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Indications and Outcomes of Select Vitreoretinal Surgery in Patients With Marfan Syndrome

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Abstract

Purpose: To report clinical indications and outcomes of select vitreoretinal surgery in patients with Marfan syndrome. **Methods:** A retrospective consecutive case series of patients with Marfan syndrome undergoing surgery was performed. Data collected included demographics, systemic and ocular history, refraction, and preoperative and postoperative examination findings. **Results:** Twenty-seven patients (39 eyes) with Marfan syndrome who underwent vitreoretinal surgery were included. Mean age at time of surgery was 37 years, and mean follow-up duration was 4 years. Surgical indications for patients with Marfan syndrome included visually significant crystalline lens subluxation (n = 25 eyes), rhegmatogenous retinal detachment (RRD) (n = 9 eyes), and dislocated intraocular lens implants (n = 5 eyes). Best-corrected visual acuity was 20/40 or better in 21 eyes undergoing surgery for lens subluxation. For patients undergoing surgery for RRD, anatomic reattachment was achieved by last follow-up in 8 eyes (89%). **Conclusions:** Pars plana lensectomy and vitrectomy for crystalline lens subluxation was the most common vitreoretinal surgery in patients with Marfan syndrome.

Keywords

Marfan syndrome, crystalline lens subluxation, rhegmatogenous retinal detachment, dislocated intraocular lens

Introduction

Marfan syndrome is a multisystem genetic disorder of connective tissue. Autosomal dominant inheritance with high penetrance is most common, but a sporadic pattern occurs in 25% of affected individuals.[1] In 1990, the causative gene was identified as *fibrillin-1* (*FBN1*), which encodes a structural protein of the extracellular matrix expressed in various body tissues.[2] In the eye, the amount of expressed fibrillin-1 varies between ocular structures but is most prominent in lens zonules.[3]

Ocular manifestations of Marfan syndrome vary between individuals as a function of their specific mutation and disease severity. Commonly, patients with Marfan syndrome develop lenticular and axial myopia during prepubescent years. Ocular features suggestive of Marfan syndrome include enlarged corneal diameter, corneal astigmatism, miosis, and iris hypoplasia.[4] The most characteristic ocular feature, ectopia lentis, may occur in up to 60% of patients with Marfan syndrome, typically before early adulthood. Other ocular complications leading to vision loss may include refractive amblyopia, open-angle glaucoma, and rhegmatogenous retinal detachment (RRD).[1]

Potential indications for vitreoretinal surgery in patients with Marfan syndrome include pars plana lensectomy and RRD repair. In patients with ectopia lentis, a proper refraction is often an adequate solution to prevent amblyopia and ameliorate symptoms. However, pars plana lensectomy is considered for more advanced cases. RRD occurs in an estimated 8% to 38% of patients with Marfan syndrome, whose risk factors may include axial myopia and zonular deficiency leading to mechanical traction on the peripheral retina.[5]

The purpose of this case series is to present the clinical indications and long-term outcomes of select vitreoretinal surgery for patients with Marfan syndrome at a single center.

Methods

This study was approved by the Institutional Review Board of the University of Miami School of Medicine Medical Sciences Subcommittee for the Protection of Human Subjects. A

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Table 1. Demographics and Surgical Outcomes of Marfan Syndrome With Crystalline Lens Subluxation or Luxation.

Parameter	Value
Age (y)	
Mean	19
Range	4-67
Sex, %	
Female	57
Male	43
Follow-up (mo)	
Mean	23
Range	5-36
Lens status, n (%)[a]	
Aphakic	15 (60)
Scleral-fixated lens	9 (90)
Anterior chamber lens	1 (10)
Mean preoperative BCVA, n (%)[a]	
>20/40	5 (20)
20/40-20/200	6 (24)
<20/200	8 (32)
Mean postoperative BCVA, n (%)[a]	
>20/40	21 (84)
20/40-20/200	3 (12)
<20/200	2 (8)
Postoperative complications, n[a]	
Secondary angle closure glaucoma	1
RRD	1
Vitreous hemorrhage and CME	1

Abbreviations: BCVA, best-corrected visual acuity; CME: cystoid macular edema; RRD, rhegmatogenous retinal detachment.
[a]Indicates number (%) of eyes.

consecutive, retrospective case series of patients with Marfan syndrome undergoing ocular surgery at Bascom Palmer Eye Institute between January 2015 and January 2024 was identified using International Classification of Diseases (ICD) Ninth Revision (ICD-9) and Tenth Revision (ICD-10) codes associated with Marfan syndrome (759.82 and Q87.4, respectively) and Current Procedural Terminology codes associated with vitreoretinal surgery (67110, 67108, 67113, 67036, 67039, 67040, 67041, 67042, 67043, and 67121) or cataract extraction (66850, 66986, 66985, 66984, 66982, and 65920). Clinic notes and operative reports were reviewed for all patients. Data collected included demographic information, prior systemic and ocular history, refractive status, and preoperative and postoperative examination findings in the affected eyes.

Results

Overall Demographics

We identified 27 patients with Marfan syndrome (39 eyes) undergoing vitreoretinal surgeries via an ICD code search and included them in the study. Patients with Marfan syndrome were excluded if they underwent anterior segment procedures for uncomplicated cataract or glaucoma. Mean age at time of surgery was 37 years (range, 4-74 years), and mean follow-up duration was 4 years (range, 2.7 months to 11.4 years).

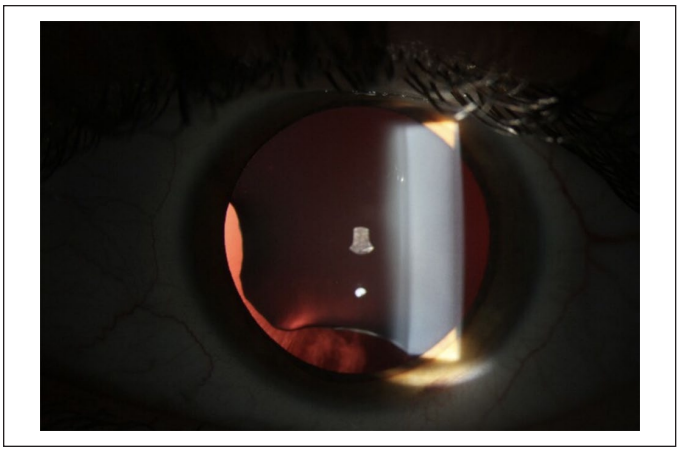

Figure 1. Dislocated crystalline lens with abnormal lens contour inferiorly.

Overall Surgical Indications

Surgical indications in patients with Marfan syndrome included a visually significant subluxated or luxated crystalline lens in 25 eyes of 14 patients (64%), RRD in 9 eyes of 9 patients (23%), and dislocated intraocular lens (IOL) implants in 5 eyes of 4 patients (13%).

Subluxated or Luxated Crystalline Lens

Demographics and surgical indications are presented in Table 1. The most frequent indication for surgery was subluxated or luxated crystalline lenses (Figure 1). Refractive limitation was the indication for surgery in all patients. Of the 8 pediatric patients, 6 were within the amblyogenic age range at the time of surgery. Aphakia was planned in 15 eyes (60%), and 10 eyes of 6 patients (40%) underwent IOL implantation during pars plana vitrectomy (PPV) or pars plana lensectomy. This included 9 scleral-fixated posterior chamber IOLs and 1 anterior chamber IOL.

Eyes undergoing PPV or pars plana lensectomy for subluxated or luxated crystalline lenses had preoperative best-corrected visual acuity (BCVA) of 20/40 or better in 5 eyes (20%), between 20/40 and 20/200 in 6 eyes (24%), and worse than 20/200 in 8 eyes (32%). Final BCVA was 20/40 or better in 21 eyes (84%), between 20/40 and 20/200 in 3 eyes (12%), and worse than 20/200 in 2 eyes (8%) at last follow-up. Postoperative mean spherical equivalent was +13.75 D (range, +5.75 to +17.875) in eyes left aphakic and −0.125 D (range, +0.25 to −1.375) in eyes that underwent secondary IOL implantation. An intraoperative retinal tear was identified and treated in 1 eye. Postoperative complications requiring further surgery included secondary angle closure glaucoma (1 eye), total RRD (1 eye), and vitreous hemorrhage and cystoid macular edema secondary to a dislocated IOL (1 eye).

Table 2. Demographics and Surgical Outcomes of Marfan Syndrome With Rhegmatogenous Retinal Detachment (n = 9 patients; 9 eyes).

Parameter	Value
Age (y)	
Mean	39
Range	15-74
Sex, %	
Female	66
Male	34
Follow-up (mo)	
Mean	22
Range	2-60
Retinal detachment, n (%)[a]	
Macula-involving	8 (89)
PVR at presentation	3 (33)
Scleral buckling/PPV	5 (56)
PPV	4 (44)
Recurrent RRD, n (%)[a]	4 (44)
Mean time to recurrent RRD under silicone oil (mo)	4
Mean preoperative BCVA, n (%)[a]	
>20/40	1 (11)
20/40-20/200	5 (55)
<20/200	3 (33)
Mean postoperative BCVA, n (%)[a]	
>20/50-20/200	2 (22)
20/200-20/800	3 (33)
< counting fingers	4 (44)

Abbreviations: BCVA, best-corrected visual acuity; PPV, pars plana vitrectomy; PVR, proliferative vitreoretinopathy; RRD, rhegmatogenous retinal detachment.
[a]Indicates number (%) of eyes.

Table 3. Demographics and Surgical Outcomes of Marfan Syndrome With Dislocated Intraocular Lens (n = 4 patients; 5 eyes).

Age	Mean 53 years Range (38-68 years)
Sex	F (0%) M (100%)
Follow-up	Mean 83 months Range (1-200 months)
Type of dislocated IOL	Scleral fixated 3 eyes (60%) Iris fixated 1 eye (20%) PCIOL in-bag 1 eye (20%)
Mean BCVA pre-op	>20/40 2 eyes (40%) 20/40-20/200 3 eyes (60%)
Mean BCVA post-op	>20/40 2 eyes (40%) 20/40-20/200 2 eyes (40%) <20/200 1 eye (20%)

Abbreviations: IOL, intraocular lens; PCIOL, posterior chamber intraocular lens.

Retinal Detachment

Nine patients with Marfan syndrome (9 eyes) were diagnosed with RRD at presentation or during follow-up. Demographics and surgical indications are presented in Table 2. Mean age in this group was 39 years (range, 15-74 years). Eight eyes with RRD at presentation had a history of lens subluxation for which they previously underwent at least 1 surgery. One patient had a remote history of prior glaucoma device implantation. Two patients had a preceding history of ocular trauma. Eight detachments (89%) involved the macula at presentation, and 1 was associated with a giant retinal tear. Proliferative vitreoretinopathy (PVR) was evident in 3 eyes (33%) at presentation. Preoperative lens status was aphakia in 7 eyes (78%) and pseudophakia in 2 eyes (22%), both of which had anterior chamber IOL implants. Five eyes (56%) underwent combined scleral buckling procedures with PPV, and 4 eyes (44%) underwent PPV alone. Intraocular tamponade with C_3F_8 gas was used in 6 eyes (66%), and silicone oil was used in 3 eyes (33%). No intraoperative complications were documented. Four patients (44%) required multiple surgeries for recurrent RRD during postoperative follow-up, each experiencing a recurrent RRD while under silicone oil tamponade. One patient re-detached 2 months after silicone oil removal, requiring 2 additional vitrectomies with silicone oil insertion. One patient experienced recurrent RRD 12 months after silicone oil insertion. Another patient detached 2 months after silicone oil insertion, and yet another patient detached 1.5 months after silicone oil insertion. In patients experiencing recurrent RRD at any time during their treatment course, a mean of 5 vitreoretinal surgeries were performed. Anatomic reattachment was achieved in 8 eyes (89%) by final follow-up. Final BCVA was between 20/50 and 20/200 in 2 eyes (22%), between 20/200 and 20/800 in 3 eyes (33%), and counting fingers or worse in the remaining 4 eyes (44%).

Dislocated Intraocular Lenses

IOL exchange or removal by PPV was performed in 4 patients with Marfan syndrome (5 eyes). Demographics and surgical indications are presented in Table 3. Prior history of ocular surgery included 4 patients with crystalline lens subluxation or luxation and insertion of a secondary IOL (3 scleral-fixated, 1 iris-fixated) and 1 patient with a dislocated posterior chamber IOL (in-the-bag). Four eyes underwent lens exchange for a scleral-sutured IOL (Alcon CZ70BD or Bausch + Lomb AKREOS). One eye required IOL repositioning with a Gore-Tex suture and had a remote history of lens subluxation with scleral-sutured IOL implantation done elsewhere. Preoperative BCVA was 20/40 or better in 2 eyes (40%) and between 20/40 and 20/200 in 3 eyes (60%). Final BCVA was 20/40 or better in 2 eyes (40%), between 20/40 and 20/200 in 2 eyes (40%), and worse than 20/200 in 1 eye (20%) at the last follow-up examination. Postoperative mean spherical equivalent was −1.62 D (range, plano to −2.00 D). No intraoperative complications were reported. One patient developed an epiretinal membrane with cystoid macular edema during follow-up and underwent PPV with membrane peel (final BCVA, 20/50). One patient developed an exposed scleral-sutured and pseudophakic bullous keratopathy during follow-up, which required 2 subsequent lamellar keratoplasties (final BCVA, hand motions).

Conclusions

The present cohort shows that crystalline lens subluxation is the most common indication of vitreoretinal surgery in patients with Marfan syndrome, with acceptable visual outcomes of pars plana lensectomy with or without secondary IOL implantation. However, RRD and dislocated IOLs were also a relatively frequent indication for vitreoretinal surgery in patients with Marfan syndrome with variable outcomes.

There are several considerations in preoperative planning for patients with Marfan syndrome since standard phacoemulsification with intracapsular IOL placement is typically not recommended with zonular instability. Pars plana lensectomy with planned aphakia or a secondary IOL implant is often considered. Fellow eyes may benefit from subsequent intervention due to anisometropia. Preoperative systemic evaluation is critical given known cardiovascular manifestations of Marfan syndrome (38% of patients in the present cohort) and the risk of thromboembolism with other conditions associated with ectopia lentis that may be misdiagnosed as Marfan syndrome, such as homocystinuria.

Oh and Smiddy[6] found similarly good vision with pars plana lensectomy for subluxated crystalline lens but found a higher rate of postoperative RRD. Twelve of the 40 patients in their cohort had Marfan syndrome, and mean final visual acuity of this subgroup was 20/30 at 2 months postoperatively.[6] Miraldi et al[7] reported on 42 eyes of patients with Marfan syndrome left aphakic after pars plana lensectomy with limited anterior vitrectomy, resulting in average BCVA improvement from 20/80 preoperatively to 20/25, and all 20/30 or better after a mean of 4.9 years. Several smaller cohorts have corroborated these findings, reporting favorable visual outcomes.[7,8]

There are additional considerations in patients with Marfan syndrome if IOL implantation is considered. In the current cohort, 1 eye developed dislocation of a scleral sutured IOL and vitreous hemorrhage 4 months after combined pars plana lensectomy or PPV and scleral-sutured IOL implantation at our institution. Five eyes underwent lens exchange for dislocated IOLs implanted at other facilities. Complications were infrequent in this series of patients undergoing pars plana lensectomy or PPV with planned aphakia, as only 1 patient developed an RRD 6 weeks after surgery. Our data may suggest a trend toward more complications in patients with IOL implantation at the time of lensectomy.[9] Similar rates of complications after IOL implantation were reported by Maharana et al,[10] with the most common being vitreous hemorrhage (6.4%), vitreous in the anterior chamber (11.1%), and endophthalmitis (1.3%). Asadi and Kheirkhah[11] reported postoperative hemorrhage (48% of eyes), late IOL dislocation due to breakage of polypropylene sutures after 7 to 10 years (24%), choroidal effusion (8%), and 1 case of endophthalmitis (4%) in pediatric patients with Marfan syndrome undergoing primary or secondary scleral-sutured IOL transplantation. Other reports note high rates of posterior capsular opacification in pediatric patients with Marfan syndrome and dislocated scleral-sutured IOLs in adult patients with Marfan syndrome compared to age- and surgeon-matched controls.[11,12] Anterior chamber IOLs and iris-fixated IOLs are commonly avoided in patients with Marfan syndrome, particularly in young patients. The anterior chamber is often excessively deep in Marfan syndrome, which can make appropriate size selection of IOLs challenging and lead to exaggerated IOL movement. Some IOLs can lead to iris pigment chafing, glaucoma, corneal decompensation, and inflammation.[13]

There is a paucity of literature assessing outcomes of RRD repair in patients with Marfan syndrome in the modern vitrectomy era.[6,14,15] Previous studies estimate up to a 70% incidence of posterior segment pathology in Marfan syndrome patients with subluxated lenses and increased rates (8% to 38%) of retinal detachments in Marfan syndrome patients with subluxated lenses or following IOL implantation.[6,16,17] Fundus examination may be difficult due to poor dilation, lens subluxation, and young age. Surgical repair may also present unique challenges such as prolonged surgical time or decreased efficacy of tamponade in the setting of aphakia.[18] Other studies report a high incidence of PVR at presentation.[6,19,20] Although anatomic reattachment was relatively favorable in our series (89%), 44% required repeat surgery for reattachment, and 22% had final BCVA better than 20/200. Better visual outcomes have been reported in a smaller series by Lee and Ang[16] with 58% of eyes achieving at least 20/40 visual acuity. Sharma et al[5] reported that 81% of patients had at least 20/200 visual acuity.

Diagnosis of Marfan syndrome in patients with suggestive ocular findings is important for ophthalmologists. Ocular findings may be the first presentation of Marfan syndrome in patients without marfanoid body habitus, leading to delayed diagnosis.[2] Diagnoses can be made clinically and confirmed with genetic tests. Prompt referral should be made to appropriate specialists, including cardiologists, to evaluate for aortic aneurysms.[20] Marfan syndrome is exclusive to *FBN1* mutations in the latest nosology.[21] *FBN1* mutations can also be associated with diseases such as acromicric dysplasia and Weill-Marchesani syndrome, among others.[22] Recent studies assessing phenotype-genotype correlations for patients with Marfan syndrome found that premature termination codon variants in *FBN1* are associated with the highest risk of aortic aneurysm,[23] but with lower risk of ectopia lentis. Improved understanding of *FBN1* mutations may allow physicians to better prognosticate for patients with Marfan syndrome and determine the frequency of follow-up for ocular manifestations.[22]

Our institution is a tertiary referral center, and a limitation of a chart review study is incomplete surgical history availability prior to arrival to our institution. An additional limitation is patients returning to the referring surgeon in many cases, limiting follow-up duration at our institution.

The current study reports indications and outcomes of select vitreoretinal surgery in patients with Marfan syndrome. Surgeries included pars plana lensectomy or PPV for visually significant lens subluxation, dislocated IOL repositioning or removal, and RRD surgery. Complications of ocular surgery may be more common in patients with Marfan syndrome, and careful preoperative refraction and counseling should occur before

recommending surgery. Furthermore, the present study and prior literature suggest a possible higher rate of complications in patients with Marfan syndrome with IOL implantation, and planned aphakia should be considered for visually significant lens subluxation.

Ethical Approval

This study was approved by the Institutional Review Board of the University of Miami School of Medicine Medical Sciences Subcommittee for the Protection of Human Subjects.

Statement of Informed Consent

Informed consent was deemed not required as no personally identifiable information is included.

Data Availability Statement

Data are not publicly available.

Declaration of Conflicting Interests

Drs. Sengillo, Kiryakoza, Uhr, da Cruz, Townsend, Smiddy, and Flynn declared no potential conflicts of interest with respect to the research, authorship, and/or publication of the article. Dr. Berrocal is a consultant for Alcon, Allergan, Zeiss, Dutch Ophthalmic Research Center, Novartis, and ProQR and has received lecturing fees from Oculus. Dr. Sridhar serves as a consultant for Alcon, Apellis, Dorc, Genentech, EyePoint, Iveric, and Regeneron. Dr. Lam receives study grant support from AGTC, Biogen, Editas, Endogena, Nanoscope, Ocugen, and Spark and serves as a consultant for Biogen, BlueRock, and Janssen.

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