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Research article

Clinical characteristics and diagnostic test for spherophakia: A retrospective analysis

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ABSTRACT

Background: This study aimed to analyze ocular characteristics in patients diagnosed with spherophakia, establish effective diagnostic criteria, and aid clinicians in prompt identification and management.
Methods: A retrospective case series identified spherophakia cases through medical records and literature searches. The case group included spherophakia patients, and the control group comprised individuals with similar eye conditions. Intraocular lens calculations used the SRK-T formula, and statistical analyses were performed using SPSS. Diagnostic efficacy was assessed through receiver operating characteristic (ROC) curve analysis.
Results: The study included 12 cases (23 eyes) from medical records and 86 patients (142 eyes) from literature sources. Characteristics of spherophakia included bilateral involvement, younger age, shallow anterior chamber depth, lens dislocation, and secondary glaucoma. A diagnostic criterion based on lens power demonstrated high sensitivity (94.3 %) and specificity (91.9 %). ROC analysis yielded area under the ROC curve (AUROC) values of 0.974 for lens power, outperforming refractive error (0.119), corneal curvature (0.465) and axial length (0.496). The lens power cutoff for diagnosing spherophakia was 31.25D.
Conclusion: The study offers crucial insights into spherophakia's clinical characteristics and presents a practical diagnostic criterion using lens power, enhancing early detection and management. Further research is needed to validate and refine these findings, establishing standardized diagnostic criteria for spherophakia.

1. Introduction

Spherophakia is an uncommon anomaly of the eye's crystalline lens, typically affecting both eyes. It is characterized by a spherical shape of the lens, leading to various ocular complications, including severe myopia and secondary glaucoma, which can ultimately

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result in irreversible blindness [1].

The diagnosis of spherophakia currently relies mainly on slit-lamp examination, ultrasound biomicroscopy (UBM), and anterior segment optical coherence tomography (OCT) to observe the lens shape [2,3]. Sometimes, the equator of the lens may not be clearly visible clinically, which could lead to misdiagnosis or missed diagnosis. Therefore, researchers are continuing to explore other methods for diagnosing spherophakia [4,5].

However, since these methods require a certain level of clinical expertise or expensive diagnostic equipment, there is an urgent need for an effective and simplified diagnostic method specifically targeting spherophakia.

The aim of the study is to analyze the ocular characteristics of patients diagnosed with spherophakia at our institution and establish effective diagnostic criteria to aid clinicians in promptly identifying and managing this condition.

2. Method

2.1. Patient selection

This retrospective study reviewed medical records to identify cases of spherophakia. Patients were included based on a confirmed clinical diagnosis of spherophakia, which was supported by clinical presentation and lens morphology observed under slit lamp examination or anterior segment OCT. To increase the sample size, a systematic literature search was conducted in the CNKI and PubMed databases using the terms "spherophakia" or "microspherophakia" until March 6, 2024.

For the inclusion of spherophakia cases, patients had to have a clinical diagnosis of spherophakia and be aged between 0 and 80 years, with no gender restrictions. Cases were excluded if they had significant refractive media opacities, missing relevant clinical data, completely dislocated lenses, or a history of lens extraction surgery.

In the control group, patients diagnosed with primary angle-closure glaucoma, high myopia, lens subluxation, microphthalmia, and age-matched normal eyes were selected to match the demographic characteristics of the spherophakia group. Inclusion in the control group required that patients were clinically ruled out for spherophakia and were aged between 0 and 80 years, with no gender restrictions. Exclusion criteria for the control group included significant refractive media opacities, missing relevant clinical data, and a history of lens extraction surgery.

The diagnostic criteria for spherophakia were based on characteristic clinical features such as progressive high myopia, shallow anterior chamber, narrow or closed angles, and lens subluxation, which are often associated with systemic conditions. These features were further validated by imaging techniques, including slit-lamp examination, ultrasound biomicroscopy (UBM), or anterior segment OCT, confirming the spherical morphology of the lens.

The study was conducted in accordance with the tenets of the Declaration of Helsinki and approved by the ethics committees of Eye Hospital of Wenzhou Medical University and informed consent was waived.

Table 1
Ocular parameters of patients with spherophakia based on medical record.

Case	SEX	AGE (year)	EYE	RE (D)	Refraction Method	K (D)	AL (mm)	ACD (mm)	POWER (D)	BCVA	Other Eye Abnormalities
1	F	16	OD	−24	Cycloplegic	49.76	21.94	1.79	65	0.05	SG,SCL
1	F	16	OS	−20	Cycloplegic	49.6	22.9	3.31	55	HM	SG,SCL
2	F	14	OD	−8	Cycloplegic	43.37	21.73	1.24	38.6	0.15	SG
2	F	14	OS	−13	Cycloplegic	43.58	22.87	1.19	41.5	0.15	SG
3	F	3	OD	−27	Small pupil	44.44	22.96	1.65	55.25		None
3	F	3	OS	−27	Small pupil	44.41	23.15	1.53	55.25		None
4	M	9	OD	−8.5	Cycloplegic	44.61	21.18	2.55	38.25	0.7	SCL
4	M	9	OS	−10	Cycloplegic	44.27	21.1	2.05	41.88	0.5	SCL
5	F	8	OD	−10.5	Cycloplegic	44.57	21.27	1.22	43	0.5	SCL
5	F	8	OS	−10	Cycloplegic	44.73	21.29	1.25	41.78	0.5	SCL
6	M	26	OD	−14	Small pupil	42.25	22.20	1.56	41.50	HM	SG
6	M	26	OS	−8	Small pupil	41.25	21.33	1.58	39	FC	SG
7	M	28	OD	−15.5	Cycloplegic	47.62	21.77	1.50	42.5	FC	SG,SCL
7	M	28	OS	−17	Cycloplegic	47.80	21.68	1.53	43.75	0.3	SG,SCL
8	F	7	OD	−9.50	Unclear	43.82	22.79	1.22	34.875	0.7	SG,SCL
8	F	7	OS	−9.50	Unclear	43.98	22.71	1.65	34.875	0.7	SG,SCL
9	F	9	OD	−2.75	Small pupil	43.64	23.17	3.26	IOL	0.9	SG
9	F	9	OS	−17.5	Small pupil	43.59	23.64	1.40	46.23	0.6	SG,SCL
10	M	18	OD	−13.75	Cycloplegic	44.66	23.55	1.44	35.66	0.8	SG,SCL
10	M	18	OS	−14	Cycloplegic	44.78	23.59	1.98	35.95	0.9	SG,SCL
11	M	47	OD	−16	Small pupil	46.77	24.94	3.51	33.24	0.7	SG,SCL
11	M	47	OS	−13.5	Small pupil	46.1	24.08	3.55	33.28	0.8	SCL
12	M	13	OD	−11.25	Cycloplegic	42.7	23.45	2.16	34.86	0.8	SG,SCL
12	M	13	OS	−9.25	Cycloplegic	42.61	23.38	2.10	33.07	0.6	SG,SCL

Note: RE: Refractive Error, K: Corneal Curvature, AL: Axial Length, ACD: Anterior Chamber Depth, POWER: Lens Power, BCVA: Best Corrected Visual Acuity.
SG: Secondary Glaucoma, SCL: Subluxated Crystalline Lens.

Intraocular Lens Calculation: The power of the intraocular lens (IOL) was determined based on preoperative refractive error, using it as the target refractive error for IOL power calculation. This calculated IOL power served as a surrogate for lens power. The calculation process involved utilizing an online intraocular lens calculation tool, employing the SRK-T formula with an A-constant set to 118.4. In instances where corneal curvature data were lacking, a standardized value of 44.00D was used as a substitute.

2.2. Statistical analysis

Statistical analyses were performed using the statistical software SPSS version 26.0 (SPSS Inc., Chicago, Illinois, United States). Normal distribution data were described using mean ± standard deviation, while non-normally distributed data were described using median and interquartile range (IQR).

The diagnostic accuracy of spherophakia was evaluated using receiver operating characteristic (ROC) curve analysis. Cut-off values were identified at the point of intersection between sensitivity and specificity. A p-value of <0.05 was considered statistically significant.

3. Results

A total of 12 cases (23 eyes) of spherophakia were collected from the medical records system, with specific data as presented in Table 1. Characteristics of spherophakia include a balanced distribution across genders, onset at a relatively young age (3–47 years old), predominantly bilateral involvement, shorter axial lengths (21.1–24.95 mm), shallower anterior chamber depths (1.19–3.55 mm), frequent association with subluxated crystalline lens (17/23), and secondary glaucoma (17/23), along with higher refractive errors (−8.0D to −27.0D). Secondary glaucoma can impact vision (ranging from hand motion perception to 0.9). Patients diagnosed and treated within the first decade generally experience relatively minor impacts on vision (ranging from 0.5 to 0.9), whereas delays in diagnosis and treatment until the second decade or later can significantly impair vision (ranging from hand motion perception to 0.9).

Additionally, a total of 142 eyes of 86 patients with spherophakia were identified from case reports in the literature, comprising 43 males and 43 females, with an average age of 22.4 ± 15.5 years. The median axial length was 22.37 mm (IQR 21.12 mm, 23.72 mm), the median corneal curvature was 44.00D (IQR 42.88D, 45.45D), the median refractive error was −12.625D (IQR -18.00D, −8.625D), and the median lens power was 38.87D (IQR 34.00D, 42.25D) [2–4,6–52].

Finally, the spherophakia case group was combined from both the medical records system and literature sources, comprising a total of 165 eyes. The median axial length was 22.33 mm (IQR 21.23 mm, 23.59 mm), the median corneal curvature was 42.26D (IQR 43.00D, 45.46D), the median refractive error was −12.81D (IQR -17.50D, −8.70D), and the median lens power was 38.98D (IQR 34.54D, 46.51D).

Regarding the control group, it included cases of primary angle-closure glaucoma (13 eyes, aged 34–77 years), high myopia (11 eyes, aged 49–77 years), lens subluxation (23 eyes, aged 3–68 years), microphthalmia (24 eyes,age 7–76 years) and an age-matched group of normal eyes (28 eyes, aged 3–25 years). In the control group, the median axial length was 22.87 mm (IQR 20.65 mm, 24.79 mm), the median corneal curvature was 44.48D (IQR 43.00D, 45.77D), the median refractive error was −0.50D (IQR -3.50D, 4.75D), and the median lens power was 23.00D (IQR 20.75D, 25.45D).

Specific eye parameters for each subgroup are detailed in Table 2. Fig. 2 illustrates the lens power across different subgroups. Significant differences in lens power are observed between the spherophakia group and each subgroup within the control group ($P < 0.001$), while no significant differences are found among the subgroups within the control group ($P = 1.000$).

ROC analysis revealed that the area under the receiver operating characteristic curve (AUROC) values for diagnosing spherophakia based on refractive error, corneal curvature, axial length, and lens power were 0.119 (95 % CI 0.065, 0.173), 0.465(95 % CI 0.377, 0.553), 0.496 (95 % CI 0.409, 0.583), and 0.974 (95 % CI 0.954, 0.993), respectively. The cutoff for lens power in diagnosing spherophakia was determined to be 31.25D, with a sensitivity of 94.3 % and specificity of 91.9 %(Fig. 1).

Table 2
Ocular Parameters of different subgroups.

Group	Number of Eyes	Age Range (years)	Median Axial Length (IQR)	Median Corneal Curvature (IQR)	Median Refractive Error (IQR)	Median Lens Power (IQR)
Spherophakia	165	2–72	22.33 mm (21.23 mm, 23.59 mm)	42.26D (43.00D, 45.46D)	−12.81D (−17.50D, −8.70D)	38.98D (34.54D, 46.51D)
Primary Angle-Closure Glaucoma	13	34–77	22.38 mm (22.03 mm, 23.49 mm)	44.38D (42.93D, 44.86D)	−0.00D (−2.87D, 2.25D)	24.00D (20.56D, 26.50D)
High Myopia	11	49–77	31.07 mm (29.75 mm, 33.03 mm)	43.66D (42.71D, 45.98D)	−21.00D (−27.00D, −14.00D)	20.75D (18.00D, 25.50D)
Lens Subluxation	23	3–68	24.00 mm (22.82 mm, 26.23 mm)	43.63D (42.87D, 45.00D)	−1.50D (−9.00D, 3.50D)	24.50D (15.00D, 34.60D)
Microphthalmia	24	7–76	17.36 mm (15.83 mm, 19.93 mm)	48.75D (45.39D, 49.80D)	10.00D (6.00D, 14.87D)	24.38D (22.25D, 25.58D)
Age-Matched Normal Eyes	28	3–25	23.26 mm (22.38 mm, 24.02 mm)	43.83D (41.85D, 44.78D)	0.00D (−1.18D, 0.93D)	22.15D (21.00D, 23.00D)

4. Discussion

This study comprehensively analyzed the clinical characteristics of spherophakia, including bilateral involvement, younger age, shorter axial length, shallow anterior chamber depth, high myopia, and secondary glaucoma. By integrating ocular parameters of spherophakia cases from the literature and comparing them with other similar ocular diseases, we proposed a diagnostic criterion based on lens power, which demonstrated high sensitivity and specificity. This provides crucial evidence for early detection and treatment of spherophakia, aiding in reducing visual impairment.

Previous studies have indicated that spherophakia is typically characterized by increased lens thickness, high myopia, and short axial length [53]. In this study, we attempted to use lens power, refractive error, corneal curvature and axial length as diagnostic parameters for spherophakia. The results showed that refractive error, corneal curvature and axial length performed poorly in diagnosis, while lens power exhibited excellent diagnostic performance. Fundamentally, the characteristics of spherophakia include increased anterior and posterior lens curvature, leading to increased lens power. Lens power, as an integrated parameter of refractive error and axial length, is better suited for distinguishing spherophakia from other similar conditions such as axial myopia and primary glaucoma, thus serving as a superior diagnostic parameter for spherophakia.

The human lens is almost spherical in early embryonic development, and gradually becomes elliptical during the postnatal emmetropization process [54]. Cook et al. used Bennett's formula to calculate the crystalline lens power and the result show that the lens power steadily decreases in premature infants from nearly 60D at birth to 45D at 5 months of age [55]. Mutti et al. conducted a prospective study on full-term infants at ages 3 and 9 months, performing cycloplegic refraction, biometry, and phakometry to calculate the crystalline power. They reported lens power values of 41.01D and 37.40D at 3 and 9 months, respectively [56]. However, in patients with spherical lenses due to abnormal lens development, the lens maintains a higher refractive power. This study found that the cutoff value for diagnosing spherical lenses based on lens power is 31.635D, which is close to the refractive power during embryonic development in humans. However, it is important to note that the lens power used in this study does not represent the true power of the lens within the eye but rather serves as a surrogate value. It is calculated based on the targeted refractive power of the implanted intraocular lens using existing refractive error measurements.

Patients with spherophakia often seek optometrists for high myopia-related concerns and ophthalmologists in the case of glaucoma [57]. The diagnostic trial conducted in this study, using lens power as a key parameter, holds practical significance for both optometrists and glaucoma specialists in the diagnosis and treatment of spherophakia.

Optometrists are advised to conduct corneal curvature and axial length examinations for highly myopic patients to differentiate between refractive and axial myopia. Suspicion of spherophakia in such patients with normal axial length and corneal curvature requires assessment of anterior chamber depth and intraocular pressure to avoid misdiagnosis of spherophakia and even secondary glaucoma. Similarly, ophthalmologists are recommended to investigate secondary factors in young patients with angle-closure glaucoma, especially those with high myopia and normal axial length, as spherophakia may contribute.

Although lens power showed good diagnostic performance in this trial, clinical practice may be more complex. In this study, we included axial myopia, primary angle-closure glaucoma, lens Subluxation, microphthalmia, and normal eyes as control groups based

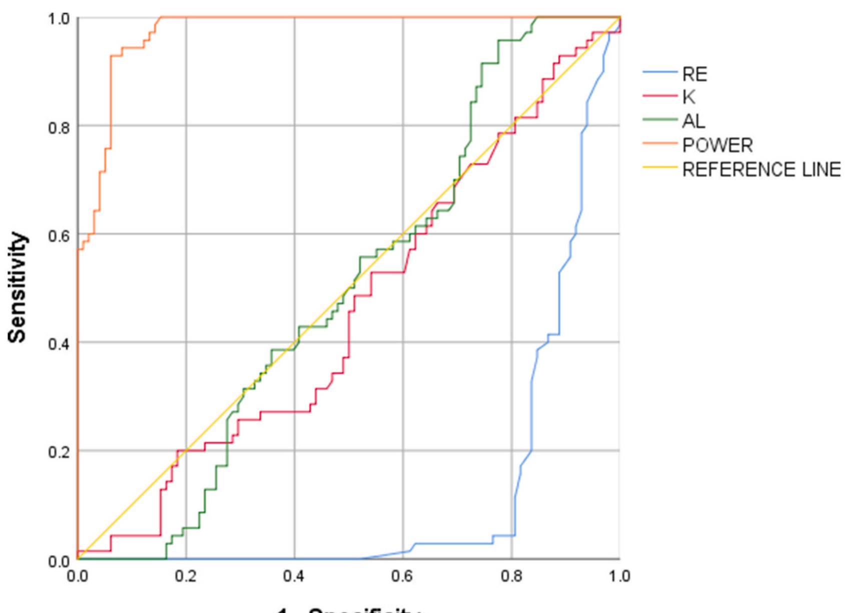

Fig. 1. This figure illustrates the ROC curve analysis for diagnosing spherophakia. The plot includes annotations for lens power (Power), axial length (AL), refractive error (RE) and corneal curvature (K).

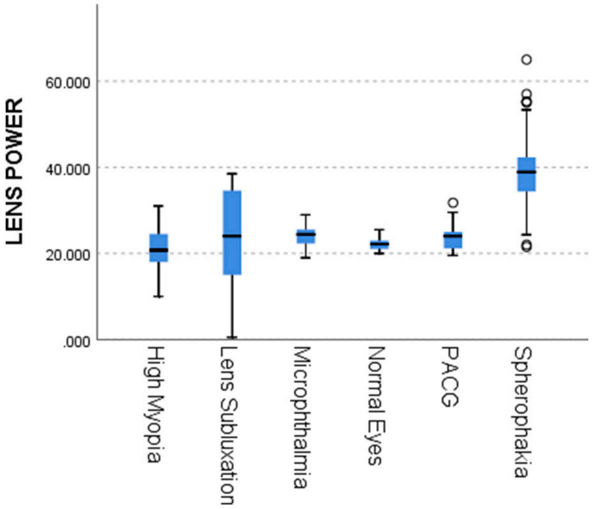

Fig. 2. Comparison of lens power among different subgroups. PACG (primary angle-closure glaucoma).

on the possible clinical characteristics of spherophakia, such as high myopia, secondary glaucoma, lens dislocation, short axial length, or normal axial length. However, there may be other similar eye conditions that were not considered. Therefore, lens power is not the gold standard for diagnosing spherophakia; it should be combined with other clinical findings to ensure diagnostic accuracy. It is important to note that spherophakia does not always present as high myopia; in some cases, it may manifest as hyperopia or high hyperopia due to lens dislocation [40]. Thus, a comprehensive assessment of anterior segment conditions through slit-lamp examination is crucial. In summary, lens power should be considered an important but not sole parameter in the diagnosis of spherophakia, and it should be combined with other factors to ensure accurate diagnosis and appropriate treatment strategies.

The strengths of this study lie in the estimation of lens power using intraocular lens (IOL) calculations, which helps distinguish spherophakia from other conditions with similar characteristics. Additionally, this study increased the sample size by incorporating more spherophakia cases extracted from literature reports. However, it is important to acknowledge some limitations of this study. Firstly, due to the limited dataset, the robustness of the results requires validation and continuous refinement in future studies. Secondly, the lack of a gold standard for diagnosing spherophakia in clinical practice raises the possibility of misdiagnosis in the control group, affecting the study's accuracy. Thus, there is a pressing need for a standardized diagnostic criterion in academic research. Thirdly, in this study, due to the limited number of cases with available lens thickness data, we were unable to conduct a diagnostic trial and compare diagnostic performance for this parameter. Moving forward, we will continue to accumulate cases with complete data on lens thickness to further enhance the study.

In summary, this study presents a comprehensive analysis of spherophakia, proposing a diagnostic criterion based on lens power with high sensitivity and specificity. The study provides valuable insights for early detection and treatment of spherophakia, aiming to reduce visual impairment.

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Data and code availability statement

Data will be made available on request.

Ethics statement

This study was conducted in accordance with the tenets of the Declaration of Helsinki and approved by the ethics committees of Eye Hospital of Wenzhou Medical University (grant number:2024–73) and informed consent was waived.

CRediT authorship contribution statement

Qiaolin Zhu: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Yujia Huo:** Writing – review &

editing, Writing – original draft, Visualization, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation. **Wenjing Lin:** Writing – original draft, Software, Methodology, Formal analysis, Data curation. **Qianqian Sun:** Methodology, Formal analysis, Data curation. **Wentao Yan:** Writing – review & editing, Writing – original draft, Supervision, Resources, Funding acquisition.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Wentao Yan reports financial support was provided by National Key R&D Program of China. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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