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Comparison of effectiveness between complete internal limiting membrane peeling and internal limiting membrane peeling with preservation of the central fovea in combination with 25G vitrectomy for the treatment of high myopic foveoschisis

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Abstract

Vitrectomy combined with internal limiting membrane peeling (ILMP) treats high myopic foveoschisis with good results, but there is a risk of iatrogenic macular holes, which may be reduced by preserving the internal limiting membrane of the central fovea. This study compared complete ILMP with partial ILMP, both combined with 25G vitrectomy, for the treatment of high myopic foveoschisis.

Thirty-three cases (33 eyes) of high myopic foveoschisis were retrospectively analyzed. They underwent 25G vitrectomy combined with C_3F_8 gas filling; Group A (20 patients, 20 eyes) underwent complete ILMP, while Group B (13 patients, 13 eyes) underwent partial ILMP to preserve the internal limiting membrane of the central fovea. Patients were followed up for 6 months and underwent best corrected visual acuity (BCVA), intraocular pressure, diopter, slit lamp microscopy, indirect ophthalmoscope, A-mode and/or B-mode ultrasound, and optical coherence tomography. Surgical complications were recorded.

Up to the last follow-up, the BCVA improved and central fovea thickness (CFT) was lower compared with before surgery in both groups (All $P < .05$). There were no significant differences in BCVA and CFT at each time point between the groups ($P > .05$). Most of the postoperative retinas of the 2 groups were completely reattached, with disappearance of the macular retinoschisis cavity. Two patients in the Group A and none in the Group B developed a macular hole during follow-up ($P = .508$).

The results did not support the superiority of partial ILMP over complete ILMP in reduced incidence of macular hole. Both methods had a similar curative effect.

Abbreviations: BCVA = best corrected visual acuity, CFT = central fovea thickness, ILMP = internal limiting membrane peeling, IOP = intraocular pressure, LSD = least significant difference, OCT = optical coherence tomography, SD = standard deviation.

Keywords: fovea centralis, myopia, treatment outcome, vitrectomy

1. Introduction

High myopic foveoschisis is considered as one of the major reasons for decreased visual acuity due to high myopia. The incidence of high myopic foveoschisis is about 9% to 34%.[1–5] The mechanism of high myopic foveoschisis is unclear, but progressive expansion of the posterior sclera, retinal, and choroidal macula atrophy, and traction of the retinal inner limiting membrane and posterior vitreous cortex may be reasons for its occurrence.[6–8]

During the natural course, macular retinoschisis may result in severe complications, such as central foveal retinal detachment, epimacular membrane, macular hole, and rhegmatogenous retinal detachment, which leads to a severe decline in visual acuity. Approximately one-half of patients with high myopia and retinoschisis develop a macular hole or retinal detachment within 2 years.[7] Hence, surgical intervention is particularly important.

Clinically, the surgical approach for high myopic foveoschisis is vitrectomy combined with internal limiting membrane peeling (ILMP), which achieves good results. Peeling of the internal limiting membrane aims to ensure the complete removal of the internal limiting membrane with weakened elasticity, as well as the collagen, cell components, and anterior membrane structure on its surface, hereby to thoroughly release the traction to the macula, as well as to reduce the occurrence of an epimacular membrane.[9,10] Nevertheless, due to the thin retina in macular retinoschisis, the peeling process is likely to cause iatrogenic

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holes, and leads to severe impairment of visual acuity. Therefore, some authors do not advocate peeling the inner limiting membrane.[11] The incidence of a macular hole after vitrectomy combined with ILMP has been reported to be 7.5% to 21.4%.[12–16]

To reduce some of the complications caused by ILMP, methods to preserve the internal limiting membrane of the central fovea while stripping the remaining part of the internal limiting membrane in the posterior pole have been suggested and achieved good outcomes.[17–20] Nevertheless, to date only a small number of patients treated with partial ILMP have been presented, and more data is needed to fully investigate this method. The aim of this study was to compare the 2 methods of ILMP to provide information to support the optimal surgical treatment of high myopic foveoschisis. We retrospectively analyzed the data of 2 groups of patients with high myopic foveoschisis. The internal limiting membrane was completely stripped in 1 group, while the internal limiting membrane of the central fovea was retained in the other group. Both groups underwent 25G vitrectomy combined with C_3F_8 gas filling. The postoperative best corrected visual acuity (BCVA), central fovea thickness (CFT), and surgical complications were observed.

2. Subjects and methods

2.1. Patients

Between October 2014 and May 2016, patients with high myopic foveoschisis who underwent 25G vitrectomy combined with ILMP in the Department of Fundus Surgery, Hebei Eye Hospital were retrospectively analyzed. The inclusion criteria (and indications for surgery) were: diopter > -6.00 D or ocular axial length >26.00 mm; visual acuity (log of the minimum angle of resolution [LogMAR]) >0.7, which decreased significantly or obvious metamorphopsia appeared recently; and macular retinoschisis shown by optical coherence tomography (OCT). The exclusion criteria were: macular hole; choroidal neovascularization; history of photocoagulation in the macular region; or accompanied with other retinopathies. This study was approved by the ethics committee of Hebei Eye Hospital (No. 2014C003). Informed consent was waived by the committee because of the retrospective nature of the study.

2.2. Data collection

Demographic data (age and gender) of all patients were obtained from their medical records. Preoperatively, they underwent BCVA, intraocular pressure (IOP), diopter, slit lamp microscopy, indirect ophthalmoscope, A-mode and/or B-mode ultrasound, and OCT examinations. BCVA referred to converting Snellen chart into logMAR. A-mode ultrasound was used to measure the ocular axial length. OCT was used to measure the CFT, which referred to the distance from the retinal neurepithelium layer to the retinal pigment epithelium layer.

2.3. Surgical procedure

According to whether the internal limiting membrane of the central fovea was preserved in the surgery, patients were divided into Groups A and B: Group A included patients who underwent vitrectomy combined with complete ILMP, while Group B included patients who underwent vitrectomy combined with ILMP with preservation of the internal limiting membrane of the central fovea.

There are no differences in the indications for the 2 surgeries. The patients selected the surgery voluntarily after a comprehensive discussion with the surgeon. Surgeries were also performed for the patients who only had high myopic foveoschisis and no retinal detachment or macular hole. All surgeries were performed by the same chief surgeon in fundus surgery. Patients were placed in the supine position, given compound phenylephrine hydrochloride eye drops (Hebei Eye Hospital) to dilate their pupils, and received 2 mL retrobulbar anesthesia of lidocaine combined with bupivacaine (1:1), followed by standard 3-incision microinvasive pars-plana vitrectomy with a 25G vitreous cutter. During the surgery, posterior detachment of the vitreous humor was made, followed by the removal of the vitreous humor and its posterior cortex with the assistance of triamcinolone acetonide (Laboratorio Italiano Biochimico Farmaceutico Lisapharma S.P.A., Italy). Subsequently, in Group A, the macular internal limiting membrane was stripped under brilliant blue staining, with a scope of the upper and lower hemal arches in the macular area. In Group B, the internal limiting membrane within the upper and lower hemal arches in the macular area was stripped under brilliant blue staining, while preserving the internal limiting membrane of the central fovea with a size of 1 PD. Patients in both groups were given gas-liquid exchange intraoperatively, and the eye was filled with 16% C_3F_8 gas. Cataract phacoemulsification via clear corneal incision was conducted for the patients with phacoscotasmus, especially central phacoscotasmus. Intraocular lens was implanted for some patients, according to the intraocular lens power measured before surgery. Postoperatively, the patients remained in the prone position for 1 week.

2.4. Follow-up

Outpatient follow-up was performed at postoperative 1, 3, and 6 months using the same equipment and methods as those before surgery. The last follow-up was considered the time point to determine the changes of BCVA and CFT, as well as reattachment of the macular retina in the affected eyes. Complete reattachment referred to a complete anatomical reattachment of the macular retina. Partial reattachment referred to a varying degree of decrease of macular retinoschisis thickness though a complete anatomical reattachment was not achieved. No reattachment meant that there was still macular retinoschisis and the macular retinoschisis thickness was not decreased or even exacerbated. The retinal reattachment rate was the complete reattachment rate plus the partial reattachment rate. During follow-up, epimacular membrane, macular hole, fundus hemorrhage, intraocular infection, hypotony, and other complications were observed.

2.5. Statistical analysis

Statistical analyses were performed using SPSS 16.0 (IBM, Armonk, NY). Continuous variables were expressed as median (range) and were analyzed using the rank-sum test. The Friedman test was used to analyze the parameters before and after surgery within groups. Repeated measures analysis of variance on ranks was adopted to analyze the parameters before and after surgery between the 2 groups. Categorical variables were expressed as frequency (percentage) and the intergroup comparisons were performed using the Fisher exact test. $P < .05$ was considered statistically significant.

3. Results

3.1. Baseline characteristics

A total of 33 patients (33 eyes) were included. Group A consisted of 9 males (9 eyes) and 11 females (11 eyes), with a mean age of

Table 1

Baseline characteristics of the 2 groups.

Characteristic	Group A (n = 20)	Group B (n = 13)	P
Age, y	50.5 (35–63)	51 (36–62)	.985
Gender			.710
Male	9 (45)	5 (38)	
Female	11 (55)	8 (62)	
IOP, mm Hg	15 (11–19)	15 (11–18)	.479
Diopter (D)	16 (8.5–21)	15.5 (9–21)	.768
Ocular axial length, mm	28.95 (26.8–32)	29.3 (27.5–31)	.725
Retinoschisis morphology			.930
Outer layer	12 (60)	8 (62)	
Mixed	8 (40)	5 (38)	
Foveal retinal detachment	8 (40)	6 (46)	.727
Preoperative BCVA (LogMAR)	1.1 (0.8–1.7)	1.1 (0.8–1.7)	.842
Preoperative CFT, μm	530 (412–600)	511 (412–592)	.413
Receiving vitrectomy+cataract surgery	7 (35)	5 (38)	.840

Data are expressed as median (range) or n (%).
BCVA = best corrected visual acuity, CFT = central fovea thickness, IOP = intraocular pressure.

50.1 ± 9.3 years (range, 35–63 years). Group B consisted of 5 males (5 eyes) and 8 females (8 eyes), with a mean age of 50.0 ± 9.6 years (range, 36–62 years). There were no significant differences between the 2 groups in age, gender, IOP, diopter, ocular axial length, BCVA, morphology of macular retinoschisis (outer layer retinoschisis, inner layer retinoschisis, and mixed retinoschisis), number of patients receiving vitrectomy+cataract surgery, and the number of patients accompanied with central foveal retinal detachment ($P > .05$) (Table 1).

3.2. Best corrected visual acuity

The results of the BCVA are shown in Table 2. In both groups, BCVA at each time point after surgery increased, with a significant difference compared with that before surgery ($P < .05$), but did not show significant difference between different time points after surgery ($P > .05$). In addition, there was no significant difference in BCVA at each time point between Groups A and B ($P > .05$).

3.3. Central fovea thickness

The results of CFT are shown in Table 3. In both groups, the CFT at each time point after surgery decreased with significant difference compared with that before surgery ($P < .05$) but did not show significant difference between different time points after surgery ($P > .05$). In addition, there was no significant difference in CFT at each time point between Groups A and B ($P > .05$).

3.4. Reattachment of the foveal retina

Up to the last follow-up, among the 20 eyes in Group A, the foveoschisis completely regressed in 15 eyes (75%), and partially regressed in 3 eyes (15%). Among the 13 eyes in Group B, the foveoschisis completely regressed in 10 eyes (77%), and partially regressed in 3 eyes (23%), in which there was severe posterior staphyloma. There was no significant difference in retinal reattachment rate between the 2 groups ($P = 1.000$) (Table 4). For the 8 patients with preoperative retinal detachment in group

Table 2

BCVA before and after surgery (LogMAR).

Group	N	Before surgery	Postoperative 1 mo	Postoperative 3 mo	Postoperative 6 mo
Group A	20	1.1 (0.8–1.7)	0.9 (0.6–1.1)*	0.9 (0.6–1.1)*	0.9 (0.7–1.2)*
Group B	13	1.1 (0.8–1.7)	1 (0.7–1.2)*	1 (0.7–1.1)*	0.9 (0.6–1.2)*

Data are expressed as median (range).
BCVA = best corrected visual acuity.
* $P < .05$, versus before surgery.
$P > .05$, Group A versus Group B at each time point.

Table 3

CFT before and after surgery (μm).

Group	N	Before surgery	Postoperative 1 mo	Postoperative 3 mo	Postoperative 6 mo
Group A	20	530 (412–600)	317.5 (250–412)*	312 (243–412)*	307 (242–412)*
Group B	13	511 (412–592)	300 (220–432)*	315 (231–432)*	300 (213–432)*

Data are expressed as median (range).
CFT = central fovea thickness.
* $P < .05$, versus before surgery.
$P > .05$, Group A versus Group B at each time point.

Table 4

Clinical data of the 2 groups.

Variable	Group A (n = 20)	Group B (n = 13)	*P*
Reattachment			1.000
Complete reattachment	15 (75)	10 (77)	
Partial reattachment	3 (15)	3 (23)	
No reattachment	2 (10)	0	
Macular hole	2 (10)	0	.508

Data are expressed as n (%).

A, complete reattachment was achieved in 7 patients, while no reattachment was found in 1 patient. For the 6 patients with preoperative retinal detachment in group B, complete reattachment was achieved in 5 patients, and partial reattachment was achieved in 1 patient. There was no difference in retinal reattachment rate in patients with high myopic foveoschisis and preoperative retinal detachment between the 2 groups ($P = 1.000$).

3.5. Complications

During follow-up, 2 cases in Group A developed a macular hole (1 was outer layer retinoschsis and 1 was outer layer retinoschsis with central fovea retinal detachment) (Fig. 1), but no cases developed a macular hole in Group B (Fig. 2); the incidence of macular hole did not show significant difference between the 2 groups ($P = .508$) (Table 4). No cases in either of the 2 groups suffered from retinal detachment, fungus hemorrhage, hypotony, endophthalmitis, or other complications. At postoperative 3 to 7 days, IOP was increased in a total of 4 cases in the 2 groups, which was stabilized after drug treatment.

4. Discussion

The aim of this study was to retrospectively compare the effectiveness and complications of patients with high myopic foveoschisis treated with 25G micro-invasive vitrectomy combined with either complete ILMP or partial ILMP (that preserved the central fovea). The results showed that there was no significant difference in effectiveness or complications between the 2 groups. The results strongly suggest that partial ILMP could be as effective as complete ILMP and this method can be considered for the treatment of high myopic foveoschisis. On the other hand, the results did not support the superiority of partial ILMP over complete ILMP in reduced incidence of macular hole.

The main concern with complete ILMP is the occurrence of macular holes. In this study, a macular hole was found during follow-up in 2 patients (10%) treated with complete ILMP, while in the group treated with partial ILMP, no case showed a macular hole. No patient showed epimacular membrane or tractive retinal detachment due to preservation of internal limiting membrane in the fovea. Nevertheless, there was no statistically significant difference in the incidence of macular hole between the 2 groups ($P = .508$), which we supposed was likely to be due to the small sample size of this study. A study with a larger sample size, a randomized controlled trial, or a meta-analysis could possibly reveal differences in complications between the 2 procedures. Shimada et al[17] conducted a controlled study of 45 patients with myopic foveoschisis combined with macular retinal superficial detachment, including a control group of 30 patients who underwent complete ILMP and a test group of 15 patients who underwent ILMP with preservation of the internal limiting membrane of the central fovea. Their results showed that 5 patients (16.7%) developed a full-thickness macular hole in the control group and none in the test group. Ho et al[18] performed peeling surgery with preservation of the internal limiting membrane of the central fovea in 8 patients with high myopic foveoschisis and did not find any case of macular hole during a 10-month follow-up. Jin et al[19] reported 20 patients who underwent vitrectomy combined with ILMP with preserved internal limiting membrane of the central fovea for the treatment of high myopic foveoschisis, and found no case of macular hole during a nearly 1-year follow-up. Kumar et al[20] used intraoperative OCT to assist their method of center-sparing internal limiting membrane peeling in 9 patients and did not find any full thickness macular hole. Taken together these studies suggest that partial ILMP has fewer risks of a macular hole than complete ILMP.

Since the retinal tissue in the fovea is very thin, especially in the fovea of patients with high myopic foveoschisis, the peeling of internal limiting membrane leads to a high risk of iatrogenic hole and leads to severe impairment of visual acuity. Peeling of the internal limiting membrane while preserving that of the central fovea requires skilled operation and proper methods. At our center and during the study period, internal limiting membrane forceps and a vitreous cutter were used to strip the internal

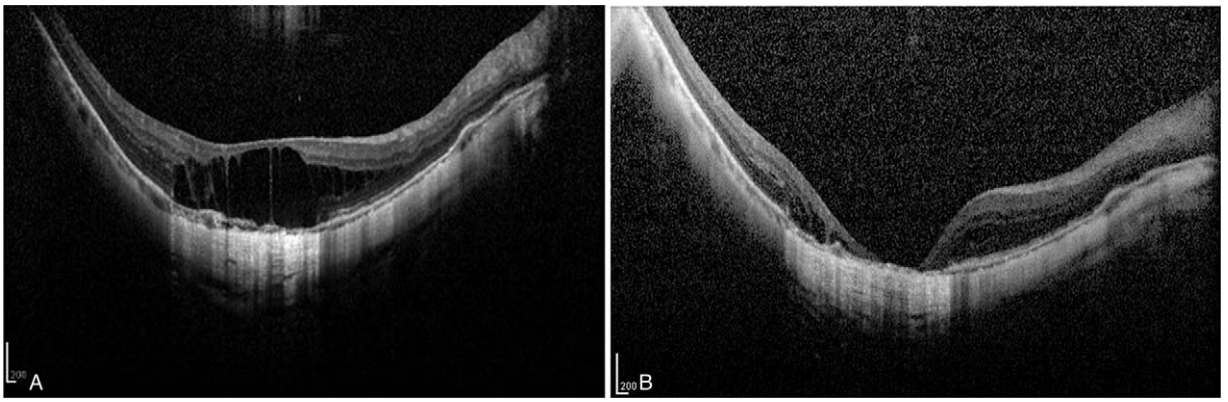

Figure 1. Complete internal limiting membrane peeling for the treatment of high myopic foveoschisis. A, Preoperative optical coherence tomography (OCT). B, OCT at postoperative 1 month: macular retinoschisis was partially improved, with visible macular hole.

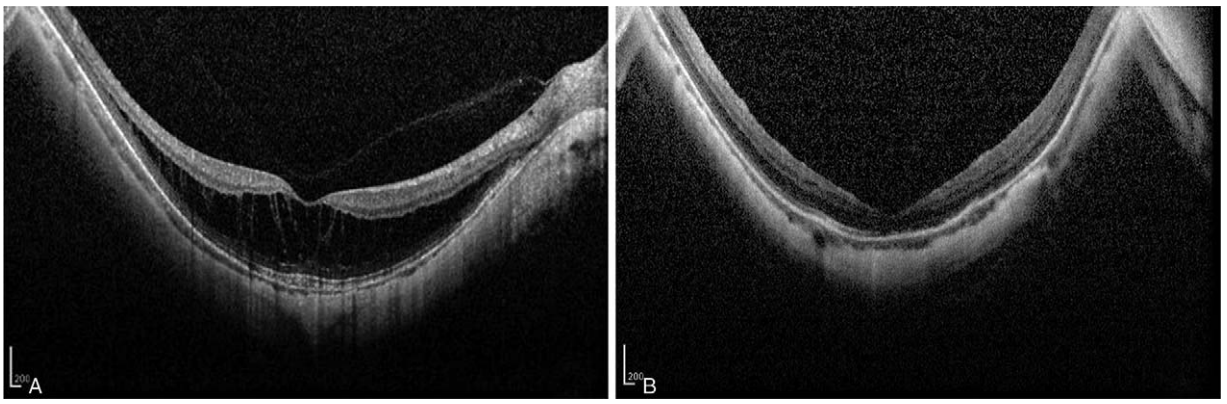

Figure 2. Internal limiting membrane peeling with preservation of the foveal internal limiting membrane for the treatment of high myopic foveoschisis. A, Preoperative optical coherence tomography (OCT). B, OCT at postoperative 6 months: the macular retinoschisis cavity had disappeared.

limiting membrane. The internal limiting membrane in the upper and lower hemal arches were divided into 4 quadrants by taking the fovea as the center, followed by peeling the internal limiting membrane in each quadrant. Firstly, peeling of the internal limiting membrane was started from the bottom section which was distant from the fovea and continued until the stripped internal limiting membrane flap was about 1 PD from the fovea. This peeling process started from a location far from the fovea and was repeated. Then, the stripped internal limiting membrane flaps were cut off using a vitreous cutter and eventually the internal limiting membrane with a size of 1 PD was preserved in the fovea. During the peeling process, only blood spots were visible in the retinal surface, which were automatically stanched without special treatment and complications such as an iatrogenic hole were not found. Nevertheless, this method required multiple rounds of clamping of the internal limiting membrane. Thus, attention should be paid during surgery to avoid extra damage to the internal limiting membrane. In the study by Shimada et al [17], the OCT at postoperative 3 months in the preservation of internal limiting membrane group showed contraction of the internal limiting membrane around the fovea, which manifested as irregular thickening of the internal limiting membrane in the fovea. This thickening of the internal limiting membrane as well as a small intraoperative trauma might be the reason for the absence of macular holes. Although a peeling method that preserves the internal limiting membrane of the central fovea largely protects the foveal retinal tissue, there is a problem to be aware of. As mentioned above, the retained foveal internal limiting membrane tends to contract after surgery. Whether this contraction will ultimately lead to decreased visual acuity, similar to the formation of an epimacular membrane, is subject to long-term observation. In addition, to reduce the contraction of the residual internal limiting membrane in the fovea, Lee et al [21] improved this surgical procedure to further reduce the area of the remaining internal limiting membrane, where only the internal limiting membrane in the caveola was retained, which could not only reduce the incidence of macular hole after vitrectomy, but also reduce the contraction of the remaining internal limiting membrane.

In this study, the postoperative BCVA was improved compared with that before surgery in both groups and the difference was statistically significant. Two patients in Group A developed a macular hole and the resulting decline of visual acuity. For patients who were accompanied by foveal detachment, the preoperative and postoperative visual acuities were poorer compared those who were not accompanied by foveal detachment. The postoperative CFT showed statistically significant difference compared with that before surgery. Most of the retina was completely reattached after surgery, with disappearance of the macular retinoschisis cavity. Patients with partial reattachment had obvious postoperative staphyloma due to a long ocular axial length.

There is controversy over intraoperative ocular fillings. Theoretically, the factors causing high myopic foveoschisis will be delimitated if the vitreous humor is removed and the internal limiting membrane is peeled, and there is no need of gas or silicone oil injection.[16] Kim et al [22] compared 2 groups of eyes receiving or not gas injection and found that there were no significant differences in postoperative visual acuity and anatomic reattachment rate of macular retinoschisis between the 2 groups. Sayanagi et al [23] found that there were no significant differences in the reattachment of macular retinoschisis and improvement of visual function between with and without gas injection after vitrectomy, but the macular structure showed a shorter recovery time in the gas-injection group. Nevertheless, in this study, all patients presented with severe conditions such as significantly decreased visual acuity or obvious metamorphopsia and some of them were accompanied by local retinal detachment. Thus, we selected to fill the vitreous cavity with C_3F_8 gas, so as to fully jack the retina to promote retina reattachment and the disappearance of the macular retinoschisis cavity. Within 3 to 7 days after surgery, 4 patients had an increased IOP, which was stabilized after drug treatment, and no serious complications due to gas filling were found.

The 25G vitrectomy system has a small puncture outlet and the incision is protected by a trocar, which reduces bleeding at the wound as well as dialysis of the retina and other complications. Another advantage is that it does not require the bulbar conjunctiva to be cut and the perfusion is easy to establish with good sealing. After surgery, the catheter can be directly pulled out and there is no need to suture, which alleviates postoperative suture-related inflammatory reactions, leads to insignificant palpebral swelling and conjunctival congestion, simplifies the operation, saves operative time and significantly relieves the foreign body sensation of patients after surgery. In this study, we filled the cavum vitreum with gas, which showed a good tightness of the incision, and there was no case of transient hypotony due to incision leakage.

The limitations of this study included its retrospective nature, which may have introduced some bias into the patient selection into the 2 groups, the small sample size, and the short 6-month follow-up (which is the routine follow-up at this institution). As this was a retrospective study, all consecutive patients that met the selection criteria were included and the number of patients were not balanced between the 2 groups. The patients selected the surgery they preferred after a thorough and comprehensive discussion with their surgeon. There are no differences in the indications for the 2 surgeries and this is probably why the baseline characteristics of the patients in the 2 groups did not differ much. Finally, due to the small sample size, multivariable analyses could not be performed to adjust the variables. The results are subject to confirmation with prospective, large-sample and long-term studies.

In conclusion, 25G vitrectomy combined with ILMP with preservation of foveal internal limiting membrane could be effective for the treatment of high myopic foveoschisis. The results did not support the superiority of partial ILMP over complete ILMP in reduced incidence of macular hole. Both methods had a similar curative effect.

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