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Research article

Feasibility of shear wave elastography for evaluating lens stiffness in patients with age-related cataracts: A quantitative analysis

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A R T I C L E I N F O

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A B S T R A C T

Background: Shear wave elastography (SWE) is a novel imaging technique that provides quantitative assessments of tissue stiffness. This non-invasive method offers real-time, quantitative measurements and has been widely applied to various tissues, providing valuable diagnostic insights.
Purpose: This study aimed to investigate the feasibility of using SWE to evaluate the stiffness of the lens in patients with age-related cataracts.
Materials and methods: A comparative analysis involving 92 patients diagnosed with age-related cataracts and 39 healthy controls was conducted. Lens stiffness was quantified using SWE measurements. The lens nucleus of all participants was graded based on the Lens Opacities Classification System II (LOCS II). Correlations between the stiffness of the lens and age were also analyzed.
Results: The study indicates that both the stiffness of the lens and the lens nucleus were significantly higher in patients with age-related cataracts compared to healthy controls ($P < 0.001$). In patients with age-related cataracts, although lens nucleus stiffness variations across different grades of cataract severity were not statistically significant, all grades displayed increased stiffness relative to healthy controls. Additionally, a significant positive correlation between lens stiffness and age was observed in all participants ($P < 0.001$).
Conclusion: SWE appears to be a promising imaging technique for quantitatively assessing the mechanical characteristics of the lens in patients with age-related cataracts.

1. Introduction

Cataracts remain the leading cause of blindness worldwide, responsible for a substantial portion of visual impairments. Research shows that as of 2020, approximately 13.4 million of the 38.5 million blind people worldwide are affected by cataracts. The prevalence of cataracts varies significantly by region: in 2015, they accounted for 21.42% and 20.13% of blindness cases in Western Europe and high-income North America, respectively. In contrast, in South and Southeast Asia and Oceania, the rates ranged from 36.58 % to

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47.29 %. Similarly, in Africa, cataracts contribute to over 40 % of blindness cases, aligning with the rates observed in Asia [1]. These differences stem from variations in healthcare access, economic conditions, and environmental factors such as ultraviolet radiation exposure [2]. Additionally, gender influences cataract prevalence, with women being more commonly affected than men [3]. These insights underscore the importance of public health strategies that address both medical and socioeconomic determinants to alleviate the global burden of blindness due to cataracts. Currently, without any preventive or pharmacological options for cataracts, surgical extraction is the sole effective treatment to regain vision impaired by this ailment. Phacoemulsification is the predominant surgical method employed for treating cataracts, and the well-established direct relationship between phacoemulsification energy levels and lens stiffness [4–7] underscores the importance of objectively grading cataracts and estimating their stiffness for effective treatment.

The Lens Opacities Classification System (LOCS) [8,9] is a well-established, widely accepted method for grading cataracts based on images obtained through slit-lamp examination. Developed to provide a more objective and consistent method for evaluating the severity and type of lens opacities, LOCS II is widely used in both clinical settings and research studies. Advances in cataract surgery and the growing reliance on phacoemulsification have made in vivo evaluation of lens stiffness increasingly valuable for reducing surgical complications and preventing vision loss.

Shear wave elastography (SWE) is a novel imaging technique that provides quantitative information on tissue elasticity. It offers distinct advantages over other imaging methods, including affordability, user-friendliness, absence of radiation, and real-time visualization. SWE has previously shown promising results in evaluating liver fibrosis, and various pathologies in kidney, breast, thyroid, and other tissues [10–13]. A previous study [14] effectively employed SWE to measure elasticity in ex-vivo porcine corneal, and a significant correlation between shear wave velocity and age-related lens hardness was demonstrated in a rabbit model using acoustic radiation force-based ultrasound elastography [15]. These findings suggest that SWE could potentially serve as a novel biomarker for characterizing the mechanical properties of the lens, offering a promising avenue for further exploration in the field of ophthalmology. However, previous investigations have mainly focused on animal models, with only limited studies utilizing SWE to assess lens stiffness in the human eye. The hypothesis of this study is that SWE can provide reliable, non-invasive quantitative measurements of lens stiffness in patients with age-related cataracts, distinguishing them from healthy controls and correlating with the severity of cataracts as graded by the LOCS II.

Therefore, the present study aimed to employ SWE to quantitatively evaluate lens stiffness in patients with age-related cataracts, based on the LOCS II grading system in comparison to healthy controls. This research seeks to provide valuable insights into the feasibility of SWE as a non-invasive imaging technique for assessing lens mechanical properties, potentially enhancing our understanding of cataract development and management.

2. Materials and Methods

2.1. Participants

From October 2021 to December 2022, we prospectively recruited consecutive participants for a comprehensive ophthalmic examination. This included an assessment of cataract severity using the LOCS II [9], conducted through slit-lamp examination by an experienced ophthalmologist. In addition, intraocular pressure was measured. For the slit-lamp examinations, tropicamide ophthalmic solution (MYDRIACYL®, Santen Pharmaceutical Co., Ltd., Shiga Plant) was used to dilate the pupils. Each participant received a single drop of this solution in each eye approximately 15 min before the commencement of the examination. The 1 % concentration of tropicamide is the standard dosage for achieving mydriasis (pupil dilation) and cycloplegia (temporary paralysis of the ciliary muscle), essential for a thorough examination of the lens and other ocular structures. The inclusion criteria for the study were as follows: (a) patients diagnosed with aged-related cataracts, (b) intraocular pressure within the normal range, and (c) completion of the informed consent form. Exclusion criteria included: (a) any cataract-related systemic disease (e.g., developmental abnormalities, trauma, metabolic disorders, genetic diseases, drug-induced changes), (b) presence of glaucoma or ophthalmopathy that obstructed lens examination; (c) poor quality images, (d) ocular diseases that hindered lens examination; (e) concurrent participation in another clinical trial.

2.2. Imaging protocol

Conventional B-mode US and SWE were acquired by the PHILIPS EPIQ7 (Philips, Bothell, WA, USA) with a linear probe (eL18-4, frequency range: 4.0–18 MHz). The measurements were performed by one of two attending sonographers (BH.Q and AL. H with 19 and 11 years of ultrasound experience and including 12 and 9 years of experience with US elastography, respectively) who were blinded to the study groups (cataracts and healthy controls). LOCS II is commonly used to categorize nuclear cataracts into four grades, based on the level and severity of cloudiness in the lens. These grades are as follows: (1) N0: transparent, with the embryonic nucleus clearly visible; (2) N1: early cloudiness. (3) N2: moderate cloudiness; (4) N3: severe cloudiness). Participants were examined in a supine position and were instructed to gently close their eyes without opening them, while looking straight upwards. Adequate coupling gel was applied to the surface of the eye to ensure image quality and measurements. The transducer was gently placed on the eye without applying pressure until stable images were obtained. Conventional B-mode US was used initially to visualize the ultrasound structure, shape, position, and echogenicity of the lens. The probe was then switched to the ultrasound elastography mode, and real-time elastography examination was displayed as grayscale with SWE images simultaneously in a dual-screen mode. Once satisfactory image quality was achieved (where the quality map showed green with no significant red areas in the region of interest over more than 3 s), a total of six SWE measurements were taken on a single axial plane across the entire lens, with an additional measurement at the center of the lens in each eye. The elastographic images were acquired at least three times for each eye. The size of the circular region of interest (ROI) was fixed at 2 mm for all measurements. Valid SWE measurements were determined by ensuring that the interquartile range (IQR) remained below 30 % of the median value [16]. A total of 18 measurements, from three consecutive SWE acquisitions, were obtained for the lens stiffness, and 3 measurements, from three consecutive SWE acquisitions, were obtained for the stiffness of the lens nucleus for each eye. The mean of these measurements was calculated and represented the Young's modulus (kPa) values used for subsequent statistical analysis. Fig. 1a, b illustrates the SWE measurements of the lens and lens nucleus.

2.3. Statistical analysis

Data analysis was performed using IBM Corporation's SPSS version 24.0 software for Windows (Armonk, NY, USA). Continuous variables were presented as means with standard deviations or medians with interquartile ranges, depending on the distribution of the data (normal or skewed). The Kolmogorov-Smirnov test was employed to assess the normality of the distribution of variables. Categorical variables were described using frequencies and percentages. Student's t-test was used to compare group differences in continuous variables with a normal distribution, while the Mann-Whitney *U* test was used for variables with skewed distribution. To assess the correlation between lens nucleus stiffness and ophthalmologic grade, a nonparametric test was used. Pearson's correlation coefficients were employed to analyze the associations between lens stiffness and age. The reliability of SWE measurements was evaluated using intraclass correlation coefficients (ICCs) for both intra- and inter-observer assessments. ICC values indicating poor agreement were below 0.40, fair to good agreement ranged from 0.40 to 0.75, and excellent agreement was represented by ICC values above 0.75. A significance level of $P < 0.05$ was considered statistically significant.

3. Results

A total of 146 participants who met the eligibility criteria were initially enrolled for SWE measurements. However, images from 15 individuals were subsequently excluded from the study. The reasons for exclusion included frequent blinking in 7 participants and difficulty in maintaining a closed eye position while looking upwards in 6 participants. Additionally, 2 participants experienced lens dislocation, resulting in suboptimal imaging quality. Consequently, 131 participants (62 men and 69 women; age range, 22–89 years) were ultimately included in the study. This group comprised 92 patients with age-related cataracts and 39 healthy controls. In total, 235 eyes (115 left eyes and 120 right eyes) were examined. The clinical characteristics of the participants are shown in Table 1.

Significant differences in lens and lens nucleus stiffness were observed between patients with age-related cataracts and healthy controls (median, 24.85 [IQR, 19.83–30.65] kPa vs. 17.24 [IQR, 13.79–20.74] kPa, $P < 0.001$; 24.30 [IQR, 18.20–30.80] kPa vs. 17.15 [IQR, 12.25–20.83] kPa, $P < 0.001$, respectively) (Fig. 2 a and b). A subgroup analysis of 45 eyes from 30 patients with age-related cataracts and 25 age-matched healthy controls showed significantly higher lens and lens nucleus stiffness in patients with age-related cataracts compared to healthy controls (median, 22.28 [IQR, 16.88–27.37] kPa vs. 18.48 [IQR, 14.02–21.98] kPa, $P = 0.007$; 21.10 [IQR, 15.20–26.40] kPa vs. 18.60 [IQR, 12.70–22.65] kPa, $P = 0.032$, respectively) (Fig. 2 c and d). Further analysis using nonparametric tests for multiple comparisons revealed significantly greater lens nucleus stiffness in patients with age-related cataracts for grades N1, N2, and N3, compared to healthy controls ($P = 0.015$, $P < 0.001$, $P < 0.001$, respectively). However, no significant differences were identified between grades N1, N2, and N3; the stiffness values were 22.45 [IQR, 16.75–26.78] kPa, 22.50 [IQR, 17.80–30.10] kPa, and 24.80 [interquartile range, 18.85–31.80] kPa, respectively (all $P > 0.05$) (Fig. 3). No significant differences were found in lens and lens nucleus stiffness between male and female patients with age-related cataracts (both $P > 0.05$) (Table 2).

Correlation analysis revealed a significant correlation between lens stiffness and age for all participants ($r = 0.410$, $P < 0.001$; Fig. 4a), as well as for patients with age-related cataracts ($r = 0.175$, $P = 0.022$; Fig. 4b). However, no significant correlation was found

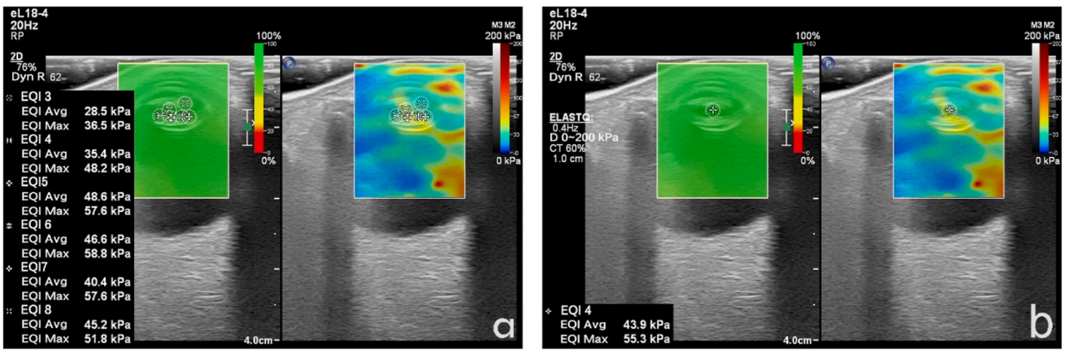

Fig. 1. Shear wave elastography measurements including the lens (a) and lens nucleus (b) in a typical 65-year-old patient with age-related cataracts in the right eye. The quality map on the left side of the image is displayed in green with no significant red regions, indicating good image quality. The elasticity map on the right side is color-coded showing the stiffness values (ranging from 0 to 200 kPa) measured in the region of interest, as indicated on the left side of the image. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 1
Clinical characteristics of participants.

Characteristic	Patients with age-related cataract	Healthy controls	All participants
Age (years)	74 (43–89)	50 (22–66)	68 (22–89)
Male (%)	45 (34.4)	17 (12.9)	62 (47.3)
Female (%)	47 (35.9)	22 (16.8)	69 (52.7)
Left eye (%)	85 (36.1)	30 (12.8)	115 (48.9)
Right eye (%)	86 (36.6)	34 (14.5)	120 (51.1)
Lens nucleus grade[a]			
0 (%)		64 (27.2)	64 (27.2)
1 (%)	20 (8.5)		20 (8.5)
2 (%)	63 (26.8)		63 (26.8)
3 (%)	88 (37.4)		88 (37.4)

Note. Unless otherwise stated, results are expressed as median (min – max) or n (%).
[a] Lens Opacities Classification System II.

between lens stiffness and age in healthy controls ($r = 0.093$, $P = 0.465$; Fig. 4c). In participants, the linear regression equation $y = 0.2445X + 7.832$ represented the relationship between age (x) and lens stiffness (y).

The intra- and inter-observer reliability ICCs were 0.74 (95% confidence interval: 0.56–0.86, $P < 0.001$) and 0.70 (95% confidence interval: 0.49–0.83, $P < 0.001$), respectively, indicating moderate to excellent reproducibility of SWE measurements. The Bland-Altman plot in Fig. 5a, b illustrates the reliabilities of SWE measurements for both intra- and inter-observer assessments.

4. Discussion

In this study, we employed shear wave elastography (SWE) to assess lens stiffness in patients with age-related cataracts, yielding findings that not only corroborate existing knowledge but also provide new insights into the biomechanical properties of the lens affected by cataracts. Our results demonstrated a significant increase in lens stiffness in patients with age-related cataracts compared to healthy controls. This increase in stiffness indicates the biomechanical changes that occur in the lens due to aging and cataract formation. Furthermore, the correlation we observed between lens stiffness and age highlights the progressive nature of these changes and underscores the potential of SWE as a diagnostic tool in the early detection and monitoring of cataract progression. By non-invasively measuring lens stiffness, surgical planning and timing can be improved, potentially leading to better patient outcomes. Additionally, an enhanced understanding of the pathophysiology of cataracts and the evolution of lens biomechanics with age and disease progression is facilitated by SWE. This makes SWE a valuable tool for ophthalmologists in early detection and monitoring, enabling more informed decisions about cataract surgery and contributing to research on cataract formation and progression.

The ocular refraction system relies solely on the crystalline lens for accommodation, enabling the eyes to accurately direct light onto the retina. The lens, a crucial component of this system, possesses a unique metabolic pattern and lacks both blood vessels and nerves. Under physiological conditions, the lens is surrounded by a low oxygen partial pressure of 0.4%–1%. This unique microenvironment is crucial for maintaining a relatively stable metabolic state within the lens, essential for its transparency and function. The low oxygen tension plays a pivotal role in minimizing oxidative stress, thereby reducing the risk of cataract formation [17–19]. Tissue elasticity can provide valuable information about its physiological and pathological characteristics. Recent findings have underscored the versatility of SWE across various tissues [20–22], thereby expanding its clinical applications. Several previous in vivo studies [23, 24] have demonstrated that the mechanical characteristics of the crystalline lens, particularly in nuclear cataracts, were typically more rigid than normal. Furthermore, lens rigidity plays a pivotal role in determining the suitability of cataract patients for phacoemulsification [25]. Concurrently, recent studies exploring elastography techniques on ocular tissues have suggested the safe application of this methodology for the human eye [26]. However, very few studies have explored SWE measurements as a means of evaluating tissue stiffness in the human eye. We found that the stiffness of the lens and the lens nucleus in patients with age-related cataracts was significantly greater than in healthy controls, including an age-matched subgroup. This is in agreement with the physical and chemical alterations to the lens associated with the development of cataracts, increased hardness and opacity occurring as a result of increased protein aggregation and inner fiber compaction [27]. In addition, we found that lens nucleus stiffness was increased across different grades of cataracts, compared to normal controls, although there were no significant differences between grades N1, N2, and N3. We consider it likely that a larger sample size would reveal significant differences with increasing grades.

In a study carried out by Mesut Ozgokce et al. [28], no significant difference in the mean shear-wave velocity was shown between patients with senile cataracts and normal subjects. Conversely, Zhou et al. [29] found that advancing age correlates with a significant decrease in the lens nucleus strain rate ratio, indicating increased lens nucleus stiffness. This discrepancy in findings highlights the complexity of understanding lens stiffness changes with age. Moreover, several factors can affect the quality of SWE images when assessing lens stiffness, including frequent blinking and difficulty in maintaining a steady gaze, leading to suboptimal image quality. To mitigate these issues, our ultrasound equipment was configured to image quality mode, with an IQR less than 30 % of the median value, minimizing the variability of the SWE measurements. In addition, SWE reproducibility, both inter- and intra-observer, was moderate to excellent in our study (as shown in Fig. 5). Additionally, we implemented patient preparation protocols involving clear instructions and practice sessions prior to imaging.

The correlation between age and lens stiffness has been widely recognized [30–32]. The prevalence of visual impairment linked to

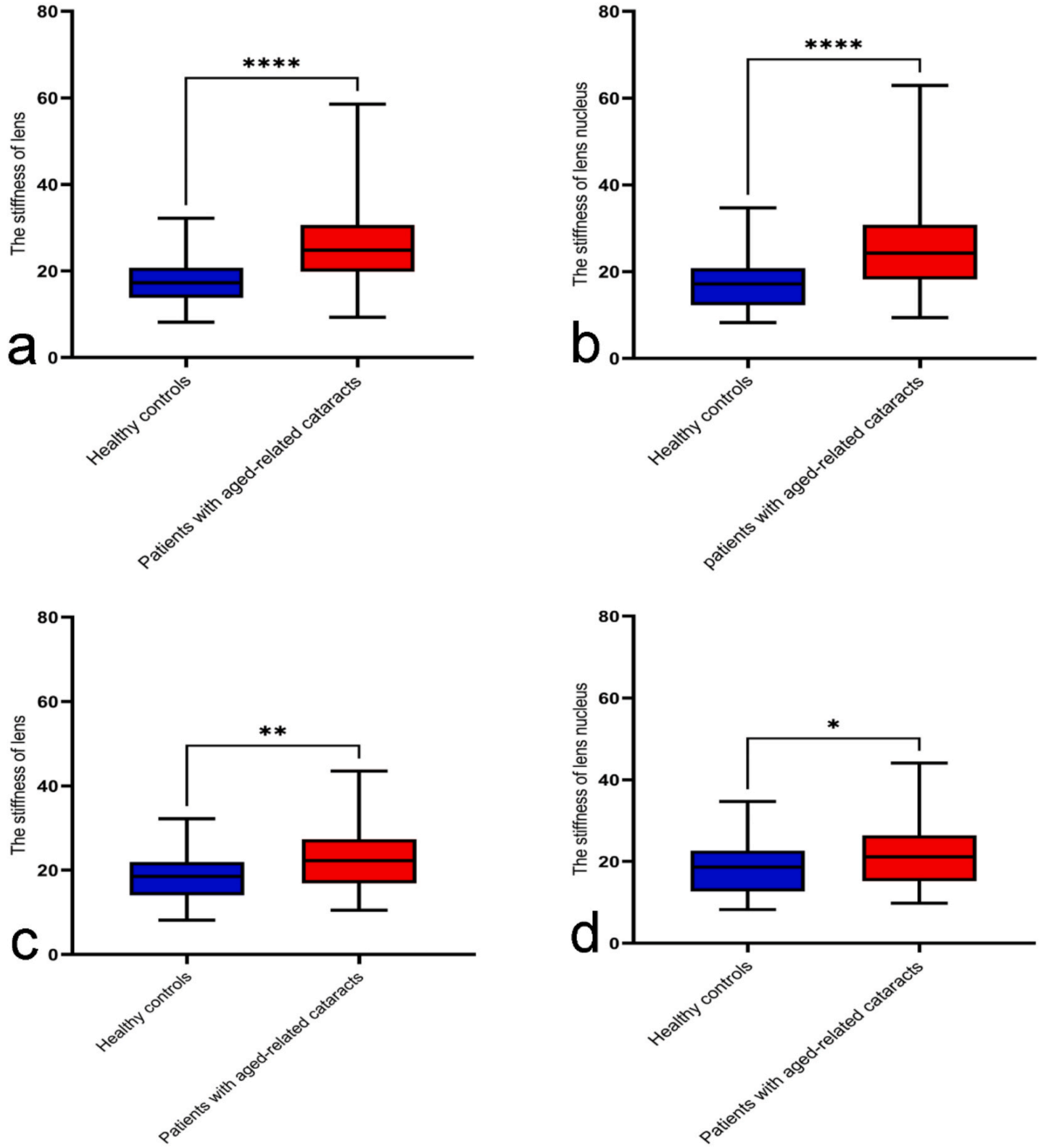

Fig. 2. Box and whisker plot showing significant difference in the stiffness of the lens (a) and the lens nucleus (b) in healthy controls compared to patients with age-related cataracts. Subgroup analysis of 45 age-matched eyes in healthy controls and patients with age-related cataracts further confirming statistically significant differences in stiffness of the lens (c) and the lens nucleus (d).

cataracts is notably increased in individuals aged ≥60 years [33], and the risks increase significantly with age, with the lens hardening further as the oxidation of the lens nucleus increases [34]. As we age, the amount of glutathione in the lens diminishes over time. This leads to not only a notable rise in lens rigidity but also a considerable reduction in the rate of surface-to-nucleus diffusion within the lens [35]. Several studies, in animals and humans [15, 36–38], have suggested that the stiffness of the lens increases with advancing age and this is considered a natural physiological alteration. In our study, we found a statistically positive correlation of lens stiffness with age in patients with age-related cataracts, consistent with prior research. This suggests that assessing the stiffness of lenses could serve as a reliable biomarker for determining cataracts associated with aging. Although lens stiffness did not correlate significantly with age in healthy controls, this may be due to the younger age of the healthy control cohort and the limited physiological and metabolic changes in their lenses.

Several limitations must be acknowledged, as they might impact the interpretation and broader applicability of our findings. First, the study was conducted with a relatively small and homogeneous sample, which may not represent the wider population affected by age-related cataracts. This limitation restricts the generalizability of our results. Second, the precision of SWE measurements can vary due to the quality of the equipment used and the skill of the operator. Ensuring consistency across measurements requires standardized

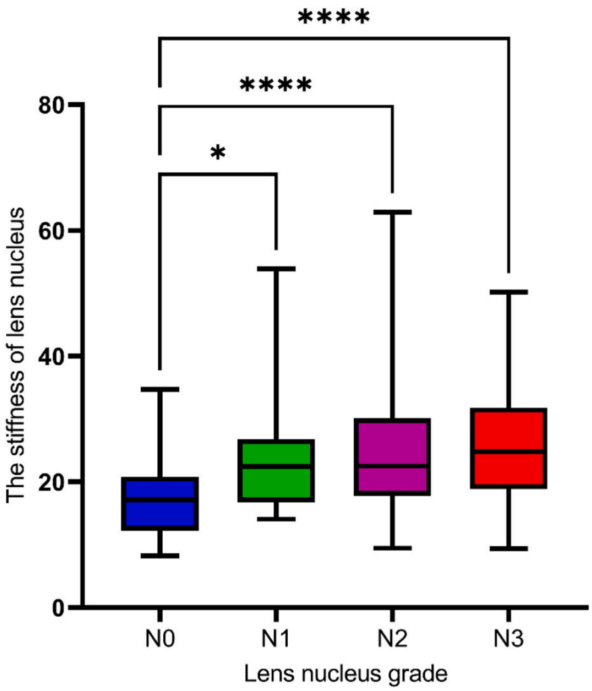

Fig. 3. Stiffness of the lens nucleus was significantly higher in patients with age-related cataracts (grades N1, N2, N3) compared to healthy controls (N0). However, no significant differences were identified between the grades N1, N2, and N3.

Table 2
Comparison of the stiffness of lens and lens nucleus in patients with age-related cataract between gender (kPa).

Characteristic	males	females	*P* value
lens	22.77(17.49–27.91)	21.90(17.38–28.16)	0.698
lens nucleus	22.35(16.50–27.40)	20.80(17.05–28.80)	0.891

Note. Except where indicated, data are medians; data in parentheses are interquartile range.

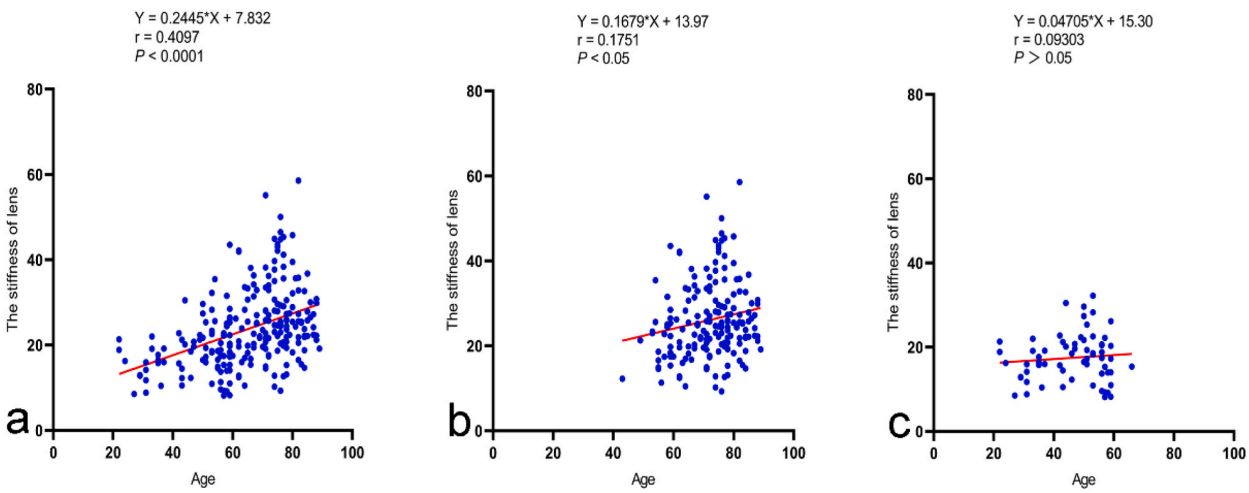

Fig. 4. Correlation analysis of lens stiffness with age of all participants (a), patients with age-related cataracts (b), and healthy controls (c). A positive correlation was observed between lens stiffness and age in all participants and patients with age-related cataracts, but no significant correlation was found in healthy controls.

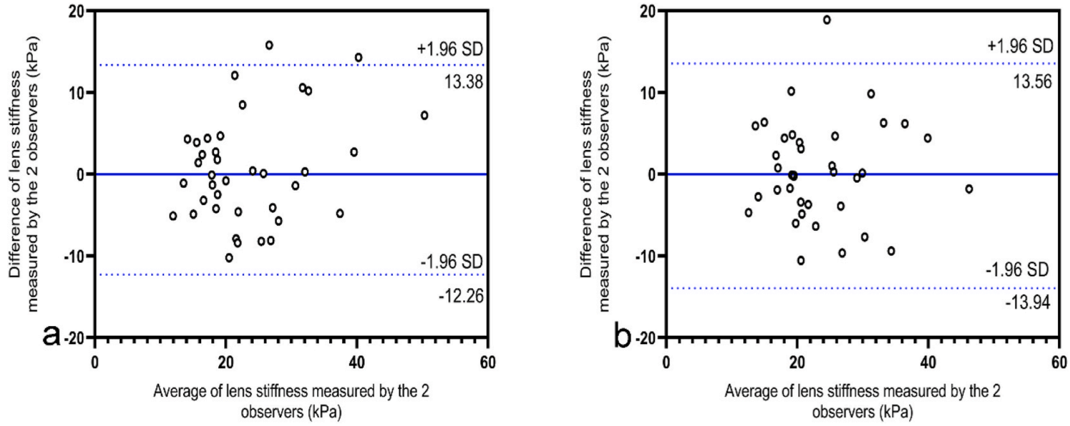

Fig. 5. A Bland–Altman plot of intra- (a) and inter-observer (b) reproducibility of shear wave elastography in participants. The solid line represents the mean, and the dotted lines represent the 95% limits of agreement, demonstrating moderate to excellent reproducibility of the measurements.

procedures and comprehensive training for all operators. Lastly, the cross-sectional design of our study limits our ability to track changes over time or to establish causal relationships between observed factors. Based on the identified limitations, we propose several key areas for future research: To enhance the robustness and generalizability of our findings, future studies should include a larger and more diverse cohort, encompassing a broad range of demographic backgrounds and cataract severities. Longitudinal studies are essential to understand the progression of lens stiffness and its clinical implications over time. Such studies could provide valuable insights into the natural history of cataracts and the long-term efficacy of potential interventions. Developing and implementing standardized protocols for SWE is crucial to improve the reliability and reproducibility of measurements across different clinical settings. This will help reduce variability introduced by technical factors and operator dependency. To establish SWE as a reliable diagnostic tool, it is imperative to conduct validation studies that compare SWE measurements with those obtained from established imaging modalities or directly correlated with clinical outcomes. These studies will help confirm the accuracy and clinical utility of SWE in the diagnosis and management of lens stiffness.

In conclusion, our study demonstrated that patients with age-related cataracts have higher lens stiffness compared to healthy controls. The findings indicate that SWE has the potential to noninvasively quantify the mechanical characteristics of the lens in the human eye, providing valuable clinical insights. This research lays the groundwork for future studies that could lead to its adoption as a standard diagnostic tool in ophthalmology, ultimately improving patient care. Further exploration in larger, diverse populations and additional studies focusing on longitudinal assessments and clinical outcomes is essential to fully establish its efficacy and utility.

Ethical statement

This study was performed with approval from the Institutional Review Board of The Second People's Hospital, Wuhu (approval number: 2021–20), and was registered in the Chinese Clinical Trial Register (ChiCTR), ChiCTR2100054913. It was conducted in strict accordance with the ethical principles outlined in the Declaration of Helsinki and the Istanbul Declaration. Written informed consent was obtained from all participants prior to their inclusion in the study, ensuring their informed participation and the protection of their rights. The study protocols were designed to ensure that no participant suffered harm or infringement of rights during the research process.

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Data availability statement

All data generated or analyzed during this study are included in this published article. Available upon request.

CRediT authorship contribution statement

Banghong Qiang: Writing – review & editing, Writing – original draft, Methodology, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Qiancheng Xu:** Writing – review & editing, Validation, Methodology, Formal analysis, Conceptualization. **Aili Hu:** Writing – review & editing, Visualization, Resources, Data curation. **Jiagui Fang:** Writing – review & editing, Software, Methodology, Investigation, Data curation. **Chunyun Shen:** Writing – review & editing, Visualization, Validation, Supervision, Software. **Yu Zhang:** Writing – review & editing, Supervision, Software, Resources, Methodology, Investigation. **Junli Wang:** Writing

– review & editing, Validation, Supervision, Project administration, Conceptualization.

Declaration of competing interest

The authors 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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