• Review Article •

# Retinoblastoma management in China: clinical challenges

*Nan Wang[1], Feng Ke[2], Jing Li[1], Liang-Yuan Xu[1], Tai-Yao Wang[1], Jian-Min Ma[1]*

[1]Beijing Ophthalmology and Visual Sciences Key Laboratory, Beijing Tongren Eye Center, Beijing Tongren Hospital, Capital Medical University, Beijing 100005, China
[2]Shiyan Renmin Hospital, Shiyan 442000, Hubei Province, China

**Correspondence to:** Jian-Min Ma. Beijing Ophthalmology and Visual Sciences Key Laboratory, Beijing Tongren Eye Center, Beijing Tongren Hospital, Capital Medical University, Beijing 100005, China. jmma@sina.com
Received: 2025-07-11 Accepted: 2025-10-23

## Abstract

● Retinoblastoma (RB) is the most common intraocular malignancy in children. In recent years, advancements in chemotherapy-based comprehensive treatment approaches and diagnostic technologies have significantly improved long-term survival rates, shifting treatment goals from saving lives toward preserving vision and enhancing quality of life. In major RB treatment centers in China, survival rates have reached levels comparable to those in developed countries. However, in some underdeveloped regions, RB continues to pose a serious threat to affected children. To further improve survival rates and quality of life for RB patients and their families in China, a series of essential measures should be implemented. These include strengthening public education to raise awareness of RB, enhancing diagnostic efficiency, promoting standardized treatment protocols, providing genetic counseling and prenatal assessment for high-risk populations, and fostering the training of specialized healthcare professionals.

● **KEYWORDS:** retinoblastoma; clinical management; chemotherapy

**DOI:10.18240/ijo.2025.12.21**

**Citation:** Wang N, Ke F, Li J, Xu LY, Wang TY, Ma JM. Retinoblastoma management in China: clinical challenges. *Int J Ophthalmol* 2025;18(12):2380-2384

## INTRODUCTION

Retinoblastoma (RB) is a life-threatening intraocular malignancy in children that can lead to blindness, disability, and death. More than half of RB patients from the Asia-Pacific region and about 1000 new cases reported annually in China[1]. Without timely intervention, the disease is often fatal. In recent years, the evolution of multimodal treatment strategies centered on chemotherapy, combined with advances in diagnostic imaging and local therapeutic techniques, has significantly improved long-term survival rates. This progress has facilitated a paradigm shift in clinical goals—from saving lives toward preserving vision and optimizing quality of life. However, patient outcomes vary considerably across regions and are closely associated with socioeconomic factors and healthcare accessibility[2]. In leading RB specialized centers in China, survival rates have exceeded 95%, matching outcomes in developed countries. Nevertheless, in underdeveloped areas, RB remains a highly lethal disease. Moreover, China continues to face challenges such as low public awareness, low rates of early diagnosis, and inadequate attention to long-term survivors. There remain urgent, unresolved issues in the diagnosis, treatment, and improvement of quality of life for patients and their families. Our institution's RB referral center has managed nearly one-third to two-thirds of nationally documented RB cases in China[3]. This substantial clinical volume provides a unique and authoritative vantage point from which to examine the specific challenges and evolving paradigms in RB management within the Chinese healthcare system, which is the primary motivation for this review. Drawing on our research group's clinical experience with nearly 3000 RB patients over 20y, this article evaluates relevant issues in China's RB clinical diagnosis and treatment.

## TARGETED PUBLIC HEALTH INITIATIVES TO ENHANCE AWARENESS AND IMPROVE EARLY DIAGNOSTIC RATES

Significant global disparities in RB survival outcomes persist. In high-income countries, universal neonatal and periodic fundus screening protocols have enabled early diagnosis, making RB a largely curable disease where treatment goals focus on preserving the globe and visual function. In stark contrast, low-income settings face a mortality risk approximately 17 times higher, with only about half of diagnosed children surviving beyond three years[4]. In China, this challenge is reflected in a national 5-year overall survival rate of 86%, which remains suboptimal compared to high-income benchmarks[5]. This gap is largely attributable to delayed diagnosis, as evidenced by our study of 2790

patients, which found that 67.1% were initially diagnosed with advanced intraocular disease [group D or E according to the International Intraocular Retinoblastoma Classification (IIRC)] and 4.2% already had extraocular extension. These figures indicate that the vast majority of patients in China present at an advanced disease stage, which is the direct cause of poorer prognosis[5-6]. The problem of delayed care-seeking is driven by a confluence of factors. These include gaps in caregiver health literacy, scarcity of medical resources, and lower income levels that can lead to treatment abandonment. Furthermore, patients from disadvantaged backgrounds often have limited access to high-level care, including timely screening and referral mechanisms. Consequently, they frequently present with late-stage disease requiring more prolonged and intensive treatment[7], which in turn exacerbates the financial burden on families and increases the likelihood of enucleation.

To address these challenges, a multifaceted approach is critical. Population-level educational campaigns targeting parents, educators, and community health workers are essential to improve recognition of early clinical signs, such as leukocoria and strabismus. Existing research indicates that health education on RB is linked to a reduced proportion of advanced-stage disease, as improved public awareness can facilitate earlier medical intervention[8-10]. Simultaneously, strengthening the frontline healthcare system is paramount for early case detection. Pediatricians and community health workers play a critical role as first-line screeners during routine well-baby visits. Their ability to recognize ominous signs, such as an abnormal red reflex or new-onset eye deviation, and to promptly refer these cases, is a crucial link in the diagnostic chain. To ensure these children reach specialists without delay, establishing robust and efficient referral pathways from local clinics to major RB treatment centers is essential. In this context, telemedicine platforms can serve as a powerful tool for preliminary remote consultation and triage, facilitating timely and appropriate referrals from underserved regions to specialized units in urban hubs. These coordinated efforts in public education and health system strengthening can promote timely medical intervention, thereby reducing enucleation rates, optimizing survival outcomes, and ultimately preserving the quality of life for affected children and their families[11].

## OPTIMIZING THERAPEUTIC STRATEGIES TO ENHANCE TREATMENT EFFICACY AND IMPROVE PROGNOSIS

The management of RB involves diverse approaches. Laser photocoagulation and cryotherapy are effective for early-stage tumors (IIRC group A and group B), while more advanced tumors require chemical intervention. Primary chemotherapeutic methods include intravenous chemotherapy (IVC), intra-arterial chemotherapy, and intravitreal chemotherapy. IVC demonstrates efficacy for familial RB, secondary tumors, and metastatic disease, improving survival rates in advanced cases[12]. However, IVC has significant limitations: systemic administration leads to substantial drug reduction due to first-pass hepatic metabolism and the blood-ocular barrier, necessitating higher dosages to achieve therapeutic concentrations and resulting in frequent complications including myelosuppression, gastrointestinal reactions, hepatic impairment, and alopecia[13]. Intra-arterial chemotherapy delivers drug concentrations up to 10 times higher than IVC through super-selective administration[14], offers shorter treatment cycles, causes fewer systemic adverse effects, and has no reported fatal complications[15]. Nevertheless, this technique is constrained by immature vasculature in infants (unsuitable for patients under 3mo or weighing <5 kg)[16], carries risks of local toxicity and ocular vascular complications[17], and remains limited in primary healthcare settings due to technical complexity and high costs. Intravitreal chemotherapy bypasses the blood-ocular barrier, maximizing intraocular drug concentration while minimizing systemic absorption, making it a reliable option for vitreous seeds[18], though strict adherence to “no-tumor” technique through pre-operative intraocular pressure reduction and cryotherapy at the injection site is essential for safety. The successful management of RB, however, extends beyond technical prowess and relies on a supportive, system-level framework. First, the complexity of the disease demands a dedicated multidisciplinary team comprising ocular oncologists, pediatric oncologists, radiologists, pathologists, and genetic counselors. This collaborative model ensures comprehensive care planning and has been shown to improve survival outcomes[11]. Second, to guarantee consistent and high-quality care across all treatment centers, it is imperative for ophthalmologists to adhere to uniform, evidence-based treatment protocols. Standardizing the approach to diagnosis, staging, and treatment minimizes outcome disparities and enhances overall clinical efficacy. Finally, the significant financial burden of therapy, including the costs of chemotherapy and serial neuroimaging for monitoring, can be a prohibitive barrier for many families. Therefore, government-sponsored financial support programs are not merely beneficial but are crucial to ensure equitable access to life- and vision-saving treatments, preventing treatment abandonment based on economic hardship. Although current treatment paradigms emphasize globe preservation and quality of life, RB’s nature as a malignant tumor dictates that treatment priorities must remain: life salvage as the primary objective, followed by globe preservation, and finally vision conservation. The central clinical dilemma lies in the fact that indiscriminate pursuit of globe salvage rates may lead to treatment delays, potentially

causing tumor progression and metastasis, ultimately endangering patient survival[11].

Therapeutic decisions are influenced by disease characteristics, treatment efficacy, and economic considerations. For patients with IIRC group D or group E disease presenting with severe intraocular structural damage, diffuse vitreous or subretinal seeding, radiological evidence of high-risk metastatic features, secondary glaucoma, phthisis bulbi, or failure of conservative management with tumor recurrence/metastasis, prompt enucleation is warranted[19]. Studies indicate that over half of enucleated specimens contain high-risk metastatic features, and persistent globe-salvage therapy in such cases correlates with poorer overall survival and increased chemotherapy burden[5]. Economic factors are equally crucial: the direct medical costs for RB patients' families in China average approximately $28 000, with non-medical expenses and income loss amounting to around $25 000, representing a significant overall economic burden[20]. Globe-salvage therapies typically require greater financial investment and longer treatment durations, demanding higher economic capacity and treatment compliance from families. Therefore, when selecting treatment strategies, several key considerations must be carefully weighed: whether globe preservation jeopardizes patient survival; whether functional vision can be safely maintained post-treatment; and whether families possess the financial and psychological capacity to withstand the associated pressures.

Following enucleation, the absence of ocular stimulation often leads to orbital development retardation on the affected side, causing facial asymmetry and deepened upper eyelid sulcus. While the safety of primary orbital implantation after failed conservative RB treatment remains debated, clinical evidence confirms its safety even in patients with optic nerve invasion, with long-term follow-up showing no increased recurrence or mortality risks[21]. Primary implantation offers multiple advantages over secondary procedures: prevents tissue contracture complicating future implantation; provides earlier stimulation for orbital and craniofacial development; achieves superior aesthetic outcomes; reduces surgical procedures; and alleviates family burdens. Although continuing orbital growth in children may lead to eventual implant volume deficiency, this can be addressed by progressively fitting larger ocular prosthesis. Based on our decade-long follow-up experience with primary implantation in infants under six months undergoing enucleation after failed globe-salvage therapy, this approach proves safe and effective[22]. Consequently, when technical expertise is available, enucleation combined with primary orbital implantation should not be restricted by patient age. To optimally address aesthetic concerns and enhance quality of life, we recommend adhering to an "implant whenever possible" principle, facilitating early orbital volume replacement to promote orbital development and improve patients' quality of life.

## IMPLEMENTING LIFELONG SURVEILLANCE, GENETIC COUNSELING, AND PRENATAL RISK STRATIFICATION FOR PROACTIVE RB PREVENTION

RB patients, particularly those with the hereditary form who carry germline mutations in the RB1 tumor suppressor gene, face a significantly elevated risk of developing second primary malignancies compared to other children[23]. Even patients with unilateral disease at presentation retain a risk of tumor development in the contralateral globe. Therefore, comprehensive patient and family education regarding the signs of tumor recurrence and second malignancies is essential, and lifelong follow-up is strongly recommended. The frequency of follow-up examinations can be gradually extended with increasing age and stability of the condition—initially scheduled every 3 to 6mo during the early phase of disease control, and later extended to annual intervals or longer. However, high-risk patients require individualized follow-up plans tailored to their specific circumstances[11]. Critically, the focus of surveillance should extend beyond the affected globe to include detailed examination of the contralateral fundus and general systemic evaluations, facilitating the early detection of new ocular tumors or second primary cancers.

When a parent has a history of RB, genetic counseling and prenatal testing are imperative. Genetic risk assessment and stratification form the foundation for screening children at high risk for RB[19]. This genetic identification enables a proactive and aggressive strategy for early diagnosis within these families. For siblings and neonates born into a family with a confirmed germline *RB1* mutation, proactive and systematic screening is non-negotiable. These at-risk children should undergo immediate and regular fundoscopic examinations according to a strict schedule, starting from birth. This proactive surveillance aims to detect tumors at their earliest, most treatable stage—often before clinical symptoms arise—thereby maximizing the potential for vision preservation and minimizing the need for invasive therapies. Furthermore, patients' understanding of genetic information influences their reproductive choices. For fetuses identified with a high risk of RB through prenatal screening, planned early-term delivery can facilitate anticipatory management for the family. This approach allows for earlier intervention, potentially leading to better visual outcomes and less invasive treatments, thereby benefiting both the patient and the family[24]. After birth, the aforementioned protocol of regular fundus examinations is crucial to detect smaller tumors at their earliest stages. This comprehensive surveillance strategy—spanning from prenatal planning to postnatal execution—maximizes survival

rates and visual potential, while reducing the future need for chemotherapy or enucleation, thereby alleviating patient suffering and lessening the family's economic burden.

## PRIORITIZING PSYCHOSOCIAL CARE TO ENHANCE SURVIVORSHIP QUALITY IN RB FAMILIES

In China's major RB treatment centers, patient survival rates now exceed 95%, enabling the vast majority of patients to achieve long-term survival. As survival outcomes improve, greater attention should be paid by healthcare providers to the quality of life of both patients and their families. A diagnosis of RB adversely affects multiple dimensions of a child's development—including psychological and social functioning[11]. Compared with their peers, these children not only face visual developmental delays but also endure lifelong fears of further vision loss, disease recurrence, second primary malignancies, and the potential of transmitting the disease to their offspring. They are also at risk of experiencing discrimination in daily life, education, and future employment. Overall, RB survivors exhibit a greater need for special educational services and tend to achieve relatively lower educational attainment[25-26]. Additionally, most parents of children with RB report symptoms of depression (73.3%), anxiety (64.2%), or stress (100%). Severe depression is more common among parents of children with multifocal disease, those with lower educational levels, and those with a history of depression[27]. Therefore, it is crucial to focus on the psychological well-being of patients and their families, provide psychological and psychiatric support, and improve their overall quality of life. At present, China faces a shortage of specialized professionals in this field, and awareness of the need for psychological intervention among patients and families remains relatively low, indicating substantial room for improvement.

In summary, the diagnosis and treatment of RB in China still needs to be further strengthened. To bridge current gaps, multidimensional strategies encompass: strengthening public health education to improve RB literacy rates, implementing risk-stratified screening protocols reducing diagnostic delays, expanding genetic counseling access to high-risk families, and cultivating specialized psycho-oncology teams through national training programs, all of which are necessary measures to improve patients' survival rate and quality of life.

## ACKNOWLEDGEMENTS

Part of the content of this article was first published in *Chinese Journal of Ocular Fundus Diseases*, Year 2023, Volume 39, Issue 10, Pages 799-802 (DOI: 10.3760/cma.j.cn511434-20230609-00265).

**Foundations:** Supported by the National Key R&D Program of China (No.2023YFC2410203); Beijing Hospitals Authority Clinical Medicine Development of Special Funding Support (No.ZLRK202503).

**Conflicts of Interest: Wang N,** None; **Ke F,** None; **Li J,** None; **Xu LY,** None; **Wang TY,** None; **Ma JM,** None.

## REFERENCES

1 Finger PT, Tomar AS. Retinoblastoma outcomes: a global perspective. *Lancet Glob Health* 2022;10(3):e307-e308.

2 Kaliki S, Vempuluru VS, Ahmad A, *et al*. Impact of race on the outcomes of retinoblastoma treated with primary enucleation: a global study of 1426 patients. *Clin Exp Ophthalmol* 2025;53(4):421-434.

3 Zhang Y, Wang YZ, Shi JT, *et al*. Clinical analysis of 2790 children with retinoblastoma: a single-center experience in China. *World J Pediatr* 2023;19(12):1169-1180.

4 Global Retinoblastoma Study Group. The Global Retinoblastoma Outcome Study: a prospective, cluster-based analysis of 4064 patients from 149 countries. *Lancet Glob Health* 2022;10(8):e1128-e1140.

5 Zhou CD, Wen XY, Ding Y, *et al*. Eye-preserving therapies for advanced retinoblastoma: a multicenter cohort of 1678 patients in China. *Ophthalmology* 2022;129(2):209-219.

6 Tomar AS, Finger PT, Gallie B, *et al*. Global retinoblastoma treatment outcomes: association with national income level. *Ophthalmology* 2021;128(5):740-753.

7 Oke I, Diller LR, Gonzalez E. Advanced retinoblastoma presenting with cataract in a child with limited access to primary care. *J Pediatr* 2022;247:171-172.

8 Liu CC, Mohmood A, Hamzah N, *et al*. Intra-arterial chemotherapy for retinoblastoma: Our first three-and-a-half years' experience in Malaysia. *PLoS One* 2020;15(5):e0232249.

9 Austoker J, Bankhead C, Forbes LJ, *et al*. Interventions to promote cancer awareness and early presentation: systematic review. *Br J Cancer* 2009;101(Suppl 2):S31-S39.

10 Wilimas JA, Wilson MW, Haik BG, *et al*. Development of retinoblastoma programs in central America. *Pediatr Blood Cancer* 2009;53(1):42-46.

11 Ma JM, Wang N. Retinoblastoma: key points and difficulties in diagnosis and treatment. *Chinese Journal of Ocular Fundus Diseases* 2023;39(10):799-802.

12 Group GRS, Fabian ID, Abdallah E, *et al*. Global retinoblastoma presentation and analysis by national income level. *JAMA Oncol* 2020;6(5):685.

13 Munier FL, Beck-Popovic M, Chantada GL, *et al*. Conservative management of retinoblastoma: Challenging orthodoxy without compromising the state of metastatic grace. "Alive, with good vision and no comorbidity". *Prog Retin Eye Res* 2019;73:100764.

14 Jabbour P, Chalouhi N, Tjoumakaris S, *et al*. Pearls and pitfalls of intraarterial chemotherapy for retinoblastoma: a review. *J Neurosurg Pediatr* 2012;10(3):175-181.

15 Biewald EM, Bornfeld N, Metz KA, *et al*. Histopathology of retinoblastoma eyes enucleated after intra-arterial chemotherapy. *Br J Ophthalmol* 2020;104(8):1171-1175.

16 Gobin YP, Dunkel IJ, Marr BP, *et al*. Combined, sequential intravenous

and intra-arterial chemotherapy (bridge chemotherapy) for young infants with retinoblastoma. *PLoS One* 2012;7(9):e44322.

17 Dalvin LA, Ancona-Lezama D, Lucio-Alvarez JA, *et al*. Ophthalmic vascular events after primary unilateral intra-arterial chemotherapy for retinoblastoma in early and recent eras. *Ophthalmology* 2018;125(11):1803-1811.

18 Farhat W, Yeung V, Ross A, *et al*. Advances in biomaterials for the treatment of retinoblastoma. *Biomater Sci* 2022;10(19):5391-5429.

19 Warda O, Naeem Z, Roelofs KA, *et al*. Retinoblastoma and vision. *Eye (Lond)* 2023;37(5):797-808.

20 Zhou YC, Cai SY, Jin M, *et al*. Economic burden for retinoblastoma patients in China. *J Med Econ* 2020;23(12):1553-1557.

21 Wang N, Liu R, Li J, *et al*. Long-term efficacy of enucleation combined with primary orbital implantation in children with retinoblastoma histopathological invasion of optic nerve. *Front Neurol* 2022;13:1013523.

22 Ke F, Li J, Wang N, *et al*. Clinical characterization and long-term postoperative outcomes of retinoblastoma patients receiving enucleation and primary orbital implantation in early infancy: an observational study. *BMC Ophthalmol* 2024;24(1):360.

23 Rossini L, Durante C, Bresolin S, *et al*. Diagnostic strategies and algorithms for investigating cancer predisposition syndromes in children presenting with malignancy. *Cancers* 2022;14(15):3741.

24 Soliman SE, Dimaras H, Khetan V, *et al*. Prenatal versus postnatal screening for familial retinoblastoma. *Ophthalmology* 2016;123(12):2610-2617.

25 Shields CL, Bas Z, Laiton A, *et al*. Retinoblastoma: emerging concepts in genetics, global disease burden, chemotherapy outcomes, and psychological impact. *Eye (Lond)* 2023;37(5):815-822.

26 van Dijk J, Oostrom KJ, Huisman J, *et al*. Restrictions in daily life after retinoblastoma from the perspective of the survivors. *Pediatr Blood Cancer* 2010;54(1):110-115.

27 Collins MLZ, Bregman J, Ford JS, *et al*. Depression, anxiety, and stress in parents of patients with retinoblastoma. *Am J Ophthalmol* 2019;207:130-143.