• Clinical Research •

Analysis of prognosis and quality of life in children with retinoblastoma

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Abstract

● **AIM:** To evaluate clinical characteristics, treatment patterns and long-term quality of life (QoL) among children with retinoblastoma (RB) managed at a single tertiary center in China.

● **METHODS:** Totally 62 consecutive patients (71 eyes) diagnosed with RB were retrospectively reviewed. The mean age at first visit was 22.13±17.87mo; 35 (56.45%) were male. Unilateral disease occurred in 53 patients (85.48%) and bilateral disease in 9 (14.52%). According to the international intraocular retinoblastoma classification (IIRC), eyes were staged as A (*n*=6), B (*n*=9), C (*n*=9), D (*n*=21), E (*n*=19), and extraocular (*n*=7). Treatments followed stage-based indications. QoL at follow-up was assessed using validated pediatric ophthalmic instruments completed by patients and/or parents.

● **RESULTS:** The mean follow-up duration was 42.9±6.49mo. Overall survival was 90.32% (56/62), mortality was 9.68% (6/62). The overall globe-preservation rate was 64.79% (46/71), and 71.88% (46/64) for intraocular RB. Eye salvage by IIRC stage was 100% for A–C, 71.43% (15/21) for D, and 36.84% (7/19) for E; no eyes were preserved in extraocular disease. Compared with the globe-preservation group, enucleated children had significantly lower scores in appearance, social functioning, and role domains on QoL measures (P<0.05). Across all PedEyeQ domains, children with preserved globes scored higher than those who underwent enucleation (P<0.05).

● **CONCLUSION:** Most children in this cohort present with intermediate-to-advanced disease, which limit eye-preservation opportunities. While survival approached contemporary benchmarks, QoL deficits are most pronounced in appearance, social participation, and role functioning after enucleation. Additionally, parents of children who underwent enucleation often experience heightened anxiety about their child's vision and social integration. These findings underscore the need for earlier detection and integrated psychosocial support alongside stage-appropriate therapy.

● **KEYWORDS:** retinoblastoma; children; quality of life; globe preservation; enucleation

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INTRODUCTION

Retinoblastoma (RB) is the most common primary intraocular malignancy in infants and young children, accounting for approximately 2% to 4% of all cancers[1]. It typically presents in infancy or early childhood. Because affected children cannot reliably report symptoms, RB is frequently diagnosed at an advanced stage. Early disease is confined to the eye, whereas progression can lead to extraocular extension *via* the optic nerve or hematogenous spread, which may be fatal[2]. Timely detection and intervention are therefore essential to reduce the need for enucleation, improve survival, and enhance prognosis[3-4]. Standardized, stage-appropriate treatment protocols aim to save life, preserve the eye when feasible, maintain useful vision, and support long-term quality-of-life (QoL). This retrospective study examines treatment approaches, prognosis, and long-term across QoL stages at presentation in children with RB managed at our center, with the goal of identifying factors associated with outcomes.

PARTICIPANTS AND METHODS

Ethical Approval We performed a single-center retrospective cohort study at Renmin Hospital of Wuhan University. Ethical approval was obtained from the institutional review board (WDRY2024-K050) in accordance with the Declaration of Helsinki. Informed consent obtained from the patient's guardian after explaining the study details.

Participants We included 62 consecutive children diagnosed with RB who presented to Renmin Hospital of Wuhan

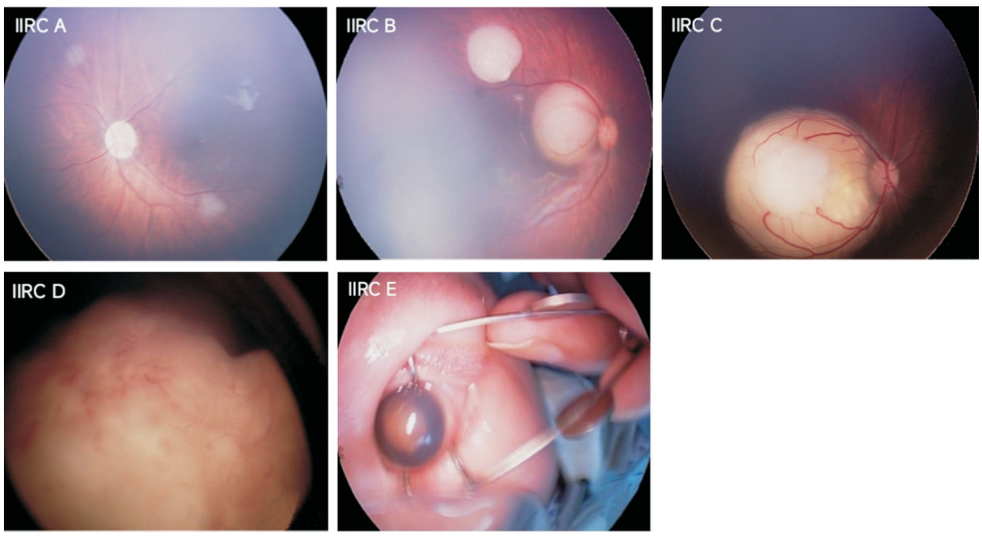

Figure 1 Fundus findings in RB patients at IIRC stages A, B, C, D and E Stage A: Small tumors (≤3 mm) away from the macula and optic nerve; Stage B: Larger tumors without vitreous or subretinal seeding; Stage C: Localized vitreous or subretinal seeding (≤3 mm); Stage D: Diffuse seeding with retinal detachment >1 quadrant; Stage E: Severe ocular damage (*e.g.*, neovascular glaucoma, intraocular hemorrhage, phthisis bulbi). RB: Retinoblastoma; IIRC: International intraocular retinoblastoma classification.

University from September 2010 to December 2020 (71 affected eyes). All children underwent bilateral examination under general anesthesia using a wide-angle pediatric retinal imaging system (RetCam; USA). Staging was assigned by an experienced ophthalmologist according to the international intraocular retinoblastoma classification (IIRC).

Orbital computed tomography (CT; Germany) and ocular magnetic resonance imaging (MRI; Germany) were obtained for all patients. For group E eyes, additional evaluations—including bone marrow cytology and cerebrospinal fluid analyses—were performed to assess extraocular involvement.

Inclusion criteria: 1) fundus examination and imaging results that meet the diagnostic criteria for RB; 2) patients who complied with follow-up visits. Exclusion criteria: 1) other malignancies; 2) dysfunction of major organs (heart, liver, or kidneys); 3) hematologic disorders; 4) immune system diseases; 5) loss to follow-up. Collected variables included sex, age, initial symptoms, laterality, interval from symptom onset to treatment, tumor diameter and growth pattern, stage, metastasis status, treatment regimen, and outcomes.

Clinical Staging Intraocular disease was staged A–E per IIRC (Figure 1). Extraocular disease was defined by imaging or pathology indicating extension beyond the globe. Complete criteria and examples are available in the Chinese RB Diagnosis and Treatment Guidelines (2019; https://rs.yiigle.com/cmaid/1164828).

Treatment Treatment was individualized according to stage. Enucleation was performed for extraocular RB and followed by systemic chemotherapy and local radiotherapy. Enucleation was also indicated for: unilateral RB at stage D or E when ocular preservation was not feasible or when reliable follow-up could not be ensured; bilateral RB with one eye at stage A and the fellow eye at stage E (removal of the stage E eye recommended); bilateral stage E disease (bilateral enucleation with parental consent); eyes with suspected viable intraocular tumor cells in which dense media opacity precluded fundus examination and staging; eyes with imaging evidence of tumor extension toward the optic nerve confined to the proximal post-laminar segment; and recurrent intraocular RB after failure of conservative therapies or when complications precluded adequate assessment and treatment of tumor aggressiveness.

For intraocular disease at other stages, eye-preserving modalities were considered, including cryotherapy, laser photocoagulation, transpupillary thermotherapy, intra-arterial chemotherapy (IAC), intravitreal chemotherapy, and focal radiotherapy.

Follow-up Protocol According to the Chinese RB Diagnosis and Treatment Guidelines (2019), the follow-up schedule for patients is as follows:1) Eye-preservation group: Examinations under anesthesia every 3–4wk until tumor control, then every 1–3mo. 2) Enucleation group: First follow-up at 3–6mo post-surgery, then every 6–12mo until disease stabilization (typically by age 6–7y).

Quality-of-Life Assessment 1) The Pediatric Quality of Life Inventory 4.0 Generic Core Scales (PedsQL 4.0) and Pediatric Quality of Life Inventory 3.0 Cancer Module (PedsQL 3.0) are used to assess QoL in relation to daily activities and cancer treatment at the final follow-up. Children ≥5y complete the survey themselves, while parents complete it on behalf of children <5y. Higher scores indicate better QoL/functional vision. 2) Pediatric Eye Questionnaires (PedEyeQ): The

PedEyeQ includes separate questionnaires for children, proxies, and parents, with three versions based on age groups: 0-4y, 5-11y, and 12-17y. The questionnaire, scoring algorithm, and lookup tables are available for free at JAEB Center (https://public.jaeb.org/pedig/view/Other_Forms).

Statistical Analysis Analyses were performed using IBM SPSS Statistics, version 25.0 (USA). Continuous variables are presented as mean±standard deviation, and categorical variables as percentages. Group comparisons used Student's *t*-test. Survival was analyzed with the Kaplan-Meier method. Between-group differences in QoL by age at diagnosis, age at follow-up, and sex were evaluated using *t* tests. A two-sided $P<0.05$ was considered statistically significant.

RESULTS

Case Characteristics of RB This study included 62 RB patients, with detailed clinical characteristics presented in Table 1. Among the patients, 35 were male (56.45%) and 27 were female (43.55%), with no statistically significant gender difference ($\chi^2=1.658$, $P=0.163$). The median age at diagnosis was 22.13mo, ranging from 1.5mo to 5.5y. The median ages for unilateral and bilateral cases were 31.42mo and 20.37mo, respectively. Of the 62 patients, 24 had right-eye-only involvement, 29 had left-eye-only involvement, and 9 had bilateral involvement. The number of unilateral cases was significantly higher than that of bilateral cases ($\chi^2=10.347$, $P<0.05$). No significant difference was found between left and right eye involvement in unilateral cases ($\chi^2=2.081$, $P>0.05$). Only 2 patients (3.24%) had a clear family history of RB. The most common initial symptom was leukocoria, observed in 32 patients (51.62%), followed by strabismus (14.52%), proptosis (8.06%), and poor vision (11.27%).

Table 1 Clinical characteristics of 62 RB patients

Characteristics	*n*	%
Gender		
Male	35	56.45
Female	27	43.55
Age at onset, y		
0-1	22	35.48
1-3	28	45.16
3-6	12	19.35
Family history		
Yes	2	3.22
None	60	96.78
Region		
Urban	40	64.52
Rural	22	35.48
Unilateral/bilateral disease		
Unilateral	53	85.48
Bilateral	9	14.52
Main symptoms		
Leukocoria	32	51.62
Strabismus	9	14.52
Poor vision	8	11.27
Proptosis	5	8.06
Eye pain	3	4.84
Physical examination findings	3	4.84
Family history	2	3.24

IIRC: International intraocular retinoblastoma classification.

Clinical Staging and Prognosis of RB Patients A total of 71 affected eyes were staged according to traditional criteria and the IIRC (Table 1): 6 eyes (8.45%) were stage A, 9 (12.68%) stage B, 9 (12.68%) stage C, 21 (29.58%) stage D, 19 (26.76%) stage E, and 7 (9.86%) extraocular. Among 64 intraocular eyes, the overall globe-preservation rate was 71.88%. Preservation by stage was 100% for A to C, 71.43% for D, and 26.84% for E; no eyes were preserved in extraocular disease (Table 2).

Regarding residence, 40 patients (64.52%) were from urban areas and 22 (35.48%) from rural areas, with a significant difference in the urban-versus-rural distribution ($t=4.389$, $P<0.001$). The mean age at diagnosis was 15.70±12.75mo in urban patients and 34.15±17.85mo in rural patients, a statistically significant difference ($t=3.409$, $P<0.001$) indicating earlier diagnosis in urban settings.

All 62 RB patients were followed regularly to monitor fundus conditions and adjust treatment. The mean follow-up was 42.9±6.49mo, ranging from 12 to 60mo. By the last visit, 6 patients had died, resulting in a mortality rate of 9.68% (6/62), while 56 patients survived, yielding an overall survival rate of 90.32% (56/62).

Quality of Life in RB Patients At the final follow-up, 56 survivors completed two QoL instruments. As shown in Table 3, the total PedsQL 4.0 score was significantly lower in the enucleation group than that in the globe-preservation group ($P<0.05$). Whereas total PedsQL 3.0 scores did not differ significantly between groups. Within PedsQL 3.0, scores for pain/discomfort, worry, and communication modules were 100 in both groups. By domain, the self-perception of appearance dimension (PedsQL 3.0) and the social and role dimensions (PedsQL 4.0) were lower in the enucleation group than in the globe-preservation group, with statistically significant differences.

Quality of Life Scores for Families of RB Patients Table 4 summarizes PedEyeQ outcomes for children, parent proxies, and parents in the globe-preservation and enucleation groups. Across all three PedEyeQ versions, scores were significantly higher in the globe-preservation group than in the enucleation group (all $P<0.05$). The median differences (with 95% confidence intervals) are reported in Table 4, highlighting consistent advantages for functional vision, social participation, and reduced frustration/worry in families of children with preserved globes.

Table 2 Treatment and eye-preservation rates in RB patients at different stages

Staging	Total	Age at diagnosis (mo, mean±SD)	Treatment duration (mo, mean±SD)	Eye preservation	Enucleation	Eye preservation rate (%)
Stage A	6	23.92±17.13	18.27±9.46	6	0	100
Stage B	9	27.18±21.07	15.26±3.47	9	0	100
Stage C	9	20.73±14.18	12.84±4.68	9	0	100
Stage D	21	24.10±16.25	20.48±11.48	15	6	71.43
Stage E	19	20.17±13.24	18.17±16.71	7	12	36.84
Extraocular stage	7	24.87±15.73	10.74±2.88	0	7	0

RB: Retinoblastoma.

Table 3 Comparison of quality of life between enucleated and eye-preserved patients

Dimension	Enucleation (*n*=17)	Eye preservation (*n*=39)	*t*	*P*
PedsQL 3.0 total score	94.1±10.0	95.0±9.6	0.52	0.61
Pain or discomfort	100	100		
Nausea	100	100		
Procedure-related nausea	84.5±24.0	90.1±20.5	0.57	0.55
Treatment anxiety	93.0±16.1	93.8±18.9	0.24	0.81
Worry	100	100		
Cognitive function	90.5±21.8	83.1±28.7	-1.44	0.16
Self-perception of appearance	81.8±27.4	93.0±18.4	2.56	0.01
Communication issues	100	100		
PedsQL 4.0 total score	97.9±4.7	99.5±1.9	2.40	0.02
Physical functioning	99.3±2.1	99.3±2.9	0.01	0.99
Emotional functioning	99.9±2.9	99.2±2.5	0.60	0.55
Social functioning	95.4±12.5	99.2±5.2	2.15	0.03
Role functioning	97.8±5.4	99.7±1.8	2.55	0.01

PedsQL 4.0: Pediatric Quality of Life Inventory 4.0 Generic Core Scales; PedsQL 3.0: Pediatric Quality of Life Inventory 3.0 Cancer Module. *t*: Student's *t*-test.

DISCUSSION

RB is a primary ocular malignancy that predominantly occurs in early childhood[1]. Each year, approximately 8000–9000 new cases are diagnosed worldwide[2], with about 3000 RB-related deaths[3-4]. The incidence, treatment patterns[5-6], prognosis and survival rates vary substantially cross countries. In high-income settings, earlier detection and advanced therapies have rendered RB a highly curable disease with nearly-universal survival. whereas in low-income countries fewer than half of affected children survive beyond three years[7]. In China, the incidence is relatively high, with an estimated 1000 to 2000 new cases annually. Against this background, we retrospectively analyzed 62 RB patients treated at our hospital, providing a preliminary assessment of stage-specific prognosis and QoL.

In our cohort, RB predominantly presents in infancy, accounting for 80.64% of cases, consistent with previous studies[8]. The median age at diagnosis was 22.13mo. Median ages for unilateral and bilateral cases was 31.42mo and 20.47mo, respectively. These figures are slightly higher than the 27mo for unilateral and 5mo for bilateral cases reported in Canada[9], but lower than the 36mo and 25mo reported in Kenya[10], suggesting delay diagnosis. Although approximately 30% of RB cases are bilateral worldwide[11], the bilateral rate in our series was 14.52%, with unilateral involvement accounting for 85.48%. This discrepancy may be due to the smaller sample size in this study compared to others[7]. The most common presenting symptom was leukocoria (53.49%), followed by strabismus (14.52%) and poor vision (11.27%), in line with the literature[12-13].

Diagnostic timing differed by residence. Children from rural areas were diagnosed significantly later than those from urban regions (mean 34 *vs* 15mo), underscoring disparities in healthcare access. Delayed presentation is clinically consequential: a >6-month lag from first symptom has been associated with approximately 70% mortality in low-resource settings[10]. Consistent with this, the prospective multicenter analysis by Das *et al*[14] linked diagnostic and treatment delays to poorer survival and reduced eye preservation in more than 1100 cases. Our data extend these observations by quantifying regional disparities within China, emphasizing the need for context-specific public health strategies (*e.g.* strengthened red-

Table 4 PedEyeQ parent questionnaire for RB patients

PedEyeQ questionnaire	Eye preservation group (*n*=39)	Enucleation group (*n*=17)	*P*	Mean difference (95%CI)
Child				
Functional vision	92.5 (75.0, 100)	70.0 (50.0, 80.0)	<0.001	17.8 (10.8, 24.9)
Bothered by eyes/vision	100 (83.7, 100)	75.0 (50.0, 90.0)	<0.001	18.3 (10.4, 26.2)
Social	100 (90, 100)	85.0 (60, 100)	<0.001	17.1 (10.2, 24.1)
Frustration/worry	77.8 (61.1, 100)	55.5 (38.9, 72.2)	<0.001	19.9 (11.3, 28.5)
Parent proxy				
Functional vision	95.0 (80.0, 100)	65.0 (50.0, 95.0)	<0.001	16.9 (8.81, 24.9)
Bothered by eyes/vision	100 (82.5, 100)	70.0 (55.0, 100)	0.002	15.0 (5.96, 24.1)
Social	100 (87.5, 100)	81.3 (56.3, 100)	<0.001	13.7 (6.02, 21.4)
Frustration/worry	87.5 (67.2, 100)	62.5 (50.0, 81.3)	<0.001	16.6 (7.80, 25.3)
Eye care	100 (75.0, 100)	75.0 (50.0, 91.7)	<0.001	14.3 (6.76, 21.8)
Parent				
Impact on parent/family	95 (70.0, 100)	70.0 (50.0, 90.0)	<0.001	13.9 (4.99, 22.7)
Worry about child's condition	65.0 (50.0, 90.0)	45.0 (30.0, 60.0)	<0.001	22.4 (11.0, 33.9)
Worry about child's self-perception/interactions	100 (78.6, 100)	50.0 (50.0, 92.9)	<0.001	20.3 (10.7, 29.9)
Worry about child's visual function	87.5 (50.0, 100)	50.0 (37.5, 56.3)	<0.001	25.6 (14.1, 37.1)

PedEyeQ: Pediatric Eye Questionnaires; CI: Confidence interval; RB: Retinoblastoma.

reflex screening, improved parental awareness, and fast-track referral pathways). Encouragingly, 62.50% of intraocular cases in our series were classified as IIRC groups D or E, indicating relatively late presentation; nevertheless, this proportion is lower than the approximately 80% late-stage burden reported before 2015[9-11], suggesting improvements in RB awareness and screening.

Treatment outcomes in our cohort reflect both progress and persistent challenges. The overall survival rate was 90.32%, comparable to recent reports from middle-income settings[15] and approaching outcomes in high-income countries[7]. Among intraocular cases, the overall globe-preservation rate was 71.88%. As expected, eye salvage declined with increasing stage: we preserved all groups A–C eyes, 71.43% of group D eyes, and 36.84% of group E eyes; no eyes were preserved in extraocular disease. These findings are consistent with prior literature. For example, Shields *et al*[16] noted intravenous chemotherapy could salvage 68% of Group D and 32% of Group E eyes, whereas adding intra-arterial chemotherapy can raise Group E salvage to 55%. Our results underscore that advanced disease still often necessitates enucleation. In fact, a recent multicenter study in China found that attempting eye-preserving therapy in Group E eyes (especially in bilateral cases) was associated with worse survival, reinforcing the life-saving role of timely enucleation[17]. In our series, all extraocular tumors underwent enucleation or orbital exenteration, consistent with the consensus that saving the child's life is paramount in late-stage RB.

Beyond survival and globe outcomes, our study uniquely examined QoL in RB survivors. We found that children who underwent enucleation experienced significantly lower QoL scores in domains of appearance, social interaction, and role functioning compared to those who retained their eye. This finding is consistent with previous literature. Studies of long-term RB survivors in high-income countries have reported relatively normal overall QoL and psychosocial adjustment[18]. For example, studies on the QoL of adult RB survivors in countries like the United States show that patients who undergo enucleation generally do not experience significant adverse effects on their cognitive, social, or psychological functions. Some studies even suggest their physical functioning may be better than that of the general population[18]. However, survivors diagnosed in childhood often face more pronounced challenges. Dhingra *et al*[19] observed that child RB survivors in India had significantly lower health-related quality of life (HRQoL) than their healthy siblings across physical, emotional, social, and school domains (P<0.01), with the greatest deficits in physical functioning and higher rates of bullying and social exclusion. Our data similarly indicate that vision loss and the presence of an ocular prosthesis can impair a child's self-confidence and social participation. A scoping review of global studies corroborates that RB survivors frequently struggle with psychosocial issues even when disease control is achieved.

The psychosocial impact of RB extends to parents and families, an area often underappreciated in clinical practice. In our cohort, parents of children who underwent enucleation reported heightened anxiety about their child's vision,

appearance, and social integration. This aligns with reports from other populations. Collins *et al*[20] found that 26.7% of parents of RB patients in the US had moderate-to-severe depression and 35.8% had significant anxiety. Batra *et al*[21] suggested that parents of RB children are more likely to experience depression or anxiety, and struggle with establishing relationships with their child. A recent survey in China revealed even higher levels of parental distress—41% with clinically relevant depression, 34% with anxiety and about 68% of parents experienced substantial fear of disease progression (FoP)[22]. Moreover, a parent's psychological condition may depend on their understanding of the disease and the child's attitude toward treatment[23]. Notably, parents in that Chinese study also reported lower emotional well-being scores than the patients themselves, reflecting how parents often bear greater long-term worry. Key risk factors for parental psychological strain include having a child with bilateral RB or advanced disease, lower parental education, and urban residency (potentially due to greater awareness of social expectations)[22]. Leske *et al*[24] surveyed the HRQoL of RB survivors and their parents, finding that parents reported lower emotional well-being scores than the children themselves. Parents expressed concern over the child's ability to compete with peers, leading to increased worries about the child's future. Parents of bilateral RB survivors were particularly likely to experience fears about cancer recurrence, the potential diagnosis of RB in siblings, guilt about the genetic transmission of RB, and even avoidance of having more children[25]. Qualitative research further underscores the profound coping challenges these families face. These findings highlight the need to provide psychological support to RB families.

In conclusion, while the survival and eye preservation rates for RB children in China have improved in recent years, most children are still diagnosed at middle or late stages, indicating a need for better public awareness and screening capabilities. Enucleation often unavoidable in late disease which carries substantial psychosocial burdens for patients and families, particularly regarding body image, social participation, and role functioning. Priorities now include integrating psychosocial support into routine care and strengthening pathways that shorten time to diagnosis. Future work should emphasize large, longitudinal cohorts to define long-term visual, psychosocial, and family-level outcomes and to evaluate targeted interventions that enhance QoL alongside survival.

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