (less other outdoor activities)
Atowa et al. [117]	Africa, Nigeria	1.25
Yang et al. [118]	North America, Canada	1.17
Data from our study	Europe, Bulgaria	Time spent outdoors <1h per day - 1.00 (p>0.05)
Time spent by performing any close-range activities		
Harrington et al. [119]	Europe, Ireland	3.7 (screen use >3 hours per day) and 2.2 (frequent reading/writing)
Singh et al. [122]	Asia, India	2.94 (reading/writing > 4 hours daily) and 8.33 (playing video games > 2 hours daily)
Wang et al. [124]	Asia, China	1.88 (moderate school load) and 2.36 (high school load)
Chiang et al. [135]	North America, USA	1.27 (watching TV 2 hours a day) and 1.28 (using a computer 1 hour a day)
Data from our study	Europe, Bulgaria	hour/day >10h - 1.27

High level of education		
Wang et al. [124]	Asia, China	2.50 (bachelor/master)
Wang et al. [126]	Asia, China	1.52 (secondary/high school education) and 3.77 (bachelor/master's degree)
Chiang et al. [135]	North America, USA	1.79 (high school education)
Yang et al. [127]	Europe, Austria	1.3–1.7 (≥completed vocational training or completed an apprenticeship) in 2013–2017 year
Shapira et al. [128]	Europe, Israel	1.16 (≥12 years of education)
Yam et al. [129]	Asia, China (Hong Kong)	1.12 (mother ≥ bachelor's degree), 1.10 (father ≥ bachelor's degree) in children; 1.81 (secondary education), 2.78 (high school), 3.47 (associate degree), 5.19 (bachelor's degree), and 6.18 (≥master's degree) in parents
Female gender		
Parrey et al. [130]	Asia, Saudi Arabia	2.56
Wang et al. [131]	Asia, China	1.54
Shapira et al. [128]	Europe, Israel	1.32
Chen et al. [132]	Asia, China	1.19 in 2001 and 1.87 in 2015.
Lim et al. [133]	Asia, Korea	1.15
Singh et al. [122]	Asia, India	0.71
Reed et al. [134]	North America, USA	0.61
Data from our study	Europe, Bulgaria	1.83

Urban environment		
Latif et al. [135]	Asia, Pakistan	1.89
Galvis et al. [136]	South America, Colombia	1.45
Shapira et al. [128]	Europe, Israel	1.20
High body mass index		
Harrington et al. [119]	Europe, Ireland	2.7
Low body mass index		
Yang et al. [127]	Europe, Austria	1.2 - 1.4 in 2013 - 2017 year
Refractive error value		
Hsu et al. [127]	Asia, China	Higher values - 0.67 faster progression; at short - distance eye-object when working at close range - 1.45
Loh et al. [121]	Asia, Singapore	Higher myopic SE at baseline - 3.6
Data from our study	Europe, Bulgaria	Higher values of SE ≤ -6.00 D - 6.43; Annual progression in SE ≤ -1.00 D - 3.43

With the advancement of technology and the capabilities of artificial intelligence, the possibilities for healthcare professionals are increasing enormously. Machine learning capabilities could certainly help researchers and clinicians, with the largest application currently being the ability to predict myopia progression. Li et al aimed to investigate the risk factors for myopia progression in primary school children and to build predictive models using machine learning (138). Of a total of 2740 children from grades 1 to 6, who were examined annually for a period of 5 years, their myopic progression was determined as the change in their cycloplegic refraction (138). Each year, risk factors were assessed and included in predictive models in a training set and then furthermore tested in an independent set using the random forest algorithm, an ensemble machine learning method that can be applied to classification and regression (138). Six variables appeared in the models predicting myopia progression over all 5 years with a predictive accuracy of over 80% - uncorrected distant visual acuity (UDVA) (mean 28%, range 22–39%), spherical equivalent (20%, 7–28%), axial length (13%, 10–14%), keratometry (K1) (7%, 4–11%), gender (6%, 2–9%) and parental myopia (3%, 1–10%) (138). Weekly reading time, reading distance and position, and frequency of meat consumption were also included as variables across years of the study (138).

Machine learning often uses many more variables in its prediction models because the emphasis is not on the significance of individual variables but rather on the ability of the machine learning model to predict the independent variable from a combination of factors (138). During the five years of the study by Li et al, UDVA always had the highest weight (28.3%) with a peak in the second year of the study, indicating that UDVA is the best predictor of myopia progression and screening for myopia (138). This means that UDVA of primary school children should be monitored frequently to identify children at risk of myopia (138). The authors also found that SE was a significant predictor variable with a peak weight in the third year of the study, followed by axial length with a moderate weight (12.6%) (138). Interestingly, continuous reading (i.e., the cut-off variable) was significant throughout the five years of the study during primary school years (138). In the study of Australian children, myopia was also not associated with time spent working at close range, as was the case in our study (138). The models of Li et al. (138) reported that time spent outdoors was not significant, as we found in our study, although it is considered in the literature as the most promising environmental factor for control of the onset of myopia by some authors. Furthermore, environmental factors are dynamic, which makes it difficult to accurately assess their impact on myopia progression. The authors nevertheless successfully built models for predicting myopia in children of different ages based on machine learning (138). The models demonstrated good prediction accuracy and interaction between the different factors, and from their results, we can observe that ocular parameters had a greater weight than environmental factors and individual genome (138).

This is both encouraging information, as it is quite difficult to modify environmental factors such as socioeconomic factors, race, gender, genetics, as well as lifestyle and habits, especially in adolescents, but at the same time it once again reinforces the key role of eye health providers in the control of myopia. Once again, it becomes clear how important their awareness, ability for timely diagnosis, individual approach, selection of the right method for myopia control, monitoring the patient's response to them, reporting the appearance of subjective symptoms, anxiety and any change in the quality of life of this very young population is. The control of myopia is definitely complex, multi-component and precise, which requires deep knowledge and empathy of eye specialists in order to provide the most useful and personalized care to patients, to guarantee their best visual outcome and the finest quality of life, in order to reduce the overall burden on the health system amidst the myopia pandemic.

A look into the future

Pilot studies in gene therapy, molecular inhibitors and neuroprotective mechanisms are providing new therapeutic targets for scientists and clinicians. Stem cell therapy could potentially address two components of myopia, according to Suriko et al., due to the scleral weakness (139). By transplanting mesenchymal stem cells that support the connective tissue and enhance dopamine production from sunlight exposure, the authors propose an innovative therapy (139). The concept is that the variety of dopamine-producing cells available for the treatment of Parkinson's disease could also be used to treat myopia (139). Velez et al reported in their work that hyperopia and microphthalmos are conditions resulting from MFRP mutations in combination with loss of function (140). In their work, it is clear that MFRP deficiency causes abnormal eye growth and significant visual comorbidities, including OAG, cystoid macular edema and exudative retinal detachment (140). Velez et al used the Mfrp rd6 /Mfrp rd6 mouse as a preclinical animal model of retinal degeneration and found that it has hyperopic refraction (140). To investigate the effect of restoring MFRP expression, the researchers delivered it to the retinal pigment epithelium via adeno-associated virus gene therapy (140). Data analysis showed that gene therapy restored retinal function and normalized axial length and that hyperopia and associated refractive errors may be amenable to gene therapy (140).

In their review, Chung and colleagues reviewed pharmacotherapies targeting vascular endothelial growth factor (VEGF) used in the treatment of retinal neovascular diseases and reported on newer generations of antiangiogenic biologic therapies, engineered proteins, implantable delivery systems and biopolymers that may allow for more sustained and long-term treatment (141). The use of gene therapy for pathological angiogenesis and the first FDA approval for the treatment of hereditary retinal diseases associated with biallelic RPE65 mutations, newer generations of viral vectors and the future application of CRISPR-Cas9 technology to suppress ocular angiogenesis in pathological retinal changes, including the complications caused by high-grade myopia, are reviewed by the authors (141). The 2025 study by Zhang et al. clarified that gene control depends largely on epigenetic changes, which are reversible, heritable and sensitive to environmental changes (142). Their work suggests that the pathophysiology and development of myopia are closely linked to gene regulation mediated by epigenetic changes (142). Recent advances in the study of epigenetic modifications, including noncoding RNAs (ncRNAs), DNA and RNA methylation, and histone modifications, have elucidated the complex interactions between genetic predisposition and environmental factors in the development of myopia (142). DNA methylation patterns of key genes, such as those involved in eye growth and signaling pathways, have been linked to the development of myopia and the regulation of axial elongation, as reviewed by these authors (142). In myopia, ncRNAs, especially microRNAs, act as master regulators of gene expression, providing a possible molecular mechanism for further controlling axial elongation and growth, and m6A RNA methylation influences myopic progression, neovascularization and axial elongation (142). Zhang and colleagues suggest that future studies should address how to make epigenetic changes reversible or prevent them altogether (142).

Studying new pathways of pathophysiology, developing novel therapies and targeting the onset, not just the progression, of myopia all seem to hold promise for properly addressing the increasing global prevalence of myopia. Combined with clarifying the environmental factors and their influence on gene expression, developing effective future strategies and individualizing the current treatment approaches appear like the very next reasonable steps.

CONCLUSIONS

1. Myopia control requires a personalized approach to patients, examining their subjective symptoms and quality of life, as well as the attitude of parents/guardians. For any approach to progression control to be successful, eye specialists must compare the individual benefit:risk ratio for the separate patients.

2. Myopia progression correlates with the age of the patient and the onset of myopia, as well as with its severity.

3. Female gender (OR 1.83), both parents having myopic refraction (OR 2.57), annual progression in SE≤-1.00D (OR 3.43), early age of onset ≤13 years (OR 4.19) and the absolute value of SE≤-6.00D (OR 6.43) emerge as risk factors for myopia progression.

4. After 2 years of follow-up, we observed a trend towards greater myopization and greater axial elongation in all age groups. Younger participants had significantly higher levels of myopic shift and axial elongation compared to older participants.

5. After analyzing the objective progression by performing highly specialized studies to report changes in AL values, it is clear that the data from our study is similar to the results of other authors - the most effective for controlling axial progression are Ortho-K lenses, followed by atropine drops and CL. We have also reported identical results for SE values.

6. The assessment of the subjective symptoms of the patients included in the study shows that pain, blurred vision and headache had the strongest impact on the visual function and normal perception of the participants. The results improve significantly already at the sixth month after the introduction of the respective control method. However, a large proportion of the atropine drops group continued to report persistent symptoms that decreased by the second year of follow-up.

7. In our study, we found that the best quality of life outcomes were reported by the group of patients corrected with multifocal and Ortho-K lenses. Increased levels of anxiety among the representative sample of patients were observed in the control group, followed by the atropine drops patients. The lowest vision-related quality of life and increased levels of anxiety were obtained by patients with monofocal glasses and/or myopia of -6.00D.

SUMMARY

High-grade myopia has a significant impact on the quality of life, the risk of pathological complications and impairment of visual function. The increasing prevalence of this socially significant ametropia requires the attention of eye specialists to the possibilities of modern medicine for early intervention and careful monitoring in order to prevent myopic progression. The burden associated with these processes has given rise to the need for a valuable and in-depth evaluation of control strategies, especially considering that earlier onset of myopia increases the economic burden throughout the life of patients and is associated with loss of productivity and independence, leading to reduced and impaired quality of life.

Although various interventions for myopia control have been proposed, consensus on strategies for their implementation has not yet been reached globally. Atropine drops and orthokeratology lenses stand out from the other available approaches with their elevated efficacy in slowing axial progression, but higher doses of atropine are associated with an increased frequency of subjective symptoms reported by patients, and Ortho-K lenses, with their high cost and risks of complications, often do not tip the scales in their favor when it comes to parental assessment. In-depth evaluation of the risks of myopia onset and progression, assessment of the individual benefit:risk ratio and quality of life in children is crucial in making clinical decisions. All approaches to myopia control have an important role in reducing the overall morbidity, as the needs and requirements of individual patients can vary greatly depending on age, attitude, access, safety, subjective needs, parental attitude, individual factors and rate of progression. Timely intervention with contact lenses and spectacles can significantly reduce the overall burden of myopia.

Further studies are needed to assess the efficacy of myopia control strategies in patients with high grade myopia, both separately and in combination therapy. In addition to traditional population-based models for predicting myopic onset and progression, individualized forecast using machine learning and age-specific refraction data is promising. Although emerging combination approaches to control axial progression are increasingly being used in clinical practice, identifying populations in need, examining and monitoring individual clinical,

subjective and quality-of-life responses remain the most important steps for clinicians in navigating the long and complex journey to successful myopia control.

CONTRIBUTIONS

Contributions of cognitive nature

1. A comprehensive review of the literature on the prevalence, progression mechanisms, diagnostic and monitoring techniques and myopia control methods that modern medicine provides for the pediatric population with myopia was conducted.

2. A detailed analysis of the currently available data in the scientific literature on the methods of myopia control, their individual efficacy and application, their advantages and disadvantages related to the annual progression in SE and AL, the subjective symptoms of patients and their quality of life on a European and global scale was carried out.

3. The data obtained by us proved that the trends in myopia progression among children and adolescents in Varna correlate with the scientific sources from other countries.

Contributions of a scientific and applied nature

1. For the first time in our country, an assessment of the subjective signs and quality of life of patients in childhood and adolescent years who underwent observation at USBOBAL-Varna was made.

2. An analysis of subjective symptoms, vision-related quality of life, anxiety levels and annual progression in SE and AL values and their relationship with socio-demographic characteristics, habits and method of myopia control was performed.

3. Questionnaires were prepared to assess vision-related quality of life and the method of correction/control and anxiety levels of children and adolescent myopes. Their application in the present study confirmed the need to validate a multi-faceted questionnaire in Bulgarian, suitable for screening a population of this specific age group and its application in clinical practice.

4. Epidemiological and clinical data were formed regarding age, gender, degree and characteristics of myopia and risk factors for its progression.

Contributions of practical nature

1. The advantages of myopia control using Ortho-K lenses in the areas of subjective symptoms, quality of life and slowing down axial progression have been established as a more reliable and safe method on the purpose of control of this socially significant ametropia.

2. A risk profile for myopia progression has been created for children and adolescents with myopia from the city of Varna.

3. A situational assessment of the quality of life related to vision and anxiety levels among a representative sample of myopic patients has been made and the factors with the strongest influence have been identified.

PUBLICATIONS RELATED TO THE DISSERTATION

1. Stoeva, M., Stefanova, D., Boyadzhiev, D., Zlatarova, Z., Nencheva, B., & Radeva, M. (2025). Assessment of the Quality of Life in Children and Adolescents with Myopia from the City of Varna. Journal of Clinical Medicine, 14(13), 4546.
2. Stoeva, M. (2025). Comparison of the efficiency of different approaches for myopia control in children and adolescents from the city of Varna for a two-year period. Bulgarian Review of Ophthalmology, 69(1).

Abstract

Aim

The aim of this study is to analyze the demographic characteristics and degree of myopia and to evaluate the clinical efficacy of the applied methods for myopia control over a period of 5 years in patients aged between 6 and 16 years from the city of Varna, who underwent follow-up at University Specialized Hospital on Eye Diseases for Active Treatment-Varna.

Materials and methods

The present study was conducted at the Department of Ophthalmology and Visual Sciences of the Medical University - Varna for a period of 5 years from 01.09.2020 to 01.09.2025. A total of 93 patients who underwent follow-up were studied, and their selection was based on precisely defined criteria - verbal patients from the city of Varna, with myopia and refractive error ≤ -2.00D, cylindrical refraction no more than 1.00D and anisometropia no more than 1.50D, aged between 6 and 16 years, with no history of ophthalmic surgeries or trauma, systemic diseases that could affect the quality of vision, without reported mental disorders and with parents/guardians who signed a declaration of informed consent. The methodology includes a documentary method through research and analysis of the published scientific literature on the types of methods for myopia control and their efficacy, analysis of the progression of axial length (AL) and refractive error in patients with myopia, the mechanism of action, indications for use and the impact of various established or modern approaches and new proposals for preventing its progression. The sociological method consisted of preparing questionnaires that met the objectives of the study and conducting a survey of the patients. Clinical methods included autorefractometry (HRK-1, Huvitz (HUVITZ Co., Ltd., Republic of Korea), skiascopy with a Heine Beta® 200 retinoscope (HEINE Ophthoecnic, Herrsching, Germany), optical biometry (ZEISS IOLMaster 700 with SWEPT Source Biometry®), corneal topography (Pentacam®, Oculus (OCULUS, Optikgeräte GmbH), history taking and visual acuity testing. The collected data from the study were statistically processed using analysis of variance (ANOVA, MANOVA), variation, correlation, regression and comparative analysis and risk assessment analysis (OR, RR) at an acceptable level of significance $p<0.05$, $p<0.01$, $p<0.001$ at a standard confidence interval of 95%. The data was statistically processed using SPSS v.20, using descriptive indicators for quantitative and qualitative variables, presented in tabular and graphical form.

Results

Over a period of 5 years (2020-2025), 92 patients with myopia were surveyed. Of these, 40 were male (43.48%) and 52 were female (56.52%). The average age of myopic patients was 11.57 years. In terms of spherical equivalent (SE) for OD and OS, 78% of the patients had low-grade myopia, nearly 82% had astigmatism and the average values of SE and |Cyl| were -4.27 D and -0.82 D, respectively. We observed more patients with low-grade myopia in males (35:22) and more women had high-grade (21:14). Most patients spent between 3 and 6 hours a day working at close range distance (n=50), followed by those who strain their visual analyzer between 6 and 10 hours (n=29). Twice as many patients spend over 10 hours (n=4) in front of a mobile device or reading than the group of patients who did it for 1 hour a day (n=2). The studied population of our patients most often spends between 1-3 hours outdoors (n=38) or between 3-6 hours a day (n=30). A much higher number of patients spend less than 1 hour a day outdoors – 21 of them. We did not find a statistically significant difference in terms of time spent at close range or outdoors at the beginning and end of the study ($p>0.05$). Regarding other family members with myopia, 56 have data on myopia in the family, or nearly 61% of all. Of these, 31 have two myopic parents, 12 – one myopic parent, 10 – a sibling and 3 – a grandparent with myopia. Regarding their age, the patients were divided into 2 groups – aged between 8 and 12 years and aged between 13 and 16 years. The number of patients in both groups was similar – 44 patients in the 13-16 group and 48 – 8-12 years. The prevalence of moderate and high myopia showed a higher frequency among the group of patients aged between 13-16 years.

The quality of life of the patients was assessed using questionnaires. Cronbach's alpha for the PREP questionnaire for all 10 factors was higher than 0.6, which indicates acceptable internal consistency. Significantly higher results were reported for overall, near and far vision, appearance, attitude, activities and hobbies, handling and perception for soft contact (MCL) and ortho-K lens wearers than for spectacle wearers ($p<0.05$). No significant difference was found between ortho-K wearers and those wearing MCL for any factor ($p>0.05$). Regarding attitude, handling, overall vision, symptoms and school environment, there were no significant differences between the control group and the atropine drops group ($p>0.05$). The worst results, especially in terms of handling, overall vision, symptoms and appearance, were observed in the atropine drops group and the control group, as well as in terms of performance in a school environment and involvement in extracurricular activities and hobbies. The Cronbach's alpha of the SCARED questionnaire for all factors was between 0.623-0.992, indicating acceptable internal consistency. Significantly worse scores on the anxiety questionnaire were given by monofocal spectacle wearers for symptoms, shyness and performance than by contact lens wearers from all groups, including the atropine drops group ($p<0.05$). Monofocal spectacle wearers had the highest anxiety scores among all other participants - median=26 ($p<0.05$), followed by the atropine drops group - median=15. No statistically significant difference was observed between MCL and Ortho-k wearers – median=2 for both groups ($p>0.05$). Students with glasses showed higher levels of anxiety than MCL wearers (26 (2, 28) vs. 2 (2, 8), p=0.001), the atropine drops group (26 (2, 28) vs. 15 (2, 20), p=0.020) and Ortho-k wearers (26 (2, 28) vs. 2 (2, 10), p=0.003). According to the distribution of patients in terms of the lowest quality of life, represented by the worst scores on the Quality of Vision and Mood Disorders Questionnaire and anxiety levels, the results were calculated for each group separately and represent 36.96% of all participants (34 out of 92 patients). Fifteen of these patients were from the monofocal glasses group – 44.12%; 12 from the atropine drops group – 35.29%, 3 from the Ortho-K group – 8.83% and 4 from the MCL wearers – 11.76%. We did not report a significant difference between the multifocal and Ortho-K lens wearers ($p>0.05$). Patients with myopia above -6.00 D had the highest anxiety scores and lower visual quality among all participants with myopia – 76.47% of the total score in the patients with the lowest scores (n=26/34), and -4.50 D for the remaining 23.53% (n=8/34). We did not find a statistically significant difference between the scores obtained by the parents and those provided by the children ($p>0.05$).

Of the studied patients, 19.56% experienced pain before the appointment of a certain method for myopia control, 57.61% had blurred vision and 26.09% - headache. A significant impact of the pain syndrome, followed by blurred vision, was observed already at the sixth month, with only 4.35% reporting pain, 14.13% for blurred vision, and 9.78% for headache. A statistically significant difference was found in the perceptions of pain and blurred vision in patients with different degrees of myopia, regardless of the method for myopia control before treatment and at the sixth month after randomization to a certain group ($p<0.001$), at the first year of applying a control method ($p<0.001$) and at the second year ($p<0.001$). A large proportion of patients in the atropine drops group continued to report blurred vision and headache, which was probably due to side effects of the drop therapy. We found a statistically significant difference in the perceptions of blurred vision and pain in patients with different degrees of myopia ($p<0.001$). The most pronounced subjective symptomatology before randomization in a certain group was observed in patients with high-grade myopia.

The smallest progression in AL was observed in the groups with Ortho-K lenses and atropine drops, and the highest – in the control group with glasses ($p<0.001$). The analysis of variance showed that the applied methods for myopia control had a statistically significant effect. We did not find a statistically significant difference in terms of the time of application of the specified control approaches, nor in terms of the combination of a certain method and time of action. The data indicates that the atropine therapy group showed a statistically significant smaller progression in the SE values compared to the MCL ($p<0.0\ 5$) and the control group ($p<0.05$). Similar results were observed in the Ortho-K lens group ($p<0.05$;$p\leq0.001$). The group of patients using atropine drops had a statistically significant difference in the mean values of progression in AL compared to the MCL group ($p<0.05$) and the control group ($p=0.001$), as well as the Ortho-K lens group ($p=0.001$; $p=0.001$). The group of patients with Ortho-K lenses showed a significantly lower progression of AL and SE, followed by the atropine therapy group, especially compared to the MCL and the control group. A trend for an increase in AL is visible, which is more pronounced after the first year of application of a method for myopia control. SE values show a decrease (more negative values), which is expected with progressive myopia. The Ortho-K group had the lowest rate of AL growth, indicating that it is most effective in slowing myopia progression. Glasses showed the highest axial growth and refractive error shift, suggesting that they are least effective in controlling progression. Atropine and MCL fall in the middle, with atropine showing better control of SE than AL. Regarding the age of the patients included in the study by groups, we observed a faster progression in SE and AL values in the group of patients between 8 and 12 years of age, and in terms of gender, in the group of female patients.

Using optical biometry and corneal topography, we examined AL, central corneal thickness (CCT), anterior chamber depth (ACD), corneal curvature (CC), corneal curvature radius (CR), axial length to corneal radius ratio (AL/CR ratio). After 2 years of follow-up, a trend towards greater myopization and greater axial elongation was observed in all age groups. Younger participants had significantly ($p<0.001$) higher levels of myopic shift and axial elongation compared to older participants (>16 years). The results showed a significant increase in AL, AL to CR ratio and ACD in both low- and high-myopia groups. CC also showed increased mean values, while in CCT and CR we observed decreased values. In the low myopia group, ACD increased with increasing AL (Pearson coefficient=0.338, $p<0.01$). In the high myopia group, we did not find a correlation with AL (Pearson coefficient=0.057, p=0.233). We obtained similar CC values for both eyes and found a correlation between refractive error and AL (Pearson coefficient=−0.579, $p<0.001$), but not with CC. The two devices demonstrated a lack of statistically significant difference in determining ACD (p=0.270), but the IOLMaster measured steeper K1 values and higher mean ▲K values than the Pentacam (p=0.001; $p<0.001$). We did not observe a statistically significant difference between the two devices when measuring patients with astigmatism (p=0.476).

From the study, we found that the risk profile for myopia progression is female gender, two myopic parents, annual progression in SE ≤1.00 D, younger age of onset - ≤ 13 years and spherical equivalent (SE) values ≤ 6.00 D. We did not find a statistically significant difference in terms of intensive near-distance activity, nor in time spent outdoors. From the surveys conducted, the average hours per day spent working at near distance of the study patients were 6.65±3.78 hours/day and the time spent in outdoor activities - 2.15±1.73 hours/day. A high number of parents prefer glasses as a means of correction (n=57), followed by MCL (n=20) and have low trust in the doctor's judgment (n=15) regarding the choice of corrective means, after completing the questionnaires from the survey. The highest number of parents choose MCL for myopia control (n=30), with the results for the other types of methods being similar - atropine drops (n=23), Ortho-K (n=20) and 19 parents noted that they were not sufficiently informed.

Conclusion

High-grade myopia has a significant impact on the quality of life, the risk of pathological complications and impairment of visual function. Its increasing prevalence requires the attention of eye specialists to the possibilities of modern medicine for early intervention and careful monitoring in order to prevent myopic progression. The burden associated with these processes has given rise to the need for a valuable and in-depth evaluation of control strategies, especially considering that its earlier onset is associated with loss of productivity and independence, which leads to a reduced and deteriorated quality of life. Although various interventions have been proposed for myopia control, consensus on strategies for their application has not yet been reached globally. Atropine drops and orthokeratology lenses stand out from the other available approaches with high efficacy in slowing axial progression. A thorough assessment of the risks of myopia onset and progression, assessment of the individual benefit:risk ratio and quality of life in children is crucial in making clinical decisions. All approaches to myopia control have an important role in reducing the overall morbidity, as the needs and requirements of individual patients vary greatly depending on age, attitude, access, safety, subjective needs, parental judgment, individual factors and rate of progression. Timely intervention with contact lenses and spectacles can significantly reduce the overall burden of myopia.

Further studies are needed on the efficacy of myopia control strategies in patients with high myopia, both alone and through combination therapy. In addition to traditional models for predicting myopic onset and progression in a population, individualized prediction using machine learning and age-specific refraction data is promising. Although emerging combined approaches to control axial progression are increasingly being used in clinical practice, identifying the populations that need them and investigating and monitoring individual clinical, subjective and quality-of-life responses remain the most important steps for clinicians in navigating the long and complex journey towards successful myopia control.

Keywords myopia control, atropine drops, orthokeratology, quality of life, efficacy

APPENDICES

Informed Consent Form

"Myopia Control"

Dear Parents,

Your children are invited to participate in our study. In this regard, we ask you to carefully read the text below and, if you agree, to sign.

Myopia is among the most common causes of vision loss in the world and creates an alarming global epidemic with devastating consequences for people's quality of life. Its high levels increase the risk of developing pathological conditions such as myopic macular degeneration, retinal detachment, glaucoma and cataracts and is a leading cause of visual impairment and blindness in many countries. Reducing the age of onset of myopia is of great importance, since the earlier the onset, the higher all the associated risks of accompanying eye conditions. Myopia control is of key importance to prevent these consequences, and its efficacy is the subject of the present scientific study. We guarantee anonymity and ethics with regard to your personal data.

1. The purpose and all necessary actions related to conducting the study were explained to me.

2. I declare that I was given the opportunity to ask any questions regarding the study in which my child will participate.

3. It was explained to me that I have the right to refuse participation.

4. I am informed that I can withdraw my consent and terminate my participation at any time without negative consequences.

5. I am informed that anonymity in the study is guaranteed and the data will be presented in a summarized form.

6. I declare that I have read this form and am aware of its content.

If you have more specific questions, you can seek information at USBOBAL, Varna, fl.2. room 215 or via phone at: 0888/605805 (lead researcher Dr. Maria Stoeva).

I give my consent for my child to participate in the "Myopia Control" study.

Date ....

Informed consent received: .... Signature: ....

Names .... Signature: ....

/research team member/

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