ORIGINAL RESEARCH

Group-Based Trajectory Modeling to Identify Factors Influencing the Development of Myopia in Patients Receiving Orthokeratology

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Purpose: To analyze the factors influencing the progression of myopia in adolescents receiving orthokeratology.

Methods: This prospective cohort study collected the data of 378 myopia patients receiving orthokeratology. The follow-up time was 12 months ranging from December 2015 to December 2019. The group-based trajectory modeling (GBTM) was used to identify similar developmental trajectories in the levels of uncorrected visual acuity and changes of axial length elongation. Univariate and multivariate logistic regression analyses were conducted to explore the influencing factors of myopia development in patients wearing orthokeratology.

Results: There was no factor having effect on visual acuity (left) and visual acuity (right) in different trajectories (all $P>0.05$). The corneal curvature K1 (left) (OR=0.382, 95% CI: 0.188–0.776), corneal curvature K2 (left) (OR=0.362, 95% CI: 0.187–0.699), degree of spherical refraction (left) (OR=0.139, 95% CI: 0.082–0.235) and spherical equivalent (left) (OR=7.276, 95% CI: 3.724–14.215) were factors associated with the changes of axial length elongation (left). The corneal curvature K1 (right) (OR=0.260, 95% CI: 0.116–0.585), corneal curvature K2 (left) (OR=0.272, 95% CI: 0.121–0.610) and degree of spherical refraction (right) (OR=0.129, 95% CI: 0.068–0.244) were correlated with the changes of axial length elongation (right). All $P<0.05$.

Conclusion: Orthokeratology is a promising method for controlling the progression of myopia. The corneal curvature, degree of spherical refraction and spherical equivalent were factors influencing the changes of axial length elongation in myopia patients wearing orthokeratology. The findings might give a reference for the application of orthokeratology in clinic.

Keywords: group-based trajectory modeling, myopia, orthokeratology, factors

Introduction

Myopia has become a global public health problem. According to a previous study, about 30% of the global population is myopic, and the rate of it may increase to 50% by 2050.[1] China has the second largest number of myopic teenagers with a prevalence of myopia as high as 59%.[2] Myopia is one of the major causes of blindness, which seriously affects the health and quality of life in patients.[3] It is imperative to find effective treatments to slow the progress of myopia. Currently, the treatments to slow the progression of myopia mainly include drugs, glasses, and laser surgery, and wearing orthokeratology is considered to be one of the most promising methods.[4] Orthokeratology is a specially designed rigid contact lens with a flat center and steep sides worn on the cornea. Previous studies have confirmed that orthokeratology can effectively improve the naked visual acuity of patients and control the development of myopia in adolescents.[5,6] Compared with surgery, orthokeratology is reversible and painless, which has become an important method for the control of myopia in teenagers and has been widely used in clinical treatment in recent years.[7]

Orthokeratology has achieved different efficacies in the treatment of adolescent myopia.[6,8] Currently, the factors affecting the control of the progress of adolescent myopia by orthokeratology and the specific population suitable for

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orthokeratology have not been determined. According to previous studies, the axial length elongation change and initial orthokeratology wearing age were important factors affecting the efficacy of orthokeratology.[9,10] Corneal curvature was also considered as an influencing factor for predicting the efficacy of orthokeratology.[11] Another study was contradicted with this conclusion, showing that neither short-term nor long-term changes in corneal curvature were associated with the efficacy of orthokeratology in white European children.[12] The factors influencing the efficacy of orthokeratology in adolescents were not consistent. This study collected the clinical data to analyze the factors influencing the progression of myopia in adolescents receiving orthokeratology treatments, which might provide a theoretical guidance for the use of orthokeratology in clinic.

Methods
Study Population
In this prospective cohort study, we enrolled 378 patients with myopia. The range of myopia in these patients was diopter ≤-6.00 D, corneal astigmatism≤-2.00 D, the best corrected visual acuity 0.5, and intraocular pressure within the normal range. Among them, we excluded 10 patients who were older than 18 years; 3 cases with contraindication for orthokeratology; 7 patients with amblyopia, strabismus, and abnormal visual function; and 358 patients were included and received orthokeratology, and the follow-up was performed. The follow-up time ranged from December 2015 to December 2019. The follow-up time was 12 months and the follow-up was conducted on 1 day, 3 months, 6 months and 12 months after wearing orthokeratology. The screen process is shown in Figure 1. The informed consents were obtained from the participants and this study was approved by the Ethics Committee of the Aier Eye Hospital Group, Kunming Air Eye Hospital. The current study complied with the Declaration of Helsinki.

Group-Based Trajectory Modeling
According to the purpose of the study, the group-based trajectory modeling (GBTM) was used to identify similar developmental trajectories in the levels of uncorrected visual acuity (diopter) and axial length elongation (mm). The survey wave was used as a timescale of trajectories to simulate the uncorrected visual acuity and axial length elongation trajectories in the sample in all waves. First, a base model without covariates was constructed to determine the number of
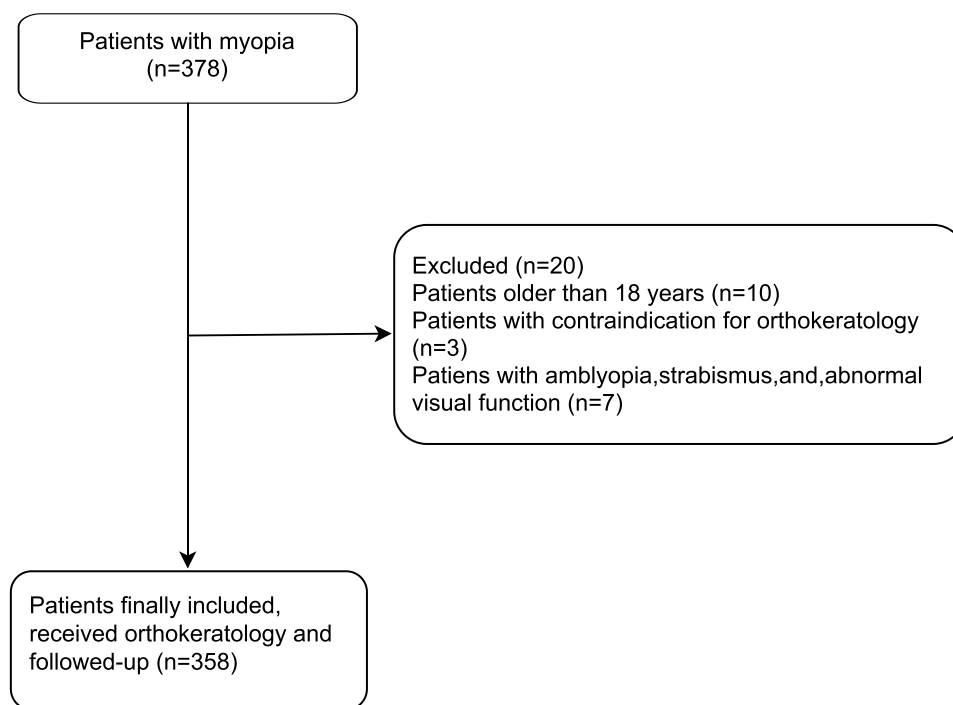

Figure 1 The screen process of the participants of the patients.

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groups and the order of the polynomial functions of the survey wave. The best-fitting model was considered as the trajectory group with the highest probability, which was based on goodness-of-fit statistics via the Bayesian information criterion (BIC) (the one whose absolute value of BIC is closest to zero is selected as the appropriate model). Second, each participant was assigned to the corresponding trajectory group according to the maximum likelihood estimation to estimate the probability of producing variance in uncorrected visual acuity and axial length elongation of each group. Third, univariate analysis and multivariate logistic regression analysis were applied to explore the influencing factors of the uncorrected visual acuity and axial length elongation at different points.

Data Collection

The clinical data of patients receiving orthokeratology were collected to evaluate the factors influencing the development of myopia. The data included wearing age (years), gender, allergic history, history of wearing glasses or orthokeratology, myopia time (month), origin of orthokeratology (China, America, Japanese or others), pupil diameter (left) (mm), pupil diameter (right) (mm), intraocular pressure (left) (mmHg), intraocular pressure (right) (mmHg), corneal curvature: K1 (left) (diopter), corneal curvature: K1 (right) (diopter), corneal curvature: K2 (left) (diopter), corneal curvature: K2 (right) (diopter), e value of corneal curvature (left), e value of corneal curvature (right), corneal thickness (left) (μm), corneal thickness (right) (μm), degree of spherical refraction (left), degree of spherical refraction (right), spherical equivalent (left) (diopter), spherical equivalent (right) (diopter), anterior chamber depth (left) (mm), anterior chamber depth (right) (mm).

Statistical Analysis

Statistical analyses were performed using SAS 9.4 and R 4.20 software. The measurement data of normal distribution were described as Mean ± standard deviation (Mean ± SD), and the independent sample t test and variance test were used for the comparisons between groups. The non-normal data were described as [M (Q1, Q3)], and the Mann–Whitney U rank sum test and Kruskal–Wallis H rank sum test were used for the comparisons between groups. The enumeration data were displayed as n (%). Chi-square test or Fisher's exact probability method were applied for the comparisons between groups. Logistic regression was conducted to explore the influencing factors of myopia development in patients wearing orthokeratology. All statistical tests were conducted by two-sided tests, and $P<0.05$ was considered statistically significant.

Results
Trajectory Grouping of Visual Acuity and Axial Length Elongation

Based on GBTM, the visual acuity of left eye [visual acuity (left)] and visual acuity (right) respectively showed two different trajectories, while the axial length elongation (left) and axial length elongation (right) were respectively divided into three trajectories according to the baseline data of 1 day after wearing, 3 months after wearing, 6 months after wearing, and 12 months after wearing orthokeratology. As shown in Figure 2A, in terms of the visual acuity (left), in trajectory 1 (Group 1), the visual acuity (left) was at a low level, so it was defined as "low-initial level group" (n=240, 67.04%). In trajectory 2 (Group 2), the visual acuity (left) was at a high level, so it was defined as "high-initial level group" (n=118, 32.96%). Similarly, for visual acuity (right), trajectory 1 (Group 1) was defined as "low-initial level group" (n=229, 63.97%). Trajectory 2 (Group 2) was defined as "high-initial level group" (n=129, 36.03%) (Figure 2B). Regarding axial length elongation (left), the population of trajectory 1 (Group 1) had a low initial level, so it was defined as "low-initial level group" (n=124, 34.64%). In trajectory 2 (Group 2), the axial length elongation (left) had a medium initial level, and it was defined as "medium-initial level group" (n=195, 54.47%). In trajectory 3 (Group 3), the population had a relatively high level of axial length elongation initially, and it was defined as "high-initial level group" (n=39, 10.89%) (Figure 2C). Similarly, for the axial length elongation (right), trajectory 1 (Group 1) indicated "low-initial level group" (n=86, 24.02%); Trajectories type 2 (Group 2) was defined as "medium-initial level group" (n=181, 50.56%); Trajectory type 3 (Group 3) was defined as "high-initial level group" (n=91, 25.42%) (Figure 2D).
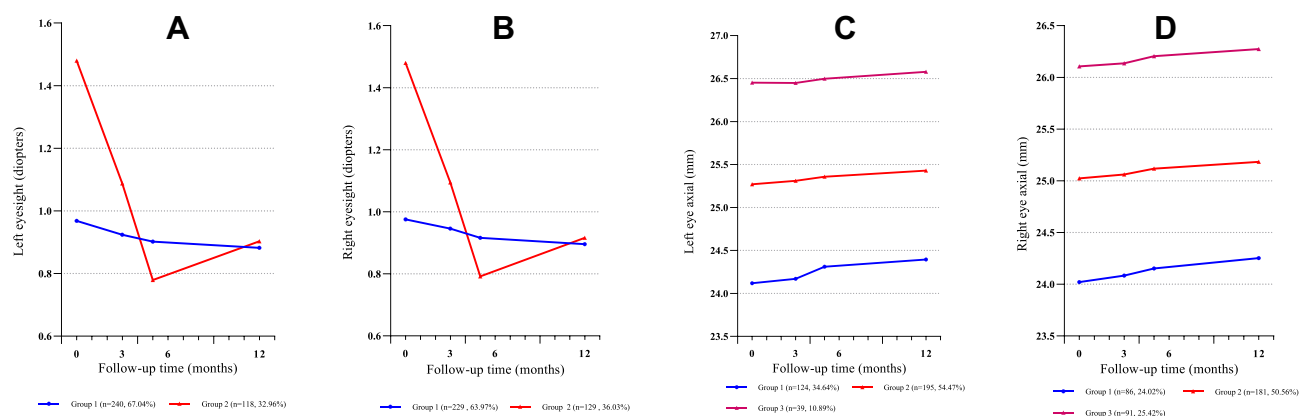
Figure 2 The trajectories of visual acuity (left) (**A**), visual acuity (right) (**B**), axial length elongation (left) (**C**) and axial length elongation (right) (**D**).

The Baseline Characteristics of Participants

A total of 358 patients with myopia who wore orthokeratology were involved in this study. The average age of patients wearing orthokeratology was 12.08±2.40 years. Among them, 139 were males, which accounted for 38.83%. Seventy (19.55%) participants had a history of allergies. A total of 323 (90.22%) had a history of glasses or orthokeratology wearing. The median myopia time was 36 months. The origins of orthokeratology were from China, the United States, Japan or some other countries. There were 296 (82.68%) patients worn orthokeratology from China, 6 (1.68%) patients worn orthokeratology from the United States, and 36 (10.06%) patients worn orthokeratology from other countries (Table 1). As exhibited in Supplementary Table 1, the visual acuity (left) decreased −0.20 diopter, and the decrease of the visual acuity (left) was statistically different between Group 1 and Group 2 (0.00 diopter vs −0.50 diopter). The visual acuity (right) decreased −0.20 diopter, and the decrease was higher in Group 2 than Group 1 (−0.50 diopter vs 0.00 diopter) (Supplementary Table 2). In terms of the axial length elongation (left), the total elongation was 0.14 mm, and statistical difference was observed in the elongations of Group 1, Group 2 and Group 3 (Supplementary Table 3). The total elongation of the axial length elongation (right) was 0.16 mm, and no significant difference was found among the elongations in Group 1, Group 2 and Group 3 (Supplementary Table 4).

Table 1 The Baseline Characteristics of Participates

Variables	Description (n=358)
Wearing age, Mean±SD	12.08±2.40
Gender, n (%)	
Male	139 (38.83)
Female	219 (61.17)
Allergic history, n (%)	
No	288 (80.45)
Yes	70 (19.55)
History of wearing glasses or orthokeratology, n (%)	
No	35 (9.78)
Yes	323 (90.22)
Myopia time (month), $M(Q_1,Q_3)$	36 (18.48)
Origin of orthokeratology, n (%)	
China	296 (82.68)
America	6 (1.68)
Japanese	20 (5.59)
Others	36 (10.06)

Table 2 Univariate Logistic Regression Results of Visual Acuity (Left)

Variables	P	OR	95% CI	
			Lower	Upper
Wearing age, Mean±SD	0.996	1.000	0.912	1.097
Gender, n (%)				
Male		Ref		
Female	0.117	1.447	0.916	2.309
Allergic history, n (%)				
No		Ref		
Yes	0.250	0.711	0.39	1.252
History of wearing glasses or orthokeratology, n (%)				
No		Ref		
Yes	0.092	2.094	0.934	5.346
Myopia time, $M(Q_1,Q_3)$				
Origin of orthokeratology, n (%)				
China		Ref		
America	0.396	0.392	0.02	2.473
Japanese	0.911	1.055	0.386	2.662
Others	0.471	0.754	0.335	1.58
Myopia time, $M(Q_1,Q_3)$	0.189	0.993	0.982	1.003
Pupil diameter (right), Mean±SD	0.130	1.25	0.941	1.682
Pupil diameter (left), Mean±SD	0.667	1.066	0.798	1.427
Intraocular pressure (right), Mean±SD	0.596	1.026	0.934	1.126
Intraocular pressure (left), Mean±SD	0.844	1.009	0.92	1.107
Corneal curvature: K1 (right), Mean±SD	0.985	1.002	0.84	1.194
Corneal curvature: K1(left), Mean±SD	0.951	1.006	0.839	1.205
Corneal curvature: K2 (right), Mean±SD	0.679	0.966	0.821	1.137
Corneal curvature: K2 (left), Mean±SD	0.985	0.998	0.849	1.175
e value of corneal curvature (right), Mean±SD	0.808	1.289	0.169	10.154
e value of corneal curvature (left), Mean±SD	0.726	0.688	0.084	5.591
Corneal thickness (right), Mean±SD	0.343	1.004	0.996	1.011
Corneal thickness (left), Mean±SD	0.131	1.006	0.998	1.013
Degree of spherical refraction (right), $M(Q_1,Q_3)$	0.841	0.981	0.81	1.187
Degree of spherical refraction (left), $M(Q_1,Q_3)$	0.740	0.968	0.797	1.175
Spherical equivalent (right), $M(Q_1,Q_3)$	0.904	0.989	0.828	1.181
Spherical equivalent (left), $M(Q_1,Q_3)$	0.871	1.015	0.846	1.217
Anterior chamber depth (right), Mean±SD	0.565	0.736	0.258	2.088
Anterior chamber depth (left) (mm), Mean±SD	0.891	0.941	0.374	2.22

Univariate Analysis of Factors Influencing Visual Acuity and Axial Length Elongation in Different Trajectories

As displayed in Tables 2 and 3, the data of univariate analysis delineated that there was no statistical difference in different trajectories in both visual acuity (right) and visual acuity (left). All $P>0.05$.

Regarding axial length elongation (left), the wearing age of orthokeratology ($F=10.074$, $P<0.001$), males ($\chi^2=13.355$, $P=0.001$), and myopia time ($\chi^2=45.157$, $P<0.001$), origin of orthokeratology ($\chi^2=13.573$, $P=0.035$), corneal curvature K1 (left) ($F=67.522$, $P<0.001$), corneal curvature K1 (right) ($F=63.271$, $P<0.001$), corneal curvature K2 (left) ($F=57.621$, $P<0.001$), corneal curvature K2 (right) ($F=45.840$, $P<0.001$), e value of corneal curvature (left) ($F=3.308$, $P=0.038$), e value of corneal curvature (right) ($F=3.486$, $P=0.032$), degree of spherical refraction (left) ($\chi^2=86.682$, $P<0.001$), degree of spherical refraction (right) ($\chi^2=58.031$, $P<0.001$), spherical equivalent (left) ($\chi^2=80.901$, $P<0.001$), spherical

Table 3 Univariate Logistic Regression Results of Visual Acuity (Right)

Variables	P	OR	95% CI	
			Lower	**Upper**
Wearing age, Mean±SD	0.457	1.035	0.946	1.132
Gender, n (%)				
Male		Ref		
Female	0.356	1.234	0.792	1.936
Allergic history, n (%)				
No		Ref		
Yes	0.149	0.657	0.365	1.147
History of wearing glasses or orthokeratology, n (%)				
No		Ref		
Yes	0.551	1.256	0.607	2.753
Myopia time, M (Q_1,Q_3)				
Origin of orthokeratology, n (%)				
China		Ref		
America	0.338	0.348	0.018	2.195
Japanese	0.231	1.741	0.693	4.372
Others	0.305	0.670	0.298	1.401
Myopia time, M (Q_1,Q_3)	0.127	0.992	0.982	1.002
Pupil diameter (right), Mean±SD	0.214	1.193	0.907	1.586
Pupil diameter (left), Mean±SD	0.623	1.076	0.805	1.443
Intraocular pressure (right), Mean±SD	0.850	1.009	0.921	1.105
Intraocular pressure (left), Mean±SD	0.923	1.005	0.915	1.103
Corneal curvature: K1 (right), Mean±SD	0.631	1.043	0.879	1.238
Corneal curvature: K1(left), Mean±SD	0.910	1.011	0.843	1.212
Corneal curvature: K2 (right), Mean±SD	0.959	0.996	0.85	1.167
Corneal curvature: K2 (left), Mean±SD	0.954	1.005	0.854	1.183
e value of corneal curvature (right), Mean±SD	0.753	0.728	0.100	5.343
e value of corneal curvature (left), Mean±SD	0.934	0.915	0.111	7.518
Corneal thickness (right), Mean±SD	0.253	1.004	0.997	1.012
Corneal thickness (left), Mean±SD	0.256	1.004	0.997	1.012
Degree of spherical refraction (right), M (Q_1,Q_3)	0.594	1.052	0.874	1.268
Degree of spherical refraction (left), M (Q_1,Q_3)	0.869	0.984	0.810	1.196
Spherical equivalent (right), M (Q_1,Q_3)	0.450	0.935	0.786	1.112
Spherical equivalent (left), M (Q_1,Q_3)	0.979	0.998	0.830	1.197
Anterior chamber depth (right), Mean±SD	0.62	1.294	0.468	3.599
Anterior chamber depth (left) (mm), Mean±SD	0.897	1.058	0.428	2.511

equivalent (right) (χ^2=54.267, P<0.001), anterior chamber depth (left) (F=8.290, P<0.001) and anterior chamber depth (right) (F=12.054, P<0.001) levels were statistically different among three trajectories (Table 4).

In different trajectories axial length elongation (right), the wearing age (F=8.774, P<0.001), males (χ^2=19.853, P<0.001), history of wearing glasses or orthokeratology (χ^2=7.218, P=0.027), myopia time (χ^2=38.353, P<0.001), corneal curvature K1 (left) (F=82.776, P<0.001), corneal curvature K1 (right) (F=94.212, P<0.001), corneal curvature K2 (left) (F=65.051, P<0.001), corneal curvature K2 (right) (F=63.505, P<0.001), degree of spherical refraction (left) (χ^2=40.912, P<0.001), degree of spherical refraction (right) (χ^2=63.585, P<0.001), spherical equivalent (left) (χ^2=39.820, P<0.001), spherical equivalent (right) (χ^2=39.820, P<0.001), anterior chamber depth (left) (F=9.530, P<0.001) and anterior chamber depth (right) (F=15.406, P<0.001) (Table 5).

Table 4 Comparisons of Characters of Axial Length Elongation (Left)

Variables	Total (n=358)	Groups			Statistical Magnitude	P
		Group 1 (n=124)	Group 2 (n=195)	Group 3 (n=39)		
Wearing age, Mean±SD	12.08±2.40	11.55±2.54	12.15±2.21	13.46±2.34	F=10.074	<0.001
Gender, n (%)					χ^2=13.355	0.001
Male	139 (38.83)	33 (26.61)	85 (43.59)	21 (53.85)		
Female	219 (61.17)	91 (73.39)	110 (56.41)	18 (46.15)		
Allergic history, n (%)					χ^2=0.589	0.745
No	288 (80.45)	98 (79.03)	157 (80.51)	33 (84.62)		
Yes	70 (19.55)	26 (20.97)	38 (19.49)	6 (15.38)		
History of wearing glasses or orthokeratology, n (%)					χ^2=5.074	0.079
No	35 (9.78)	18 (14.52)	15 (7.69)	2 (5.13)		
Yes	323 (90.22)	106 (85.48)	180 (92.31)	37 (94.87)		
Myopia time, M (Q$_1$, Q$_3$)	36 (18, 48)	21 (12, 36)	36 (18, 48)	48 (36, 60)	χ^2=45.157	<0.001
Origin of orthokeratology, n (%)					χ^2=13.573	0.035
China	296 (82.68)	100 (80.65)	165 (84.62)	31 (79.49)		
America	6 (1.68)	1 (0.81)	2 (1.03)	3 (7.69)		
Japanese	20 (5.59)	6 (4.84)	13 (6.67)	1 (2.56)		
Others	36 (10.06)	17 (13.71)	15 (7.69)	4 (10.26)		
Pupil diameter (left), Mean±SD	6.55±0.77	6.51±0.69	6.53±0.80	6.79±0.89	F=2.104	0.124
Pupil diameter (right), Mean±SD	6.69±0.80	6.67±0.66	6.67±0.85	6.84±0.94	F=0.784	0.457
Intraocular pressure (left), Mean±SD	15.30±2.42	15.26±2.47	15.25±2.33	15.58±2.69	F=0.315	0.730
Intraocular pressure (right), Mean±SD	15.39±2.38	15.38±2.39	15.40±2.32	15.38±2.67	F=0.004	0.996
Corneal curvature: K1 (left), Mean±SD	42.47±1.24	43.25±1.01	42.19±1.11	41.22±0.91	F=67.522	<0.001
Corneal curvature: K1(right), Mean±SD	42.55±1.27	43.33±1.07	42.31±1.14	41.26±0.86	F=63.271	<0.001
Corneal curvature: K2 (left), Mean±SD	43.89±1.39	44.73±1.07	43.57±1.28	42.64±1.20	F=57.621	<0.001
Corneal curvature: K2 (right), Mean±SD	43.89±1.37	44.66±1.09	43.62±1.26	42.76±1.41	F=45.840	<0.001
e value of corneal curvature (left), Mean±SD	0.55±0.11	0.56±0.11	0.55±0.11	0.52±0.10	F=3.308	0.038
e value of corneal curvature (right), Mean±SD	0.54±0.11	0.56±0.11	0.54±0.11	0.51±0.09	F=3.486	0.032
Corneal thickness (left), Mean±SD	549.48±30.25	546.86±29.05	551.44±32.14	549.03±24.70	F=0.835	0.435
Corneal thickness (right), Mean±SD	549.14±29.82	546.50±29.23	551.02±30.98	548.36±25.60	F=0.872	0.419
Degree of spherical refraction (left), M (Q$_1$,Q$_3$)	−3.25 (−4.00, −2.50)	−2.50 (−3.25, −2.00)	−3.25 (−4.00, −2.75)	−4.75 (−5.50, −4.10)	χ^2=86.682	<0.001
Degree of spherical refraction (right), M (Q$_1$,Q$_3$)	−3.50 (−4.25, −2.50)	−3.00 (−3.50, −2.25)	−3.50 (−4.25, −2.75)	−4.7 5 (−5.50, −4.25)	χ^2=58.031	<0.001
Spherical equivalent (left), M(Q$_1$,Q$_3$)	3.50 (2.75, 4 0.38)	3.06 (2.31, 3.75)	3.75 (3.00, 4.63)	5.13 (4.38, 6.00)	χ^2=80.901	<0.001
Spherical equivalent (right), M(Q$_1$,Q$_3$)	3.75 (2.75, 4.75)	3.25 (2.50, 4.00)	3.75 (2.75, 4.75)	5.10 (4.50, 5.88)	χ^2=54.267	<0.001
Anterior chamber depth (left), Mean±SD	3.88±0.26	3.82±0.21	3.91±0.29	3.99±0.21	F=8.290	<0.001
Anterior chamber depth (right) (mm), Mean±SD	3.87±0.21	3.81±0.21	3.89±0.21	3.99±0.19	F=12.054	<0.001

Table 5 Comparisons of Characters of Axial Length Elongation (Right)

Variables	Total (n=358)	Groups			Statistical Magnitude	P
		Group 1 (n=86)	Group 2 (n=181)	Group 3 (n=91)		
Wearing age, Mean±SD	12.08±2.40	11.37±2.63	12.04±2.36	12.85±2.02	F=8.774	<0.001
Gender, n (%)					χ^2=19.853	<0.001
Male	139 (38.83)	22 (25.58)	65 (35.91)	52 (57.14)		
Female	219 (61.17)	64 (74.42)	116 (64.09)	39 (42.86)		
Allergic history, n (%)					χ^2=0.175	0.916
No	288 (80.45)	68 (79.07)	147 (81.22)	73 (80.22)		
Yes	70 (19.55)	18 (20.93)	34 (18.78)	18 (19.78)		
History of wearing glasses or orthokeratology, n (%)					χ^2=7.218	0.027
No	35 (9.78)	13 (15.12)	19 (10.50)	3 (3.30)		
Yes	323 (90.22)	73 (84.88)	162 (89.50)	88 (96.70)		
Myopia time, M (Q_1, Q_3)	36 (18, 48)	18 (12, 36)	30 (18, 48)	48 (36, 60)	χ^2=38.353	<0.001
Origin of orthokeratology, n (%)					χ^2=9.769	0.135
China	296 (82.68)	73 (84.88)	146 (80.66)	77 (84.62)		
America	6 (1.68)	0 (0.00)	2 (1.10)	4 (4.40)		
Japanese	20 (5.59)	3 (3.49)	14 (7.73)	3 (3.30)		
Others	36 (10.06)	10 (11.63)	19 (10.50)	7 (7.69)		
Pupil diameter (left), Mean±SD	6.55±0.77	6.38±0.66	6.59±0.77	6.64±0.86	F=2.703	0.068
Pupil diameter (right), Mean±SD	6.69±0.80	6.55±0.69	6.75±0.80	6.73±0.89	F=1.940	0.145
Intraocular pressure (left), Mean±SD	15.30±2.42	15.28±2.39	15.34±2.36	15.22±2.59	F=0.069	0.934
Intraocular pressure (right), Mean±SD	15.39±2.38	15.49±2.48	15.39±2.33	15.28±2.41	F=0.167	0.846
Corneal curvature: K1 (left), Mean±SD	42.47±1.24	43.52±0.94	42.47±1.06	41.48±1.01	F=82.776	<0.001
Corneal curvature: K1(right), Mean±SD	42.55±1.27	43.65±0.99	42.55±1.06	41.53±0.98	F=94.212	<0.001
Corneal curvature: K2 (left), Mean±SD	43.89±1.39	44.98±1.00	43.88±1.20	42.90±1.28	F=65.051	<0.001
Corneal curvature: K2 (right), Mean±SD	43.89±1.37	44.96±1.02	43.85±1.17	42.96±1.33	F=63.505	<0.001
e value of corneal curvature (left), Mean±SD	0.55±0.11	0.57±0.11	0.54±0.11	0.54±0.10	F=2.525	0.082
e value of corneal curvature (right), Mean±SD	0.54±0.11	0.57±0.11	0.53±0.11	0.54±0.10	F=2.549	0.080
Corneal thickness (left), Mean±SD	549.48±30.25	548.28±29.99	549.31±31.27	550.94±28.64	F=0.166	0.847
Corneal thickness (right), Mean±SD	549.14±29.82	548.51±29.99	548.73±30.35	550.54±28.88	F=0.135	0.873
Degree of spherical refraction (left), M (Q_1, Q_3)	−3.25 (−4.00, −2.50)	−2.75 (−3.25, −2.25)	−3.25 (−4.00, −2.50)	−3.75 (−4.75, −3.00)	χ^2=40.912	<0.001
Degree of spherical refraction (right), M (Q_1, Q_3)	−3.50 (−4.25, −2.50)	−2.75 (−3.25, −2.25)	−3.50 (−4.25, − 2.75)	−4.25 (−5.00, -3.50)	χ^2=63.585	<0.001
Spherical equivalent (left), M (Q_1, Q_3)	3.50 (2.75, 4.38)	3.13 (2.50, 3.78)	3.50 (2.75, 4.38)	4.30 (3.25, 5.50)	χ^2=39.820	<0.001
Spherical equivalent (right), M (Q_1, Q_3)	3.75 (2.75, 4.75)	3.00 (2.25, 3.75)	3.75 (2.75, 4.50)	4.75 (3.75, 5.50)	χ^2=39.820	<0.001
Anterior chamber depth (left), Mean±SD	3.88±0.26	3.79±0.19	3.89±0.30	3.96±0.20	F=9.530	<0.001
Anterior chamber depth (right) (mm), Mean±SD	3.87±0.21	3.79±0.20	3.88±0.22	3.96±0.18	F=15.406	<0.001

Table 6 Logistic Regression Analysis of Axial Length Elongation (Left)

Model	Variables	β	SE	Wald	P value	OR	95% CI	
							Lower	Upper
Model 1	Constant	65.526	9.169	51.068	<0.001	–	–	–
	Corneal curvature: K1 (left)	−0.962	0.361	7.075	0.007	0.382	0.188	0.776
	Corneal curvature: K2 (left)	−1.016	0.335	9.149	0.003	0.362	0.187	0.699
	Degree of spherical refraction (left)	−1.971	0.267	54.298	<0.001	0.139	0.082	0.235
Model 2	Constant	−9.1584	1.4658	39.0387	<0.001	–	–	–
	Spherical equivalent (left)	1.9846	0.3417	33.7337	<0.001	7.276	3.724	14.215

Notes: Model 1: Group 2 vs Group 1, Group 1 as the control group. Model 2: Group 3 vs Group 1, Group 1 as the control group.

Table 7 Logistic Regression Analysis of Axial Length Elongation (Right)

Model	Variables	β	SE	Wald	P	OR	95% CI	
							Lower	Upper
Model 1	Constant	84.632	13.560	38.949	<0.001	–	–	–
	Corneal curvature: K1 (right)	−1.346	0.413	10.585	0.001	0.260	0.116	0.585
	Degree of spherical refraction (right)	−2.047	0.325	39.601	<0.001	0.129	0.068	0.244
	Corneal curvature: K2 (left)	−1.303	0.412	9.983	0.002	0.272	0.121	0.610
Model 2	Constant	136.8	40.128	11.614	0.001	–	–	–
	Corneal curvature: K1 (right)	−4.843	1.402	11.931	0.001	0.008	0.001	0.123
	Degree of spherical refraction (right)	−3.829	1.211	9.991	0.002	0.022	0.002	0.233

Notes: Model 1: Group 2 vs Group 1, Group 1 as the control group. Model 2: Group 3 vs Group 1, Group 1 as the control group.

Multivariate Analysis of Factors Influencing Visual Acuity and Axial Length Elongation in Different Trajectories

According to results of the multivariate logistic regression analysis on the visual acuity (left) and visual acuity (right), no factor was found to have a statistical effect on visual acuity (left) and visual acuity (right). All *P*>0.05.

The data of multivariate logistic regression analysis on axial length elongation (left) showed that in Model 1, compared with Group 1, the corneal curvature K1 (left) (OR=0.382, 95% CI: 0.188–0.776, *P*=0.007), corneal curvature K2 (left) (OR=0.362, 95% CI: 0.187–0.699, *P*=0.003) and degree of spherical refraction (left) (OR=0.139, 95% CI: 0.082–0.235, *P*<0.001) were protective factors for the axial length elongation (left) in Group 2. In Model 2, compared with Group 1, spherical equivalent (left) (OR=7.276, 95% CI: 3.724–14.215, *P*<0.001) was a risk factor for the axial length elongation in Group 3 (Table 6).

As shown in Table 7, the results of multivariate logistic regression analysis on axial length elongation (right) depicted that in Model 1, relative to Group 1, the corneal curvature K1 (right) (OR=0.260, 95% CI: 0.116–0.585, *P*=0.001), corneal curvature K2 (left) (OR=0.272, 95% CI: 0.121–0.610, *P*=0.002) and degree of spherical refraction (right) (OR=0.129, 95% CI: 0.068–0.244, *P*<0.001) were protective factors for the axial length elongation (right) in Group 2. In Model 2, compared with Group 1, the corneal curvature K1 (right) (OR=0.008, 95% CI: 0.001–0.123, *P*=0.001) and degree of spherical refraction (right) (OR=0.022, 95% CI: 0.002–0.233, *P*=0.002) were protective factors for axial length elongation (right) in Group 3.

Discussion

This study analyzed the factors influencing the progression of myopia in 358 patients with orthokeratology. The results revealed that there was no factor having effects on visual acuity (left) and visual acuity (right) statistically in different trajectories. The corneal curvature K1 (left), corneal curvature K2 (left), degree of spherical refraction (left) and spherical

equivalent (left) were factors associated with the changes of axial length elongation (left). The corneal curvature K1 (right), corneal curvature K2 (left) and degree of spherical refraction (right) levels were correlated with the changes of axial length elongation (right). The findings of our study might help identify patients suitable for using orthokeratology.

The axial length elongation of the eyeball is the main reason for the gradual deepening of myopia and is regarded as an index of myopic progression.[13] Under normal circumstances, the axial length of the eyes is about 21 mm in children aged 5–6 years, 21.5 mm in children aged 7–8 years, 22 mm in children aged 9–10 years, 24 mm in children aged 17–18 years. In clinic, the axial length greater than 24 mm is considered myopia.[14] Kong et al followed up 724 myopic children with orthokeratology for 6 months-65 months, and found that corneal curvature was an independent factor affecting the control effect of myopia.[15] A previous study revealed that the corneal curvature might be a predictor for the changes of axial length elongation in myopic children with orthokeratology.[16] Zhong et al analyzed the changes of corneal curvature before and after wearing orthokeratology in 32 myopic children and found that the changes of axial length elongation were 54–69% slower in those with higher levels of corneal curvature.[17] According to the data in a study of Kang et al, orthokeratology can cause significant changes in the peripheral corneal refraction and corneal topography, especially on the first night of wearing, the peripheral corneal refraction and corneal refractive power in patients on the meridian level have the greatest changes, and the peripheral retina also produce myopic defocus.[18] Corneal curvature includes the horizontal keratometry (K1) and vertical keratometry (K2).[19] In our study, the results showed that the corneal curvature K1 (left) and corneal curvature K2 (left) were protective factors for the axial length elongation (left). Additionally, the corneal curvature K1 (right) and corneal curvature K2 (left) were protective factors for the axial length elongation (right) in Group 2, indicating a higher corneal curvature was negatively correlated with the changes of axial length elongation in patients with medium initial level of axial length. The degree of spherical refraction represents the degree of myopia or hypermetropia and minus indicates myopia in patients.[20] A previous study demonstrated that a higher myopia degree could lead to a better effect on myopia controlling in patients wearing orthokeratology.[21] The study of Kakita et al also confirmed that the effect of orthokeratology was better on patients with higher degrees of myopia.[22] Herein, the degree of spherical refraction was identified as a protective factor in patients with medium initial levels compared with low initial levels, suggesting a higher initial degree of spherical refraction may have better effects on myopia control in patients with orthokeratology. This may be due to the myopic defocus around the retina can delay or prevent the increase of myopia. Patients with a higher degree of myopia can achieve better shaping degree and change in peripheral refractive light by orthokeratology. Previously, a study reported that the degree of spherical equivalent was negatively associated with the changes of diopter in adolescents wearing orthokeratology.[23] In the current study, compared with Group 1, spherical equivalent was a risk factor for the axial length elongation in Group 3, suggesting a higher spherical equivalent degree might have a longer axial length elongation (left) in patients. This may be due to the small samples in Group 3 of left eyes. Although this was not consistent with the results in previous studies, orthokeratology had good overall effects in controlling axial length elongation in all three groups.

The present study evaluated the factors affecting the development of myopia in patients receiving orthokeratology based on GBTM. GBTMs are substantially being used in clinical research to map the developmental course of symptoms and assess heterogeneity in response to clinical interventions.[24] GBTMs could clearly observe the development trajectories of development of myopia at different time points. The results delineated that the trajectories visual acuity in both groups achieved good controlling effects after 1 year. The trajectories of axial length elongation after wearing orthokeratology all developed slowly. These data suggested that orthokeratology could effectively control the development of myopia, which might be a promising method for myopia treatment in the clinic. There were some limitations in the present study. Firstly, the corneal curvature K2 of the left eye was identified as a factor influencing the axial length elongation of the right eye, but the deep regulatory mechanisms of it was not explored in this study and required to be investigated in further studies. Secondly, the small sample size was relatively small in Group 3 of left eyes, which might decrease the statistical power of our study. Thirdly, we did not explore whether the results may differ in patients of left-handed and right-handed and the influence of the dominant eye of the patients was not determined. In the future, more well-signed studies with large scale sample size were called for to confirm the findings of this study.

Conclusions

Our study analyzed the factors associated with the progression of myopia patients with orthokeratology via GBTM. The results depicted that the corneal curvature, degree of spherical refraction and spherical equivalent were factors associated with the changes of axial length elongation in myopia patients. Orthokeratology may be a promising method for controlling the progression of myopia. The findings might give a reference for the application of orthokeratology in clinic.

Ethics Approval and Informed Consent

The informed consents were obtained from the participants and this study was approved by the Ethics Committee of the Aier Eye Hospital Group, Kunming Air Eye Hospital ((2019) 0102). Written informed consents were obtained from the participants. All methods were performed in accordance with the relevant guidelines and regulations.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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