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Original Article

Establishment and validation of a prognostic model for controlling adolescents' myopia progression through repeated low-level red-light therapy

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Abstract: Background/Purpose: Repeated low-level red-light (RLRL) therapy has emerged as a possible intervention to control myopia progression. This study aimed to establish and validate a prognostic model for controlling adolescents' myopia progression with RLRL therapy, considering demographic, lifestyle, and ophthalmic parameters. Methods: A retrospective cohort study was conducted on adolescent myopic patients admitted to Cangzhou Central Hospital from January 2022 to June 2023. Patients were divided into a control group and an RLRL treatment group based on their treatment method. Various demographic, lifestyle, and ophthalmic parameters were assessed to identify predictors for treatment response. A comprehensive evaluation using logistic regression and nomogram analysis was performed to identify significant factors associated with treatment outcomes. Results: The study included a total of 145 patients, comprising 82 in the control group and 63 in the RLRL group. RLRL therapy demonstrated significantly better effectiveness in controlling myopia progression, with a reduction of -0.62 ± 0.24 D in the RLRL group compared to -0.75 ± 0.36 D in the control group (P=0.010). Furthermore, the RLRL group exhibited improved visual acuity (logMAR) of 0.12 ± 0.06 compared to 0.15 ± 0.07 in the control group (P=0.015). Moreover, baseline demographic and ophthalmic characteristics showed significant associations with treatment outcome, emphasizing the multifaceted nature of myopia response to RLRL therapy. The nomogram analysis demonstrated high predictive performance, with an AUC of 0.994. Conclusion: This study demonstrates the effectiveness and safety of RLRL therapy in controlling myopia progression among adolescents. The establishment of a prognostic model incorporating demographic, lifestyle, and ophthalmic factors offer a promising approach for predicting treatment outcome.

Keywords: Myopia, adolescents, repeated low-level red light, prognostic model, treatment outcome, personalized medicine

Introduction

The escalating prevalence of myopia, particularly among adolescents, poses a significant public health concern globally [1]. Current estimates suggest that nearly 50% of the world's population will be affected by myopia by 2050, with a substantial portion experiencing high myopia [2]. This trend highlights the urgency for effective interventions that can mitigate myopia progression during the critical years of adolescent ocular development [3]. Traditionally, interventions such as pharmaceutical treatments, optical devices, and lifestyle modifications have been employed to curb myopia progression, yet challenges remain in optimizing efficacy and minimizing associated risks [4].

Repeated low-level red light (RLRL) therapy has garnered attention as a novel approach to managing myopia progression [5]. This innovative intervention exploits specific wavelengths of red light to exert biological effects on ocular tissues, possibly influencing mechanistic pathways involved in myopia development [6]. Recent studies suggest that red light may stimulate choroidal cells, modulate gene expression, and influence choroidal dopamine release,

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potentially regulating ocular growth and refractive errors [7]. These insights provide a foundation for exploring RLRL therapy's utility in the clinical management of adolescent myopia, yet rigorously designed studies are needed to substantiate these therapeutic claims [8].

Current evidence underscores the multifactorial pathogenesis of myopia, with genetic, environmental, and lifestyle factors intricately interwoven [9]. The onset and progression of myopia during adolescence coincide with critical periods of ocular growth, rendering the identification of efficacious management strategies imperative [10]. Despite promising preliminary findings regarding RLRL therapy, the variability in treatment response necessitates a personalized approach [11]. Understanding the nuanced interplay between demographic factors (such as age and family history), lifestyle behaviors (including screen time and outdoor activity), and ophthalmic characteristics (such as axial length and myopic degree) is crucial for predicting treatment outcome [12].

Recent advancements in biophysical research elucidate potential mechanisms through which RLRL therapy influences myopia progression [13]. The interaction between red light and ocular tissues may impact circadian rhythms and melatonin synthesis, pathways critically involved in ocular growth regulation [14]. Additionally, red light's potential anti-inflammatory and neuroprotective effects could alter the ocular microenvironment, reducing factors that exacerbate myopia progression [15]. This scientific rationale, coupled with a need for personalized treatment strategies, underscores the significance of advancing the understanding and clinical application of RLRL therapy.

Moreover, the integration of a prognostic model into clinical practice could significantly improve individualized care approaches [16]. By delineating associations between specific prognostic factors and treatment outcomes, clinicians can deliver more targeted and precise interventions. This approach aligns with the precision medicine paradigm and addresses the unique challenges posed by adolescent myopia progression, ultimately improving myopia management strategies.

This study aims to evaluate rigorously the efficacy and safety profile of RLRL therapy, while also accounting for the myriad factors that influence treatment responsiveness. To this end, a retrospective cohort design was utilized to assess adolescents receiving RLRL therapy in comparison to control counterparts, evaluating both clinical outcomes. Through a comprehensive evaluation of contributing factors, including demographic, lifestyle, and baseline ophthalmic characteristics, this research aims to construct a predictive framework that enhances intervention selection and maximizes therapeutic benefit.

Materials and methods

Study design and participants

This study employed a retrospective cohort design to evaluate the effectiveness and safety of RLRL therapy in controlling myopia progression among adolescents. We selected adolescent myopia patients admitted to Cangzhou Central Hospital from January 2022 to June 2023 and divided them into a control group and an RLRL treatment group based on their treatment method. We analyzed the prognosis of the RLRL group and classified the patients into a poor prognosis group and a good prognosis group. The study was approved by the institutional review board (IRB) of Cangzhou Central Hospital (No.2024-1236-01) and adhered to the principles outlined in the Declaration of Helsinki.

Inclusion criteria [17]: Aged 6-14 years; spherical diopter ranged from -1.00 to -6.00 D, and astigmatism was less than -2.00 D; interocular difference in equivalent spherical diopter was less than 1.00 D; intraocular pressure ranged 10-21 mmHg; central corneal thickness was >0.45 mm, corneal curvature ranged 39.00-46.00 D; normal routine ophthalmic examination; myopia progression of at least 0.50 D in the past year; cycloplegic spherical equivalent refraction (SER) ≤-1.00 D, with a best-corrected visual acuity (BCVA) of 1.0 or 20/20 or better in both eyes.

Exclusion criteria: Other ophthalmic diseases; systemic or autoimmune diseases; contraindications for corneal reshaping lens wear such as dry eye, keratitis, or keratoconus; history of contact lens wear, ocular surgery, or prior myopia control treatment; refractive disparities >1.50, poor compliance, or inability to attend

follow-up visits; congenital ocular abnormalities, myopia secondary to other conditions (e.g., retinopathy of prematurity), media opacity in the eye, or active inflammation on the ocular surface.

Sample size and statistical power assessment

The sample size was determined by the number of patients meeting the inclusion and exclusion criteria at Cangzhou Central Hospital from January 2022 to June 2023. Statistical power analysis was conducted using G*Power 3.1.9.7, selecting the "Means: Difference between two independent means (two groups)" option based on t-tests. A post hoc analysis was conducted with the following parameters: two-tailed test, effect size d =0.5, and α error probability =0.05. The sample sizes for the two groups were then used to calculate the power (1-β error probability), resulting in a value of 0.842, indicating an ideal statistical power.

Treatment approach

The RLRL treatment group utilized a table-mountable device (Eyerising; Suzhou Xuanjia Optoelectronics Technology, China) that emits red light at 650 ± 10 nm from semiconductor laser diodes, with an illuminance level of 1600 lux from pupil to fundus. Participants, consisting of children and their parents, were instructed to engage in two 3-minute sessions of RLRL therapy daily, ensuring a minimum 4-hour interval between each session. During the therapy, subjects were positioned in front of the device with both eyes open. Each cycle of treatment spanned 3 months, with a follow-up examination at the end of each cycle, involving routine internal and external ocular examinations, which were duly recorded in the patient's file. The entire treatment period extended over 6 months.

Control group: Participants only wore corrective glasses without any special treatment. Follow-up appointments were scheduled every 3 months, during which routine internal and external ocular examinations were performed and recorded in patient's file. The treatment duration was also 6 months.

Effectiveness criteria: During the treatment period, myopia progression of ≤0.25 D and axial elongation of ≤0.1 mm were considered effective and deemed as the Good Prognosis group. The other patients were deemed as the Poor Prognosis group.

Demographic and basic data collection

Demographic and ophthalmic characteristics were collected at baseline, including age, gender, ethnicity, parental myopia prevalence, socioeconomic status, outdoor activities, parental education level, daily screen time, room illuminance, reading distance, daily reading time, night light exposure, sleep duration, and being particular about food.

Ophthalmic data collection

Before lens fitting, both groups underwent examinations including uncorrected visual acuity, slit-lamp biomicroscopy, dilated fundus examination, standard subjective refraction, and non-contact tonometry, as routine assessments. Patient's uncorrected visual acuity and corneal curvature were recorded. Additionally, measurements of intraocular pressure (IOP), axial length (AL), corneal thickness (CT), anterior chamber depth (ACD), and lens thickness (LT) were obtained. The non-contact tonometer (NT-2000, NIDEK, Japan) was used to measure the IOP of both eyes of all patients, with three readings taken per eye, and the average value recorded. AL, CT, ACD, and LT were measured using the IOLMaster 700 (ZEISS, Germany), with five measurements taken for each eye and the average recorded. Patient attendance rates for examinations and compliance with spectacle wear requirements were also documented. Contrast sensitivity was evaluated using the CGT-1000 Contrast Glare tester (Takagi Seiko in Nagano, Japan). Pupil size ranged from 2.5 to 4 mm at a distance of 35 cm. Assessments were conducted under various conditions: bright adaptation at 85 cd/m^2, bright adaptation with glare, dark adaptation at 3 cd/m^2, dark adaptation with glare, as well as monovision. Additionally, glare contrast sensitivity was measured after approximately 10 minutes of dark adaptation, all assessments conducted under the patient's best corrected visual acuity.

Outcome measures

After six months of treatment, a follow-up examination was conducted for both groups to

Table 1. Demographic characteristics of participants

Data	Control group (n=82)	RLRL group (n=63)	t/χ^2	*p* Value
Age (years)	9.78 ± 1.58	9.31 ± 1.94	1.607	0.110
Gender (M/F)	42 (51.22%)/40 (48.78%)	31 (49.21%)/32 (50.79%)	0.058	0.810
Ethnicity (Han/others)	70 (85.37%)/12 (14.63%)	55 (87.30%)/8 (12.70%)	0.112	0.738
Parental Myopia (Y/N)	50 (60.98%)/32 (39.02%)	45 (71.43%)/18 (28.57%)	1.723	0.189
Socioeconomic Status (Low/Medium/High)	20 (24.39%)/45 (54.88%)/17 (20.73%)	18 (28.57%)/30 (47.62%)/15 (23.81%)	0.754	0.686
Outdoor activities (hours/week)	6.14 ± 1.56	6.24 ± 1.65	0.373	0.710
Education level of parents (years)	12.56 ± 2.53	12.85 ± 2.36	0.704	0.482
Daily screen time (hours)	4.15 ± 1.06	4.27 ± 1.15	0.651	0.516
Room illuminance (lux)	352.69 ± 50.26	361.23 ± 60.48	0.928	0.355
Reading distance (cm)	31.15 ± 5.16	32.46 ± 5.13	1.519	0.131
Daily reading time (hours)	1.58 ± 0.57	1.48 ± 0.65	0.985	0.326
Night light exposure (Y/N)	65 (79.27%)/17 (20.73%)	48 (76.19%)/15 (23.81%)	0.196	0.658
Sleep Duration (hours/night)	7.14 ± 1.04	7.24 ± 1.14	0.550	0.583
Particular about food (Y/N)	40 (48.78%)/42 (51.22%)	29 (46.03%)/34 (53.97%)	0.108	0.743

document the progression of myopia. The primary outcomes included myopia progression and visual acuity (logMAR). Secondary outcomes comprised contrast sensitivity, corneal thickness, anterior chamber depth, as well as side effects or adverse events.

Statistical analysis

Clinical data were collected using the FreeEDC software. Before data analysis, a standardized data cleaning process was conducted to identify and rectify any inconsistencies, errors, or missing values. Specifically, this involved a thorough examination of the dataset, elimination of duplicate entries, correction of data input errors, and handling of missing values. The data were analyzed using SPSS 29.0 and Free Statistics software versions 2.0. Categorical data were expressed as [n (%)] and compared using chi-square test. Continuous variables were first tested for normal distribution using the Shapiro-Wilk method. Normally distributed data were expressed as mean ± SD and compared between groups using t-test. Spearman correlation analyses were used to assess the associations between categorical variables, with a favorable prognosis coded as 1 and an unfavorable prognosis coded as 0. Variables demonstrating significant differences in both difference analysis and correlation analysis were included as covariates in logistic regression analysis and nomogram analysis. Calibrate plot and Receiver operation characteristics (ROC) plot were used to evaluate the performance of the nomogram model. $P<0.05$ was considered significant.

Results

Demographic and basic data

The demographic characteristics of the two groups were similar at baseline (**Table 1**). No significant differences were observed between the RLRL group and the control group in terms of age, gender distribution, ethnicity, parental myopia prevalence, socioeconomic status, outdoor activities, parental education level, daily screen time, room illuminance, reading distance, daily reading time, night light exposure, sleep duration, or dietary preferences (all $P> 0.05$), indicating the two groups were comparable.

Baseline ophthalmic characteristics

Baseline ophthalmic characteristics were evaluated in both groups (**Table 2**), and no significant differences were observed between the two groups in terms of myopia severity distribution, contrast sensitivity, axial length, corneal curvature, corneal thickness, intraocular pressure, lens thickness, anterior chamber depth, attendance rate, or compliance with eyewear (all $P>0.05$). These findings indicate that at baseline, the ophthalmic characteristics were comparable between the two groups. Further investigation will be crucial to determine the effect of RLRL therapy on these ophthalmic parameters and its potential effectiveness in controlling adolescents' myopia progression.

Ocular parameters after 6 months treatment

After 6 months of treatment, significant differences were found between the two groups in

Table 2. Baseline ophthalmic characteristics of participants

Data	Control group (n=82)	RLRL group (n=63)	t/χ^2	*p* Value
Myopia (-D)			0.291	0.865
0-3 D	36 (43.90%)	30 (47.62%)		
3 D-6 D	32 (39.02%)	24 (38.10%)		
>6 D	14 (17.07%)	9 (14.29%)		
Contrast sensitivity	1.54 ± 0.26	1.48 ± 0.19	1.542	0.125
Axial length (mm)	24.18 ± 1.06	24.34 ± 1.09	0.890	0.375
Corneal curvature	42.79 ± 1.13	42.56 ± 1.19	1.187	0.237
Corneal thickness (μm)	537.16 ± 23.49	539.84 ± 23.17	0.685	0.494
Intraocular pressure (mmHg)	13.19 ± 1.33	13.12 ± 1.49	0.298	0.766
Lens thickness	3.23 ± 0.24	3.29 ± 0.26	1.439	0.152
Anterior chamber depth (mm)	3.36 ± 1.15	3.32 ± 1.12	0.210	0.834
Attendance rate (%)	95.14 ± 5.48	96.45 ± 4.58	1.530	0.128
Compliance with eyewear (Y/N)	70 (85.37%)/12 (14.63%)	57 (90.48%)/6 (9.52%)	0.856	0.355

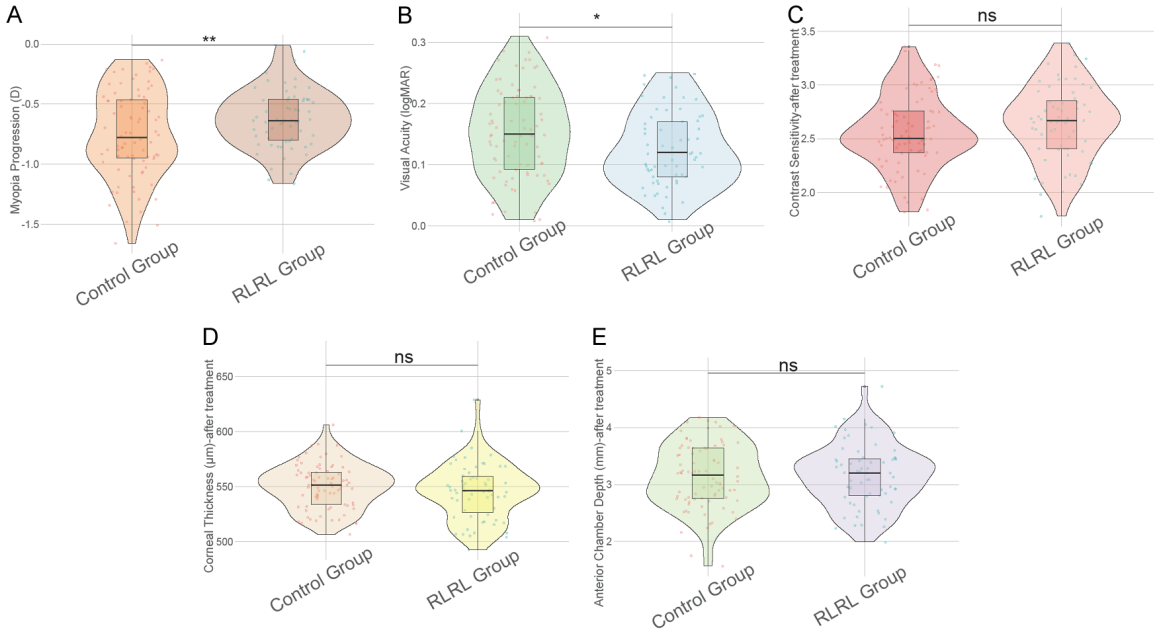

Figure 1. Ocular parameters after 6 months treatment. A: Myopia progression (D); B: Visual acuity (logMAR); C: Contrast sensitivity after treatment; D: Corneal thickness (μm) after treatment; E: Anterior chamber depth (mm) after treatment. ns: no significant difference; *: P<0.05; **: P<0.01.

myopia progression (-0.62 ± 0.24 D vs. -0.75 ± 0.36 D, t=2.621, P=0.010) and visual acuity (logMAR) (0.12 ± 0.06 vs. 0.15 ± 0.07, t=2.467, P=0.015) (**Figure 1**). However, no significant differences were observed in contrast sensitivity (t=1.495, P=0.137), corneal thickness (t=1.227, P=0.222), or anterior chamber depth (t=0.168, P=0.867) between the two groups. These findings indicate that RLRL therapy is associated with a significant reduction in myopia progression and improvement in visual acuity, suggesting its potential as an effective intervention for controlling myopia progression in adolescents.

Side effects and adverse events

Comparison of side effects and adverse events between the RLRL group and the control group revealed no significant differences in eye irritation, dry eye symptoms, headache, blurred vision, and photophobia (all P>0.05) (**Table 3**).

Table 3. Side effects and adverse events

Data	Control Group (n=82)	RLRL Group (n=63)	χ^2	*p* Value
Eye Irritation (Y/N)	0 (0%)/82 (100%)	1 (1.59%)/62 (98.41%)	1.311	0.252
Dry Eye Symptoms (Y/N)	3 (3.66%)/79 (96.34%)	1 (1.59%)/62 (98.41%)	0.570	0.450
Headache (Y/N)	1 (1.22%)/81 (98.78%)	2 (3.17%)/61 (96.83%)	0.672	0.412
Blurred Vision (Y/N)	2 (2.44%)/80 (97.56%)	0 (0%)/63 (100%)	1.558	0.212
Photophobia (Y/N)	0 (0%)/82 (100%)	1 (1.59%)/62 (98.41%)	1.311	0.252

Table 4. Baseline demographic characteristics of patients with poor and good prognosis after RLRL therapy

Data	Poor prognosis (n=25)	Good prognosis (n=38)		*p* Value
Age (years)	10.16 ± 2.45	8.69 ± 1.26	3.131	0.003
Gender (M/F)	10 (40.00%)/15 (60.00%)	21 (55.26%)/17 (44.74%)	1.406	0.236
Ethnicity (Han/others)	23 (92.00%)/2 (8.00%)	32 (84.21%)/6 (15.79%)	0.825	0.364
Parental myopia (Y/N)	22 (88.00%)/3 (12.00%)	23 (60.53%)/15 (39.47%)	5.577	0.018
Socioeconomic status (Low/Medium/High)	13 (52.00%)/6 (24.00%)/6 (24.00%)	5 (13.16%)/24 (63.16%)/9 (23.68%)	12.819	0.002
Outdoor activities (hours/week)	5.33 ± 1.21	6.27 ± 1.24	2.972	0.004
Education level of parents (years)	12.16 ± 2.15	13.34 ± 2.06	2.186	0.033
Daily screen time (hours)	4.69 ± 0.53	4.15 ± 1.08	2.318	0.024
Room illuminance (lux)	350.16 ± 50.79	354.24 ± 55.48	0.295	0.769
Reading distance (cm)	31.15 ± 3.16	32.96 ± 3.13	2.237	0.029
Daily reading time (hours)	1.51 ± 0.46	1.47 ± 0.26	0.441	0.661
Night light exposure (Y/N)	24 (96.00%)/1 (4.00%)	24 (63.16%)/14 (36.84%)	8.966	0.003
Sleep duration (hours/night)	7.11 ± 1.08	7.21 ± 1.06	0.364	0.717
Particular about food (Y/N)	18 (72.00%)/7 (28.00%)	11 (28.95%)/27 (71.05%)	11.251	0.001

These findings suggest that RLRL therapy was not associated with increased incidence of adverse events compared to the control group, indicating a favorable safety profile of this intervention.

Baseline demographic characteristics of patients with poor and good prognosis after RLRL therapy

As shown in **Table 4**, the poor prognosis group exhibited significantly elder age (10.16 ± 2.45 vs. 8.69 ± 1.26 years, P=0.003), higher prevalence of parental myopia (88.00% vs. 60.53%, P=0.018), lower socioeconomic status (Low/Medium/High: 52.00%/24.00%/24.00% vs. 13.16%/63.16%/23.68%, P=0.002), reduced outdoor activities (5.33 ± 1.21 vs. 6.27 ± 1.24 hours/week, P=0.004), lower parental education level (12.16 ± 2.15 vs. 13.34 ± 2.06 years, P=0.033), shorter reading distance (31.15 ± 3.16 vs. 32.96 ± 3.13 cm, P=0.029), higher daily screen time (4.69 ± 0.53 vs. 4.15 ± 1.08 hours, P=0.024), increased night light exposure (96.00% vs. 63.16%, P=0.003), and a stronger emphasis on particular food habits (72.00% vs. 28.95%, P=0.001) compared to the good prognosis group. No significant differences were observed in gender distribution (P=0.236), ethnicity (P=0.364), room illuminance (P=0.769), daily reading time (P=0.661), sleep duration (P=0.717), and attention to food particulars (P=0.002) between the two groups. These findings underscore the potential influence of demographic and lifestyle factors in the effectiveness of RLRL therapy, highlighting the need for personalized approaches in managing adolescent myopia progression.

Baseline ophthalmic characteristics of patients with poor and good prognosis after RLRL therapy

As shown in **Table 5**, the poor prognosis group showed a significantly higher proportion of individuals having high myopia (>6 D) compared to the good prognosis group (24.00% vs. 7.89%, P=0.028). Additionally, the good prognosis group exhibited significantly shorter axial length (22.83 ± 1.05 mm vs. 23.48 ± 1.02 mm, P=0.018) and a higher attendance rate (92.79 ± 4.16% vs. 90.15 ± 5.22%, P=0.030) compared to the poor prognosis group. No significant differences were found in contrast sensitivity

Table 5. Baseline ophthalmic characteristics of patients with poor and good prognosis after RLRL therapy

Data	Poor prognosis (n=25)	Good prognosis (n=38)		*p* Value
Myopia (-D)			7.155	0.028
0-3 D	7 (28.00%)	23 (60.53%)		
3 D-6 D	12 (48.00%)	12 (31.58%)		
>6 D	6 (24.00%)	3 (7.89%)		
Contrast sensitivity	1.14 ± 0.13	1.18 ± 0.12	1.252	0.215
Axial length (mm)	23.48 ± 1.02	22.83 ± 1.05	2.431	0.018
Corneal curvature	41.33 ± 1.06	41.29 ± 1.08	0.145	0.885
Corneal thickness (μm)	532.18 ± 23.06	533.04 ± 22.82	0.146	0.885
Intraocular pressure (mmHg)	14.23 ± 1.16	14.15 ± 1.29	0.250	0.803
Lens thickness	3.15 ± 0.16	3.17 ± 0.14	0.524	0.602
Anterior chamber depth (mm)	3.97 ± 1.53	3.86 ± 1.56	0.276	0.784
Attendance rate (%)	90.15 ± 5.22	92.79 ± 4.16	2.226	0.030
Compliance with eyewear (Y/N)	21 (84.00%)/4 (16.00%)	36 (94.74%)/2 (5.26%)	2.017	0.156

Table 6. Correlation analysis between various factors and patient prognosis in patients undergoing RLRL therapy

Data	r	*p* Value
Age (years)	0.370	0.003
Parental myopia (Y/N)	-0.298	0.018
Socioeconomic status (Low/Medium/High)	0.261	0.039
Outdoor activities (hours/week)	0.355	0.004
Education level of parents (years)	0.271	0.031
Daily screen time (hours)	-0.282	0.025
Reading distance (cm)	0.275	0.029
Night light exposure (Y/N)	-0.377	0.002
Particular about food (Y/N)	-0.423	<0.001
Myopia (-D)	-0.334	0.007
Axial length (mm)	-0.297	0.018
Attendance rate (%)	0.274	0.030

(P=0.215), corneal curvature (P=0.885), corneal thickness (P=0.885), intraocular pressure (P=0.803), lens thickness (P=0.602), anterior chamber depth (P=0.784), or compliance with eyewear (P=0.156) between the two groups. These findings suggest that baseline myopia severity and axial length, along with treatment attendance, may play a role in predicting the outcome of RLRL therapy in controlling adolescents' myopia progression.

Correlation analysis between patient prognosis and measures with a significant difference

As shown in **Table 6**, a significant correlation was found between patient prognosis and age (r=0.370, P=0.003), parental myopia (r=-0.298, P=0.018), socioeconomic status (r=-0.261, P=0.039), outdoor activities (r=0.355, P=0.004), education level of parents (r=0.271, P=0.031), daily screen time (r=-0.282, P=0.025), reading distance (r=0.275, P=0.029), night light exposure (r=-0.377, P=0.002), emphasis on particular food habits (r=-0.423, P<0.001), myopia severity (r=-0.334, P=0.007), axial length (r=-0.297, P=0.018), and attendance rate (r=0.274, P=0.030) in patients undergoing RLRL therapy. These results suggest that various demographic, lifestyle, and ophthalmic factors are associated with the patient prognosis of adolescents undergoing RLRL therapy for myopia control, underscoring the multifaceted nature of treatment response. These findings emphasize the importance of considering a wide range of factors when assessing patient prognosis and its potential influence on therapeutic outcomes, thus highlighting the need for comprehensive and personalized approaches in managing myopia progression in adolescents.

Logistic regression analysis of factors affecting patient prognosis in patients undergoing RLRL therapy

As shown in **Table 7**, the odds ratio analysis revealed that age (OR=0.623, 95% CI 0.425-0.852, P=0.007), parental myopia (OR=0.209,

Table 7. Logistic regression analysis of factors affecting prognosis in patients undergoing RLRL therapy

Data	Odds ratio	95% CI	B	Beta	*p* Value
Age (years)	0.623	0.425-0.852	2.712	-0.473	0.007
Parental myopia (Y/N)	0.209	0.044-0.741	2.238	-1.565	0.025
Socioeconomic status (Low/Medium/High)	2.178	1.052-4.844	2.021	0.779	0.043
Outdoor activities (hours/week)	1.88	1.214-3.143	2.637	0.631	0.008
Education level of parents (years)	1.317	1.028-1.739	2.081	0.275	0.037
Daily screen time (hours)	0.487	0.237-0.897	2.145	-0.72	0.032
Reading distance (cm)	1.221	1.026-1.493	2.104	0.200	0.035
Night light exposure (Y/N)	0.071	0.004-0.399	2.456	-2.639	0.014
Particular about food (Y/N)	0.158	0.049-0.467	3.225	-1.842	0.001
Myopia (-D)	0.367	0.161-0.771	2.535	-1.002	0.011
Axial length (mm)	0.540	0.304-0.895	2.268	-0.617	0.023
Attendance rate (%)	1.135	1.014-1.289	2.093	0.126	0.036

95% CI 0.044-0.741, P=0.025), daily outdoor activities (OR=1.88, 95% CI 1.214-3.143, P=0.008), education level of parents (OR=1.317, 95% CI 1.028-1.739, P=0.037), daily screen time (OR=0.487, 95% CI 0.237-0.897, P=0.032), reading distance (OR=1.221, 95% CI 1.026-1.493, P=0.035), night light exposure (OR=0.071, 95% CI 0.004-0.399, P=0.014), emphasis on particular food habits (OR=0.158, 95% CI 0.049-0.467, P=0.001), myopia severity (OR=0.367, 95% CI 0.161-0.771, P=0.011), axial length (OR=0.540, 95% CI 0.304-0.895, P=0.023), and attendance rate (OR=1.135, 95% CI 1.014-1.289, P=0.036) were significantly associated with the patient prognosis in adolescents undergoing RLRL therapy. These outcomes underscore the role of diverse demographic, lifestyle, and ophthalmic factors in influencing patient prognosis, thus emphasizing the need for personalized and comprehensive strategies to address the complex interplay of these variables in the management of myopia progression.

Nomogram for patient prognosis prediction in patients undergoing RLRL therapy

A nomogram was constructed incorporating the significant factors in logistic regression analysis for predicting patient prognosis in patients undergoing RLRL therapy (**Figure 2A**). Using ten-fold cross-validation, the model reached an AUC of 0.994, with a specificity of 1.000 and sensitivity of 0.947 (**Figure 2C**). The mean absolute error was 0.056 based on 1000 bootstrap repetitions (**Figure 2B**).

Discussion

The increasing prevalence of myopia among adolescents has raised significant public health concerns globally [18]. This study investigated the potential of repeated low-level red-light (RLRL) therapy for controlling myopia progression in adolescents. The findings shed light on several important factors associated with the effectiveness and safety of RLRL therapy, providing valuable insight into the prognostic model for managing adolescent myopia.

The significant reduction in myopia progression and improvement in visual acuity observed in the RLRL treatment group emphasize probable effectiveness of RLRL therapy in controlling adolescent myopia. The effectiveness of RLRL therapy in controlling myopia progression can be attributed to several underlying mechanisms. RLRL may exert its effects through the stimulation of choroidal cells and modulation of gene expression associated with myopia progression [19]. Previous studies [20] have suggested that red light therapy may influence choroidal dopamine release, which in turn, modulates eye growth and myopia development. The interaction between red light and choroidal cells could help regulate axial elongation and refractive error progression, thereby offering a possible explanation for the reduction in myopia progression observed among adolescents undergoing RLRL therapy in this study [21].

Additionally, red light therapy has been implicated in the regulation of circadian rhythms

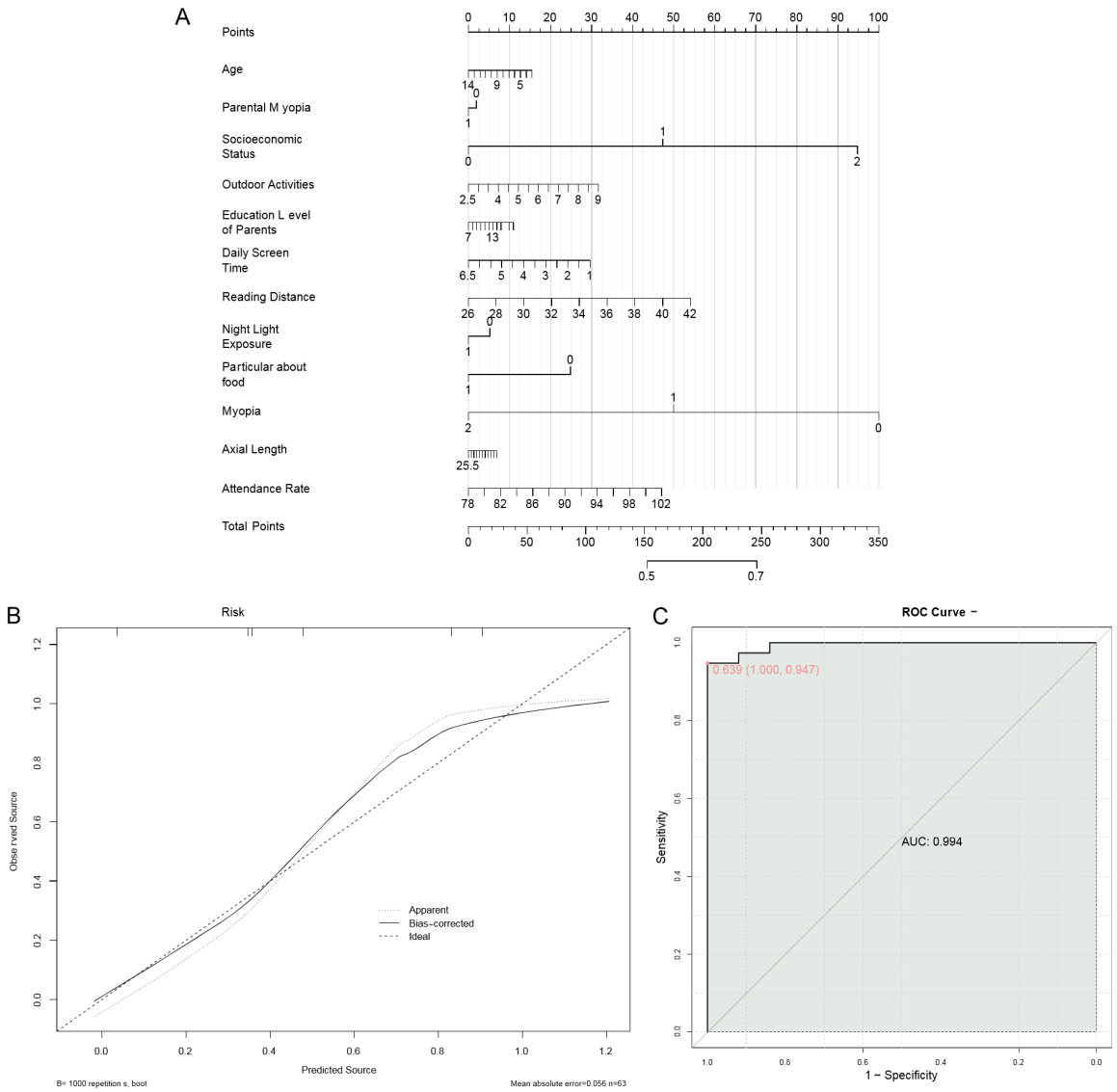

Figure 2. Nomogram for predicting prognosis of patients undergoing RLRL therapy. A: Nomogram; B: Calibrate plot; C: ROC plot.

and melatonin production, both of which are crucial for ocular development and myopia control [22]. By influencing the release of melatonin and the synchronization of circadian rhythms, RLRL therapy may impact the signaling pathways associated with eye growth, further contributing to its effectiveness in managing adolescent myopia progression. Moreover, the potential anti-inflammatory and neuroprotective effects of red light may help modulate the ocular microenvironment, mitigating factors that exacerbate myopia progression [23].

The favorable safety profile of RLRL therapy observed in our study is highly encouraging. The absence of statistically significant differences in adverse events between the RLRL and control groups indicates that RLRL therapy is well-tolerated, without leading to an increased incidence of eye-related discomfort or adverse reactions. This suggests that RLRL therapy holds promise as a safe intervention for myopia control in adolescents.

Our study also revealed the influence of various demographic and lifestyle factors on the prognosis of RLRL therapy in adolescents. Factors such as age, parental myopia, socioeconomic status, outdoor activities, education level of parents, daily screen time, reading distance,

night light exposure, and particular food habits were found to be significantly associated with treatment outcomes. The age-related impact on treatment outcomes may be attributed to the dynamic nature of ocular development during adolescence [24]. Younger individuals may exhibit greater ocular plasticity and responsiveness to therapeutic interventions, potentially enhancing the effectiveness of RLRL therapy in modulating ocular growth and refractive development [25]. The strong association of parental myopia with treatment outcomes suggests a genetic predisposition to myopia development and progression. Genetic factors contribute significantly to the pathogenesis of myopia, influencing the response to therapeutic interventions. Adolescents with a family history of myopia may exhibit distinct ocular characteristics and growth patterns, influencing their response to RLRL therapy. Socioeconomic disparities may impact treatment outcomes through various mechanisms, including access to healthcare and education resources, lifestyle choices, and environmental factors. Lower socioeconomic status may be associated with reduced access to outdoor activities, increased screen time, and suboptimal dietary habits, all of which can affect the progression of myopia and the response to RLRL therapy. Engagement in outdoor activities has been correlated with a reduced risk of myopia development and progression. Increased exposure to natural light and distant visual stimuli during outdoor activities may exert protective effects against myopia, potentially influencing the response to RLRL therapy [26]. The mechanisms underlying the protective role of outdoor activities could involve light exposure, visual stimulation, and factors related to environmental and lifestyle influences. The education level of parents may reflect broader environmental and lifestyle factors that can impact myopia progression. Higher parental education levels may be associated with increased awareness of ocular health, adoption of healthy visual habits, and better access to eye care services, potentially influencing treatment outcomes. Furthermore, parental education may influence adolescents' lifestyle and reading habits, impacting ocular development and their response to RLRL therapy [27]. Prolonged screen time has been linked to an increased risk of myopia development and progression. Excessive near work, such as prolonged digital device usage, may contribute to accommodative dysfunction and increased near-induced visual stress, potentially influencing the response to RLRL therapy. Reducing screen time and adopting appropriate visual ergonomics may positively impact treatment outcomes by mitigating near-induced ocular changes [29, 30]. Excessive exposure to artificial light at night has been associated with disrupted circadian rhythms and potential impacts on ocular health. Night light exposure may influence treatment outcomes by affecting melatonin production, sleep quality, and overall ocular physiology. Addressing nighttime environmental factors may positively influence treatment responses by promoting optimal circadian regulation and supporting ocular health [28].

The influence of these factors on the effectiveness with RLRL therapy underscores the need for personalized and comprehensive approaches in managing myopia progression. The multifaceted nature of myopia demands a holistic assessment of individual characteristics and behaviors to optimize treatment outcomes. These factors play a pivotal role in guiding patient selection, predicting treatment response, and personalizing intervention strategies to maximize efficacy [31, 32].

Our establishment of a prognostic model for controlling adolescents' myopia progression represents a significant step toward personalized treatment strategies for myopia management. The incorporation of demographic, lifestyle, and ophthalmic parameters into the model underscores the comprehensive nature of our approach.

The high predictive performance of the model, as indicated by the AUC, specificity, and sensitivity, highlights its potential for clinical use in identifying patients most likely to benefit from RLRL therapy. The nomogram analysis further enhances the practical applicability of our findings, providing a visual tool for assessing patient prognosis and predicting treatment outcomes based on individual characteristics.

The development and validation of our prognostic model offer a valuable framework for personalized decision-making in myopia management. The model's predictive accuracy can aid clinicians in identifying individuals who may benefit from early intervention with RLRL therapy, thus optimizing treatment allocation and

improving the overall effectiveness of myopia control strategies.

The findings of this study emphasize the importance of evaluating a wide range of demographic, lifestyle, and ophthalmic factors when assessing patient prognosis and its influence on therapeutic outcome. The establishment of a prognostic model and a comprehensive nomogram analysis offers a promising approach for predicting treatment outcome and developing personalized strategies for managing adolescent myopia through RLRL therapy [35]. However, further research is warranted to elucidate the specific mechanisms by which RLRL therapy exerts its effects on myopia progression and to validate the prognostic model in diverse patient populations. Long-term follow-up studies and randomized controlled trials will be essential for comprehensively evaluating the safety, efficacy, and long-term outcome of RLRL therapy for managing myopia progression among adolescents. Additionally, the integration of genetic, environmental, and lifestyle factors into the prognostic model may enhance its predictive power and its utility for personalized treatment strategies [33, 34].

Despite the valuable insights provided by this study, several limitations should be considered. The retrospective cohort design may introduce selection bias and limit the ability to establish causality. Future prospective studies with larger sample sizes and longer follow-up periods are necessary to validate our findings. Additionally, the study focused on short-term treatment outcome, and long-term effects of RLRL therapy on myopia progression require further investigation. Furthermore, the specific mechanisms by which RLRL therapy affects choroidal dopamine levels and its relationship with myopia progression warrant in-depth exploration through experimental studies.

Conclusion

This study provides valuable insight into the potential of RLRL therapy for controlling myopia progression among adolescents. The established prognostic model with comprehensive evaluation of demographic, lifestyle, and ophthalmic factors emphasize the multifaceted nature of treatment response and the need for personalized approaches in managing adolescent myopia.

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Disclosure of conflict of interest

None.

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