Original Article

Multilayered Inverted Internal Limiting Membrane Flap Technique in Optic Disc Pit Maculopathy

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Abstract

Objectives: To evaluate the anatomical and visual outcomes of the multilayered inverted internal limiting membrane (ML-ILM) flap technique in the treatment of optic disc pit maculopathy (ODPM).

Materials and Methods: In this retrospective interventional case series, medical records and macular spectral-domain optical coherence tomography images of patients who underwent combined pars plana vitrectomy with ML-ILM flap surgery for ODPM were analyzed. Best-corrected visual acuity (BCVA) and central macular thickness (CMT) at postoperative 6 months were compared with baseline findings. Intraoperative and postoperative complications, fluid resolution time, and recurrence during follow-up were recorded.

Results: Five eyes of 5 patients with ODPM were included in the study. According to the preoperative macular fluid characteristics, 2 patients had only intraretinal fluid, while 3 patients had intraretinal and subretinal fluid. The preoperative median BCVA was 1.0 logarithm of the minimum angle of resolution (logMAR) (range, 1.0-1.3 logMAR), and the CMT was 560 µm (range, 452-667 µm). At the 6-month postoperative follow-up, the median BCVA was 0.40 logMAR (range, 0.1-0.7 logMAR), and CMT was 315 µm (range, 265-326 µm) (p=0.042 and p=0.043, respectively). During the 6-month follow-up period, no recurrence or full-thickness macular hole formation was observed.

Conclusion: The ML-ILM flap technique is a preferable surgical option to achieve both high anatomical and functional success and flap stabilization.

Keywords: Multilayered inverted internal limiting membrane flap, optic disc pit maculopathy, pars plana vitrectomy

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Introduction

Optic disc pit (ODP) is one of the cavitary anomalies of the optic nerve head and is typically congenital and unilateral.[1] It has been suggested that ODP may develop as a result of herniation of dysplastic primitive retinal tissue within a pocket into the subarachnoid space through a defect in the lamina cribrosa.[2,3] ODP is a rare pathology, with an estimated incidence of 2/10,000, and occurs equally in men and women.[4,5,6] It arises most commonly in the inferotemporal aspect of the optic nerve head.[5] Although ODP is often asymptomatic, 25-75% of patients may develop vision-threatening maculopathy, a condition which is referred to as ODP maculopathy (ODPM) and is characterized by cystoid macular changes and/or serous macular detachment.[7,8] Various techniques have been used in the treatment of ODPM, including peripapillary barrier laser photocoagulation, pars plana vitrectomy (PPV) and posterior vitreous detachment (PVD) induction, gas endotamponade with or without laser, and internal limiting membrane (ILM) peeling, but the results have been controversial.[9,10,11,12] The inverted ILM flap technique was first reported in the treatment of ODPM by Mohammed and Pai[13] and was subsequently adopted by many vitreoretinal surgeons.[14,15,16,17]

In the inverted ILM flap technique, which is frequently used in macular hole surgery, flap separation or rupture may occur due to intraoperative fluid-air exchange or failure to maintain postoperative patient positioning. To prevent these undesirable situations that may result in surgical failure, the multilayered inverted (ML) ILM flap technique was recently introduced and is reported to be effective in the treatment of macular hole.[18,19,20] ODPM patients undergoing ILM flap surgery also face postoperative risks comparable to those associated with the single-layered inverted ILM flap technique. However, to our knowledge there is no previous study evaluating the ML-ILM flap technique in the treatment of ODPM.

This study aimed to evaluate the visual and anatomical outcomes of PPV combined with the ML-ILM flap technique in the management of ODPM.

Materials and Methods

Patient Selection

The medical records of patients who were diagnosed with ODPM confirmed by spectral domain-optical coherence tomography (SD-OCT) in a tertiary ophthalmology clinic between January 2016 and October 2023 and underwent PPV with inverted ILM flap surgery were retrospectively examined. The patients' demographic data, detailed preoperative and postoperative ophthalmological examination findings, and previous macular SD-OCT images were recorded. Patients who underwent ML-ILM flap surgery performed by the same experienced vitreoretinal surgeon were included in the study; those whose surgeries involved techniques other than the ML-ILM flap technique (detailed below) were excluded. Patients with a postoperative follow-up of less than six months and patients with additional ocular or systemic disease that may cause visual impairment were also excluded. The study was conducted in accordance with the principles of the Declaration of Helsinki. Bezmialem Vakıf University Local Ethics Committee approval was obtained for the study (ethics committee decision number: 2024/212-09, date: 15.05.2024) and the written consent of the patients or their legal guardians was on file.

Preoperative Assessment

The best-corrected visual acuities (BCVA), intraocular pressures (IOP), and anterior and posterior segment examination findings on record were noted for all patients. Detailed imaging of the macula was performed with SD-OCT (Spectralis OCT, Heidelberg Engineering, Heidelberg, Germany). Central macular thickness (CMT) was recorded from cross-sectional 25 A-scan SD-OCT images of the macula. The presence of subretinal and/or intraretinal fluid and ellipsoid zone (EZ) integrity were evaluated qualitatively from cross-sectional SD-OCT images.

Surgical Procedure

All surgeries were performed by a single experienced vitreoretinal surgeon (H.Ö.) under general anesthesia, starting with 23-gauge (G) PPV via a standard three-port transconjunctival scleral entry. After central vitrectomy, intravitreal triamcinolone acetonide (KENACORT-A intramuscular/intraarticular retard 40 mg ampule; Deva Holding Inc., İstanbul, Türkiye) was used to induce PVD. The ILM was stained using a dual dye (OCUBLU ILM/ERM Blue, Miray Medical, Bursa, Türkiye). Using 23G Eckhart ILM forceps, at least 3 inverted ILM flaps were created from the area between the fovea and optic disc toward the optic disc head (Figure 1). The ML-ILM flaps were inverted and placed so as to cover the ODP but were not used to plug the pit. The ILM was peeled in an area of two disc diameters around the temporal fovea (Figure 2A). Parts of the inverted ILM flaps that extended beyond the optic disc were trimmed using a vitrector (Figures 2B and 2C). Fluid-air exchange was then performed, taking care not to separate the ILM mound from the optic disc head. During fluid-air exchange, the globe was gently tilted nasally. This allowed the fluid on the retinal surface to be aspirated from nasal to the optic disc using a 23G silicone-tipped backflush needle and the ILM flaps were stabilized over the ODP with air (Figure 3). ILM flap formation and stabilization were done without the use of perfluorocarbon fluid. The surgery concluded with intraocular air tamponade and subconjunctival ceftazidime (ZIDIM 1 g intramuscular/intravenous vial, Tüm Ekip Pharmaceuticals Inc., İstanbul, Türkiye) and dexamethazone (DEKSAMETAZON-PF 8 mg/2 mL solution, Polifarma Medical, Tekirdağ, Türkiye) injection. After extubation, the patients were placed in a lateral lying position according to which eye was operated (left side for the right eye, right side for the left eye) to support the spread of the flaps over the optic disc. Patients were instructed to

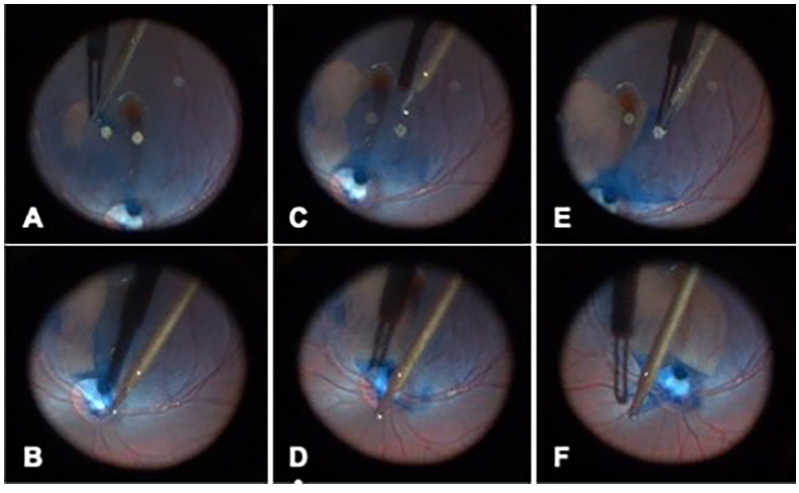

Figure 1. Intraoperative images of a patient with optic disc pity maculopathy showing staining of the internal limiting membrane (ILM) with trypan blue (0.06%) followed by the creation of the inverted multilayered ILM (ML-ILM) flap. Three inverted ML-ILM flaps were made from the macular area between the fovea and optic to the optic pit. Creation of the first flap is shown in images A and B, the second flap in images C and D, and the third flap in images E and F

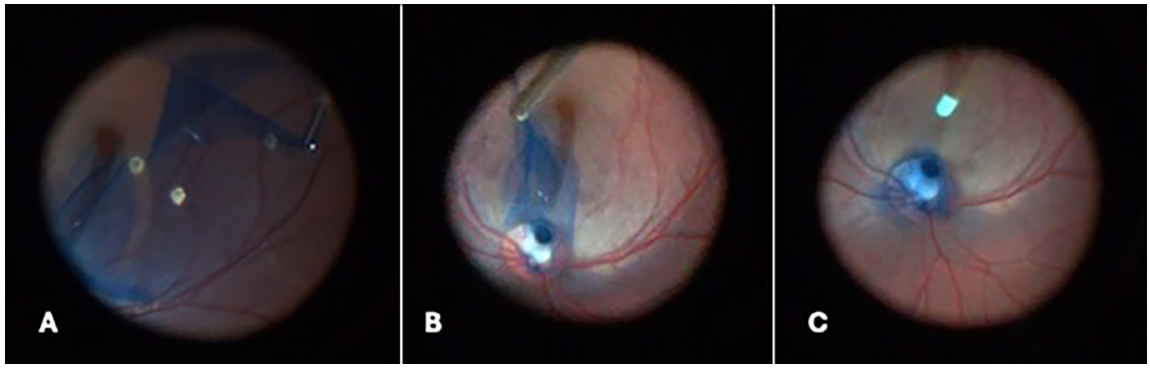

Figure 2. (A) After creating three internal limiting membrane (ILM) flaps, the remaining ILM was peeled between the vascular arcades in the posterior pole without creating a flap. (B) Excess ILM flap extending beyond the optic disc was trimmed using a vitrector. (C) The ILM flaps were stacked over the optic disc using a 23-gauge silicone-tipped backflush needle

maintain this positioning for 2 days postoperatively. All patients were prescribed topical 0.5% moxifloxacin (MOXAI 0.5% eye drops, Abdi İbrahim Medical Inc., İstanbul, Türkiye) and 0.1% dexamethasone (ONADRON SIMPLE 0.1% eye/ear drops, İ.E. Ulagay Medical Inc., İstanbul, Türkiye) 5 times a day for 2 weeks postoperatively. Any intraoperative and early postoperative (within the first 2 weeks) complications were noted.

Postoperative Evaluation

Findings from ophthalmological examinations conducted at postoperative 1 day, 2 weeks, and 1, 3, and 6 months were obtained from patient records. Macular SD-OCT imaging performed at all follow-up visits starting from postoperative 2 weeks was evaluated. BCVA and IOP values, anterior and posterior segment examination findings, CMT, residual macular fluid pattern, EZ integrity, and presence of recurrence at postoperative 1-, 3-, and 6-month follow-ups were recorded (Figure 4).

Statistical Analysis

Statistical analysis was performed using SSPS version 20.0 statistical software (IBM Corp, Armonk, NY, USA). Categorical variables were presented as numbers (percentages) and continuous variables were presented as median (range). Statistical analysis of BCVA was performed by converting Snellen values to logarithm of the minimum angle of resolution (logMAR). For continuous variables, Wilcoxon signed-rank test was used to compare initial findings to those at postoperative 6 months. $P<0.05$ was accepted as statistical significance.

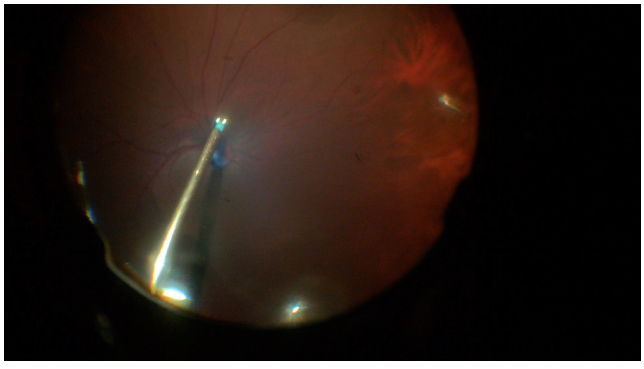

Figure 3. Image of the intraoperative fluid-air exchange phase. The globe was gently tilted nasally and the fluid on the retinal surface was passively aspirated from nasal to the optic disc using a 23-gauge silicone-tipped backflush needle. Thus, the internal limiting membrane flaps were stabilized over the optic disc pit with air

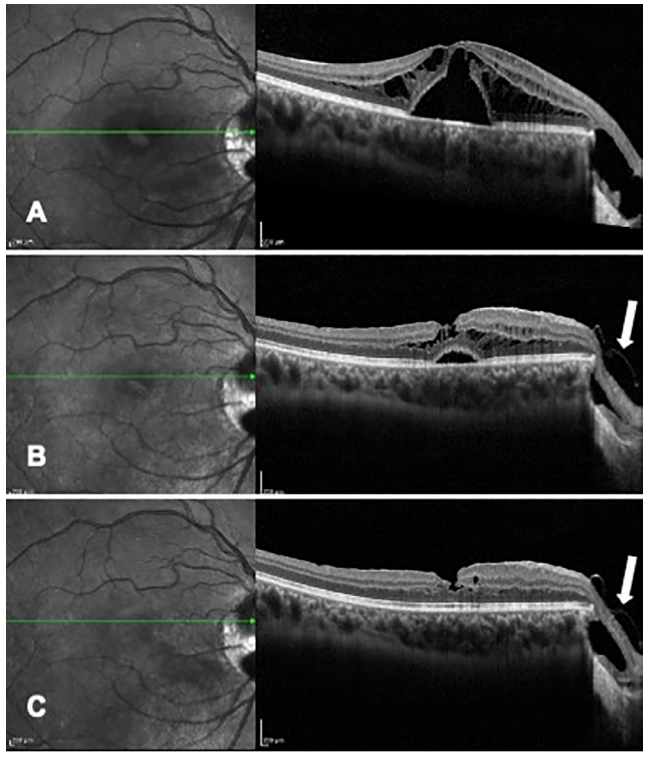

Figure 4. Preoperative and postoperative fovea-centered cross-sectional optical coherence tomography (OCT) images of a patient with optic disc pity maculopathy in the right eye (patient 1, 17-year-old female). (A) Preoperative OCT images. The OCT cross-section shows the coexistence of retinochisis and serous macular detachment (bilaminar fluid pattern). (B) OCT image at postoperative 3 months shows minor intraretinal cystoid spaces with minimal serous macular detachment. In the cross-section, the inverted internal limiting membrane flap (arrow) can be seen over the optic disc. (C) OCT image at postoperative 6 months shows the intraretinal and subretinal fluid have been resorbed and the flap (arrow) remains in situ over the optic disc

Results

Five eyes of 5 patients diagnosed with ODPM who underwent surgery using the ML-ILM flap technique were included in the study. The median age was 29 years (range, 17-34 years), and 3 patients (60%) were female. ODP was located temporal to the optic disc in all cases. Preoperative median BCVA was 1.0 logMAR (range, 1.0-1.3 logMAR) and CMT was 560 µm (range, 452-667 µm). According to the macular fluid characteristics on preoperative SD-OCT imaging, 2 patients had intraretinal fluid only, while 3 patients had both intraretinal and subretinal fluid. At postoperative 6 months, the median BCVA was 0.4 logMAR (range, 0.1-0.7 logMAR) and CMT was 315 µm (range, 265-326 µm) (p=0.042 and p=0.043, respectively). The comparison of the patients' preoperative and postoperative 6-month clinical characteristics is summarized in Table 1. EZ disruption was observed in 3 patients (60%) preoperatively and persisted at postoperative 6 months in 2 patients (40%). No intraretinal or subretinal residual fluid was observed in any patient at 6 months and no recurrence was detected during follow-up. None of the patients had intraoperative or postoperative complications such as cataract or full-thickness macular hole. The demographic and clinical characteristics of all patients are presented in Table 2.

Discussion

Although uncomplicated ODP remains asymptomatic, maculopathy may develop over time and asymptomatic patients should be followed closely for ODPM. Complicated ODP can cause severe visual impairment, warranting an aggressive treatment approach.[5,9,10,11] The main aim of treatment in ODPM is to stop fluid passage to the macular area, which causes visual impairment. Various treatment modalities have been trialed for this purpose.[10,11] However, there is currently no gold standard treatment defined for ODPM. One of the first described treatment modalities was laser photocoagulation of the temporal edge of the ODP, but this approach has been abandoned in recent years because it can cause papillomacular bundle damage, resulting in permanent vision loss.[10] PPV is often preferred in the current management of ODPM.[9,10] The main reason for choosing PPV in ODPM is PVD induction, because traction from the vitreous and posterior hyaloid on the peripapillary and macular area allows fluid ingress through the ODP and can promote separation of the retinal layers, thereby facilitating the passage of fluid into the retina.[21,22,23] Studies in the literature have shown that PPV and posterior hyaloid separation are effective for resolving maculopathy.[23,24] PPV can be performed alone or combined with various techniques such as juxtapapillary laser photocoagulation, radial optic neurotomy, and ILM peeling or flaps.[25,26,27,28] However, a meta-analysis by Zheng et al.[25] failed to demonstrate significant superiority of any of these methods over the others.

It has been noted that ILM peeling may be an important surgical maneuver to ensure the successful resolution of ODPM through eliminating tangential traction on the retina.[29] Marticorena et al.[30] reported a case in which treatment with a second intervention performed after ILM peeling was successful after initial failure with PVD and laser. In a retrospective analysis of patients who underwent PPV and gas tamponade with or without ILM peeling, Skaat et al.[31] reported that serous macular detachment persisted in patients without ILM peeling. In contrast, a recently published multicenter study indicated that ILM peeling did not provide any additional benefit.[32] More recent studies have investigated the idea of covering the ODP with an ILM flap, as used in the treatment of macular holes.[16,33,34] As an autologous physiological tissue, ILM placed over the optic pit can form a permanent barrier that acts as a physiological dam against fluid ingress to the macula through the pit opening, and may induce gliosis and cell proliferation in the ODP cavity.[14,34] Supporting this hypothesis, recent studies have concluded that the inverted ILM flap brings about functional and anatomical restoration and is an effective and safe treatment option for ODPM.[14,15,16,17]

The inverse ILM flap technique is already known to provide successful outcomes in macular hole surgery.[35] However, various flap-related problems can occur in macular hole surgery, such as incorrect ILM flap orientation, flap loss to the cutter probe, and postoperative flap dehiscence. The ML-ILM flap technique was recently introduced as a surgical modification to reduce these risks and has yielded higher rates of anatomical closure compared to standard ILM peeling and PPV.[18,19] In the present case series, we have shown for the first time that the ML-ILM flap technique, which was 100% successful at the end of the 6-month follow-up period, can be used as an effective treatment option in the treatment of ODPM. Unlike the single-layered inverted ILM flap technique previously preferred in the treatment of ODPM, this method is believed to be advantageous

Table 1. Demographic characteristics of the patients and their clinical status at baseline and six months after surgery with the multilayered inverted internal limiting membrane flap technique

	Preoperative median (range)	Postoperative 6 months median (range)	p
Age, years	29 (17-34)		-
Gender, female/male (%)	3 (60%)/2 (40%)		-
BCVA, logMAR	1.0 (1.0-1.3)	0.4 (0.1-0.7)	**0.042***
CMT, µm	560 (452-667)	315 (265-326)	**0.043***
Impaired EZ integrity, n (%)	3 (60%)	2 (40%)	1.000**

*Wilcoxon signed-rank test, **McNemar test, BCVA: Best-corrected visual acuity, logMAR: Logarithm of the minimum angle of resolution, CMT: Central macular thickness, EZ: Ellipsoid zone

Table 2. Demographic and clinical characteristics of the patients

Patient information		Preoperative				Postoperative 1 month				Postoperative 3 months				Postoperative 6 months			
Patient	Age, sex	BCVA	MCT	Retinal fluid	EZ defect	BCVA	MCT	Retinal fluid	EZ defect	BCVA	MCT	Retinal fluid	EZ defect	BCVA	MCT	Retinal fluid	EZ defect
1	17, F	20/400 (1.3)	560	IRF+SRF	+	20/200 (1.0)	385	IRF	+	20/40 (0.3)	335	IRF	-	20/40 (0.3)	326	-	-
2	22, F	20/200 (1.0)	524	IRF	-	20/200 (1.0)	455	IRF	-	20/50 (0.4)	380	IRF	-	20/25 (0.1)	315	-	-
3	34, M	20/200 (1.0)	645	IRF+SRF	+	20/100 (0.7)	486	IRF + SRF	+	20/100 (0.7)	285	IRF	+	20/100 (0.7)	265	-	+
4	30, F	20/400 (1.3)	667	IRF+SRF	+	20/200 (1.0)	385	SRS	+	20/100 (0.7)	345	-	+	20/100 (0.7)	325	-	+
5	29, M	20/200 (1.0)	452	IRF	-	20/200 (1.0)	286	–	-	20/50 (0.4)	288	-	-	20/50 (0.4)	286	-	-

F: Female, M: Male, BCVA: Best-corrected visual acuity (Snellen fraction with corresponding logMAR values in parentheses), CMT: Central macular thickness, EZ: Ellipsoid zone, IRF: Intraretinal fluid, SRF: Subretinal Fluid, -: Absent, +: Present, logMAR: Logarithm of the minimum angle of resolution

in terms of flap stabilization. Previous studies have reported that intraoperative perfluorocarbon fluid, viscoelastic material, and silicone or gas tamponades may be selected for flap stabilization.[36,37] However, the presence of an anatomical orifice in ODP may allow intraocular tamponades to pass into the subretinal, intraretinal, or even intracranial spaces and cause various complications.[38,39,40] As multiple ILM flaps are stacked in the ML-ILM technique, flap stabilization was achieved under air tamponade alone, without the need for gas or silicone tamponade. In addition, perfluorocarbon fluid was specifically avoided when creating flaps to prevent the risk of toxic retinopathy that may occur as a result of perfluorocarbon fluid ingress to the intraretinal space via the cavitary opening.

There are also studies indicating that creating ILM flaps in eyes with ODPM can cause macular hole formation.[41,42] Some vitreoretinal surgeons have recommended fovea-sparing ILM peeling to prevent this complication.[15,43] However, in eyes where the ILM is retained, it has been reported that a full-thickness macular hole may occur if performing PPV with gas tamponade and laser photocoagulation.[44] Ultimately, there are limited data regarding whether ILM peeling causes full-thickness macular hole in eyes with ODPM, and some have suggested that macular hole formation may be associated with posterior hyaloid detachment.[16,45] Furthermore, it is known that ODPM itself can also lead to the formation of a full-thickness macular hole.[9] Although the development of iatrogenic full-thickness macular hole associated with ILM peeling was not observed in any of the cases in the present series, patients should be followed closely for this complication in the postoperative period.

A limited number of studies have shown that successful outcomes can be obtained by plugging various biological structures other than ILM into the pit opening for a similar purpose.[17,46,47,48] However, as the potential for occlusive vasculitis and progressive peripapillary retinal nerve fiber layer thinning has been reported, especially with scleral plugs, ILM flaps can be considered advantageous considering these complications.[49,50] In this case series, the multiple ILM flaps created were not placed in the pit opening as a plug, but were only placed over the optic pit and stabilized. The fact that the ILM flap technique utilizes the patient's own tissue eliminates the described risks associated with external tissue.

Although there is no clear consensus on the fluid source that causes maculopathy in ODPM, suggested sources are cerebrospinal fluid, vitreous fluid, or leakage from dural vessels in the pit base.[9,11] OCT imaging greatly facilitates the recognition of the intraretinal and/or subretinal fluid accumulation causing ODPM. Moreover, OCT imaging is useful in the preoperative and postoperative evaluation of EZ integrity, which is closely related to visual prognosis, as well as in postoperative follow-up for recurrence and investigating for the presence of residual fluid. ODPM may manifest with retinochisis in the outer retinal layers due to the ingress of intraretinal fluid, or macular neurosensory detachment due to the ingress of subretinal fluid. The coexistence of both subretinal and intraretinal fluid in ODPM was named the bilaminar pattern and reported at a rate of 83.3% by Karacorlu et al.[51] In our case series, the bilaminar fluid pattern was observed in 60% of the patients. In addition, there are studies reporting that as with other macular pathologies, EZ disruption may be associated with poor visual prognosis in ODPM. In our case series, we noted that patients with postoperative EZ defect (patients 3 and 4) had an increase of less than 3 lines in Snellen

BCVA. In one case (patient 1), the preoperative EZ defect resolved postoperatively and BCVA increased by more than 3 lines. The authors of a previous case report also documented a dramatic visual gain (increase from counting fingers to 6/6) in a young patient with an outer retinal hole after ILM peeling with SF6 gas tamponade.

Study Limitations

One of the main limitations of this study is the small case number and lack of a control group that would allow comparison with another method. However, as mentioned previously, ODPM is a rare macular pathology. Nevertheless, achieving surgical success in all five patients using the ML-ILM flap may serve as a guide for future studies. In addition, evaluating the patients' 6-month outcomes can be considered another limitation. Although it was reported in an earlier case presentation that resolution could continue for up to 22 months, achieving complete resolution by the end of a 6-month period in all patients also suggests that this technique may be effective in the short term.

Conclusion

To our knowledge, this study is the first to investigate the effectiveness of the ML-ILM flap technique in the treatment of ODPM, and the results demonstrate that this method seems to be a preferable option in the management of ODPM to ensure both high anatomical and functional success and flap stabilization. Larger ODPM case series in which the ML-ILM flap technique is applied and prospective studies comparing it with other surgical techniques are needed.

Ethics

Ethics Committee Approval: Bezmialem Vakıf University Local Ethics Committee approval was obtained for the study (ethics committee decision number: 2024/212-09, date: 15.05.2024).

Informed Consent: Written consent of the participants or their legal guardians is on file.

Authorship Contributions

Surgical and Medical Practices: H.Ö., Concept: H.Ö., Design: H.Ö., F.K., Data Collection or Processing: G.E.A., B.P.A., Analysis or Interpretation: H.Ö., F.K., Literature Search: G.E.A., B.P.A., Writing: H.Ö., F.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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