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Outcomes of 25-gauge vitrectomy with air tamponade for idiopathic macular hole repair surgery

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25G 玻璃体切除联合空气填充治疗特发性黄斑裂孔

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摘要

目的:观察对于特发性黄斑裂孔行 25G 玻璃体切除联合空气填充治疗后的解剖和视功能结果。

方法:前瞻性干预性分析。27 例(30 眼)特发性黄斑裂孔患者接受 25G 经睫状体平坦部玻璃体切除术,同时行白内障超声乳化抽吸联合人工晶体置入和玻璃体腔无菌空气填充。所有患者在术前和术后 3mo 进行最佳矫正视力(logMAR 视力)、视野检查和多焦视网膜电流图(multifocal electroretinography, mfERG)检查,使用 OCT 明确黄斑裂孔闭合情况。

结果:首次手术后 28 眼的黄斑裂孔闭合,平均 logMAR 视力由术前的 0.72±0.22 提高到术后的 0.29±0.18($P<0.001$)。中心 10°视野检查中,平均偏差(mean deviation, MD)由术前的-3.59±1.83 dB 减少到术后的-2.51±1.36 dB($P<0.001$),平均模式标准差(pattern standard deviation, PSD)由术前的 1.86±0.68 dB 减少到术后的 1.33±0.32 dB($P=0.001$)。MfERG 中可见术后中心凹和旁中心凹区域的平均振幅明显升高,而 4-6 环区域的平均潜伏期明显延长($P<0.05$)。疾病病程长短($P<0.001$)和 1 环区域的术前 N1 波振幅($P=0.001$)对术后最佳矫正视力有预测作用。

结论:特发性黄斑裂孔患者行 25G 玻璃体切除联合空气填充,术后保持 1d 的面向下体位,有很好的解剖成功率和视功能结果。

关键词:特发性黄斑裂孔;玻璃体切除术;空气填充;视野;多焦视网膜电流图

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Abstract

• AIM: To evaluate the anatomic and visual outcomes of 25-gauge vitrectomies combined with air tamponade for the treatment of idiopathic macular hole (IMH).

• METHODS: Thirty eyes of 27 patients with IMH were included in this prospective interventional study. All patients underwent 25-gauge pars plana vitrectomy (PPV) combined with phacoemulsification and air tamponade. Best corrected visual acuity (BCVA, logMAR), perimetry and multifocal electroretinography (mfERG) were conducted before and after the operation. Anatomical changes were evaluated with optical coherence tomography (OCT).

• RESULTS: The macular holes closed successfully in 28 eyes after the primary vitrectomy. The mean BCVA improved from 0.72±0.22 logMAR preoperatively to 0.29±0.18 logMAR postoperatively ($P<0.001$). In the visual field of central 10°, the average mean deviation (MD) decreased from -3.59±1.83 dB preoperatively to -2.51±1.36 dB postoperatively ($P<0.001$) and the average pattern standard deviation (PSD) decreased from 1.86±0.68 dB preoperatively to 1.33±0.32 dB postoperatively ($P=0.001$). The retinal response densities of mfERG in the foveal and perifoveal area increased significantly, and implicit times of rings 4-6 prolonged significantly ($P<0.05$). The symptom duration and baseline N1 amplitude densities at ring 1 had a significant impact on postoperative BCVA ($P<0.001$, $P=0.001$, respectively).

• CONCLUSION: The 25-gauge PPV and air tamponade with 1 day prone positioning produce favorable anatomic and functional outcomes.

• KEYWORDS: idiopathic macular hole; pars plana vitrectomy; air tamponade; perimetry; multifocal electroretinography

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INTRODUCTION

Idiopathic macular hole (IMH) is a full-thickness dehiscence of the neural retinal tissue in the fovea. If left untreated, it often leads to severe central visual impairment, with over a third of patients experiencing a drop in vision to levels of 20/200 or worse[1]. It is believed to originate in a pathologic vitreomacular interface. Despite of many studies on IMH in recent years, the precise pathogenesis of IMH still remains elusive. Evidence from ocular imaging has suggested that firm foveal vitreous adhesion and abnormal vitreomacular traction may constitute the main pathogenic factor[2]. Four stages (1-4) of IMH have been described by Gass[3], often with increasing severity of visual loss as the stage of the hole progresses.

The first report on successful IMH closure by pars plana vitrectomy (PPV) was published in 1991 by Kelly and Wendel[4]. Modifications in vitrectomy instrument have been advocated to improve morphological and functional outcomes, including 23-gauge or 25-gauge vitrectomy with sutureless self-sealing sclerotomies[5-6]. With smaller gauge instruments, there is greater instrument flexibility, allowing reduction of surgical time and postoperative inflammation, and gaining wide acceptance. Currently, the standard surgical procedure for IMH is PPV with peeling of the internal limiting membrane (ILM) and intraocular long-acting gas tamponade, followed by prone positioning for several days. The anatomic closure rate after the first surgical attempt using the aforementioned techniques was around 98%, or even higher[7-8]. However, most patients suffer from discomfort and noncompliance when maintaining the prone positioning for extended periods. Some patients are even unable to maintain a prone positioning.

Assessment of the visual outcomes of IMH repair does not only involve measuring visual acuity. Visual problems due to central retinal dysfunction also include visuospatial distortion and scotoma, which can be better assessed by perimetry and multifocal electroretinography (mfERG)[9]. However, most previous studies on the functional outcomes of IMH repair surgery have concentrated on the development of visual acuity and safety of dye-assisted ILM peeling. In the present study, we performed a 3mo evaluation of the closure rate of IMH after air tamponade with limited postoperative prone positioning for only 1d, and assessed the macular function by visual acuity measurement, perimetry and mfERG, eliminating the influence of dye.

SUBJECTS AND METHODS

In this prospective interventional case series, 30 eyes of 27 consecutive patients underwent 25-gauge PPV and ILM peeling for IMH (stage Ⅱ-Ⅳ of Gass's classification). All surgery was performed at between January 2015 and July 2016. Patients with confirmed diagnosis of full-thickness IMH were considered for inclusion. Exclusion criteria included intraocular pressure (IOP) >21 mmHg, high myopia, traumatic macular holes, visible epiretinal fibrosis, previous cataract or retinal surgery, and any eye or systemic disorders that may impair visual function. The study was performed in accordance with the Declaration of Helsinki and informed consent was obtained from each patient.

The diagnosis and staging of IMH, as well as the anatomic changes postoperatively were made by slit-lamp ocular fundus examination and optical coherence tomography (OCT) (Fourier-Domain Topcon 3D OCT-1000™, Topcon Medical Systems Inc., Paramus, NJ, USA). Retinal function was assessed in all patients preoperatively and postoperatively, over a period of 3mo. Best-corrected visual acuity (BCVA) was measured using a retroilluminated logarithm of the minimum angle of resolution (logMAR) chart (Precision Vision, La Salle, IL, USA) with an initial testing distance of 4 meters, and the BCVA expressed as logMAR units was obtained for statistical analysis. Visual field of central 10° was evaluated using 10-2 Swedish Interactive Threshold Algorithm program (SITA; Humphrey Field Analyzer Ⅱ 750, Carl Zeiss Meditec Inc., Dublin, CA, USA). The visual field reliability criteria included < 20% fixation loss and <20% false positive and false negative rates. The visual field charts were reviewed to compare the mean deviation (MD) and pattern standard deviation (PSD) defects before and after surgery. Other data recorded included the symptom durations and IOP.

Surgical Procedure All surgery was performed by an experienced surgeon (Xian WG). The surgical procedure involved phacoemulsification, intraocular lens implantation and standard sutureless 3-port, 25-gauge PPV using the Alcon (Fort Worth, TX, USA) Constellation 25-gauge vitrectomy system. The posterior hyaloid was detached at the optic disc after core vitrectomy using active aspiration, and a subtotal vitrectomy was then performed. During vitrectomy, a vitreous cutter was set to 2 500 cycles per minute, and its maximum aspiration vacuum was 500 mmHg. The triamcinolone acetonide (TA)-assisted ILM peeling was performed using ILM forceps over a circular area centered of the macular hole and of a diameter of approximately two optic disc diameters. The peripheral retina was checked carefully for any iatrogenic, peripheral retinal breaks, after which a total fluid-air exchange was performed under low air pressure (30 mmHg). After the surgical procedures, the trocars were removed and the conjunctiva was repositioned over the sclerotomy sites. All patients were instructed to maintain a prone position for 1d (no less than 10h).

Multifocal Electroretinography MfERG was evaluated by VERIS Science™ 4.0 (Visual Evoked Response Imaging System, Electro-Diagnostic Imaging, Redwood City, CA, USA). The first-order kernel responses were recorded according to the International Society for Clinical Electrophysiology of Vision guidelines for basic mfERG[10]. Three dimensional topography represented the retinal response density (amplitude per retinal area, nV/deg^2). The rings 1-6 correspond to the fovea, 4, 7, 12, 16, and 22 degrees, respectively[11]. In the average curves, two cursors were placed in the first negative trough-N1, and first

Table 1 The demographic and clinical characteristics of the enrolled subjects

Patient	Age (a)	Gender	Eye	Stage of IMH	Duration (mo)	Preoperative logMAR BCVA	Postoperative logMAR BCVA
1	61	F	OD	3	4	0.9	0.2
2	56	F	OD	4	3	0.9	0.3
3	68	F	OD	4	6	0.8	0.4
4	52	F	OD	3	0.5	0.3	-0.1
5	65	F	OD	2	1	1.0	0.1
6	72	F	OS	4	2	1.0	0.4
7	61	F	OD	4	3	0.7	0.4
8	60	F	OD	3	5	1.0	0.5
9	64	F	OS	2	3	1.0	0.4
10	58	M	OS	2	4	0.4	0.0
11	54	M	OS	3	3	1.0	0.3
12	49	M	OS	2	3	0.4	0.1
13	58	F	OD	2	4	0.8	0.1
14	53	F	OS	2	3	0.8	0.4
15	62	F	OD	2	2	0.5	0.3
16	58	F	OS	3	12	1.0	0.5
17	54	F	OS	3	3	0.6	0.4
18	52	F	OS	2	4	0.5	0.0
19	70	F	OS	4	6	0.7	0.4
20	49	F	OS	3	1	0.3	0.0
21	56	F	OD	2	3	0.6	0.3
22	69	F	OS	4	12	1.0	0.5
23	70	M	OS	3	2	0.6	0.3
24	58	M	OD	2	1	0.8	0.1
25	64	M	OS	4	1	0.6	0.3
26	46	M	OS	2	5	0.6	0.4
27	62	M	OS	4	12	0.8	0.5
28	65	M	OD	4	8	0.6	0.4
29	68	M	OD	2	6	0.9	0.5
30	58	F	OS	3	3	0.5	0.2

IMH: Idiopathic macular hole; BCVA: Best corrected visual acuity; logMAR: Logarithm of the minimum angle of resolution.

positive peak-P1. Amplitude density of N1 was measured from the baseline to the N1 trough. Amplitude density of P1 was measured from the N1 to P1 peak. The implicit times of N1 and P1 were measured from the onset of the stimulation. Before recording, pupils were fully dilated using topical 0.5% tropicamide.

Statistical Analysis Changes in functional (BCVA, perimetry and mfERG) outcomes observed after surgery were compared with baseline values (3mo versus baseline) using the Student's t-test. Bivariate correlation test was used to assess the relationship between postoperative BCVA and the characteristics of IMH. Multiple linear regression analysis of postoperative BCVA was completed, with adjustment for the patient's age, stage of IMH, baseline BCVA, symptom duration and preoperative mfERG results. SPSS V13.0 for Windows software (SPSS, Chicago, IL, USA) was used for statistical analysis. The threshold of statistical significance was set at $P<0.05$.

RESULTS

The demographic and baseline characteristics of the subjects were shown in the Table 1. The mean age of the 27 patients (9 males, 18 females) was 60.2±7.1 (range 46-72) y. The average duration of the 30 eyes from initial onset of symptoms, such as decreased vision or metamorphopsia, to surgery was 4.2±3.2 (range 0.5-12) mo. According to the Gass classification, 12 (40%) cases of stage 2, 9 (30%) cases of stage 3, and 9 (30%) cases of stage 4. There were no remarkable intra-and postoperative complications.

Three months after surgery, the macular holes successfully closed in 28 eyes (Figure 1), and the BCVA increased significantly from 0.72±0.22 logMAR (range 1.0 to 0.3) to 0.29±0.18 logMAR (range 0.5 to -0.1) ($P<0.001$).

In terms of the different stages or symptom durations, stage 2 subjects achieved better BCVA than that of stage 4 (0.23 *vs* 0.40, $P=0.007$); BCVA was better than 0.3 (20/40 in Snellen visual acuity) in 8 (66.7%) subjects of stage 2, while only 2 (22.2%) subjects of stage 4; subjects with shorter durations (<6mo) also achieved better BCVA than those with longer durations (≥6mo) (0.23 *vs* 0.46, $P<0.001$); BCVA was better than 0.3 in 16 (69.6%) subjects of that with shorter durations (<6mo), while all 7 subjects

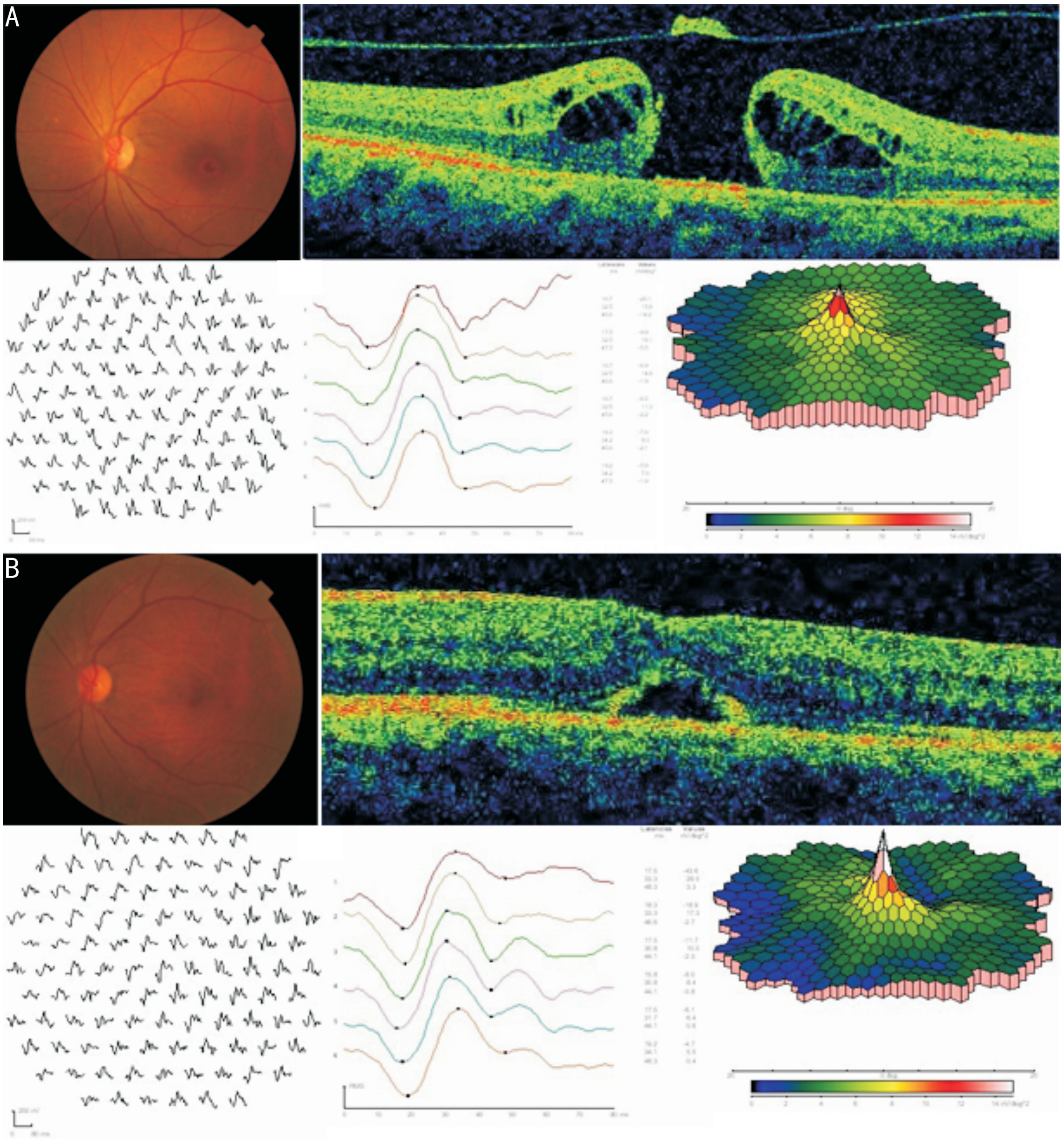

Figure 1 The fundus photograph, optical coherence tomography (OCT) image, and multifocal electroretinography (mfERG) of Patient 30 pre-and post-operatively. The three-dimensional density plots, trace arrays, and ring average of the first-order kernel responses were shown. A: Before IMH repair surgery; B: 3mo after IMH repair surgery. The macular hole closed and the peak amplitude increased significantly at the 3mo follow-up visit. The patient's BCVA improved significantly from 0.5 logMAR to 0.2 logMAR.

with longer durations (≥6mo) had BCVA worse than 0.3. Twenty-four subjects completed the perimetry of central 10°, in which the percentage of significantly depressed points with confidence limits of $P \leqslant 0.05$ and $P \leqslant 0.01$ were calculated. Three months after surgery, the scotoma in the central field decreased or disappeared; the MD significantly decreased from -3.59 ± 1.83 to -2.51 ± 1.36 dB ($P<0.001$) and the PSD significantly decreased from 1.86 ± 0.68 to 1.33 ± 0.32 dB ($P=0.001$). No patients developed a new visual field defect postoperatively. No significant differences regarding the development of MD and PSD were noted in terms of the different stages and symptom durations.

Twenty-eight subjects completed the mfERG tests. The functional outcomes estimated by the mfERG were good, with increased retinal response densities at the fovea and perifoveal area (Figure 2).

The N1 and P1 amplitude densities in area of ring 1 (fovea) and ring 2 (perifoveal area of 4 degrees from the center) both increased significantly ($P<0.001$) 3mo postoperatively. For stage 2 subjects, the preoperative N1 and P1 amplitude densities of ring 1, the postoperative N1 amplitude densities of rings 1-6 and P1 amplitude densities of rings 1-4 were significantly higher than that of stage 4 ($P<0.05$); for stage 3 subjects, the postoperative N1 amplitude densities of rings 2-6 and P1 amplitude densities of rings 2-3 were significantly higher than that of stage 4 ($P<0.05$). For subjects with symptom duration less than 6mo, the preoperative N1 and P1 amplitude densities of rings 3-4, the postoperative N1 amplitude densities of rings 1-6 and P1 amplitude densities of rings 1-4 were significantly higher than that with longer durations (≥6mo) ($P<0.05$). Besides, N1 implicit times were significantly prolonged in area of rings 3-6

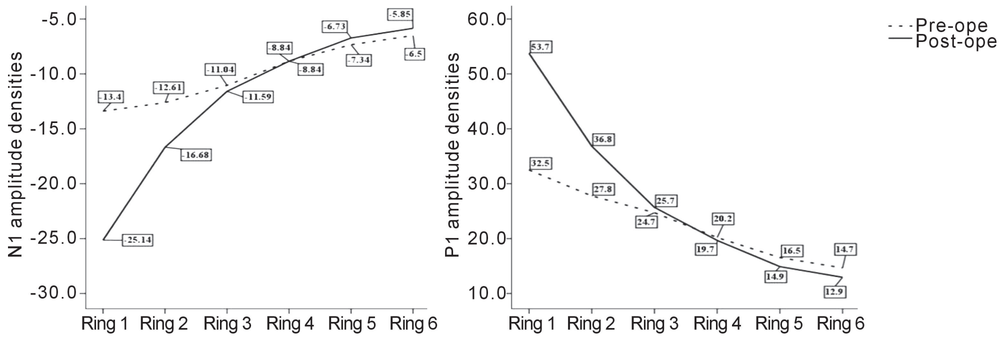

Figure 2　Two line charts showing the mean preoperative N1 and P1 amplitude densities of rings 1-6 and that at the 3mo follow-up visit. The N1 and P1 amplitude densities increase significantly in area of rings 1 and 2 postoperatively ($P<0.05$).

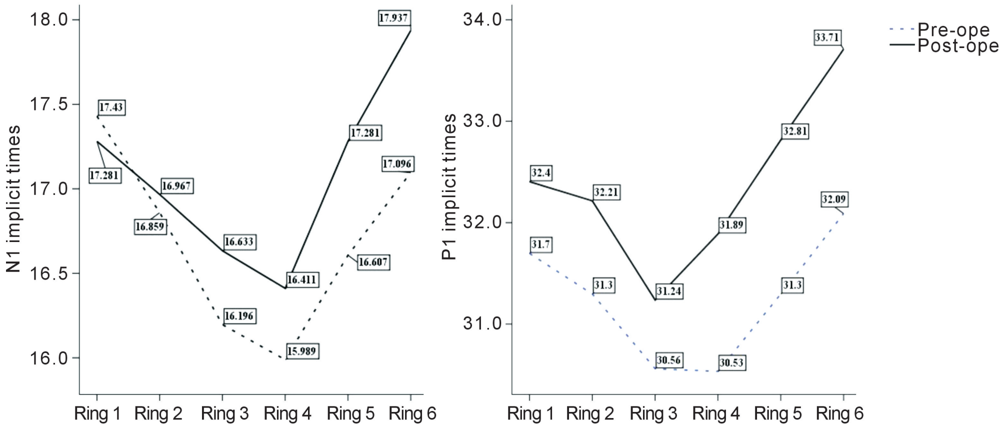

Figure 3　Two line charts showing the mean preoperative N1 and P1 implicit times of rings 1-6 and that at the 3mo follow-up visit. The N1 implicit times prolonged significantly in area of rings 3-6 postoperatively ($P<0.05$). The P1 implicit times prolonged significantly in ring 2 and rings 4-6 ($P<0.05$).

($P<0.05$), and P1 implicit times were significantly prolonged in ring 2 ($P=0.029$) and rings 4-6 postoperatively ($P<0.05$, Figure 3).

Multiple linear regression analysis demonstrated that symptom duration and preoperative N1 amplitude densities of ring 1 had a significant impact on postoperative BCVA (Table 2).

The 16 cases whose postoperative BCVA were better than 0.3 (20/40 in Snellen visual acuity) had shorter durations (2.5mo *vs* 6.1mo, $P=0.002$), better baseline BCVA (0.63 *vs* 0.82, $P=0.018$), higher preoperative N1 amplitude densities of rings 1-3 and P1 amplitude densities of rings 1-5 ($P<0.05$) than those with worse visual acuity. Eight (50%) of the 16 cases were stage 2 and 2 (12.5%) were stage 4. Of the other 14 cases, 4 (28.6%) were stage 2 and 7 (50%) were stage 4.

DISCUSSION

The current study reports some interesting findings about the visual function outcomes after the IMH repair surgery with air tamponade. In this study, most patients showed a satisfactory recovery. The anatomic success rate was 93.3%, and the overall functional results confirmed that this surgical procedure generally leads to favorable visual outcomes.

In the study, the anatomic failure was observed in 2 subjects, both of which were stage 4 and had a symptom for 12mo.

Table 2　Factors associated with postoperative logMAR BCVA

Parameters	B^1	P	95% *CI*
Age	0.067	0.664	-0.007-0.011
Stage of IMH	0.025	0.870	-0.063-0.074
Preoperative logMAR BCVA	0.231	0.165	-0.086-0.469
Symptom duration	0.339	0.027[3]	0.003-0.039
Preoperative N1[2]	0.437	0.011[3]	0.003-0.020

[1]Standardized partial β Coefficient in linear regression models; [2]Preoperative N1 amplitude density of ring 1 in multifocal electroretinography; [3]Significant level is set at the 0.05 level (two-tailed); CI: Confidence interval; IMH: Idiopathic macular hole; BCVA: Best corrected visual acuity.

Advanced stage with relative long symptom duration could hinder the anatomic success of IMH repair surgery. We found that the postoperative logMAR BCVA improved significantly, and 16 eyes (53.3%) achieved 0.3 (20/40 in Snellen visual acuity) or better at the 3mo postoperatively. These results were comparable with those of previously published data[8, 12-13]. A common complication of vitreous surgery in phakic eyes is nuclear sclerotic cataract progression. In this study, all the patients underwent cataract extraction and PPV in the same time, so there is no lens opacity interfering with a reliable measurement of visual acuity.

The central 10° field was reviewed to evaluate the changes of central retinal function. Along with the closure of macular hole and increase in visual acuity, decrease of central field defects and amelioration of metamorphopsia occurred. We did not observe new scotoma in the central field, which could be a complication after ILM peeling[14]. Visual field defects caused by fluid-air exchange is another common complication[15]. In our study, the air pressure was 30 mmHg and the period of time was short, so we speculate that the negative effect was limited. Many studies revealed that the potential toxicity of dyes led to unfavorable visual outcomes such as indocyanine green[16], so the ILM was systematically peeled without dye to eliminate the potential toxic effect on retinal function.

MfERG is an objective method developed by Sutter and Tran[17] which described the changes of retinal function due to regional disorders in the outer retinal layers[18]. It has been used to evaluate retinal function for IMH and proved to be a good measure to observe the functional changes. Apostolopoulos *et al*[9] reported the similar mfERG results, but they only compared areas 1 and 2, which covered about the central 9 degrees of the retina. MfERG demonstrates the macular dysfunction topographically with reduced amplitudes, in which all the six rings were measured and compared according to the distribution of outer retina cells. In our study, we evaluated the changes of mfERG response densities in all the six rings. The findings showed marked decreases in N1 and P1 amplitude densities of rings 1 and 2 preoperatively. These decreases in foveal (ring 1) and perifoveal (ring 2) area seemed to reflect the loss of photoreceptors and retinoschisis or the intraretinal splitting involving perifoveal area. Three months after surgery, the significant increases of N1 and P1 amplitude densities of rings 1-2, along with the improvements in visual acuity, seemed to reflect the closure of the macular hole and the corresponding reattachment of the perifoveal retinoschisis[19]. MfERG response densities in area of rings 3-6 corresponding to 7 to 22 degrees from the fovea were not improved significantly. These observations were consistent with those of previous studies[9,19-20]. According to Hood *et al*[21], the waveform of mfERG can be considered as a combination of ON and OFF-bipolar cell contributions plus smaller contributions from inner retina and photoreceptors. Our findings may demonstrate the elevated electrical activities of the central retina. Restoration of the intraretinal neural network after closure of the macular hole and reattachment of the retinoschisis can promote the increase of retinal electrophysiological responses.

However the implicit times of rings 1-2 did not reduce in the meantime, which may indicate that implicit time is insensitive in assessing retinal dysfunction associated with macular hole. Long-term follow-up is needed to ascertain whether there is permanent prolongation of implicit times. Furthermore, implicit times in outer rings were significantly prolonged, which may suggest the direct damage to the nerve fiber layer caused by ILM peeling and alternation of retinal physiology in the macular region[22]. Symptom duration and preoperative N1 amplitude densities of ring 1 had a significant impact on postoperative BCVA. However, P1 amplitude densities of ring 1 did not affect the postoperative BCVA significantly, which may result from the large variation in P1 amplitude densities of ring 1, since ring 1 contains only a single hexagon[23]. The relationship between mfERG outcomes and visual acuity was not detected in previous studies[9,19], which may be due to the fact that their mfERG test did not detect the two elements of average curves, N1 and P1. Their different estimation may interfere with the final analysis. Further studies are needed to ascertain the relation between mfERG responses and visual acuity outcomes.

There are several limitations to our study. First, since all the patients underwent combined cataract surgery with IMH repair, it may be difficult to interpret the visual acuity improvement absolutely from the IMH closure. Second, the limited follow-up period 3mo may make the functional outcomes less reliable. We need to investigate the anatomic and visual outcomes in these patients with a long-term follow-up.

In summary, the present study shows that 25-gauge PPV and air tamponade with 1d prone positioning lead to favorable anatomic and functional outcomes, suggesting that air tamponade with a short prone positioning period may be sufficient for the closure of IMH, especially the early stage IMH. Our observations also prove that mfERG is of great value for IMH evaluation as a prognostic tool, as well as for postoperative assessment.

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