Ophthalmic Research

Ophthalmic Surgery

Ophthalmic Res 2025;68:147–155
DOI: 10.1159/000544002

Received: July 22, 2024
Accepted: January 29, 2025
Published online: February 11, 2025

Cataract Surgery in Eyes with Microphthalmos and/or Uveal Coloboma

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Keywords
Cataract · Coloboma · Comorbidity · Microphthalmos · Phacoemulsification

Abstract
Introduction: Cataract may cause severe visual impairment in eyes with microphthalmos (MO) and uveal coloboma (UC). Despite their similarities, distinguishing between these conditions is crucial for cataract surgery. We aimed to compare complications, nucleus hardness, surgical strategies, and outcomes of cataract surgery between MO and UC. ***Methods:*** This retrospective comparative study included 19 eyes with MO and 20 with UC. Preoperative, intraoperative, and postoperative data of eyes that underwent cataract surgery were analysed. ***Results:*** MO eyes had lower high-hardness nucleus rates (p = 0.002) than UC. The most common preoperative complications in the MO and UC groups were glaucoma (37.5%) and retinal detachment (15.4%), respectively. No significant differences in the phacoemulsification (p = 0.45) or intraocular lens implantation (p > 0.99) rates between the two groups. Extracapsular cataract extraction was performed in five eyes (25%), and posterior capsular rupture was the most common surgical complication (15%) in the UC group. Combined surgery was mainly used to deal with high or unstable intraocular pressure (IOP; 77%) in the MO group versus posterior pars plana vitrectomy (85.71%) in the UC group to treat vitreoretinal pathologies. Corrected distance visual acuity was significantly improved in both MO (p = 0.0005) and UC (p < 0.001) groups, while IOP was decreased (p = 0.03) in the MO group. ***Conclusion:*** Eyes with MO and UC exhibited distinct cataract grades and complications, necessitating varied surgical strategies; while cataract surgery has proven to be effective in improving the visual acuity in both groups. Our findings hold significant value for guiding clinical treatment decision-making.

Introduction

Microphthalmos (MO)-anophthalmos-coloboma is a group of structurally and clinically correlated congenital ocular malformations that may cause severe visual impairment [1, 2]. These are uncommon conditions with

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prevalence estimated at 2–17, 0.6–4.2, and 2–14 per 100,000 births, respectively [3].

MO is characterised by short axial length (AL; 2 standard deviations less than the healthy average) [4] and is classified as simple or complex. Simple MO and, in particular, nanophthalmos are not associated with ocular malformations; their clinical features include a microcornea, shallow anterior chamber, short AL, increased lens/volume ratio, and thick sclera [5]. Contrastingly, complex MO is associated with ocular malformations such as coloboma due to optic fissure closure disorders [6]. Uveal coloboma (UC) occurs when an optic fissure fails to close appropriately during foetal development, resulting in a tissue gap that affects the iris, ciliary body, retina, choroid, and optic nerve [7].

With overlapping phenotypes and genetic heterogeneity, differentiation between MO and UC is often overlooked [8, 9]. However, when cataract surgery is required, which significantly improves visual acuity, the differences between MO and UC are noticeable, but there is a lack of relevant comparative research. In this study, we assessed the clinical features, surgical procedures, therapeutic outcomes, and complications associated with cataract surgery, hoping to provide a reference for clinicians.

Methods

Research Participants

This study included patients with MO or UC who underwent cataract surgery at Qilu Hospital of Shandong University from October 2014 to December 2023. MO was defined as an AL <20.0 mm [10]. If MO and UC were both present, then colobomatous MO (CBMO) was diagnosed.

UC diagnosis was based on iris or choroid coloboma observed on slit-lamp fundus examination. Iris coloboma appear as a fan shaped defect between about 4 and 6 points below the iris, and the defect and the pupil together form a "keyhole" shape. Choroidal coloboma is characterised by a circular, fan shaped, or large area of irregular defects below the choroid, which has a white appearance. A small quantity of tortuous choroidal blood vessels can be observed in the defect area. Choroidal coloboma can be connected to or completely wrapped around the optic disc. Patients with eyeball atrophy or traumatic or iatrogenic coloboma were excluded. All surgeries are performed by a number of experienced surgeons, all of whom have senior professional titles.

Data

Data on patient sex, age, biological parameters, preoperative/postoperative corrected distance visual acuity (CDVA), preoperative/postoperative intraocular pressure (IOP), comorbidities, nuclear hardness (Emery-Little grade), UC type, surgical procedures, and surgical complications were collected. Postoperative follow-up ranged from 2 months to 7 years. CDVA was converted to the logarithm of the minimum angle of resolution (logMAR) for statistical analysis. logMAR values corresponding to count fingers, hand movements (HMs), light perception, and no light perception were substituted with 2.10, 2.40, 2.70, and 3.00 logMAR, respectively [11]. The biometrical parameters included AL, anterior chamber depth (ACD), keratometry, and horizontal corneal diameter (HCD). AL, ACD, and keratometry were obtained using the IOL 500 Master system (Carl Zeiss Meditec AG, Jena, Germany). If ACD or AL could not be measured via optical measurements, then ultrasound biomicroscopy (SW-3200; Suowei, Tianjin, China) or A/B ultrasound (SW-2100; Suowei) were used. HCD was measured using the light band of the slit-lamp microscope or the white-to-white distance measured using the IOL Master system.

Statistical Analysis

GraphPad Prism 8.0.1 (GraphPad Software, La Jolla, CA, USA) was used for data analysis. Normal distribution was tested using the Shapiro-Wilk test. Normally distributed continuous data are presented as mean ± standard deviation, whereas non-normally distributed data were reported as median (P25, P75). The independent-samples t test, paired t test, or Mann-Whitney U test was used to analyse quantitative data as appropriate. Enumeration data are expressed as percentages and were analysed using Fisher's exact test. p values <0.05 were considered statistically significant.

Results

Preoperative Evaluation

Clinical Characteristics

In total, 39 eyes (31 patients; 14 men, 17 women; median age: 47 years) that underwent cataract surgery were analysed. For these, 19 eyes (14 patients) were diagnosed with MO, including 16 with nanophthalmos and 3 with CBMO, and 20 eyes (17 patients) were diagnosed with UC.

Biometrical Parameters

Biometry measurements included unoperated eyes. The mean AL in MO was significantly shorter than that in UC. The mean ACD in MO was significantly shallower

Table 1. Biometrical parameters of MO and UC

Biometrical parameters	MO			UC			*p* value
	mean/median	SD/(25%, 75%)	*n*	mean/median	SD/(25%, 75%)	*n*	
HCD, mm	10.85	8.625, 11.30	20	9.50	9.00, 11.00	19	0.38[a]
ACD, mm	2.11	0.50	12	2.89	0.71	20	<0.01*[b]
AL, mm	17.86	1.57	24	24.74	2.02	21	<0.01*[b]
K (D)							
K1 (D)	45.78	2.43	14	42.74	1.60	22	<0.01*[b]
K2 (D)	47.73	2.21	14	44.53	1.24	22	<0.01*[b]

ACD, anterior chamber depth; AL, axial length; K, keratometry; HCD, horizontal corneal diameter; K1, minimum keratometry; K2, maximum keratometry. *Statistically significant difference between MO and UC group ($p < 0.05$). [a]*p* value by Mann-Whitney test. [b]*p* value by independent *t* test.

than that in UC. The minimum keratometry in MO was significantly steeper than that in UC, as was the maximum keratometry. The mean HCD in MO and UC did not differ significantly (Table 1).

Comorbidities Affecting Visual Acuity and Surgical Strategy

Preoperative comorbidities affecting visual acuity in patients with MO included glaucoma (9/24, 37.5%), uveal effusion (4/24, 16.7%), and retinal detachment (RD) (3/24, 12.5%). The comorbidities of UC included RD (4/26, 15.4%) and subluxation of the lens/intraocular lens (IOL; 3/26, 11.5%).

Nuclear Hardness

The hardness of the lens nucleus in MO was mostly grade II and below (16/19, 84.2%). In UC, grades III–V were observed in 11/20 eyes (55.0%); this was considered high-hardness. A higher proportion of eyes with UC had a high-hardness nucleus compared to eyes with UC (p = 0.002).

Surgery

Overall, cataract surgery was performed on 19 eyes (14 patients) in the MO group and 20 eyes (17 patients) in the UC group. The proportion of cataracts extracted using phacoemulsification was 84.21% (16/19) in the MO group and 70.00% (14/20) in the UC group (p = 0.45). Notably, five eyes (25.00%) in the UC group underwent extracapsular cataract extraction (ECCE), which was not performed in any eyes in the MO group. IOL implantation was successfully achieved in 13 eyes (68.42%) in the MO group compared with 14 eyes (70.00%) in the UC group ($p > 0.99$).

Combined surgery was performed in 13 eyes (68.42%) in the MO group, with 76.92% (10/13) of these cases addressing complications related to abnormal and unstable IOP levels. In the UC group, combined surgery was performed on 7 eyes (35.00%), with the majority (85.71%, 6/7) undergoing posterior pars plana vitrectomy (PPPV) to address vitreoretinal pathologies (Tables 2, 3).

Within the MO group, we further categorised eyes based on AL and the presence of combined coloboma. Phacoemulsification and IOL implantation were successfully performed in all 8 patients with nanophthalmos and an AL >18 mm. Combined surgeries in this subgroup included goniosynechialysis in three eyes. Of the other eight eyes, five underwent phacoemulsification, and the remaining three underwent lens aspiration surgery with an irrigation/aspiration handpiece but without phacoemulsification. Additional combined procedures included anterior vitrectomy (five eyes), sclerectomy (three eyes), trabeculectomy (one eye), and surgical peripheral iridectomy (one eye). One eye that developed RD and choroidal detachment following cyclophotocoagulation was treated with PPPV and silicone oil tamponade. IOLs were implanted in four eyes; however, implantation failed in other cases due to a low corneal endothelial cell count or limited potential for visual improvement due to poor fundus conditions.

In all three eyes with CBMO, phacoemulsification and PPPV were performed. Two of these eyes required silicone oil tamponade due to RD. However, no IOLs were implanted in these cases because of poor fundus conditions (Table 2).

Table 2. Surgical data of MO

Case	Eye	Complication	AL	Nucleus hardness	Surgery	Preoperative DCVA	Postoperative DCVA	Surgical complication
Nanophthalmos: AL >18 mm								
1	L	Purtscher-like retinopathy	19.76	III	Phacoemulsification + IOL	20/125	20/100	
2	R	–	19.61	II	Phacoemulsification + IOL + GSL	20/20	20/20	
	L	Angle-closure glaucoma	19.37	II	Phacoemulsification + IOL + GSL	20/67	20/33	
3	R	Angle-closure glaucoma	19.88	II	Phacoemulsification + IOL + GSL	20/67	20/50	
4	R	Amblyopia	18.58	II	Phacoemulsification + IOL	20/100	20/50	
	L	Amblyopia	18.93	II	Phacoemulsification + IOL	20/160	20/50	
5	R	Amblyopia	18.95	II	Phacoemulsification + IOL	20/32	20/25	
	L	Amblyopia	18.93	II	Phacoemulsification + IOL	20/25	20/25	
Nanophthalmos: AL <18 mm								
6	R	Angle-closure glaucoma, optic atrophy	16.44	II	Sclerectomy + aVTX + phacoemulsification + IOL + trabeculectomy	HM	HM	
	L	RD, choroid detachment, optic atrophy	16.49	II	Phacoemulsification + PPPV	HM	HM	
7	L	Angle-closure glaucoma, uveal effusion, optic atrophy	17.50	IV	Sclerectomy + phacoemulsification + IOL	CF	20/200	
8	R	Angle-closure glaucoma, uveal effusion	15.72	II	Sclerectomy + phacoemulsification	CF	20/100	Choroid detachment
9	L	Malignant glaucoma, optic atrophy	14.88	II	Phacoemulsification + aVTX	LP	LP	Subretinal haemorrhage, choroid detachment
10	R	Angle-closure glaucoma, corneal endothelial decompensation, optic atrophy	17.74	II	Lens aspiration + aVTX + SPI	NLP	LP	
11	R	Amblyopia	17.50	I	Lens aspiration + aVTX + IOL	20/500	20/200	
	L	Amblyopia	17.99	I	Lens aspiration + aVTX + IOL	20/250	20/167	
Colobomatous MO								
12	R	RD, iris + choroidal coloboma (disc abnormalities)	19.35	II	Phacoemulsification + PPPV + SOT	HM	HM	

Table 2 (continued)

Case	Eye	Complication	AL	Nucleus hardness	Surgery	Preoperative DCVA	Postoperative DCVA	Surgical complication
13	L	RD, iris + choroidal + disc coloboma	19.32	II	Phacoemulsification + PPPV+ SOT	HM	CF	PCR
14	R	Iris + choroidal + disc coloboma	16.00	III	Phacoemulsification + PPPV	LP	HM	

AL, axial length; aVTX, anterior vitrectomy; CDVA, corrected distance visual acuity; CF, count fingers; GSL, goniosynechialysis; HM, hand movements; IOL, intraocular lens implantation; LP, light perception; NLP, no light perception; PCR, posterior capsular rupture; PPPV, posterior pars plana vitrectomy; SOT, silicone oil tamponade; SPI, surgical peripheral iridectomy; VTX, vitrectomy.

Postoperative Assessment

Visual Acuity and IOP

In the MO group, the median preoperative CDVA was 1.40 (0.50, 2.40) logMAR, and it improved to 0.90 (0.40, 2.40) logMAR after surgery (p < 0.01). The median preoperative CDVA in the UC group was 1.70 (1.08, 2.10) logMAR, and it improved to 0.90 (0.50, 1.08) logMAR after surgery (p < 0.01). There was no significant difference in pre- and postoperative CDVA values between groups (p = 0.63 and p = 0.96). However, mean preoperative IOP was significantly higher in the MO group than in the UC group (28.97 ± 19.62 mm Hg vs. 16.34 ± 4.82 mm Hg; p = 0.01). Postoperatively, the mean IOP in the MO group decreased to 16.14 ± 3.52 mm Hg (p = 0.03), with no significant difference between pre- and postoperative IOP in the UC group (16.16 ± 5.7 mm Hg; p = 0.91). Postoperative IOP did not differ significantly between the groups (p = 0.98).

Overall, CDVA improved in 13 eyes (68.4%) in the MO group. The mean preoperative CDVA in the eight eyes with nanophthalmos with an AL >18 mm was 0.46 ± 0.33 logMAR; this improved to 0.26 ± 0.18 logMAR postoperatively (p = 0.03). CDVA improved in all eyes. The CDVA of the eight eyes with nanophthalmos with an AL <18 mm increased from 2.15 ± 0.63 logMAR to 1.73 ± 0.89 logMAR. The CDVA of one eye with CBMO was maintained at HM, one eye increased from HM to count fingers, and one eye increased from light perception to HM. The preoperative CDVA and postoperative CDVA of eyes with nanophthalmos and an AL >18 mm were better than those of eyes with nanophthalmos and an AL <18 mm or CBMO (p < 0.01).

In the UC group, CDVA improved in 18 eyes (90%). Postoperative CDVA was unchanged in one eye due to retinal reasons, and it decreased in one eye due to postoperative macular oedema. The difference in the efficiency of surgical techniques and approaches between these two groups was not statistically significant (p = 0.107).

Surgical Complications

In the MO group, iridocele and choroid detachment were observed in two eyes and subretinal haemorrhage was observed in one eye. Posterior capsular rupture (PCR) occurred in one eye with CBMO. PCR was the most common complication in the UC group (three eyes, 15%). One eye showed persistent intraocular hypertension after vitreoretinal surgery, and one eye had macular oedema 6 months after silicone oil removal.

Discussion

Cataract surgery can significantly improve visual acuity in patients with MO and UC, but it often increases surgical risk and results in poor prognosis; therefore, in-depth analysis and optimisation of cataract surgery methods in MO and UC are needed. Owing to the low prevalence of MO and UC, studies on cataract surgery are limited [12–14]. This report summarised and compared clinical features, surgical methods, effects, and complications of cataract surgery in patients with MO and UC.

Angle-closure glaucoma is a common complication of MO due to shallow anterior chambers, short AL, and elevated lens-to-eyeball volume ratios [5, 15]. Furthermore, abnormal scleral thickening may lead to uveal effusion, resulting in increased vitreous pressure, anterior displacement of the lens-iris septum, and further narrowing of the anterior chamber [16]. Angle-closure glaucoma and uveal effusion were also the most common complications in MO in our study, and MO showed higher IOP than the normal-scope and UC groups.

Table 3. Surgical data of UC

Case	Eye	Fundus finding	Type of coloboma	Nucleus hardness	Surgery	Preoperative BCVA	Postoperative BCVA	Surgical complication
1	R	–	Iris + choroid + disc	II	Phacoemulsification + IOL	20/500	20/167	
2	L	RD	Iris + choroid + disc	IV	Phacoemulsification + PPPV + SOT	NLP	LP	High IOP
3	L	Macular membrane	Choroid	II	Phacoemulsification + IOL	20/1000	20/50	
4	R	–	Iris + choroid	III	Phacoemulsification + CTR + IOLS + aVTX	20/200	20/67	
5	L	Grey appearance of retina	Iris + choroid	II	Phacoemulsification + IOL	HM	CF	
6	L	–	Iris + choroid	I	Lens aspiration + IOL	CF	20/333	
7	R	RD	Iris + choroid	II	Phacoemulsification + PPPV + SOT	20/133	20/333	Macular oedema
8	R	–	Iris + choroid	IV	Phacoemulsification + IOL	CF	20/100	
9	R	Atrophy of macular area	Iris + choroid	V	ECCE + PPPV	20/1000	20/200	PCR
	L	Atrophy of macular area	Iris + choroid	V	ECCE + PPPV	20/500	20/200	PCR
10	R	RD, macular hole	Choroid	III	Phacoemulsification + PPPV + IOL	20/1000	20/200	
11	L	–	Iris	III	Phacoemulsification + IOL	CF	20/67	
12	R	–	Iris + choroid	III	ECCE + IOL	20/500	20/200	
	L	–	Iris + choroid	IV	ECCE	20/400	20/133	PCR
13	L	RD	Iris + choroid	III	Phacoemulsification + PPPV + SOT	HM	20/250	
14	R	–	Iris	II	Phacoemulsification + IOL	HM	20/80	
	L	–	Iris	II	Phacoemulsification + IOL	20/200	20/67	
15	L	Diabetic retinopathy	Iris + choroid	III	ECCE + IOL	CF	20/167	
16	L	–	Iris + choroid	II	Phacoemulsification + IOL	20/80	20/50	
17	L	–	Iris + choroid	II	Phacoemulsification + IOL	20/133	20/50	

aVTX, anterior vitrectomy; CF, count fingers; CDVA, corrected distance visual acuity; CTR, capsular tension ring; ECCE, extracapsular cataract extraction; HMs, hand movements; IOL, intraocular lens implantation; IOLS, intraocular lens suspension; LP, light perception; NLP, no light perception; PCR, posterior capsular rupture; PPPV, posterior pars plana vitrectomy; SOT, silicone oil tamponade; VTX, vitrectomy.

The MO group had shorter AL, steeper corneas, and shallower ACD compared with the UC group, which is not surprising considering the diagnostic standards for both groups. However, there was no significant difference in HCD between the two groups. The HCD of relative anterior MO was reported to be 10.6 ± 0.38 mm [17], and no data were found for MO eyes. UC can be associated with normal-sized or microcorneas [18], and HCD in eyes with isolated iris coloboma was reported at 11.06 ± 0.42 mm [19]. These differences may stem from different inclusion criteria. Structural differences are important in the assessment and treatment of cataracts in MO and UC.

Adult patients with chorioretinal coloboma have a 29–42% risk of RD [20, 21]. In our study, RD was the most common complication in the UC group (incidence of 18.2%), and different types of colobomas (chorioretinal vs. uveal) may account for the differences in RD rates.

CBMO is rare, with no definite information regarding its prevalence and only sporadic cases reported in the literature [9, 22]. Interestingly, none of the three eyes with CBMO included in our study presented with angle-closure glaucoma or uveal effusion, while two developed RD. The underlying mechanisms require further investigation.

In our study, most cataracts in the MO group were early- or mid-stage, and this has not been reported previously. This may be because patients first visit doctors for glaucoma-related symptoms such as eye pain, and the main purpose of cataract extraction was to relieve pupil block and peripheral pre-iris adhesion caused by the posterior "push" mechanism [15]. Phacoemulsification allows good control and helps maintain the anterior chamber and IOP during surgery, which could help reduce complications [23]. In our study, 84.21% of patients with MO underwent phacoemulsification, and no PCR occurred in patients with nanophthalmos. One case of PCR occurred in a CBMO eye.

Most cataracts in the UC group were mid- and late-stage cataracts with high-hardness nuclei. Two studies also found that most cataracts in UC were nuclear sclerosis [24, 25]. When ECCE must be performed, which occurred in 25% of our eyes with UC, one must ensure that the range of the anterior capsule tear is large enough and the pupil is sufficiently dilated; otherwise, PCR can easily occur. Chaurasia et al. [26] included 10 eyes with high nuclear hardness; nine eyes underwent ECCE or small-incision cataract surgery, and six eyes underwent PCR. In our study, all three cases of PCR occurred in 5 patients who underwent ECCE.

The rate of successful IOL implantation did not differ between the MO and UC groups. However, within the MO group, implantation rates differed among patients with nanophthalmos and an AL >18 mm (8/8, 100%), with nanophthalmos and an AL <18 mm (4/8, 50%), and with CBMO (0/3, 0%) (p = 0.006). The underlying reasons may include more severe structural abnormalities, worse expected CDVA improvement after surgery, and more complications in patients with nanophthalmos and an AL <18 mm and CBMO than in patients with nanophthalmos and an AL >18 mm.

The accuracy and degree of selection of IOL measurements for MO are challenging. Studies have suggested that the Haigis formula is most suitable for patients with nanophthalmos and small eyes (AL <22 mm) [27, 28]. However, the IOL power required to achieve emmetropia is often greater than 34 D, with some exceeding 40D. In clinical practice, IOLs with a degree ≥34 D are difficult to obtain, making piggyback IOL implantation an optional refractive procedure in nanophthalmic eyes [29, 30].

For eyes with MO, high IOP and increased positive vitreous pressure during cataract surgery should be considered because this may increase the risk of PCR, iris prolapse, and suprachoroidal haemorrhage [31]. Yalvac et al. [32] reported that trabeculectomy + mitomycin-C + inferior sclerotomy was effective and safe for glaucoma control in patients with nanophthalmos. Combined with partial vitrectomy, the lens can be shifted posteriorly to deepen the anterior chamber and reduce the IOP [33].

RD is the most common complication of choroidal coloboma [20, 21]; therefore, PPPV and gas/silicone oil filling should be combined [14, 34]. Combined vitreoretinal surgery is necessary for CBMO [2]. Consistent with several studies [12, 13], cataract surgery in the MO group resulted in significantly improved CDVA and significantly decreased IOP. However, CBMO had little benefit in improving vision, and the main purpose of cataract surgery was to provide a better surgical field of view to facilitate vitreoretinal surgery.

In the UC group, there was a general trend toward worsened visual acuity with more severe anomalies [35]. The mean final follow-up CDVA was significantly improved, as reported in previous studies [14, 25, 26], suggesting that, despite the complexity and difficulty of cataract surgery in eyes with UC, vision can be improved.

Our study had some limitations. In some patients, biometric data were missing because of poor coordination, such as that caused by nystagmus, and turbid dioptric media. Additionally, this retrospective review included a small number of cases. However, our findings still provide valuable information for ophthalmologists to plan cataract surgery and improve outcomes for patients with MO and UC.

Conclusion

This was the first study to compare differences in cataract surgery between MO and UC, two conditions that are frequently confused. Phacoemulsification emerged as the predominant procedure. Nevertheless, due to higher IOP, MO requires concurrent anti-glaucoma surgery, For MO with an AL <18 mm, cataract surgery often requires other surgical procedures, such as anterior vitrectomy and sclerectomy, and is associated with higher surgical risks. UC may require additional vitrectomy to manage concomitant vitreoretinopathy or posterior capsule rupture due to a harder nucleus. In general, the CDVA was significantly improved in both the MO and UC groups, whereas the IOP was considerably decreased in the MO group. In particular, all three eyes with CBMO exhibited severe intraocular structure abnormalities, necessitating additional PPPV surgery, and poor vision prognosis; thus, surgery performed by experienced fundus surgeons was suggested. Cataract surgery in eyes with MO and UC is challenging; therefore, clinicians should ensure sufficient doctor-patient communication, adequate preoperative evaluation, individualised surgery plans, and careful intraoperative manipulations.

Statement of Ethics

This retrospective study adhered to the principles of the Declaration of Helsinki and was approved by the Qilu Hospital of Shandong University Ethics Committee (reference number: 2019052). Written informed consent to participate in the study has been obtained from the participants.

Conflict of Interest Statement

The authors have declared that no competing interest exists.

Funding Sources

This work was supported by the Natural Science Foundation of Shandong Province (Grant No. ZR2020MH174).

Author Contributions

Leyi Wang and Bozhao Wang designed and conducted the study, analysed and interpreted the data. Leyi Wang, Bozhao Wang, Ying Wang, and Xin Wang collected the data. Leyi Wang and Bozhao Wang wrote the manuscript. Hongling Yang translated the manuscript. Ran Wu checked spelling and grammar mistakes. Yan Cui reviewed the manuscript and ensured that the methodology and results of the study were correct. All authors reviewed and approved the manuscript.

Data Availability Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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