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Analysis of Efficacy of Vitrectomy on Myopic Foveoschisis and Its Associated Factors

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Abstract: *This paper aims to investigate the surgical efficacy of vitrectomy on myopic foveoschisis (MF) and its related factors. We reviewed the clinical data of MF patients who received vitrectomy surgery in the Department of Ophthalmology of the First Affiliated Hospital of Zhengzhou University between January 2020 and August 2022, and analyzed the efficacy of vitrectomy surgery in treating MF. Furthermore,we investigated the correlation between preoperative clinical characteristics of the eyes affected by MF and surgical efficacy. Our results are as follows: A total of 56 MF patients (61 eyes) were included in this study, with a mean age of 56.39±10.39 (33-75) years. After surgery, 50 eyes (82.0%) showed improved visual acuity compared with the preoperative period, 12 eyes (19.7%) got MF reattached, and 33 eyes (54.1%) got MF partially reattached, and MF did not further develop in all eyes during postoperative follow-up. Compared with MF eyes with improved postoperative visual acuity, MF eyes with unimproved postoperative visual acuity had longer axial length (P=0.036), with a higher incidence of severe MF (P=0.004), but the incidences of vitreous adhesion and epi-retinal membrane(ERM), and central foveal thickness(CFT) were not significantly different between the two groups of MF eyes (P>0.05). Compared with MF eyes got reattached or partially reattached, the axial length of MF eyes that were not reattached were longer (P<0.001), with a similarly higher proportion of severe MF eyes (P=0.003), but there were no significant differences in the incidence of vitreous adhesion and ERM ,and the CFT between the two groups of MF eyes (P>0.05). Univariate and multivariate regression analyses showed that preoperative grading of the condition as severe was an independent risk factor for difficulty in improving visual acuity in postoperative MF eyes (P=0.030), and a long axial length was an independent risk factor for difficulty in resetting the MF in postoperative MF eyes (P=0.004). In conclusion, our study can significantly improve that vitrectomy surgical treatment is safe and effective for most MF patients, and preoperative grading of severe MF and long ocular axis are risk factors for relatively poor surgical outcomes in eyes with MF.*

Keywords: *Myopic foveoschisis, High myopia, Vitrectomy, Surgical efficacy, ATN classification system*

1. Introduction

Myopic foveoschisis(MF) is a macular lesion with a relatively high incidence in patients with high myopia, and is a current hot spot in the study of retinopathy associated with high myopia[1]. In recent years, many studies have suggested that MF is a pathological stage before the development of macular hole associated with high myopia, and that it is better than macular hole in terms of its therapeutic effect[1-4]. If the development of the lesion can be effectively controlled at this stage, avoiding or delaying the formation of macular schisis will be of great significance in protecting the visual function of patients with high myopia.

Vitrectomy is one of the main clinical modalities for the treatment of MF, but there are fewer studies evaluating the efficacy of vitrectomy for the treatment of MF. Understanding the efficacy of vitrectomy surgery for the treatment of MF and its associated factors can help determine the scope of vitrectomy surgery in MF patients, and the results of this study will help clinicians make better medical decisions, which may improve the prognosis of MF patients. Therefore, the aim of this study was to investigate the efficacy of vitrectomy surgery for MF and its associated factors, which is reported as follows.

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2. Objects and Methods

2.1 Subject of the Study

The clinical data of MF patients who received vitrectomy surgery at the First Affiliated Hospital of Zhengzhou University between January 2020 and August 2022 were reviewed, and information on the patients' gender, age, visual acuity, intraocular pressure, macular retinoschisis characteristics, results of ocular examinations, surgical methods and intra-operative and post-operative complications were collected. Before statistical analysis, visual acuities recorded in different visual acuity formats were first converted to logMAR visual acuity format[5, 6] . The inclusion and exclusion criteria of patients were as follows:

Inclusion criteria: (1) myopia >600 diopters and ocular axial length ≥26mm[7] ; (2) MF diagnosis in accordance with international standards[8] ; (3) vitrectomy surgery for MF; (4) postoperative follow-up ≥ 6 months.

Exclusion criteria: (1) concomitant ocular diseases such as uveitis, diabetic retinopathy, central serous chorioretinopathy, retinal detachment, etc., which may affect the assessment of MF condition and surgical efficacy; (2) heavy dioptric system clouding, which does not allow for the acquisition of clear OCT and/or fundus images.

2.2 Research Methodology

The main surgical steps were as follows: (1) routine 23G vitrectomy to remove the vitreous body; (2) indocyanine green staining the internal limiting membrane, peeling the internal limiting membrane within the range of the vascular arch (or the ERM if present); (3) gas-liquid exchange, and sterile air filling the vitreous chamber. For those with obvious lens clouding, cataract extraction + IOL implantation was performed simultaneously. The patient is kept in the downward-facing position after surgery, and the duration of this position is determined by the absorption of gas in the vitreous cavity, usually for 5-7 days.

The degree of traction, atrophy, and choroidal neovascularization in different MF eyes was evaluated according to the ATN classification of highly myopic maculopathy[1, 2]. On the basis of the ATN classification, MF eyes were classified as mild or severe according to the severity of MF[1, 9].The specific classification and grading methods were as follows: (1) ATN classification: 1) A0: no myopic retinal lesions, A1: tessellated fundus only, A2: diffuse chorioretinal atrophy, A3: patchy chorioretinal atrophy, and A4: complete macular atrophy; 2) T0: no macular schisis, T1: inner or outer foveoschisis or lamellar macular hole, T2: inner +outer foveoschisis, T3: foveal detachment, T4:full-thickness macular hole, T5: macular hole retinal detachment; 3) N0: no myopic CNV;N1:macular lacquer cracks, N2a: active CNV, N2b: Fuchs spot/scar; (2) MF severity grading: if the MF affected eye had an atrophy (A) or a tractional (T) grading of ≥3 or a neovascularization (N) grading of ≥2, then it was defined as severe MF, and the MF affected eyes that did not meet the criteria were defined as mild MF.

The degree of preoperative lens clouding was assigned based on the LOCS III classification system[10] and differences in dioptric system were compared between MF subgroups with different surgical outcomes. Vitreous adhesion, ERM and CFT measurements were based on OCT images of the macula. The CFT was measured from the inner border of the internal limiting membrane to the outer boundary of the retinal pigment epithelium.[11] Postoperative changes in visual acuity were evaluated as follows[12] :The visual acuity at the last follow-up visit was defined as an increase or decrease of ≥0.3 logMAR units from the preoperative level; or it was defined as no change in visual acuity <0.3 logMAR units[1] . The criteria for determining whether the anatomical structure of the macular cleft was restored after surgery were that: reattached: ≥80% reattachment in the extent of the macular retinoschisis after surgery compared with the preoperative period; partially reattached: ≥40% reattachment in the extent of the macular retinoschisis, but <80%; and not reattached: <40% reattachment in the extent of the retinoschisis[13, 14] .

2.3 Statistical Methods

The statistical analyses were performed with SPSS for Windows, version.22.0. The Kolmogorov-Smirnov test was applied to assess whether the data in each group conformed to normal distribution. Continuous variables were expressed as means±standard deviation. For continuous variables that conformed to normality, t-test was applied to compare data between two groups. For continuous variables that did not conform to normality, the rank sum test was applied to compare data between two groups.

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Chi-square test or Fisher exact test was applied to compare differences in rates between subgroups. Logistic regression analysis was applied to assess the correlation between different preoperative parameters and surgical outcomes in eyes with MF. All statistical tests were two-sided tests, and statistical significance was $P < 0.05$.

3. Results

3.1 Clinical Characteristics and Surgical Outcomes of MF Patients

A total of 56 MF patients (61 eyes) were finally included in this study, 12 males (13 eyes) and 44 females (48 eyes), with a mean patient age of 56.39±10.39 (33-75) years. The median follow-up time after surgery was 11 months (6-15 months). Preoperative mean visual acuity in MF eyes was 0.98 ± 0.54, mean CFT was 541.16 ± 100.52 um, and mean axial length was 29.20 ± 1.40 mm. According to the ATN classification system: in the included MF eyes, 22 eyes with atrophy (A) were classified as A1, 23 eyes as A2, 10 eyes as A3, and 6 eyes as A4; 13 eyes with traction (T) was classified as T1 in 13 eyes, T2 in 29 eyes, and T3 in 19 eyes; and neovascularization (N) was classified as N0 in 42 eyes, and N1 in 19 eyes. Among the MF eyes, 26 eyes were classified as severe (with macular atrophy and macular traction in 9 MF eyes meeting the criteria for severe MF), and 35 eyes were classified as mild. Among the included MF eyes, ERM were seen in 12 eyes, vitreous adhesion was seen in 17 eyes, and a total of 7 eyes were IOL eyes before surgery. All MF eyes were successfully operated without intraoperative complications. 46 eyes received cataract extraction combined with IOL implantation. 4 eyes developed transient intraocular pressure and 6 eyes developed transient corneal edema after surgery, and all of these postoperative complications subsided within 24 hours. By the final follow-up, no further macular retinoschisis had progressed in any of the MF eyes, with 12 eyes (19.7%) having a reattached retinoschisis and 33 eyes (54.1%) having a partially reattached retinoschisis. The proportion of eyes with a reattached or partially reattached retinoschisis in eyes with severe and mild MF was 53.8% (14 eyes) and 88.6% (31 eyes). By the time of the final follow-up, there was no further decrease in visual acuity in any of the MF eyes, with 50 eyes (82.0%) having improved visual acuity and 11 eyes (18.0%) having the same visual acuity, and the proportion of MF eyes with improved visual acuity in the eyes with severe and mild MF was 65.4% (17 eyes) and 94.3% (33 eyes), respectively. There was no significant difference in lens clouding LOCS III scores between MF eyes with and without improved postoperative visual acuity ($P_{\text{cortex}} = 0.209$, $P_{\text{nucleus}} = 0.769$, $P_{\text{posterior capsular}} = 0.700$).

3.2 Comparison of Clinical Characteristics of MF Eyes with Different Surgical Outcomes

Compared with MF eyes with improved postoperative visual acuity, MF eyes with unimproved postoperative visual acuity had a longer axial length (P=0.036), with a higher proportion of eyes with severe ATN classification (P=0.004), but the incidence of preoperative vitreous adhesion, ERM and CFTs were not significantly different between the two groups (P>0.05), see Table 1.

Compared with the MF eyes in which the retinoschisis were reattached or partially reattached after surgery, the axial length of the MF eyes in which the retinoschisis were not reattached were longer ($P < 0.001$), with a higher proportion of eyes with a severe ATN classification ($P = 0.003$), but the incidence of preoperative vitreous adhesion, ERM and CFTs did not differ significantly between the two groups ($P > 0.05$), see Table 1.

3.3 Correlation Analysis between Different MF Clinical Characteristics and Surgical Outcomes

To further investigate the correlation between clinical characteristics of MF and surgical efficacy, we sequentially substituted the above indexes with preoperative visual acuity, age, and gender into univariate and multivariate logistic regression analysis models, and the results showed that MF eyes with a severe ATN classification were an independent risk factor for difficulty in improving visual acuity postoperatively (P=0.030, see Table 2), and that a long axial length was an independent risk factor for difficulty in restoring retinoschisis postoperatively independent risk factor (P=0.004, see Table 3). As severe MF was defined in this study based on two factors, atrophy (A) and traction (T), we further compared the strength of the correlation between the above two factors (A and T) and postoperative visual acuity benefit, and the results showed that the presence of preoperative macular atrophy was more correlated with the difficulty in further improvement of visual acuity in the postoperative period ($P=0.013$) compared with macular traction ($P=0.505$).

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Table 1: Comparisons of clinical characteristics between MF groups with different postoperative prognosis

	VA improved	**VA stable**	***P***	**MF reattached or partial reattached**	**MF failed to reattach**	***P***
Vitreous adhesion	28.0% (14/50)	27.2% (3/11)	0.961	22.2% (10/45)	37.5% (6/16)	0.233
ERM	16.0% (8/50)	36.4% (4/11)	0.124	20.0% (9/45)	18.8% (3/16)	0.914
CFT	537.90±84.57	556.00±159.01	0.593	530.13±88.38	572.19±126.93	0.152
axial length	29.03±1.30	29.99±1.58	**0.036**	28.70±1.12	30.61±1.11	**<0.001**
MF severe MF	34.0% (17/50)	81.8% (9/11)	**0.004**	31.1% (14/45)	75.0% (12/16)	**0.003**

Note: MF, Myopia foveoschisis; ERM, Epi-retinal membrane; CFT, Central foveal thickness.

Table 2: Logistic regression analysis evaluating the ability of different parameters to predict visual prognosis of MF eyes

Variable	**Category**	**Univariate analysis**		**Multivariate analysis**	
		OR (95% CI)	***P***	***OR (95% CI)***	***P***
visual acuity	/	1.111 (0.0.333, 3.710)	0.864	5.395 (0.758,38.418)	0.092
sex	male	2.603 (0.626,10.820)	0.188	0.628 (0.122,3.233)	0.578
	female	Ref.		Ref.	
age	/	0.960(0.899,1.025)	0.222	0.975(0.902,1.054)	0.528
Vitreous adhesion	yes	0.964 (0.223,4.167)	0.961	0.262(0.042,1.639)	0.152
	no	Ref.		Ref.	
ERM	yes	1.969 (0.428,8.067)	0.385	4.208 (0.725,24.412)	0.109
	no	Ref.		Ref.	
MF severity	severe	8.735 (1.694, 45.036)	0.010	10.446 (1.255, 86.929)	**0.030**
	non-severe	Ref		Ref	
CFT	/	1.002(0.995,1.008)	0.587	0.996(0.989,1.003)	0.223
axial length	/	1.699 (1.014, 2.845)	0.044	1.568 (0.821,2.995)	0.173

Note: MF, Myopia foveoschisis; ERM, Epi-retinal membrane; CFT, Central foveal thickness.

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Table 3: Logistic regression analysis evaluating the ability of different parameters to predict anatomical prognosis of MF eyes

Variable	Category	Univariate analysis		Multivariate analysis	
		OR (95% CI)	***P***	***OR (95% CI)***	***P***
visual acuity	/	3.422 (1.118,10.473)	0.031	1.840 (0.305,11.091)	0.506
sex	male	3.257 (0.893,11.879)	0.074	3.560 (0.402,31.554)	0.254
	female	Ref.		Ref.	
age	/	0.975(0.922,1.031)	0.379	0.968 (0.892,1.049)	0.426
vitreous adhesion	yes	2.722 (0.810,9.149)	0.105	0.974 (0.085,11.227)	0.983
	no	Ref.		Ref.	
ERM	yes	1.067 (0.245,4.641)	0.931	1.640 (0.148,18.124)	0.686
	no	Ref.		Ref.	
MF severity	severe	6.643 (1.818, 24.270)	0.004	2.603 (0.283, 23.959)	0.398
	non-severe	Ref		Ref	
CFT	/	1.004(0.998,1.010)	0.159	1.003 (0.994,1.012)	0.507
axial length	/	5.605 (2.203, 14.260)	<0.001	6.289 (1.795,22.036)	**0.004**

Note: MF, Myopia foveoschisis; ERM, Epi-retinal membrane; CFT, Central foveal thicknes

4. Discussion

With this study, we found that vitrectomy is safe and effective for most patients with MF, and that eyes with MF whose preoperative MF condition is graded as severe are likely to have poor postoperative visual acuity enhancement. The longer the axial length of the eye in the eye with MF, the greater the risk that the retinoschisis will be difficult to reattach postoperatively.

The ATN classification system is a new classification proposed by researchers in recent years for highly myopic macular lesion[2]. Unlike the old classification, the ATN classification system is a more comprehensive way of evaluating myopic macular lesion[2, 15]. Since the introduction of the ATN classification system, many studies have evaluated its value in the assessment of high myopia, and the superiority of the ATN evaluation system has been demonstrated in many different types of myopic macular lesion[1, 15, 16] . Based on the ATN classification, Fang D et al. proposed a method for grading MF, which differentiated MF into mild and severe based on the ATN macular atrophy, traction and neovascularization classifications[1] . In the same way as previous studies[1], in this study, we also found some differences in surgical efficacy between eyes with mild and severe MF, with eyes with severe MF having a lower likelihood of postoperative visual acuity improvement and a greater risk of incomplete reattachment of the foveoschisis postoperatively compared with eyes with mild MF. On this basis, we analyzed the correlation between preoperative mild and severe MF grading and vitrectomy efficacy in eyes with MF by applying a multifactorial regression model. The results showed that severe MF was an

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independent risk factor for postoperative visual acuity improvement in eyes with MF, and among the two factors of macular atrophy and traction on the basis of the severe MF grading, macular atrophy was more associated with postoperative visual acuity improvement.

Several studies[17,18] have shown that macular atrophy causes the most severe degree of central vision loss among the pathologic changes in the fundus caused by high myopia. According to the ATN classification system, A4 complete macular atrophy as the final stage of atrophic lesions can be caused by the late progression of A3 patchy choroidal atrophy involving the central concave or by choroidal retinal atrophy due to the regression of macular neovascularization (MNV), whereas most of the A4 progresses from MNV[19]. There is no effective treatment for old MNV and macular atrophy, so preventing further progression of MNV to atrophic lesions is important for preserving vision in patients with high myopia. In addition, MNV-associated macular atrophy generally does not occur in eyes with complete disappearance of MNV, and visual acuity can be maintained well[20] . In addition, anti-VEGF therapy, as the first-line treatment for MNV, has a clear efficacy and safety profile, suggesting that patients with high myopia with MNV should be treated early and aggressively.

Vitreous adhesion and the ERM are common ocular concomitant manifestations in eyes with MF, and several previous studies have suggested that vitreous adhesion and the ERM are involved in the pathogenesis of MF through the application of shear forces to the retina at the site of adhesion[3, 21-23] . However, unlike many of the other causative factors of MF, the effects of vitreous adhesion and ERM on the retina are to some extent temporary, and the retinoschisis induced by these factors may resolve spontaneously as the adhesion is released or the tension is reduced. Several studies have observed self-resetting of MF after vitreous adhesion detachment or ERM breaks in patients with MF[4, 24-26]. The phenomenon of vitreous adhesion detachment has been observed in several studies in MF patients. This phenomenon not only suggests the immediacy of the effects of vitreous adhesion and ERM, but also suggests that in some eyes with MF, the damage to retinal tissue caused by vitreous adhesion and ERM may be mild and reversible. In contrast, in the present study, we did not find a significant correlation between vitreous adhesion or ERM and surgical outcomes in eyes with MF. Further histologic studies in the future will help to reveal the mechanisms of vitreous adhesion and ERM in the pathogenesis of MF.

The thickness of the fovea is an important indicator of macular disease, and changes in the thickness of it are associated with the condition and prognosis of most macular diseases[27, 28]. However, we did not find a significant correlation between preoperative CFT and surgical outcomes in MF patients in this study. Compared with other macular diseases such as wet macular degeneration and diabetic macular edema, the lesion characteristics of MF are somewhat unique. Histologically, many MF eyes show only elongated henle fibers[29], with no or minimal tissue fracture.[21, 29] This histologic feature of MF dictates that an increase in CFT may not accurately reflect the true damage in MF eyes within the range of henle fiber tolerance. This may account for the weak correlation between CFT and MF treatment outcome.

The increase in the ocular axis is the initial factor in the development of MF and is the pathologic basis for choroidal atrophy and retinal traction[2, 4] . For the MF eyes in this study, the primary surgical procedure was vitrectomy and peeled the internal limiting membrane; therefore, the ocular axial length was the only major indicator of MF that did not change from the preoperative period. In the between-group comparisons, we found significant axial differences between MF eyes with different anatomical gains, and subsequent univariate and multivariate regression analyses indicated that a long axial length was an independent risk factor for difficult resetting of the macular schisis in MF eyes after surgery. This result suggests that failure to improve posterior scleral staphyloma may account for the difficulty in reattaching the retinoschisis after vitrectomy in these MF eyes, and future exploration of vitrectomy combined with posterior scleral reinforcement surgery may improve outcomes in this subset of MF eyes.

This study has certain limitations: (1) the sample size of this study is relatively small, thus making it difficult to draw more definitive conclusions from this study alone, but even so, this study provides a research framework for future prospective studies with large samples; (2) the postoperative follow-up period of the patients in this study is relatively short; (3) this study is retrospective, thus making it difficult to avoid the inherent shortcomings of retrospective studies.

From this study we conclude that vitrectomy is safe and effective for most patients with MF. Preoperative grading of the condition as severe and long ocular axis are factors associated with relatively poor surgical outcomes in patients with MF.

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Author contributions

All authors have designed the study, developed the methodology, performed the analysis, and written the manuscript. All authors have read and agreed to the published version of the manuscript.

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