

COMPARISON OF TECHNIQUES: INVERTED FLAP AND CONVENTIONAL INTERNAL LIMITING MEMBRANE REMOVAL IN IDIOPATHIC MACULAR HOLE SURGERY

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SUMMARY

Aim: To compare functional and anatomical outcomes between the inverted flap technique and conventional removal of the internal limiting membrane (ILM) in the surgical management of idiopathic macular hole (IMH).

Material and methods: We retrospectively evaluated the anatomical and functional results in 67 eyes of 65 patients operated on for IMH. The patients were operated on either using the conventional ILM peeling technique (first group) or with the inverted ILM flap technique (second group). 43 eyes of 41 patients were included in the first group, 24 eyes of 24 patients in the second group. We indicated for surgery only patients with IMH stage 2–4 according to the Gasse classification. Best corrected visual acuity (VA) was always determined before and two months after surgery. Furthermore, a comparison of both techniques was made according to the average letter gain after surgery, and the effect of surgery was evaluated using OCT with regard to whether IMH closure succeeded. For both techniques, 25G PPV with SF6 tamponade was performed.

Results: Hole closure took place in 41 eyes with conventional ILM removal. In one eye, the hole did not close even after reoperation with the same technique. Median ETDRS letter gain was 7.0. VA remained the same in 2 eyes (4.7%), worsened in 7 cases (16.2%), and improved in all other cases (79.0%). In 16 eyes (37.2%), VA improved by 2 or more lines of ETDRS charts. Using the inverted flap technique, the hole was closed in all 24 monitored eyes. Median ETDRS letter gain was 9.5. VA remained the same in 2 eyes (8.3%), worsened in 2 cases (8.3%), and improved in all other cases (83.3%). In 12 eyes (50.0%), VA improved by 2 or more lines of ETDRS charts. There were no serious complications intraoperatively or postoperatively.

Conclusion: Our study demonstrated the safety and efficacy of both methods. Although the results were not statistically significant, the inverted flap technique recorded a greater ETDRS letter gain (9.5 vs. 7.0) and proportion of closed holes (100% vs. 95.3%) compared to the conventional ILM peeling technique in our set of eyes.

Key words: macular hole, 25-gauge vitrectomy, MLI peeling, inverted flap technique, trypan blue, gas tamponade

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INTRODUCTION

Idiopathic macular hole (IMH) is a concept defining a foveal retinal defect throughout the full thickness from the internal limiting membrane (ILM) up to the outer segments of the photoreceptors, which leads to central scotoma (Fig. 1 and 2). The disease is conditioned by age, and is most often diagnosed between the ages of 60 and 70 years. Women are affected three times more frequently than men [1]. In 11.7% of cases it may occur bilaterally [1]. The risk of development of IMH in the other eye is approximately 9.1% over the course of 6 years [2] and is significantly higher in the case of persistent vitreomacular traction

(VMT) [3]. The incidence of IMH is approximately 7.8 cases per 100 000 of the population per year [1]. The Gass classification divides IMH into 4 stages. In stage 1 the defect is incomplete, the patient is mostly asymptomatic, while in the other stages the defect afflicts the full thickness of the fovea. In stage 2 IMH is less than 400 µm, in stage 3 over 400 µm. In the first three stages VMT persists.

In stage 4 IMH can be of any size, with complete separation of the posterior vitreous membrane. Symptomatic IMH in stage 1 and all IMH in stage 2 are indicated for surgical solution. The gold standard in IMH surgery is suture-free 25G pars plana vitrectomy (PPV) with ILM peeling. The anatomical success rate of IMH surgery is

93–98% [4–6]. Nevertheless, in the case of holes over 400 μm the attained success rate is only 40–80 % [7].

In 2010 Michalewska et al. first described the inverted ILM flap technique for the treatment of large macular holes (MH). They discovered that their technique achieved better anatomical and visual outcomes in comparison with conventional ILM peeling [8]. In recent years several studies have indicated that the inverted ILM flap technique may be more effective for the treatment of large macular holes than conventional ILM peeling [9–11]. In the case of holes of less than 400 μm the results of both techniques are comparable [12,13].

The objective of our study is to compare the functional and anatomical outcomes between the inverted ILM flap technique and conventional ILM peeling on idiopathic macular holes at our center.

MATERIAL AND METHOD

Design of study and characteristics of cohort

We retrospectively evaluated the anatomical and functional results in patients operated on for IMH during the period from December 2019 to January 2024 at the Department of Ophthalmology at the Faculty of Medicine and Dentistry of Palacký University and the University Hospital Olomouc. From December 2019 to January 2023 all the patients were operated on using the technique of conventional ILM peeling (first group), and subsequently up to the end of the observed period only using the inverted flap technique (second group). In total this concerned 67 eyes of 65 patients. The first group included 43 eyes of 41 patients with an average age of 71.1 years (43–85), the second group included 24 eyes of 24 patients with an average age of 70.1 years (59–88). Only patients with stage 2–4 IMH according to the Gass classification were indicated for surgery. Before the operation we examined best corrected visual acuity (VA) on ETDRS charts for each patient. We examined the anterior segment on a slit lamp, and we examined the finding on the posterior segment of the eye biomicroscopically. The performance

of OCT (Heidelberg Spectralis) and measurement of intraocular tension using a noncontact tonometer (TX-20P Full Auto Tonometer) was also a standard component of the examination on each patient. The same spectrum of examination as before surgery was also performed at the postoperative follow-up, which we conducted two months after surgery. We considered a condition in which the edges of the MH were closed to represent anatomical success. Functional success was determined by a gain of ETDRS letters. Patients with secondary types of MH, with stage 1 IMH, advanced glaucomatous optic neuropathy, mature cataract, keratopathy deteriorating VA, and intermediate and advanced age-related macular degeneration were excluded from the study.

Surgical technique

The patients were operated on by a single surgeon (MH) with the aid of suture-free 25G PPV. After inserting the trocars transconjunctivally via the pars plana, core vitrectomy was performed, followed by ablation of the posterior vitreous membrane. Peeling of the ILM (and if applicable also any present epiretinal membrane) was performed with the aid of micro-forceps. Trypan blue was used for easier identification of the membranes, applied into the vitreous cavity. The extent of ILM peeling was 2–3 PD (papilla diameter) on average. Using the case of conventional ILM peeling, this was followed by suction of the content of the MH. In the case of the inverted flap technique of ILM removal, the flap from the ILM was left on the edge of the MH, which was not truncated and was not handled further, and no suction of the content of the MH was performed afterwards. Before the end of the procedure, the retinal periphery was checked for the purpose of detecting cracks, with the aid of scleral indentation. In all cases SF6 tamponade was used. All the procedures were performed under retrobulbar anesthesia. After the operation it was recommended that the patients keep their heads in a prone position for 3 days, with the greatest emphasis on maintaining this position for the first 24 hours after surgery.

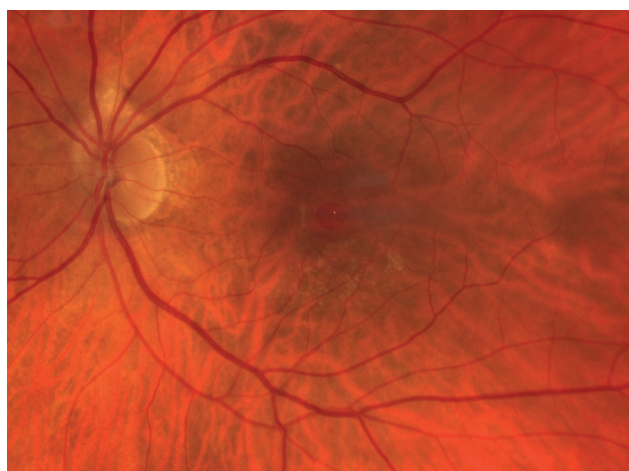


Figure 1. Photo of the macular hole (Zeiss Clarus 700)

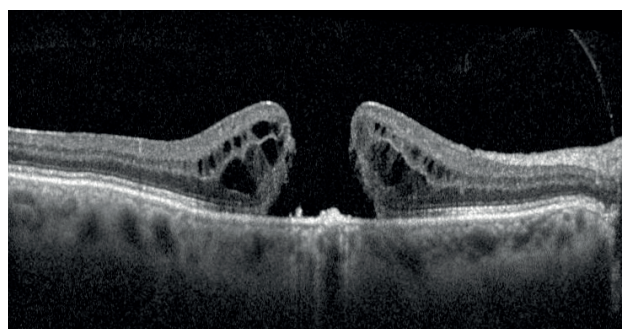


Figure 2. OCT image of the macular hole in the 4th stage (Heidelberg Spectralis OCT)

Statistical analysis

The software IBM SPSS Statistics for Windows, Version 23 (Armonk, NY: IBM Corp.) was used for the data analysis. A Mann-Whitney U test was used for a comparison of the groups according to the type of operation in the quantitative parameters. In the qualitative parameters the groups were compared with the aid of a Fischer's exact test. The normality of data was tested using a Shapiro-Wilk test. All the tests were performed on a level of significance of 0.05.

RESULTS

No significant difference was demonstrated between the groups of patients according to age at the time of surgery, according to size of macular hole (Table 1 and 2), according to sex, laterality of the eye and condition of the lens (Table 3).

Both groups are equal in the above parameters. Anatomical success, namely full closure of MH, was achieved in 41 eyes (95.3%) using the technique of conventional ILM peeling, and in all 24 eyes (100%) operated on using the inverted ILM flap method. No significant difference was demonstrated between the groups of patients in the outcome of the operation (Table 4). An assessment of the functional effect of the operation using the technique of conventional ILM peeling

is presented in Table 5, and using the inverted flap method in Table 6.

In both groups a significant increase in the number of letters was demonstrated after surgery ($p < 0.0001$). In the first group VA remained the same in 2 eyes (4.7%), worsened in 7 cases (16.2%) and improved in all other cases (79.0%). In 16 eyes (37.2%) VA improved by 2 or more rows of ETDRS charts.

In the second group VA remained the same in 2 eyes (8.3%), worsened in 2 cases (8.3%) and improved in all other cases (83.3%). In 12 eyes (50.0%) VA improved by 2 or more rows of ETDRS charts. No significant difference was demonstrated between the groups in the change of the number of letters after surgery (Table 7).

We divided both groups into three subgroups on the basis of the size of MH (small less than 250 μm , medium between 250–400 μm and large over 400 μm), and compared the difference in the gain of ETDRS letters. In all the subgroups the average gain of letters was large in the case of the inverted ILM flap technique, but the results were not statistically significant (Table 8).

At the end of the operation, all sclerotomies were sufficiently sealed and did not require suturing. We have not recorded hypotonia during the postoperative period. We have also not recorded any perioperative or postoperative complications.

Table 1. Comparison of patient groups in age and size of macular hole

	Inverted ILM flap			Conventional ILM peeling			P-value
	Median	Average	Min–max	Median	Average	Min–max	
Age at time of surgery	69.0	70.1	59–88	73.0	71.1	43–85	0.185
Hole size in μm	352	370	128–688	381	377	46–724	0.784

ILM – internal limiting membrane

Table 2. Comparison of patient groups in size of macular hole divided into three categories

		Inverted ILM flap		Conventional ILM peeling		P-value
		Quantity	Percentage	Quantity	Percentage	
Size of MH	Small (under 250 μm)	8	33.3%	14	32.6%	0.997
	Medium (between 250–400 μm)	6	25.0%	11	25.6%	
	Large (over 400 μm)	10	41.7%	18	41.9%	

ILM – internal limiting membrane, MH – macular hole

Table 3. Comparison of patient groups in sex, laterality of eye, and lens status

		Inverted ILM flap		Conventional ILM peeling		P-value
		Quantity	Percentage	Quantity	Percentage	
Sex	Male	7	29.2%	12	27.9%	0.913
	Female	17	70.8%	31	72.1%	
Laterality	OD	9	37.5%	24	55.8%	0.151
	OS	15	62.5%	19	44.2%	
Lens status	Clear	4	16.7%	12	27.9%	0.050
	Cataract	14	58.3%	12	27.9%	
	Arterphakia	6	25.0%	19	44.2%	

ILM – internal limiting membrane, OD – right eye, OS – left eye

DISCUSSION

Kelly et al. demonstrated that an improvement of VA is directly caused by closure of MH [14]. In order to achieve this goal it is necessary to select the best possible available surgical technique for MH on the basis of quality evidence. Conventional ILM peeling was first presented as a new method of rectifying MH by Park et al. in 1999 [15]. Remo-

val of the ILM became an essential surgical procedure in the majority of MH operations. It has enabled a higher probability of closure of MH and reduced the incidence of recurrence [16–18]. Thanks to its effectiveness, the spectrum of indications for treatment of other macular pathologies has been extended [15,19–20]. Nevertheless, in demanding cases such as large MH (> 400 µm) and macular holes associated with high myopia, the surgical outcomes are

Table 4. Comparison of patient groups in anatomical outcomes of surgery

		Inverted ILM flap		Conventional ILM peeling		P-value
		Quantity	Percentage	Quantity	Percentage	
Result of the surgery	Unclosed MH	0	0.0%	2	4.7%	0.533
	Closed MH	24	100.0%	41	95.3%	

ILM – internal limiting membrane, MH – macular hole

Table 5. Assessment of the functional effect of surgery using conventional ILM peeling technique

	Conventional ILM peeling				Wilcoxon signed-rank test p-value
	Median	Average	Minimum	Maximum	
Baseline BCVA in letters of ETDRS	47.0	43.7	2	69	< 0.0001
BCVA in letters of ETDRS after surgery	51.0	52.4	1	75	

ILM – internal limiting membrane, ETDRS – Early Treatment Diabetic Retinopathy Study, BCVA – best-corrected visual acuity

Table 6. Assessment of the functional effect of surgery using inverted ILM flap technique

	Inverted ILM flap				Wilcoxon signed-rank test p-value
	Median	Average	Minimum	Maximum	
Baseline BCVA (ETDRS letters)	45.0	39.9	2	60	0.0001
BCVA after surgery (ETDRS letters)	53.5	51.0	2	77	

ILM – internal limiting membrane, ETDRS – Early Treatment Diabetic Retinopathy Study, BCVA – best-corrected visual acuity

Table 7. Comparison of patient groups in the number of letters of ETDRS before surgery, after surgery, and their difference

BCVA (ETDRS letters)	Inverted ILM flap			Conventional ILM peeling			P-value
	Median	Average	Min–max	Median	Average	Min–max	
Baseline	45.0	39.9	2–60	47.0	43.7	2–69	0.175
After surgery	53.5	51.0	2–77	51.0	52.4	1–75	0.804
Difference after surgery	9.5	11.0	-8 to +27	7.0	8.5	-16 to +48	0.127

ILM – internal limiting membrane, ETDRS – Early Treatment Diabetic Retinopathy Study, BCVA – best-corrected visual acuity

Table 8. Comparison of subgroups of patients in the difference of the number of letters ETDRS after surgery

Difference in BCVA after surgery (letters ETDRS)	Inverted ILM flap			Conventional ILM peeling			P-value
	Median	Average	Min–max	Median	Average	Min–max	
IMH up to 250 µm	9.0	10.5	-1 to +27	9.5	8.0	-16 to +20	0.811
IMH between 250 to 400 µm	13.5	11.2	-8 to +23	1.0	5.3	-4 to +18	0.226
IMH over 400 µm	9.5	11.4	0 to 27	4.5	10.8	-7 to +48	0.401

ILM – membrana limitans interna, IMH – idiopathic macular hole, ETDRS – Early Treatment Diabetic Retinopathy Study, BCVA – best-corrected visual acuity

usually worse. [21]. In these cases there is an endeavor to ensure the most extensive ILM peeling, by which the entire macula can be covered for the purpose of increasing the flexibility of the tissue with the aim of closing the MH. The physiological impacts of excessive peeling have not been fully studied, but evidence exists relating to the anatomical consequences such as damage and shrinkage of the Müller cells, asymmetrical shift of the macula (downwards and/or nasally), thinning of the temporal retina, reduction of the distance between the fovea and the optic nerve, disruption of the optic nerve fiber layer, and microscotomas [8,22–23]. Deterioration of retinal function in the parafoveal region has also been described 3 months after surgery in the sense of extension of the time of leading through the outer retinal layers on ERG [24]. Approximately 10 years later a modified technique of ILM peeling was proposed by the authors Michalewska et al. for the treatment of large macular holes. The trimmed flap of the peeled ILM was left attached to the edges of the hole and folded over its surface. The presumed mechanism of effect is the induction of gliosis of the retina from inside the macular hole by means of the flap of the ILM (serving as “scaffolding”) in order to increase the probability of MH closure. This approach, in addition to removing all the tractional forces from the surface of the retina, enables greater sparing of the ILM and potentially a reduction of certain consequences of extensive peeling [8, 25]. Michalewska et al. state a 98% rate of anatomical success in the case of large MH (> 400 µm) [8]. In the case of holes of less than 400 µm, the results of both techniques are comparable in the international literature [12–13]. Intraocular tamponade and postoperative positioning are of fundamental importance for the closure of MH [6]. No convincing evidence exists that would give preference to long-term acting gas over short-term acting gas in macular hole surgery [26]. In a study conducted by Modi et al., the authors did not find any statistically significant difference in the degree of attained anatomical success, the improvement of postoperative VA and postoperative complications (increase of intraocular pressure, incidence of glaucoma and the formation of visually significant lens opacity) between SF6 and C3F8 tamponade, regardless of the stage, size and length of existence of the hole [26].

Nonetheless, the choice of a long-term acting gas delays visual convalescence by 4–6 weeks after surgery. At our center, in operations for IMH we always choose the short-term acting tamponade SF6. The need for duration of the tamponade still remains unclear, and thus also the need for positioning, which is usually very arduous and unpleasant for the patient [6]. We most often encounter a recommendation for the prone position of the head, for a period of 3–14 days [6,27–28]. At our center the standard procedure is to place patients in the prone position for 3 days. In the case of serious musculoskeletal complaints, we individualize the length of positioning. We do not ordinarily indicate stage 1 MH for a surgical solution unless they are symptomatic. Furthermore, there is a risk of postoperative development of a full defect in this case [6]. In an extensive multicentric study observing the outcomes of PPV

in the case of stage 1 MH, full thickness macular hole developed in 37% of eyes following PPV in comparison with 4% of eyes that were randomized into a group for observation [6,29]. Up to January 2023 we performed IMH surgery only using the technique of conventional ILM peeling. Based on the results of the last studies and international experiences, in which the inverted ILM flap technique has proven to be more effective at least in the case of large holes over 400 µm [9–11], since February 2023 we have switched to the inverted flap technique, which we use to operate on all patients with IMH regardless of its size. In terms of the duration of the operation, safety and the demand factor of performance, our surgeons have not found any significant difference between the two techniques. The objective of this study was to verify our decision regarding preference of the inverted ILM flap technique. The data we obtained point to a greater average gain of ETDRS letters in all size categories of IMH (Table 8) and a greater degree of IMH closure (Table 4) using the inverted flap technique, which supports our decision. However, the results were not significant. The strengths of the study are that all the operations were performed by a single surgeon, examination of best corrected VA before and after the operation was performed by experienced staff and an OCT scan was used to evaluate the success of the operation. On the other hand, the weaknesses of our study were the size of the cohort, the retrospective character of the study, the fact that the patients were not randomized and that manual measurement of the size of the hole was performed on an OCT scan, which may have led to distortion of the size on an individual basis. Both groups also included patients with cataract, which may have reduced postoperative best corrected VA and interfered with the results. In order to reduce this impact on the quality of the study, we compared the percentage representation of various states of the lens (artraphakia, clear lens and cataract) between the groups, and the difference in representation was not significant (Table 3). At the same time, advanced cataracts were operated on before the actual IMH operation. The size of the cohort may have been the cause of the insignificant results. Further clinical research with a more extensive cohort of patients could provide a more definitive answer to the question of which technique is more effective, and in what kind of situation.

CONCLUSION

Our study demonstrated that both methods are safe and effective. In our cohort of patients, a greater average gain of ETDRS letters in all size categories and a greater degree of anatomical success was achieved using the inverted ILM flap technique. However, the results were not statistically significant, probably as a result of the small size of the cohort. Further clinical trials are required in order for us to obtain a definitive answer to the question of which technique is more appropriate for IMH surgery. Our results are comparable with the international literature.

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