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Standardized Assessment of Health-Related Quality of Life in Patients with Congenital Aniridia

Standardisierte Erfassung der gesundheitsbezogenen Lebensqualität bei Patienten mit kongenitaler Aniridie

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ABSTRACT

Introduction Congenital aniridia is a rare panocular disorder that is associated with varying degrees of impairment of visual acuity. The COST Action (CA18116) developed a survey (aniridia-net.eu) to assess patient-reported experiences with congenital aniridia and its impacts on vision and daily life. Here, we correlate the survey responses of German patients with congenital aniridia with clinical ophthalmology data acquired at the Homburger Aniridia Center.

Patients and Methods The patients completed the German-language version of a 20-point ANIRIDIA-NET survey. The survey included demographic information, the most common symptoms caused by the disease, difficulties caused by visual impairment in various life situations, and the frequency of using visual aids in daily life. As for clinical data, best-corrected visual acuity (BCVA) as well as corneal, lens, and glaucoma status were collected.

Results A total of 71 participants, 27 (38.0%) children and 44 (61.7%) adults, completed the questionnaire, with an age range of 28.8 ± 20.2 years (6–78 years). Among them, 55 (77.4%) reported daily light sensitivity, 34 (47.8%) experienced dry eyes, 17 (23.9%) had fluctuating vision, 11 (15.4%) reported eye pain, and 5 (7.0%) experienced daily watering eyes. Older patients reported significantly more eye complaints than children ($p < 0{,}001$). Notably, patients with more advanced aniridia-associated keratopathy (AAK) exhibited a discernibly lower quality of life ($\rho = 0.28$, $p = 0.027$). Similarly, cataract surgery early in life was associated with a more pronounced decline in quality of life ($\rho = -0.36$, $p = 0.002$). Thirty-five (49.2%) patients never needed assistance for their commute to school/work, 27 (38.0%) and

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22 (30.9%) never needed assistance for their daily routines at home or various social activities, respectively. Regarding the use of visual aids, 39 (24.9%) reported that they always used visual aids at work or school, 24 (33.8%) during social activities, and 32 (45.1%) during free time activities.

Conclusions Although congenital aniridia is associated with reduced visual acuity, the majority of affected individuals, especially during childhood, report that they were able to manage personal communication and various life situations independently and without significant difficulties, despite their eye-related issues. Visual aids serve as crucial support for them during their transition into adulthood and as they age. Symptoms of congenital aniridia subjects, described by the ANIRIDIA-NET survey, correlated well with clinical findings. Therefore, the questionnaire may provide important information for the treating ophthalmologist for follow-up examination of these patients and improvement in their life quality.

ZUSAMMENFASSUNG

Einleitung Kongenitale Aniridie ist eine seltene panokulare Störung, die mit unterschiedlich starken Beeinträchtigungen der Sehschärfe einhergeht. Im Rahmen der COST-Aktion (CA18116) wurde eine Umfrage (aniridia-net.eu) entwickelt, um die Erfahrungen von Patienten mit kongenitaler Aniridie und deren Auswirkungen auf das Sehen und das tägliche Leben zu erfassen. Im Folgenden werden die Antworten deutscher Patienten mit kongenitaler Aniridie mit klinischen ophthalmologischen Daten des Homburger Aniridie-Zentrums in Beziehung gesetzt.

Patienten und Methoden Die Patienten füllten die deutschsprachige Version eines 20 Punkte umfassenden ANIRIDIA-NET-Fragebogens aus. Der Fragebogen umfasste demografische Informationen, die häufigsten durch die Krankheit verursachten Symptome, die durch die Sehbehinderung verursachten Schwierigkeiten in verschiedenen Lebenssituationen und die Häufigkeit der Verwendung von Sehhilfen im täglichen Leben. Was die klinischen Daten betrifft, so wurden die bestkorrigierte Sehschärfe (BCVA) sowie der Hornhaut-, Linsen- und Glaukomstatus erhoben.

Ergebnisse Insgesamt 71 Teilnehmer, 27 (38,0%) Kinder und 44 (61,7%) Erwachsene, füllten den Fragebogen aus, mit einer Altersspanne von 28,8 ± 20,2 Jahren (6–78 Jahre). Von ihnen berichteten 55 (77,4%) über tägliche Lichtempfindlichkeit, 34 (47,8%) über trockene Augen, 17 (23,9%) über schwankende Sehkraft, 11 (15,4%) über Augenschmerzen und 5 (7,0%) über täglich tränende Augen. Ältere Patienten berichteten signifikant häufiger über Augenbeschwerden als Kinder ($p < 0{,}001$). Vor allem Patienten mit fortgeschrittener Aniridie-assoziierter Keratopathie (AAK) wiesen eine deutlich geringere Lebensqualität auf ($\rho = 0{,}28$, $p = 0{,}027$). Ebenso war eine Kataraktoperation in einem frühen Lebensalter mit einer stärkeren Verschlechterung der Lebensqualität verbunden ($\rho = -0{,}36$, $p = 0{,}002$). Fünfunddreißig (49,2%) Patienten brauchten nie Hilfe auf dem Weg zur Schule/Arbeit, 27 (38,0%) und 22 (30,9%) brauchten nie Hilfe bei ihren täglichen Routinen zu Hause bzw. bei verschiedenen sozialen Aktivitäten. Was die Verwendung von Sehhilfen betrifft, so gaben 39 (24,9%) an, dass sie bei der Arbeit oder in der Schule immer Sehhilfen verwendeten, 24 (33,8%) bei sozialen Aktivitäten und 32 (45,1%) bei Freizeitaktivitäten.

Schlussfolgerungen Obwohl die kongenitale Aniridie mit einer verminderten Sehschärfe einhergeht, berichtet die Mehrheit der Betroffenen, insbesondere in der Kindheit, dass sie trotz ihrer augenbedingten Probleme in der Lage waren, die persönliche Kommunikation und verschiedene Lebenssituationen selbstständig und ohne größere Schwierigkeiten zu bewältigen. Sehhilfen sind für sie eine wichtige Unterstützung beim Übergang ins Erwachsenenalter und im Alter. Die in der ANIRIDIA-NET-Umfrage beschriebenen Symptome von Personen mit kongenitaler Aniridie korrelierten gut mit den klinischen Befunden. Daher kann der Fragebogen dem behandelnden Augenarzt wichtige Informationen für die Nachuntersuchung dieser Patienten und die Verbesserung ihrer Lebensqualität liefern.

Introduction

Congenital aniridia is a rare, panocular, genetically determined disease, which is characterized by total or partial iris hypoplasia from birth [1, 2]. This rare disorder (incidence 1:60 000 to 1:90 000) [3] is inherited in an autosomal dominant manner with a high penetrance and variable expressivity. Two-thirds of the cases are familial, others are sporadic. PAX6 gene-associated forms and other forms should be differentiated.

PAX6 is a highly conserved gene [2] and its mutation leads to a disturbance of the entire embryonic eye development. Patients are diagnosed after birth with iris hypoplasia [4], anterior polar cataract [4], choroidal coloboma, foveal hypoplasia [4, 5], nystagmus, optic disc hypoplasia, and other optic nerve abnormalities [5]. There is almost, in all subjects, visual loss [1] and often reduced color vision [1, 6]. In addition, patients develop early complications such as glaucoma, cataract, dry eye syndrome, and aniridia-associated keratopathy (AAK), which can lead to corneal blindness later in life. The PAX6 gene mutation is also associated with limbal stem cell insufficiency, making the keratopathy difficult to treat [1, 2]. Furthermore, when intraocular surgery is performed, there is a risk of developing aniridia fibrosis syndrome, with inflammatory intraocular scarring, often followed by hypotony and phthisis [3].

Aniridia is often accompanied by systemic diseases [7], therefore, nowadays it is often referred as “aniridia syndrome” or “PAX6 syndrome”. The most common associated conditions are WAGR syndrome (Wilms tumor, aniridia, genitourinary abnormalities, and mental retardation), Gillespie syndrome, hearing impairment, intelligence loss, diabetes mellitus, and pituitary hypoplasia. In patients having only PAX6 syndrome, there often are obesity, early manifestation of diabetes type II, hypothyroidism, auditory perception deficits, and anomalies in brain morphology (e.g., hypoplasia of corpus callosum).

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There is a significant and progressive visual impairment in the majority of congenital aniridia patients, in addition, with ocular discomfort. During their life, patients require continuous monitoring by an ophthalmologist and a variety of complex conservative and surgical treatments to maintain their vision [2].

Quality of life (QoL) is increasingly becoming an important criterion in the evaluation and treatment of eye diseases. Functional measurements may not always provide adequate characterization of the burden of disability in day-to-day activities from the patient's perspective [8, 9]. Visual disability limits social interactions and independence of the affected person, thus influencing their daily activities, emotional state, social involvement, and mobility [8, 10]. People with aniridia have a permanent visual impairment, which is generally not correctable by eyeglasses, contact lenses, or surgical interventions. In addition, surgical interventions may actually accelerate visual loss in congenital aniridia. Interventions to improve visual function of these patients are based on the use of low vision aids, learning compensatory skills, and training in the use of technology aids. There are currently no surveys on the subjective limitations and challenges in the daily life of patients with congenital aniridia, so this study could provide important information for future organization of care.

Our purpose was to collect experiences of German-speaking patients with congenital aniridia using the ANIRIDIA-NET survey, and to analyze the correlation of QoL and the clinical data at the Homburger Aniridia Center.

Patients and Methods

This retrospective, cross-sectional, descriptive survey-based study was conducted with congenital aniridia patients of the Homburg Aniridia Center at Saarland University Medical Center in Homburg/Saar, Germany. The Ethical Committee of the Medical Council of Saarland approved our study (Nr 132/22), which followed the principles of the Declaration of Helsinki. Only patients providing written informed consent were included in the study. In case of minors, their guardians signed our informed consent form.

Inclusion criteria were patient age more than 6 years (these subjects were considered capable of providing insightful assessment of their daily challenges) and being a resident in Germany. Patients received the questionnaire via post, including a patient information sheet, patient consent form, and data privacy statement as well as a post-paid envelope.

In addition, patient data of the electronic medical record system of the Department of Ophthalmology of Saarland University were collected, such as genetic mutation, ocular and systemic diagnoses, local and systemic therapy, and previous intraocular surgeries. Best-corrected visual acuity (BCVA), intraocular pressure measurement results, and slit lamp examination findings were also recorded.

The used questionnaire was designed through ANIRIDIA-NET, which is a pan-European network of researchers and other interest groups concerned with aniridia, and its German version was handed out to our patients. The questionnaire is available in 13 languages at https://aniridia-net.eu/survey. The questions referred to information regarding demographics of the patients (age and gender), the frequency of eye complaints; use of electronic devices such as computers or mobile phones and, accordingly, the need for special software for their use; interaction with other people at school, work, and in the family; need for visual aid; need for help and/or support from other people during daily activities. Additionally, using the COST survey, self-assessed life quality (as very good, good, satisfactory, poor, and very poor) was investigated, and lastly, patients reported whether they had filled out the questionnaire themselves or with the help of someone else. At the end of each question, patients could provide their comments to express their experiences or perspective in an unrestricted way.

Optotype BCVA was converted into decimal and logMAR BCVA. Non-optotype vision recorded as counting fingers, hand motion, light perception, and no light perception was approximated as 0.016, 0.0063, 0.002, and 0.001, respectively, according to the WHO definitions of distance vision impairment [8] · LogMAR visual acuity under 0.5 was classified as mild or no visual impairment; 1.0–0.5 moderate impairment; 1.3–1.1 severe impairment; above 1.3 blindness.

The examination findings were grouped into corneal, lens, and glaucoma findings. AAK was graded from 0–4, as defined by previous authors [6]. Grade 0 consists of intact limbal border and no corneal lesions; Grade 1 is characterized by partial or complete limbal invasion from vessels and conjunctival tissue, reaching 1 mm from the limbus; Grade 2 consists of conjunctival tissue invading the peripheral and mid-peripheral cornea, leaving the central 2–3 mm of cornea transparent; Grade 3 is characterized by a diffuse, translucent, vascularized pannus affecting the entire cornea, including the visual axis; Grade 4 is the most advanced form, with an opaque, thick, and irregular pannus covering the entire ocular surface [11].

In addition to the keratopathy grade, the necessity of permanent use of therapeutic contact lenses and previous corneal surgeries (including corneal transplantation) were also recorded. Furthermore, due to early development of cataract and secondary glaucoma, the need for surgery and age at the time of surgery were collected. Finally, information on the type and frequency of topical therapy (eye drops) used by patients was gathered.

The information obtained from the questionnaires and the clinical findings was statistically analyzed to evaluate how children and adults navigated their daily challenges. We analyzed how the frequency of visual symptoms correlated with the efficacy of school-related tasks for children and work-related tasks for adults. Second, the impact of face recognition and face-to-face communication in social interactions and completing school and work tasks was evaluated. In addition, we analyzed how the self-assessed QoL was correlated to the patients' genetic mutations, BCVA, the age at which the first surgical intervention occurred, the cumulative count of surgeries, the frequency of eye drop administration per day, and the frequency of yearly visits to ophthalmologists.

Statistical analysis

Data collection and statistical analysis were performed using SPSS (IBM SPSS Statistics for Windows, Version 20, Armonk, NY, USA). Continuous data were described as the mean, standard deviation, minimum, and maximum. We used Spearman and Pearson correlation tests for categorical and continuous variables, respectively; p values < 0.05 were considered statistically significant.

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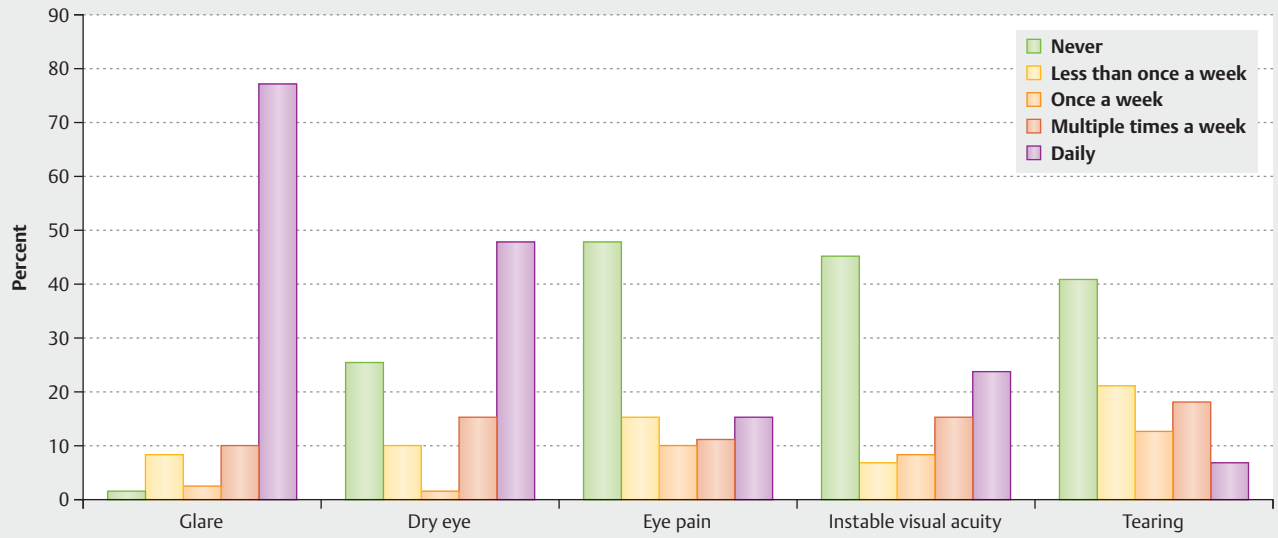

▶ **Fig. 1** Frequency of eye symptoms. The X-axis shows the most common symptoms in aniridia patients and the Y-axis shows the percentage of patients that reported them. The columns reflect the frequencies, described as: never, less than once a week, once a week, multiple times a week, and daily.

Results

Demographic data

There were 207 patients who received a letter to participate in the study and 71 (34.1%) completed the survey. Out of the selected sample, 41 individuals (19.8%) did not receive our correspondence due to changed address information. Of the respondents, 37 (52.1%) were female, 31 (43.4%) were male, and 3 (4.2%) were diverse (nonbinary, gender fluid, agender, or other). The mean age was 28.8 ± 20.7 (range 6–78) years. Of the participants, 27 (38.0%) were children and 44 (61.7%) were adults.

Questionnaire-based data

The most common reported symptom was glare, occurring daily in 55 (77.4%) of the patients. Another 34 (47.8%) reported daily dry eye symptoms, 17 (23.9%) fluctuating eyesight, 11 (15.4%) eye pain, and 5 (7.0%) had daily teary eyes. ▶ **Fig. 1** shows a summary of the frequency of these eye symptoms. Older patients reported significantly more eye complaints than children ($p < 0.001$). No statistically significant correlation was found between eye symptoms and the self-assessed ability to complete school tasks in children and work tasks in adults (Spearman's Rho correlation test, $p = 0.96$ and $p = 0.25$, respectively).

Most of the participants [47 (66.2%)] reported using special software or devices to use a computer, whereas 32 (45.1%) needed software to use a mobile phone. Patients mostly used the Magnifier tool to complete computer tasks. Online and live communication never posed problems for 47 (66.2%) patients, yet 28 (39.6%) always encountered problems at interpreting facial cues and facial expressions. Twenty-six patients (36.6%) never faced difficulties during personal communication with schoolmates (13 [18.3%]) or colleagues (13 [18.3%]). Due to their visual impairment, 40 (56.3%) participants had faced difficulties in understanding and completing tasks at school and 26 (36.6%) in engaging with other children or pupils of the same age. At work, 25 (52.2%) of the adults reported sometimes having issues completing their work tasks and 18 (40.9%) in socializing with their colleagues due to their restricted vision.

Furthermore, the need for assistance during daily life was explored. Twenty-seven (38.0%) of the patients indicated they never sought assistance with household routines. Thirty-five (49.3%) were capable of independently attending school or work, and 24 (33.8%) occasionally encountered challenges in engaging in social activities such as shopping, sports, dining out, and attending events. Twenty-seven (38.0%) were independent during their daily routines at home, and 22 (30.9%) in various social activities. Patients commented that they have no issues in places they were familiar with. Daily routine activities could also be managed without the need of visual aids for most patients. Activities such as differentiating food in one's plate, choosing drinks and dishes at the kitchen, choosing their clothes, finding their personal belongings, and performing daily hygiene was possible for most patients alone and with or without visual aids. The data is summarized in the bar diagrams in ▶ **Figs. 2** and **3** below. Children and adults showed no differences in their responses ($p > 0.05$).

Visual aids play an important role in the ability of patients to navigate through life. Thirty-nine (24.9%) reported always using visual aids at work or school, 24 (33.8%) during social activities, and 32 (45.1%) during free time activities. On the other side, other participants never used them for communication [30 (42.2%)], social activities [16 (22.5%)], travelling [13 (18.3%)], or for studying/working [7 (9.8%)]. The column diagram in ▶ **Fig. 3** summarizes their answers.

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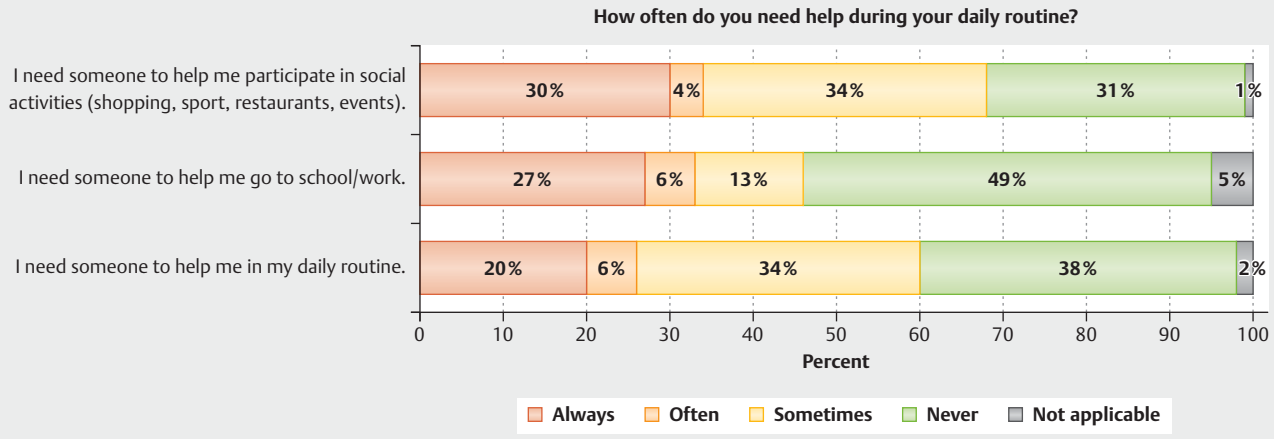
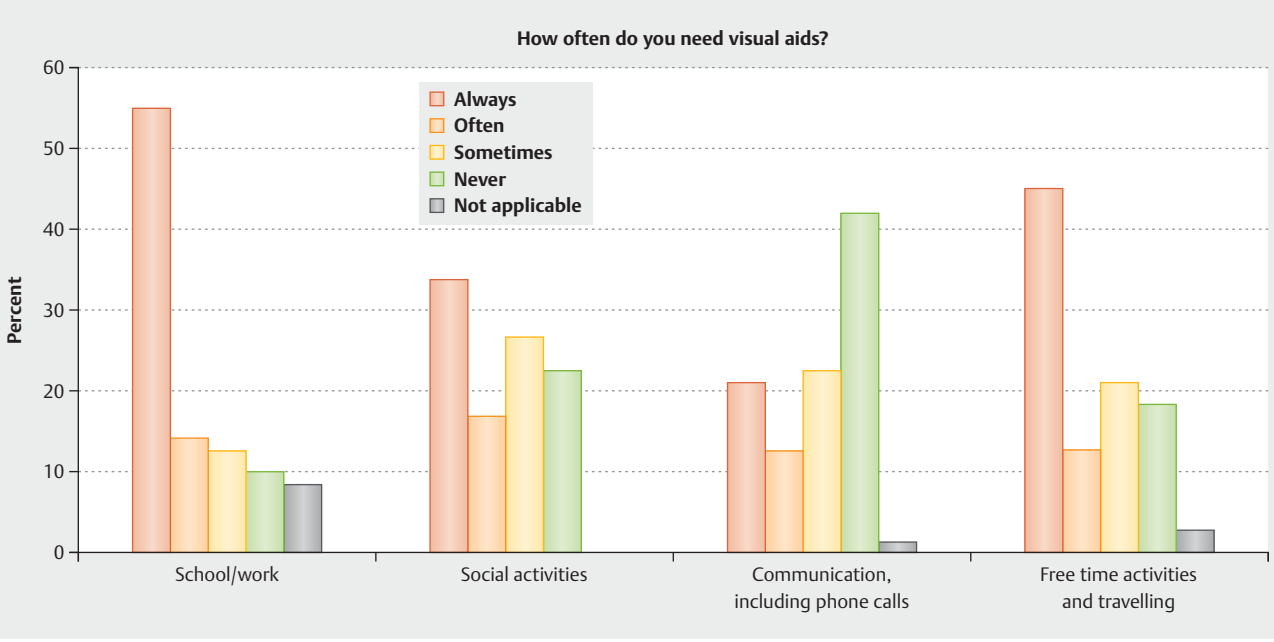


▶ **Fig. 2** Bar diagram to illustrate the frequency with which patients expressed the need for assistance in various aspects of their daily routines. On the vertical axis, distinct daily activities are depicted, while the horizontal axis shows the percentage of patients who indicated their requirement for aid using categories such as "always", "often", "sometimes", and "never". The frequencies are shown in different colors and inside the bars the number of patients is annotated.



▶ **Fig. 3** Column diagram depicting how often patients need visual aids during school/work, social activities, communication, and free time activities. The vertical axis shows the percentage of patients, and the columns reflect the frequencies denoted by categories such as "always", "often", "sometimes", and "never". "Not applicable" shows the patients who did not answer.

Conversely, when it came to engaging in novel or infrequent tasks, 24 (33.8%) patients occasionally sought assistance, while 22 (31.0%) consistently relied on help. Twenty-five (35.2%) participants relied on assistance for attending medical appointments, while 24 (33.8%) managed without it. Nearly half of the patients [34 (47.9%)] required up to six visits per year to the ophthalmologist. Corneal and glaucoma complications are the main reason that patients with congenital aniridia visit the ophthalmologist. There was a strong correlation between the frequency of visits to an ophthalmologist and the severity of AAK (Pearson test $r = 0.51$, $p = 0.01$), as well as presence of glaucoma (Pearson test $r = 0.76$, $p = 0.01$).

Ultimately, 31 patients (43.7%) autonomously completed the questionnaire without assistance, while 28 patients (39.4%) re-

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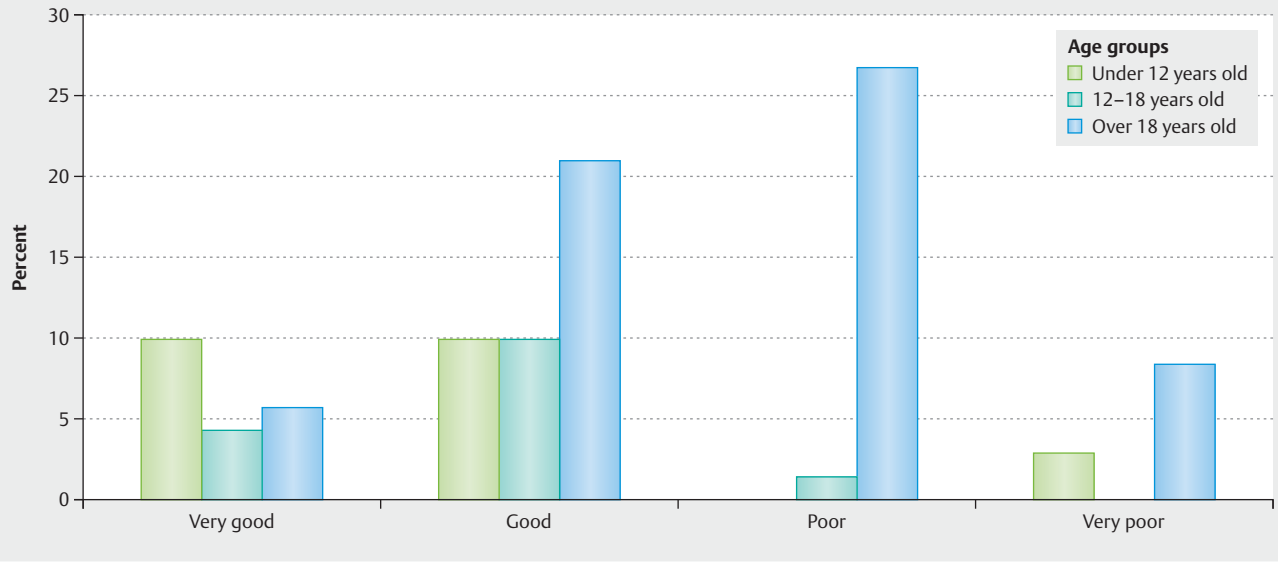

▶ **Fig. 4** Self-assessed quality of life (QoL) across children and adults. The Y-axis demonstrates the self-assessed QoL, the X-axis the percentage of patients. They are divided into three groups: children under 12 years old, those between 12 and 18, and adults. Spearman's Rho correlation revealed a moderately higher QoL in children compared to adults; ρ = .44, p < 0.001, n = 71.

▶ **Table 1** Frequency of the genetic mutations and systemic diseases. Among "other genetic mutations," one patient had Gillespie syndrome, one had an ELP4 gene-related aniridia [40], and one patient had no known genetic mutation despite testing.

	n (%)
Genetic mutation	
▪ PAX6	39 (54.9%)
▪ WAGR	4 (5.6%)
▪ Other	3 (4.2%)
▪ Not tested	12 (18.3%)
Systemic disease	
▪ Yes	27 (38.0%)
▪ No	44 (61.9%)

▶ **Table 2** Best-corrected visual acuity (BCVA) in the participants.

LogMAR BCVA	n (%)	Descriptive statistics
Mild or no impairment (< 0.5)	17 (23.9%)	
Moderate impairment (0.5–1.0)	26 (36.6%)	Mean value 0.14 ± 0.15
Severe impairment (1.3–1.1)	9 (12.7%)	Minimum 0.001
Blindness (> 1.3)	14 (19.7%)	Maximum 0.800

quired comprehensive aid for its completion. The remaining 12 patients (16.9%) sought partial assistance.

Self-assessed quality of life

A significant proportion of patients, comprising 29 individuals (40.8%), assessed their QoL as "good," while an additional 20 patients (20.2%) deemed it "satisfactory." Notably, patients with more advanced AAK exhibited a discernibly lower QoL (Spearman correlation test ρ = 0.28, p = 0.027, n = 61; ▶ **Fig. 5**). Similarly, earlier cataract surgery was associated with a more pronounced decline in QoL (Spearman correlation ρ = − 0.36, p = 0.002). Conversely, the existence of glaucoma, history of glaucoma surgery, and the age at which surgery was performed revealed no significant correlation with the self-assessed QoL (as indicated by the Spearman correlation test, yielding p values of 0.089, 0.975, and 0.108, respectively). Furthermore, the type of genetic mutation, visual acuity (BCVA), use of eye drops, and total number of surgeries had no significant correlation to QoL (Spearman correlation test p > 0,05). Children self-reported a moderately higher life satisfaction compared to adults (ρ = 0.44, p < 0.001, n = 71). The data is summarized at ▶ **Fig. 4**.

Clinical data

The information collected from our clinical records was summarized in the following tables. An overview of the genetic mutation present in the patients, the presence of systemic diseases, and BCVA are given in ▶ **Tables 1** and **2**. Furthermore, the presence of complications like AAK, cataract, glaucoma, and their need for surgery are presented in ▶ **Tables 3**, **4** and **5**, respectively. ▶ **Fig. 6** also depicts how many of the patients needed surgery for these three compliations, separated in under and above 18 years old.

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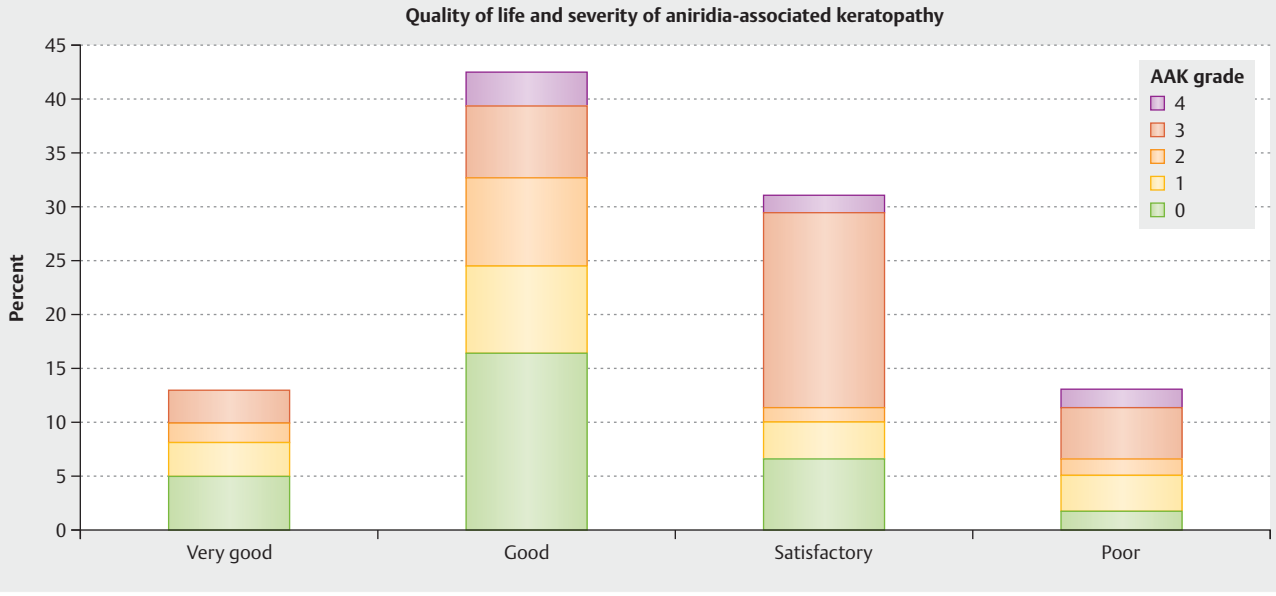

▶ **Fig. 5** Self-assessed quality of life (QoL) according to the aniridia-associated keratopathy (AAK) grade. The Y-axis depicts the percentage of patients and the X-axis their QoL. The AAK is illustrated in different color bars. The Spearman correlation test showed that patients with more advanced AAK exhibited a lower QoL; $\rho = 0.28$, $p < 0.027$, $n = 61$.

▶ **Table 3** Frequencies of patients with aniridia-associated keratopathy and its grade, need for therapeutic contact lenses, corneal surgery (such as pannectomy, amniotic membrane transplantation, phototherapeutic keratectomy, and corneal graft) and corneal transplantation, within the analyzed subjects.

Cornea	n (%)
Aniridia-associated keratopathy	
▪ Grade 0	18 (25.4%)
▪ Grade 1	11 (15.5%)
▪ Grade 2	8 (11.3%)
▪ Grade 3	20 (28.2%)
▪ Grade 4	4 (5.6%)
Patients who permanently needed therapeutic contact lenses	8 (11.3%)
Patients who underwent corneal surgery	21 (29.6%)
Patients who received a corneal graft	18 (25.4%)

▶ **Table 4** Frequencies of patients with cataract, surgical cataract intervention, and age at first intervention within the analyzed subjects.

Cataract	n (%)
Patients with cataract	52 (73.2%)
Patients who underwent cataract surgery	30 (42.3%)
Age of first cataract surgery	
▪ Under 12	11 (15.5%)
▪ 12–18 years old	6 (8.5%)
▪ 19–49 years old	17 (23.9%)
▪ Above 50	1 (1.45)

Discussion

This study is part of a larger survey conducted by the "COST Action ANIRIDIA-NET" (European Cooperation in Science in Technology, COST action CA18116) in several European countries, aiming to assess the QoL related to visual impairment of patients with congenital aniridia. Our work focused on a subgroup of patients in Germany who additionally had clinical data available, in addition to the self-reported survey data. Moreover, we obtained information on perceived QoL from the patients.

In this study, patients reported a good or satisfactory QoL and few limitations in their daily activities, despite their significant visual impairment. Children reported a moderately better QoL than adults ($p < 0.001$). Similarly, a study of young adults with primary congenital glaucoma showed a good QoL regardless of their visual field, surgical intervention, and medication [12]. This may suggest that QoL may be influenced by factors other than clinical indices. However, a study conducted among children aged 0–11 years who had undergone surgery for congenital or developmental cataracts found that their QoL was lower compared to the control group. [13]. Likewise, studies of patients with visual impairment due to glaucoma [14], age-related macular degeneration [14,

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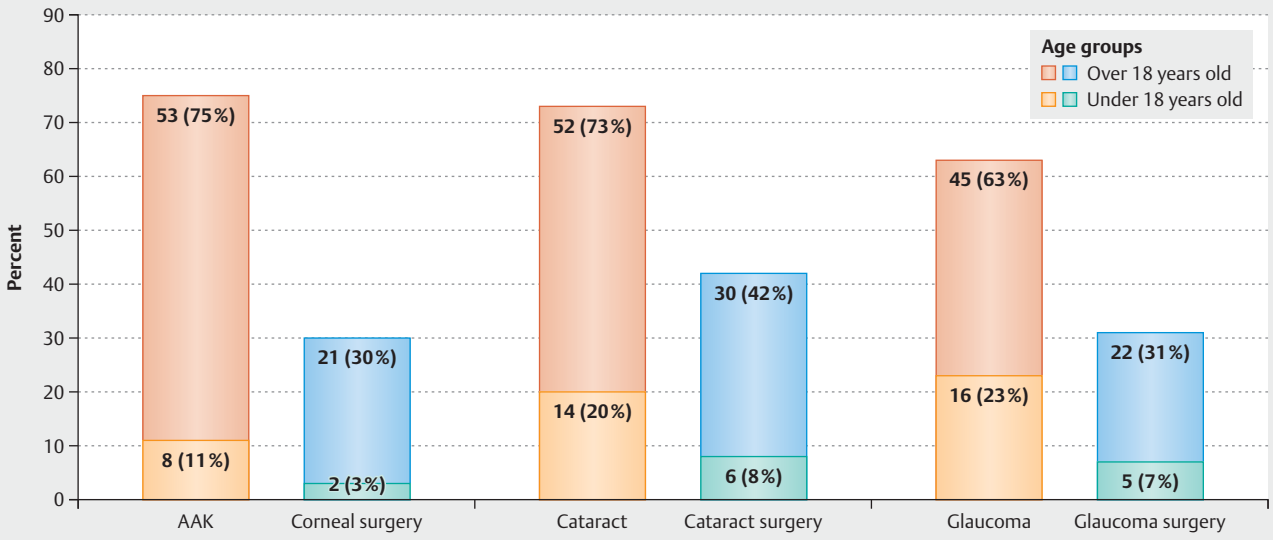

▶ **Fig. 6** Column diagram showing the frequencies of aniridia complications, along with the corresponding need for surgical intervention for patients under and over 18 years old, shown in light and deep brown, respectively. The first column in each group shows the number of patients who have aniridia-associated keratopathy (AAK), cataract, and glaucoma (labeled in the horizontal axis) and the adjacent column conveys the subset of patients who underwent surgery to address these complications, according to age (green – under 18 years, blue – over 18). In brackets, the percentage of patients is indicated in comparison to the total number of patients.

▶ **Table 5** Frequencies of patients with glaucoma, surgical glaucoma intervention, and age at first intervention, within the analyzed subjects.

Glaucoma	n (%)
Patients with glaucoma	45 (63.4%)
Patients who underwent glaucoma surgery	22 (31.0%)
Age of first glaucoma surgery	
▪ Under 12	7 (9.9%)
▪ 12–18 years old	1 (1.4%)
▪ 19–49 years old	14 (19.7%)
▪ Above 50	2 (2.8%)
▪ No data available	47 (66.2%)

15], or senile cataract [16] have reported a lower QoL. Notably, these patients had previously experienced normal vision, and the adaptation to reduced visual acuity occurred later in life. Conversely, patients with keratoconus exhibited a reduced QoL even in early stages with normal BCVA [17]. Keratoconus commonly affects young and active individuals (onset typically between 9.2 and 28.0 years) [18, 19], so its diagnosis may result in heightened anxiety and reactivity to stressful situations [20]. Another study involving 125 low vision patients found that those who developed low vision after the age of five had more fragile mental health, scoring higher for depression and anxiety compared to individuals with congenital low vision [21]. Both groups, however, reported a lower vision-related QoL compared to healthy controls. Our findings suggest that the good perceived QoL in congenital aniridia patients may be due to early adaptation to their environment, as they have never experienced "normal" vision and have learned to adjust from a young age.

Our study showed a moderately higher QoL reported among children compared to adults. One reason could be the onset of secondary complications and particularly the ocular surface damage after 10 years of age and progressing thereafter [22]. Studies in adults have shown that visual impairment later in life is commonly associated with a lower QoL [23, 24]. However, these studies were usually conducted in adults with cataract, glaucoma, or macular degeneration, who have had a lifetime of normal sight. A 3-year cross-sectional study among adults aged 60–96 years found that visual impairment was significantly associated with more activity limitations and fewer socioeconomic, social, and psychological resources [25]. Adults with congenital aniridia have a baseline visual impairment; however, we could hypothesize that, as responsibilities increase in adulthood and the disease follows its progressive course. Activity limitation as well as financial and social strains can be a cause of their lower QoL compared to younger participants.

Visual aids played an important role in patients' autonomy, especially at school or work and during leisure activities. Participants commented on the use of specific tools and applications on mobile smart phones and computers, such as Zoom Text magnifier/reader and Voice Over. However, many commented that they struggled at school because they could not read the text on the blackboard because it was too small or too far away. Providing

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the right optical aid is essential for these patients. Edge filters can be used to improve contrast sensitivity and control glare. To magnify text and objects, optical magnifiers such as hand-held and stand magnifiers, simple high-plus spectacles, and telescopic spectacles can be used. For high magnification requirements (> 6×), an electronic reading device should usually be used. There is no universal low vision aid, and these aids can only help in specific situations (e.g., reading). Individual fitting is required to maximize residual vision and reduce the patient's disability (alleviation of symptoms and photophobia), thereby improving their QoL [26]. Aniridia is a disease with continuous deterioration over the years, therefore visual acuity-adapted low vision aids are necessary, and an evaluation of the sufficiency of low vision aids should be done regularly [27].

The mean visual acuity was 0.14 ± 0.15 (logMAR 0.85 ± 0.79). A similar level of acuity was reported [15] in 125 patients in Sweden and Norway, whose Snellen visual acuity was 0.19. A visual acuity threshold of logMAR 1.0 (20/200 equivalent) in the better-seeing eye is used to define "serious" vision impairment by WHO criteria and logMAR 1.3 is considered legal blindness. In Germany, the threshold for legal blindness is logMAR 1.69 (1/50 equivalent), according to Versorgungsmedizin-Verordnung (Teil A.6.a der Anlage zu § 2 VersMedVO). In this study, 9 (12.7%) met the criteria for serious visual impairment (WHO) and 14 (19.7%) for legal blindness. Jacobson found a higher proportion of aniridia patients with legal blindness at presentation (38%) [28]. Despite the low visual acuity, most patients reported being able to complete their tasks at school and work and participate in social activities independently. Half of the patients only sometimes had difficulties in completing their work and school tasks. These patients are restricted in the range of jobs available to them and face impediments in many other jobs [29]. An adjustment of the work and school environment through glare reduction, contrast enhancement and adjusted lighting, desktops with screen reading, screen magnification, and/or optical character recognition (OCR) software, larger prints, and tactile or talking devices can facilitate task performance for people with low vision.

Among our participants, 36.6% of children and 40.9% of adults reported sometimes having difficulties in socializing; however, the context of these situations is not known, for example, if it is with family or friends or in new surroundings with strangers. Twenty-eight (39.6%) always encountered problems at interpreting facial cues and facial expressions, potentially constraining their social interactions and communication. In 1998, Huurre and Aro [30] found that adolescents with visual impairment often had less friends and reported more feelings of loneliness and difficulties making friends. However, their psychosocial development was similar to that of their peers without visual impairment. Whether this is true for aniridia specifically is not known. Studies in adults have usually found a restriction in social participation among older adults who suffer from age-related vision loss, but those results are not generalizable to the present population. Strategies like fostering a friendship network, family support, and peer counseling can facilitate adaptation and improve psychological well-being and health-related QoL [31] in patients with congenital aniridia.

Familiarity with the environment was an important factor influencing patients' independence. Notably, 33.8% of individuals sought occasional assistance, while 31.0% required consistent aid. This dependency on assistance, especially in a familiar environment, could potentially impede their capacity to readily engage in new activities, both within educational settings and workplaces. The rehabilitation of individuals with significant visual impairment encompasses various components, with one key aspect being orientation and mobility training. In Germany, this training is provided by the DBSV (Deutscher Blinden- und Sehbehindertenverband e. V.). The primary objective of this training is to enhance individuals' mobility beyond their homes. Through targeted instruction and support, the program assists visually impaired individuals in developing skills to confidently navigate and engage with their external environment. In addition, the DBSV provides access to training of DLA – daily living activities, so that the patients can be enabled to do their household work, cook, do the washing and ironing, etc., without harming themselves.

Providing appropriate support for children with congenital aniridia is essential, particularly before and during the progression of their condition, as they must develop skills to cope with both growing up and the gradual loss of their vision. Early multidisciplinary care, involving ophthalmologists, geneticists, occupational therapists, orientation and mobility specialists, orthoptists, physiotherapists, and special education teachers, is crucial for offering holistic management of their needs. In German-speaking countries, the nonprofit organization and self-help group for Aniridia and WAGR Syndrome offers valuable support for affected patients and their families, fostering a sense of community and shared experiences.

Psychological support and fostering social inclusion are equally important in helping these children navigate the emotional and social challenges that come with visual impairment. To promote independence, interventions should focus on improving literacy, training in alternative communication methods, providing appropriate low vision aids, and offering mobility training. Additionally, utilizing the right technologies can enhance their daily functioning [32]. Despite these recognized needs, there is a significant gap in high-quality studies that measure the impact of rehabilitation services on health-related QoL for children and young adults with visual impairment, particularly for those with congenital aniridia, highlighting a critical area for future research [32].

Complications such as AAK, cataract, and glaucoma are some of the causes of progressive visual loss in patients with congenital aniridia [33].

Cataract and its visual significance are some of the most important components in patients with aniridia. In our study, 52 (73.2%) patients had cataract and 17 (23.9%) of them underwent surgery between 19 and 49 years of age. Cataract surgery early in life was associated with a lower QoL. This may be due to intraoperative challenges such as poorer surgical visibility due to reduced corneal transparency, altered intraocular anatomy with a shallow anterior chamber, and a compromised zonular apparatus [34]. Postoperatively, patients are susceptible to exacerbation of AAK, glaucoma, and anterior segment fibrosis syndrome (AFS). Although surgery should be performed if visual acuity is compromised, it is a high-risk procedure and should be performed by an experienced

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cataract surgeon after careful preoperative evaluation [9]. Iris reconstruction can be combined with cataract surgery [34] to improve visual acuity and photophobia, but its implantation is challenging and high risk. Patients are often accustomed to glare and iris prostheses provide little benefit; therefore, they are generally not recommended nowadays [34, 35].

AAK is a direct result of limbal epithelial stem cell deficiency and leads to recurrent corneal erosion, ulceration and scarring, and ultimately progressive vision loss, even when excluding cataract and glaucoma [36]. Patients often have concomitant Meibomian gland dysfunction, tear film insufficiency, and decreased corneal sensitivity, all of which correlate with the severity of corneal disease [7]. The ocular surface pathology leads to classical symptoms of dry eye, eye pain and tearing, and the need for continuous use of artificial tears and, sometimes, therapeutic contact lenses. Of our patients, 29.6% had corneal surgery and 25.4% had a corneal transplantation. Viberg et al. [37] reported that the visual acuity gain among transplanted corneas was modest at best, and the majority of patients had complications, such as recurrence of AAK in the graft, rejection, and glaucoma. In our patients, 61 (85.9%) were affected by AAK, similar to values reported by Latta et al. [3]. It was also one of the main reasons for more frequent visits to the ophthalmologist. Collectively, these factors likely contribute to the lower reported QoL among patients with advanced AAK ($p = 0.027$).

In our study, glaucoma, surgical interventions, and early surgery did not exhibit a correlation with the QoL. However, they emerged as frequent reasons for regular visits to the ophthalmologist. The prevalence of glaucoma in our group was 63.4%, aligning with findings from previous reports [7]. Onset typically occurs around the age of 8 [38], and its incidence tends to increase with age. Given its potential to cause blindness and the challenges associated with diagnosis, especially in young children, monitoring, and treatment, aniridic glaucoma can have a profound impact on vision.

Several studies have suggested that chronic inflammation begins early in life, but complications like AAK, dry eye disease, and cataract only become clinically relevant in early adulthood [22]. This early window could be a critical target for future treatments aimed at halting disease progression. It is essential for all patients to use preservative-free artificial tears and medications to optimize the ocular surface. Novel therapies, such as immunomodulators and gene therapy, may help regulate PAX6 levels [39]. Additionally, surgical interventions, especially cataract surgery, should be carried out in specialized centers experienced in managing these complex cases. Proactively addressing ocular surface issues and utilizing preventive strategies during this key period could help delay complications, preserving vision and enhancing long-term QoL.

The same survey used for gauging the experiences in patients with congenital aniridia in Hungary showed similar results. The tested group exhibited minimal limitations in personal communication and showcased a high degree of independence in daily routine activities. Additionally, the study identified a correlation between higher age and an increased requirement for assistance during activities, as well as a reliance on visual aids [40].

Limitations

This study has several limitations. Primarily, the response rate is relatively low, with 34.1% of the intended participants responding to the questionnaire. Incorrect address information was one of the reasons. Second, it is uncertain whether patients with more advanced stages of AAK, cataract, or secondary glaucoma could access and read the questionnaire. This could be a reason for bias in the reported QoL towards a more positive outlook. Additionally, the survey was based on self-reported, thereof subjective data, and there was no control group with normal vision for comparative analysis. Moreover, the clinical data was gathered from the patient's most recent examination at the clinic, which may not accurately represent their condition at the time of completing the questionnaire. The time gap between the examination and the survey ranged from a few weeks to up to a year. Patients with more severe symptoms tend to visit the clinic more frequently, while those with milder symptoms often attend only annual checkups. This variability raises questions about the reliability of the correlations between clinical findings and reported symptoms. To enable a more comprehensive understanding of the impact of various aspects of congenital aniridia and its treatment on patients' lives, future studies with enhanced methodologies and broader participant inclusion are necessary.

Conclusion

In conclusion, this study, part of the larger COST Action ANIRIDIA-NET survey in Germany, revealed that patients with congenital aniridia reported a generally good QoL despite significant visual impairment. Children exhibited a moderately better QoL than adults, suggesting early adaptation to the condition contributes to their well-being, while progressive ocular pathology and vision loss typically start to appear in early adulthood. Visual aids played a crucial role in autonomy, especially in education and work. While most participants coped well with daily tasks, challenges arose in social interactions, emphasizing the importance of support networks. Cataract surgery early in life as well as AAK and common complications were associated with lower QoL. Overall, adaptation strategies, personalized visual aids, and social support play key roles in enhancing QoL for individuals with congenital aniridia.

Symptoms of congenital aniridia subjects, described by the ANIRIDIA-NET survey, correlated well with clinical findings. Therefore, the survey may well support follow-up examinations of the patients. Survey responses regarding personal communication and the use of visual aids did not correlate with the clinical measures. Nevertheless, the information obtained may give important practical information to the treating ophthalmologist for improving the QoL of congenital aniridia subjects.

CONCLUSION

Already known:

- Patients with congenital aniridia suffer from significant and progressive visual impairment and require complex treatments during their life to maintain their remaining vision.

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Newly described:

- Despite their visual challenges, self-reported QoL among aniridia patients in Germany was generally good, particularly in children, possibly due to early adaptation. Onset of progressive ocular pathology and vision loss typically starts to appear in early adulthood.
- Cataract surgery early in life as well AAK and frequent complications were associated with a diminished QoL.
- The ANIRIDIA-NET survey effectively correlated symptoms of the patients with clinical findings, providing valuable support for follow-up examinations.

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Conflict of Interest

The authors declare that they have no conflict of interest.

References

[1] Landsend ECS, Lagali N, Utheim TP. Congenital aniridia – A comprehensive review of clinical features and therapeutic approaches. Surv Ophthalmol 2021; 66: 1031–1050

[2] Käsmann-Kellner B, Seitz B. Aniridiesyndrom. Ophthalmologe 2014; 111: 1145–1156

[3] Latta L, Figueiredo FC, Ashery-Padan R et al. Pathophysiology of aniridia-associated keratopathy: Developmental aspects and unanswered questions. Ocul Surf 2021; 22: 245–266

[4] Calvão-Pires P, Santos-Silva R, Falcão-Reis F et al. Congenital Aniridia: Clinic, Genetics, Therapeutics, and Prognosis. Int Sch Res Notices 2014; 2014: 1–10

[5] Lee H, Khan R, O'Keefe M. Aniridia: current pathology and management. Acta Ophthalmol 2008; 86: 708–715

[6] Pedersen HR, Hagen LA, Landsend ECS et al. Color Vision in Aniridia. Invest Ophthalmol Vis Sci 2018; 59: 2142

[7] Käsmann-Kellner B, Seitz B. Kongenitale Aniridie oder PAX6-Syndrom? Ophthalmologe 2014; 111: 1144

[8] Kuyk T, Liu L, Elliott JL et al. Health-related quality of life following blind rehabilitation. Qual Life Res 2008; 17: 497–507

[9] Patrick DL, Erickson P. Assessing health-related quality of life for clinical decision-making. In: Springer ebooks; 1993: 11–63

[10] Daruich A, Duncan M, Robert MP et al. Congenital aniridia beyond black eyes: From phenotype and novel genetic mechanisms to innovative therapeutic approaches. Prog Retin Eye 2023; 95: 101133

[11] Lagali N, Wowra B, Fries FN et al. Early phenotypic features of aniridia-associated keratopathy and association with PAX6 coding mutations. Ocul Surf 2020; 18: 130–140

[12] Gothwal VK, Mandal AK. Quality of Life and Life Satisfaction in Young Adults with Primary Congenital Glaucoma. Ophthalmol Glaucoma 2021; 4: 312–321

[13] Gu S, Hu Y, Zhao Y, Chen L et al. A Retrospective Study on the Eye-Related Quality of Life, Functional Vision, and Their Determinants Among Children Following Congenital and Developmental Cataracts Surgery and Its Impact on Their Families Using the PedEyeQ. Front Public Health 2022; 10: 788384

[14] Karadeniz Ugurlu S, Kocakaya Altundal AE et al. Comparison of vision-related quality of life in primary open-angle glaucoma and dry-type age-related macular degeneration. Eye (Lond) 2017; 31: 395–405

[15] Inan S, Cetinkaya E, Duman R et al. Quality of life among patients with age-related severe macular degeneration assessed using the NEI-VFQ, HADS-A, HADS-D and SF-36 tests. A cross-sectional study. Sao Paulo Med J 2019; 137: 25–32

[16] Cicinelli MV, Buchan JC, Nicholson M et al. Cataracts. Lancet 2023; 401: 377–389

[17] Labiris G, Giarmoukakis A, Sideroudi H et al. Impact of keratoconus, cross-linking and cross-linking combined with photorefractive keratectomy on self-reported quality of life. Cornea 2012; 31: 734–739

[18] Kennedy RH, Bourne WM, Dyer JA. A 48-year clinical and epidemiologic study of keratoconus. Am J Ophthalmol 1986; 101: 267–273

[19] Sideroudi H, Flockerzi E, Jullien T et al. Risk Factors for Keratoconus Progression in Children Compared with Young and Middle-aged Adults. Klin Monbl Augenheilkd 2023; 240: 751–760

[20] Kymes SM, Walline JJ, Zadnik K et al. Changes in the quality-of-life of people with keratoconus. Am J Ophthalmol 2008; 145: 611–617.e1

[21] Choi SU, Chun YS, Lee JK et al. Comparison of vision-related quality of life and mental health between congenital and acquired low-vision patients. Eye (Lond) 2019; 33: 1540–1546

[22] Fries FN, Moslemani K, Utheim TP et al. Early ocular surface and tear film status in congenital aniridia indicates a supportive treatment window. Br J Ophthalmol 2024; 108: 30–36

[23] Brennan M, Cardinali G. The use of preexisting and novel coping strategies in adapting to age-related vision loss. Gerontologist 2000; 40: 327–334

[24] Brennan M, Su YP, Horowitz A. Longitudinal associations between dual sensory impairment and everyday competence among older adults. J Rehabil Res Dev 2006; 43: 777–792

[25] Brown RL, Barrett AE. Visual impairment and quality of life among older adults: an examination of explanations for the relationship. J Gerontol B Psychol Sci Soc Sci 2011; 66: 364–373

[26] Agarwal R, Tripathi A. Current Modalities for Low Vision Rehabilitation. Cureus 2021; 13: e16561

[27] Perrault MA, Lauer G, Voss S et al. Visual Impairment and Low Vision Aids–A Comparison between Children and Adults. J Pers Med 2023; 13: 1608

[28] Jacobson A, Mian SI, Bohnsack BL. Clinical outcomes and visual prognostic factors in congenital aniridia. BMC Ophthalmol 2022; 22: 235

[29] Lennie P, Van Hemel SB, eds. Visual Impairments. Determining Eligibility for Social Security Benefits. Washington, D.C.: National Academies Press; 2002

[30] Huurre TM, Aro HM. Psychosocial development among adolescents with visual impairment. Eur Child Adolesc Psychiatry 1998; 7: 73–78

[31] Wang CW, Chan CLW, Chi I. Overview of Quality of Life Research in Older People with Visual Impairment. Adv Aging Res 2014; 3: 79–94

[32] Elsman EBM, Al Baaj M, van Rens GHMB et al. Interventions to improve functioning, participation, and quality of life in children with visual impairment: a systematic review. Surv Ophthalmol 2019; 64: 512–557

[33] Fries FN, Náray A, Munteanu C et al. The Effect of Glaucoma Treatment on Aniridia-Associated Keratopathy (AAK) – A Report from the Homburg Register for Congenital Aniridia. Klin Monbl Augenheilkd 2023. DOI: 10.1055/a-2194-1580

[34] Boden KT, Szurman P. Cataract Surgery in Aniridia. Cataract Surgery. Essentials in Ophthalmology. Cham: Springer; 2022: 283–290

[35] Romano D, Bremond-Gignac D, Barbany M et al. Artificial iris implantation in congenital aniridia: A systematic review. Surv Ophthalmol 2023; 68: 794–808

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[36] Mayer CS, Baur ID, Storr J et al. Bilateral Artificial Iris implantation in patients with bilateral iris defects. Am J Ophthalmol Case Rep 2021; 22: 101108

[37] Viberg A, Vicente A, Samolov B et al. Corneal transplantation in aniridia-related keratopathy with a two-year follow-up period, an uncommon disease with precarious course. Acta Ophthalmol 2023; 101: 222–228

[38] Muñoz-Negrete FJ, Teus MA et al. Aniridic glaucoma: An update. Arch Soc Esp Oftalmol (Engl Ed) 2021; 96 (Suppl. 1): S52–S59

[39] van Velthoven AJH, Utheim TP, Notara M et al. Future directions in managing aniridia-associated keratopathy. Surv Ophthalmol 2023; 68: 940–956

[40] Csidey M, Grupcheva C, Stachon T et al. Congenital aniridia patients' experience on their visual impairment in Hungary. Orv Hetil 2023; 164: 1342–1349

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