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A new method of treating macular holes

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PURPOSE. *To evaluate the effect of pars plana vitrectomy (PPV) combined with joining of the hole edges on the closure of full-thickness macular holes.*
METHODS. *In a prospective consecutive clinical trial, standard PPV with internal limiting membrane (ILM) maculorhexis was performed in 25 eyes from 25 patients with stage 3 or 4 idiopathic macular holes (Group A). The retina was massaged gently around the hole from the periphery to the center in order to approximate the edges as closely as possible. The edges of the macular hole were then joined with forceps and gently pressed together. At the end of surgery, air was used for intravitreal tamponade. Patients were required to remain in a face-down position for 1 day postoperatively. For the comparison, a retrospective analysis of outcomes of surgical treatment of 27 eyes of 27 patients with stage 3 to 4 idiopathic macular hole (Group B), whose surgery included standard three-port PPV, followed with ILM peeling, was performed. The closed macular holes were categorized into two patterns based on optical coherence tomography: flat/closed and flat/open.*
RESULTS. *The overall closure rate was 92±5.4% over a minimum follow-up period of 6 months in Group A, and 86±6.2% in Group B. Best-corrected visual acuity improved from 0.1±0.014 (ranged from 0.02 to 0.5) before surgery to 0.29±0.03 (ranged from 0.2 to 0.7) after surgery in Group A, and from 0.1±0.05 (ranged from 0.05 to 0.4) before surgery to 0.22±0.04 (ranged from 0.05 to 0.4) after surgery in Group B. No significant difference was found in absolute light sensitivity of macula, intraocular pressure, or lens opacification. A common postoperative complication in Group A was retinal pigment epitheliopathy, which developed in 18 cases (72%).*
CONCLUSIONS. *Mechanical joining and compression of the retinal edges during surgery for stage 3 or 4 idiopathic macular holes appears to yield a promising anatomic and functional result. (Eur J Ophthalmol 2007; 17: 246-51)*

KEY WORDS. *Macular hole surgery, Optical coherence tomography, Pars plana vitrectomy*

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INTRODUCTION

Full-thickness macular holes are an important cause of central vision loss. Since the initial report of pars plana vitrectomy (PPV) for macular holes in 1991 by Kelly and Wendel (1), vitreous surgery has established itself as the standard treatment for macular holes. Various adjuncts have been used in order to improve the closure rate of macular hole surgery. These adjuncts include intraoperative applications of transforming growth factor-β_2 (TGF-β_2) (2), autologous serum (3) and autologous platelet concentrates (4), laser photocoagulation to the bed of the macular hole (5), and internal limiting membrane (ILM) peeling (6, 7).

Usually this surgery results in glial plug formation, preventing fluid passing into the retina, hole edge attachment to the underlying pigment epithelium layer of the retina, and visual acuity improvement (8). However, glial cells at

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the bed of the hole are incapable of perceiving light.
The aim of the present study was to assess the clinical efficiency of surgical treatment of patients with idiopathic macular holes, the purpose of which was to achieve perfect closure of the macular hole using retinal tissue.

MATERIALS AND METHODS

In a prospective consecutive clinical trial conducted between January 2004 and October 2004 at the Irkutsk Branch of IRTC "Eye Microsurgery," we reviewed 25 eyes from 25 patients (Group A) who had undergone surgery for idiopathic full-thickness macular holes consistent with Stage 3 or 4 according to the classification proposed by Gass (9, 10). For the comparison, a retrospective analysis of outcomes of surgical treatment of 27 eyes of 27 patients with stage 3 or 4 idiopathic macular hole (Group B), whose surgery included standard three-port PPV, followed with internal limiting membrane peeling, was performed.
Before and after surgery all patients underwent ocular examination, including measurements of visual acuity, central visual field using Amsler's test, and automated perimetry by Dicon LD-400, A- and B-ultrasound scanning. The anterior segment, vitreous, and fundus were examined by slit lamp using contact lenses.
A complete ocular examination was performed, including slit-lamp examination, dilated fundus examination, color fundus photography, and optical coherence tomography (OCT). The baseline clinical characteristics of the patients are summarized in Table I.
The majority of patients were women. The macular holes were classified as stage 3 in 14 patients (66%) and stage 4 in 11 patients (44%) in Group A, in comparison to 18 (67%) and 9 (33%) in Group B. The duration of the macular hole symptoms was relatively prolonged. Epiretinal membranes were determined in more than one third of patients, this being an indirect indicator of the long-standing nature of the lesions and of the severity of degenerative retinal changes. The macular hole diameter exceeded 500 μm in all cases. All 52 eyes were phakic before surgery.
Distant best-corrected visual acuity (BCVA) in Group A in 12 patients (48%) was less than 0.1, in 8 patients (32%) it was equal to 0.1, in 3 patients (12%) it was 0.2, and in 2 patients (8%) it was 0.25. Distant BCVA in Group B in 8 cases (30%) was less than 0.1, in 10 (37%) it was equal to 0.1, in 4 patients (15%) it was 0.2, and in 5 patients (18%) it was 0.3.
Patients with myopia greater than 6 diopters, and with traumatic and secondary macular holes, were excluded.
Patients were informed about the purpose of the study and gave their written informed consent. All surgical procedures in this study were performed by the same surgeon (S.A.).
A standard subtotal three-port PPV was performed in all cases. Following core vitrectomy, preretinal vitreous cortex was removed from the retinal surface. In cases with partial vitreous detachment, this was separated from the posterior pole with the vitreotome tip in maximal aspiration mode. Where present, epiretinal membranes were removed using intraocular forceps. After air-fluid exchange, a total of 0.2 mL of 0.5% indocyanine green (ICG) dye solution was injected into the vitreous cavity over the macu-

TABLE I - BASELINE CHARACTERISTICS BEFORE SURGERY

Index	Values	
	Group A	Group B
Number of patients	25	27
Number of eyes	25	27
Age, yr (range)	66.6 (57–78)	65.7 (61–76)
Male, n (%)	3 (12)	3 (11)
Female, n (%)	22 (88)	24 (89)
Macular hole duration, mo (range)	18.7 (10–36)	16.1 (5–24)
BCVA (range)	0.1±0.014 (0.02–0.25)	0.1±0.05 (0.05–0.4)
Axial length, mm	23.2±0.25	22.8±0.17
Macular hole size, μm (range)	638.9±24.95 (552–849)	542.4±38.61 (521–865)
Complete vitreous detachment, n (%)	11 (44)	9 (33)
Epiretinal membranes, n (%)	9 (36)	7 (26)

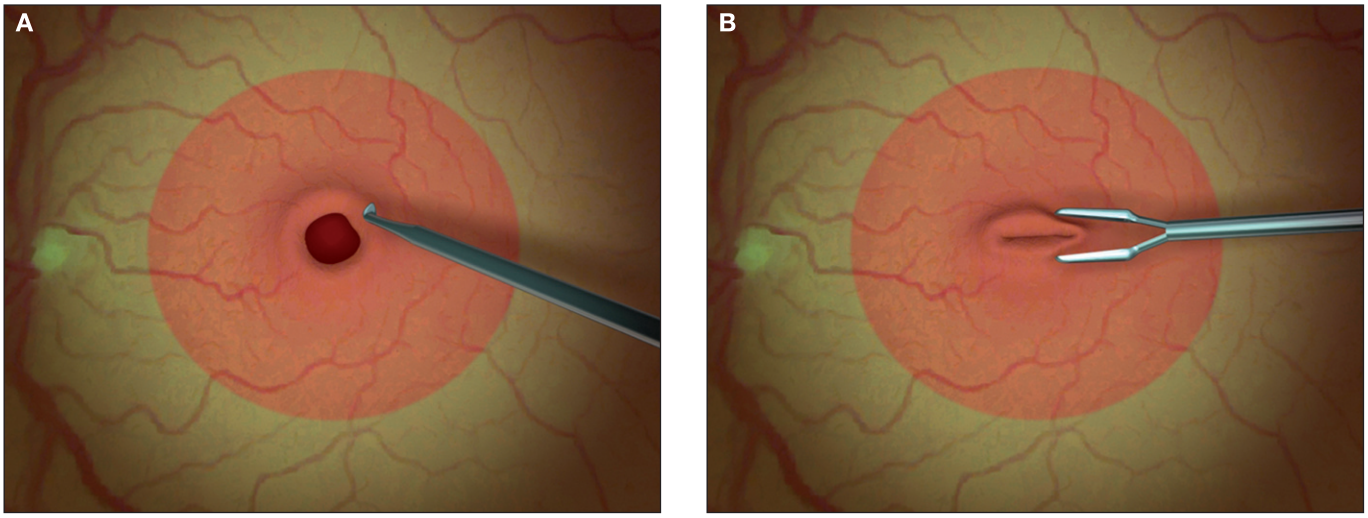

Fig. 1 - *Schematic diagram of the procedure.* **(A)** *A vitreal spatula is used to massage the retina around the hole to minimize its size.* **(B)** *After the edges have been approximated, the opposing hole edges are joined and pressed together to encourage adhesion.*

la. Then ICG was replaced by balanced irrigational solution. Internal limiting membrane (ILM) peeling was performed around the macular hole with forceps. ILM removal mobilizes the retina and facilitates the ensuing steps in the procedure. Then in Group A a spatula was used to smooth the retina around the hole from the periphery to the center. The edges of the macular hole were approximated as closely as possible by gentle manipulation with the retinal spatula, and the hole became smaller or was closed at the end of the procedure (Fig. 1A). In most cases, however, complete closure was not achieved because of the large size of the holes or retinal rigidity. In these circumstances massage was employed to modify the hole contour, first making it oval and then slit-like. With extreme precision, in order to minimize trauma to the retina and pigment epithelium, the edges of the slit-like hole were joined with forceps and then pressed lightly together to provoke aseptic inflammation and stimulate adhesion of contiguous tissues. Complete sealing of the edges of the retinal defect was achieved by several such compressions (Fig. 1B). To ensure the integrity of retinal sealing, it is important to establish the absence of any tendency to dehiscence at the hole edges for 5–10 seconds. At the end of the surgery, sterile air was used for gas tamponade. Patients remained in the face-down position for 1 day postoperatively.

After treatment the patients were reviewed after 1 week and after 1, 3, 6, and 12 months. The minimum follow-up period was 6 months. The postoperative anatomic status of the macular holes was categorized using three defined end-points (elevated/open, flat/open, flat/closed), as suggested by Tornambe et al (11).

RESULTS

The postsurgical characteristics of the patients are summarized in Table II.

Group A

As a result of treatment, a total positive effect (flat/closed and flat/open) was achieved in 23 patients (92%). In this group complete sealing (flat/closed) was recorded in 21 eyes, and attachment of the hole edges with chorioretinal scar formation (flat/open) in 2 eyes. Enlargement of macular holes (elevated/open) was noted in the remaining 2 eyes. In most patients with macular hole closure, ophthalmoscopy confirmed the disappearance of the hole and restoration of the foveal reflex. OCT demonstrated the fine delicate scar at the site where the retinal edges had sealed (Fig. 2).

BCVA was elevated significantly after the procedure to a mean of 0.32±0.03 ($p<0.001$). For 1 month after surgery BCVA remained unstable. Three months after surgery it was sufficiently stable. BCVA was >0.1 in 22 eyes (88 %), and 0.5 in 4 eyes (16 %). The maximum BCVA (0.7) was recorded in one eye. Absolute light sensitivity at zone 30

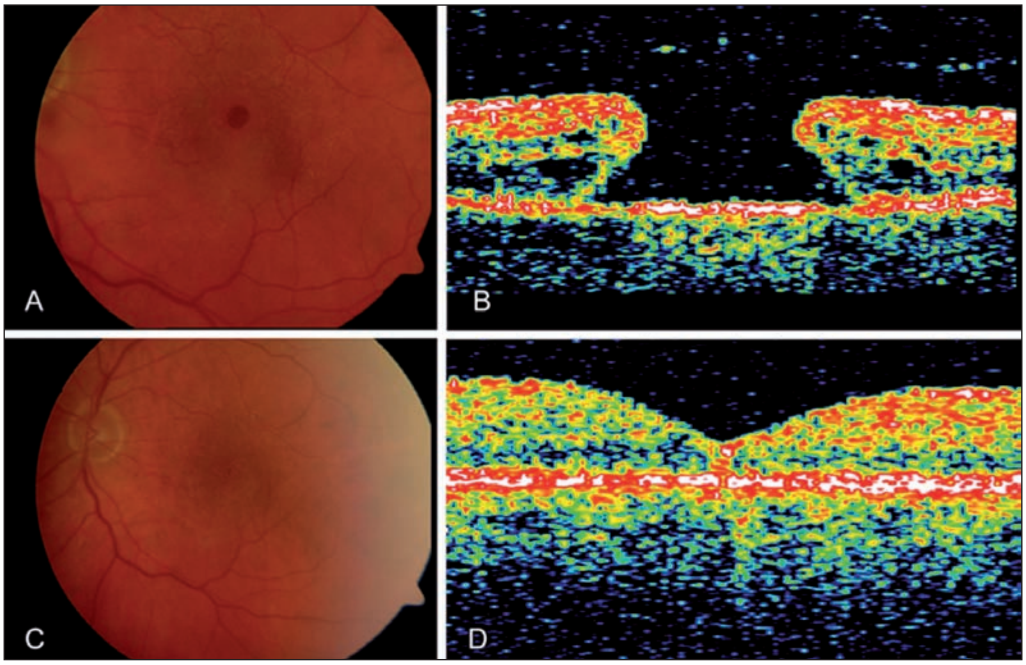

Fig. 2 - *Macula of Patient, 67 years old, stage 4 macular hole before treatment. Duration of symptoms: 24 months.* **(A)** *Photograph of full-thickness macular hole before surgery. Retinal defect at macular center with intraretinal edema around the hole. Complete vitreous detachment.* **(B)** *Optical coherence tomography (OCT) image of the same hole showing full-thickness retinal defect at the center. Hole diameter is 563 µm. Intraretinal edema around full-thickness macular hole.* **(C)** *Photograph of macular area at 3 months after surgery. The hole is invisible. Dyspigmentation is present at the center of the fovea.* **(D)** *OCT image demonstrating complete hole closure. Retinal thickness at the center is increased to 122 µm, fovea at the edge decreased to 169 µm, best-corrected visual acuity 0.5.*

degrees from a point of fixation of the macula (Dicon LD-400, program 7) was a mean 24.2±8.3 dB.

Mean intraocular pressure remained within normal limits (19.6 ± 0.37 mm Hg) and in all cases was consistent with preoperative values. Progression of lens opacification was noted in 3 patients (12%). During the follow-up period two of these patients underwent cataract extraction. Small retinal hemorrhages were noted in 8 eyes (32%) at the site where the forceps gripped the ILM during the maculorhexis procedure. The hemorrhages resolved spontaneously and no functional deterioration was noted.

Group B

Three months after surgery a positive effect was achieved in 24 patients (88%). However, complete sealing (flat/closed) was noted only in 14 eyes. Enlargement of macular holes (elevated/open) was noted in the 3 eyes. BCVA was elevated after treatment to a mean of 0.22±0.04 (p<0.001). BCVA was >0.1 in 18 eyes (67%). The maximum BCVA was 0.4. Mean intraocular pressure was 20.3±0.21 mm Hg. Absolute light sensitivity was a mean 24.6±8.7 dB. Lens opacification was noted in 6 eyes (22%).

DISCUSSION

Initially, the anatomic closure rate in macular hole surgery was 58% (1). At present, postoperative anatomic success rates reported in the literature vary between 86% and 95% (6, 12-14). Brooks has reported 100% macular hole

TABLE II - ANATOMIC AND FUNCTIONAL SUCCESS RATE

Group	Anatomic effect				Functional effect	
	Total positive	**Flat/closed**	**Flat/open**	**Elevated/open**	**Mean BCVA**	**Light sensitivity (dB)**
A	24 (92%)	22 (84%)	2 (8%)	2 (8%)	0.32±0.03	24.2±8.3
B	24 (88%)	14 (52%)	10 (37%)	3 (15%)	0.22±0.04	24.6±8.7

closure following vitrectomy (7). At the same time controversy surrounds both the definition of macular hole closure and the guidelines for treating this condition.

Various adjuncts have also been studied in order to promote glial scar formation that improves closure rates in macular hole surgery. These adjuncts include ILM peeling, intraoperative applications of transforming growth factor-$ß_2$, autologous serum and autologous platelet concentrates, and laser photocoagulation to the retinal pigment epithelium (RPE) in the bed of the macular hole (2-7, 12, 14).

The existing classifications of positive treatment results, i.e., types of closure, suggest that they can be divided into two basic groups:

1. The macular hole is closed without a foveal defect in the neurosensory retina.
2. A foveal defect of the neurosensory retina persists postoperatively although the entire rim of the macular hole is attached to the underlying RPE with flattening of the cuff (11, 15).

It is evident that infill of the hole bed by retinal tissue yields the best functional result. Our method of treatment results in infilling of the hole bed mainly by retinal tissue with resorption of intraretinal edema (Fig. 2). Main condition for macular holes closing is mobility of a retina around holes. ILM peeling provides insufficient mobility, especially in chronic macular hole**s**. The break edges were pulling together by massage and fixed by compression.

The retinal destructive changes in the zone of compression are of minimal extent.

A shorter duration of symptoms is associated with smaller preoperative macular hole size which, in turn, probably results in complete sealing of the macular hole without exposed RPE after surgery. Complete sealing of the macular hole without exposed RPE is associated with better visual acuity and greater visual improvement (16).

According to the literature, postoperative visual acuity depends in many respects on length of time for which the hole has been present (17). Kelly and Wendel noted that the best functional results were obtained when symptoms had been present for less than 6 months (1).

The diameter of the macular holes in our patients was rather large and exceeded 500 µm, and because they had been present for longer than 1 year on average, the holes could be described as chronic. Nevertheless a positive result was achieved in 23 patients (92%). Moreover, in 21 of these complete hole closure was recorded: the hole was no longer visible and OCT demonstrated union of the hole edges and restoration of foveolar indentation. In a further two cases, attachment of the hole edges to RPE was found, with elimination of edema around the hole and infilling of the bed with glial tissue. At the same time OCT demonstrated degenerative changes to the underlying pigment epithelium and choriocapillaries.

Visual acuity was improved in patients with positive results. An inverse dependence was noted between level of visual improvement and degree of dystrophic changes. Thus, in two patients with pigment chorioretinal scarring up to 800 µm in diameter at the site of the macular hole, visual acuity did not exceed 0.1, although retinal edema around the hole subsided.

We agree with the conclusion of Uemoto et al, who showed that postoperative visual acuity does not correlate with macular configuration as evaluated postoperatively by OCT (18). The restoration of the foveolar depression seen on OCT could be due not only to the renewal of near-normal foveal architecture, but also to the formation of a dystrophic area at the site of hole. Therefore attention should focus not just on the presence or absence of a central depression, but also on the degree of restoration of retinal layers, and particularly of the neuroepithelial layer.

Cataract is one of the most frequent complications of macular hole surgery and is encountered in 13–95% of cases (19, 20). The reduced incidence of cataract formation is noteworthy in the patients operated in our series. One of the main causes of cataract formation is prolonged gas blockade of the lens. The method proposed here does not require prolonged gas blockade of the macular hole. Instead it is sufficient to use air.

There have been reports of complications such as endophthalmitis or raised intraocular pressure when different additional agents are used for macular hole blockade (Cohen S. Intraocular djuvants, macular hole surgery, and endophthalmitis. 1998. Vitreous Soc Online J. Available at: http//www.vitreoussociety.org) (21, 22). In an analysis of 11,350 vitrectomies performed for macular holes in the United States, the incidence of endophthalmitis following PPV with autologous blood products was 0.13%. By comparison, the incidence of endophthalmitis following PPV without autologous blood products was 0.01%.

In the series reported here we decided not to insert into the eye any additional agents that might even theoretically cause such complications. The use of air instead of long-standing gas enabled us to reduce patients' time in the face-down position to just 24 hours.

The most frequent and, in our opinion, typical complication encountered with the procedure described here is the development of pigment epitheliopathy in the central macula. Manifestations in the form of separate pigment deposits or areas of dyspigmentation were noted in 18 patients (72%). The phototoxic effect of the light guide and microscope may result in this condition (23). Potential retinal and retinal pigment epithelial damage related to ICG-assisted ILM peeling has been reported (24). However, the mechanical manipulations required for the approximation and joining of the hole edges might also damage the pigment epithelium of the macular retina and produce macular dyspigmentation.

In two cases a positive result was not achieved. In these cases the macular hole and edema remained. We believe these failures were due to inadequate mobilization and approximation of the hole edges during the massage stage, resulting in subsequent dehiscence of the edges.

Absence of significant difference in absolute light sensitivity of macula, intraocular pressure, and lens opacification allows us to conclude that the offered method damages a retina no more than traditional methods of treatment.

Because this was not a randomised study, we are unable to make any conclusive recommendations regarding the use of this technique in macular hole surgery. However, as is evident from the results reported above, the surgical technique developed for Stage 3 and 4 macular hole repair – which involves vitrectomy, ILM peeling, mechanical approximation, and compression of the hole edges in combination with air tamponade – completely closes the macular hole, restores near-normal macular architecture, and improves visual acuity. This procedure results in fewer complications by comparison with other similar surgical techniques.

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