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INVERTED INTERNAL LIMITING MEMBRANE FLAP TECHNIQUE FOR MACULAR HOLE COEXISTENT WITH RHEGMATOGENOUS RETINAL DETACHMENT

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Purpose: To report the clinical features and treatment outcomes of patients with macular hole coexistent with rhegmatogenous retinal detachment surgically treated with pars plana vitrectomy and inverted internal limiting membrane flap technique.

Methods: Eleven consecutive patients with rhegmatogenous retinal detachment and macular hole who underwent vitrectomy and internal limiting membrane peeling with the inverted flap technique between December 2017 and February 2021 were retrospectively evaluated. The main outcome measures were retinal reattachment rate, macular hole closure rate, and postoperative best-corrected visual acuity. A nonsystematic literature review was performed to compare the study outcomes with those previously reported.

Results: The primary retinal reattachment rate was 90% (10/11) with one surgery and 100% with 2 surgical procedures. Macular hole closure was achieved in all patients (11/11). All patients showed an improvement in visual acuity at the final postoperative visit, and the mean postoperative best-corrected visual acuity was 0.60 ± 0.32 logarithm of the minimum angle of resolution (20/80 Snellen equivalent).

Conclusion: Vitrectomy with the inverted internal limiting membrane flap technique achieved not only favorable anatomical retinal reattachment rates but also an encouraging recovery of central macular anatomy and visual function in patients with macular hole coexistent with rhegmatogenous retinal detachment.

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Macular hole (MH) retinal detachment (RD) is a common complicating factor in highly myopic eyes, but it can also rarely occur in nonmyopic eyes secondary to rhegmatogenous RD associated with peripheral breaks. In such cases, the noncausal MH could happen as a consequence of vitreous traction after posterior vitreous detachment, proliferative vitreoretinopathy, or ocular trauma.[1–4] Pars plana vitrectomy combined with internal limiting membrane (ILM) peeling is the recommended treatment modality for highly myopic eyes.[5,6] Furthermore, the inverted ILM flap technique has been reported to achieve a higher MH closure rate than traditional ILM peeling in myopia.[7,8] Macular hole coexistent with a rhegmatogenous RD (MH-RRD) is relatively uncommon, with an incidence rate of only 2.3% to 4%.[1,2]

Previous studies described the outcomes of ILM peeling for MH-RRD in nonmyopic eyes, and the mere presence of an additional MH was associated with adverse factors of poor visual outcomes and high rates of proliferative vitreoretinopathy at presentation,[2]

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leading to low MH closure[9] and high reoperation rates.[10] To our knowledge, there is no evidence of the use of the inverted ILM flap technique in this cohort of patients. Therefore, the purpose of this study was to evaluate the anatomical and functional effectiveness of the inverted ILM flap technique for MH closure in addition to standard RD repair in eyes with MH-RRD.

Materials and Methods

Study Design and Population

This retrospective, single-center, single-surgeon (T.S.) case series was approved by the institutional review board of the Canton Vaud Health Department and was conducted according to the tenets of the Declaration of Helsinki. Written informed consent was obtained from the patients or their legal representatives before study participation.

The subjects were consecutive patients who underwent pars plana vitrectomy (PPV) for MH-RRD between December 2017 and February 2021. Patients presenting with clinical symptoms of high myopia such as posterior staphyloma, chorioretinal atrophy, and macular schisis were excluded from the study. The diagnosis of MH was made either preoperatively with slit-lamp ophthalmoscopy and optical coherence tomography (OCT) examination or intraoperatively at the time of the vitrectomy by a senior vitreoretinal surgeon (T.S.). In the cases where MH was diagnosed intraoperatively, OCT scans were performed postoperatively to confirm the diagnosis.

All patients underwent comprehensive ophthalmologic examinations, including measurement of the best-corrected visual acuity (BCVA), slit-lamp ophthalmoscopy, and swept-source OCT examination (DRI-OCT Triton, Topcon, Japan). Postoperative follow-up was set at least 6 months after the surgery and comprised BCVA measurements, slit-lamp examinations, indirect ophthalmoscopy assessments, and an OCT scan. Visual acuity was measured using Snellen charts converted to logarithm of the minimum angle of resolution (logMAR) for statistical analysis. The main outcome measures were retinal reattachment rate, MH closure rates, and the change in postoperative BCVA from baseline.

A nonsystematic literature search was also performed to review studies reporting the outcomes of MH-RRD surgery. The research was conducted by searching PubMed Central, MEDLINE, and Scopus databases using the following keywords: "Macular," "Hole," "Retinal," "Detachment," "Rhegmatogenous," "Internal Limiting Membrane," "ILM," and "Inverted" "Flap" "Peeling." Furthermore, the reference list of all identified articles was examined to identify any studies not captured by electronic searches. We included only studies in English published after the year 2000.

Surgical Technique

Surgery was performed using a standard 3-port, 23-gauge pars plana vitrectomy technique with a wide-angle noncontact viewing system. Internal drainage of subretinal fluid through a posterior retinal break was performed, and the peripheral retinal breaks were treated with endolaser photocoagulation. Internal limiting membrane peeling assisted with trypan blue staining and ILM flap trimming were then performed with the previously described zero aspiration technique[11] (Figure 1). Briefly, a roughly two-disc diameter ILM was peeled toward the fovea and trimmed with zero suction to leave a residual island of ILM attached at the fovea and positioned inside the MH. Silicone oil was used as a tamponade in all cases. Silicone oil removal was performed at least 3 months after RD surgery. One phakic patient (Patient number 8) underwent cataract surgery combined with silicone oil removal.

Statistical Analysis

The Wilcoxon signed rank test for nonparametric data was used to analyze changes in preoperative and postoperative BCVA. All statistical analyses were performed using SPSS software (Version 25.0; SPSS

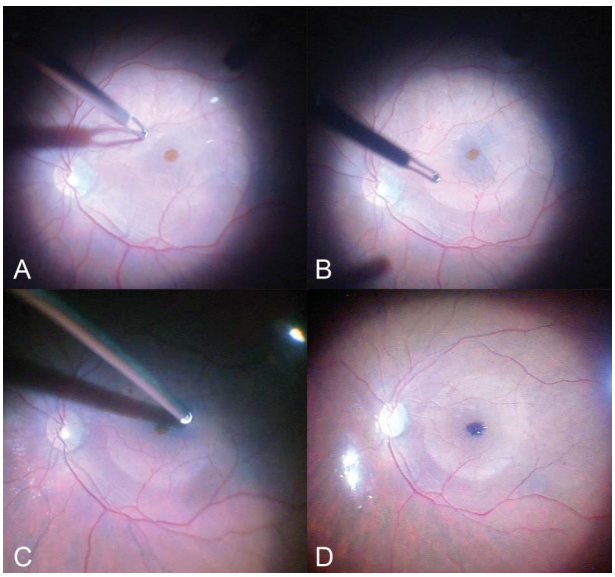

Fig. 1. Intraoperative images. The ILM is peeled and the flap is created (**A** and **B**). The ILM flap is then trimmed with the zero aspiration technique[11] (**C**) and inserted inside the MH under perfluorocarbon liquid (**D**).

Table 1. Patient Characteristics

Patient Number	Age	Sex	Eye	Lens Status	PVR	Tamponade	MH	RD	Preoperative BCVA	Postoperative BCVA	Follow-up	Comments
1	9	M	L	PPK	Grade B	Silicon oil	Closed	Attached	HM	20/80	13 months	S. Marfan
2	23	M	L	PK	—	Silicon oil	Closed	Attached	20/160	20/32	18 months	—
3	41	M	L	PK	—	Silicon oil	Closed	Attached	HM	20/125	19 months	—
4	47	M	L	PK	Grade CP-3	Silicon oil	Closed	Attached	CF	20/160	10 months	—
5	61	M	R	PPK	—	Silicon oil	Closed	Attached	LP	20/25	8 months	—
6	64	F	L	PPK	—	Silicon oil	Closed	Attached	LP	20/63	11 months	Required a second surgical procedure
7	75	F	R	PPK	—	Silicon oil	Closed	Attached	LP	20/40	16 months	—
8†	78	M	R	PK	—	Silicon oil	Closed	Attached	HM	20/100	6 months	—
9†	81	F	L	PPK	Grade B	Silicon oil	Closed	Attached	CF	20/200	13 months	—
10	59	F	L	PK	Grade B	Silicon oil	Closed	Attached	LP	20/200	8 months	—
11	48	M	R	PK	—	Silicon oil	Closed	Attached	HM	20/80	6 months	Amblyopy

†MH diagnosed preoperatively.
CF, counting fingers; F, female; HM, hand movement; L, left; LP, light perception; M, male; PK, phakic; PPK, pseudophakic; PVR, proliferative vitreoretinopathy; R, right.

Inc, Chicago, IL). *P*-values <0.05 were considered statistically significant.

Results

Of the 11 patients who met the inclusion criteria, 7 were men and 4 were women. The median patient age was 59 years (range, 9–81 years). The clinicodemographic patient characteristics are shown in Table 1. All patients had an MH-RRD with peripheral retinal tears. The estimated duration of the detachment before retinal reattachment surgery ranged from 1 day to 2 months. All patients had a macula-off RRD. In 2 patients, the coexisting MH was identified preoperatively, whereas the MH was hidden by retinal folds and was thus diagnosed intraoperatively in the remaining 9 patients (Table 1). The postoperative follow-up ranged from 6 to 19 months (mean, 11.6 ± 4.5 months). No intraoperative surgical complications were recorded. During the first month postoperatively, four patients developed a transient intraocular pressure increase requiring medical treatment with antiglaucomatous eye drops. It was managed after silicone oil removal. The silicone oil had been removed in all patients at the final follow-up. Two phakic patients required cataract surgery at 3 and 5 months postoperatively, and one patient developed postoperative cystoid macular edema 2 months after silicone oil removal. The patient subsequently underwent a dexamethasone intravitreal *implant*.

Anatomical Outcomes

The primary retinal reattachment rate was 90% (10/11). Patient 6 developed a retinal re-detachment 20 days after the silicone oil removal. This required vitrectomy, retinectomy, and a second temporary silicone oil tamponade. The retina remained attached at the final follow-up visit (6 months), leading to a final retinal reattachment rate of 100%. Macular hole closure was achieved in all patients (11/11). Notably, the MH remained closed and did not reopen even as the peripheral retina was re-detached in Patient 6.

Visual Outcomes

Vision improved postoperatively in all patients. The mean preoperative BCVA was 2.41 ± 0.30 logMAR (range, 0.9–3, 20/5,000 Snellen equivalent; patients with light perception were excluded). The mean BCVA at the final postoperative visit was 0.60 ± 0.32 logMAR (range, 0.1–1, 20/80 Snellen equivalent). The postoperative BCVA significantly improved compared with preoperative BCVA ($P = 0.003$). The

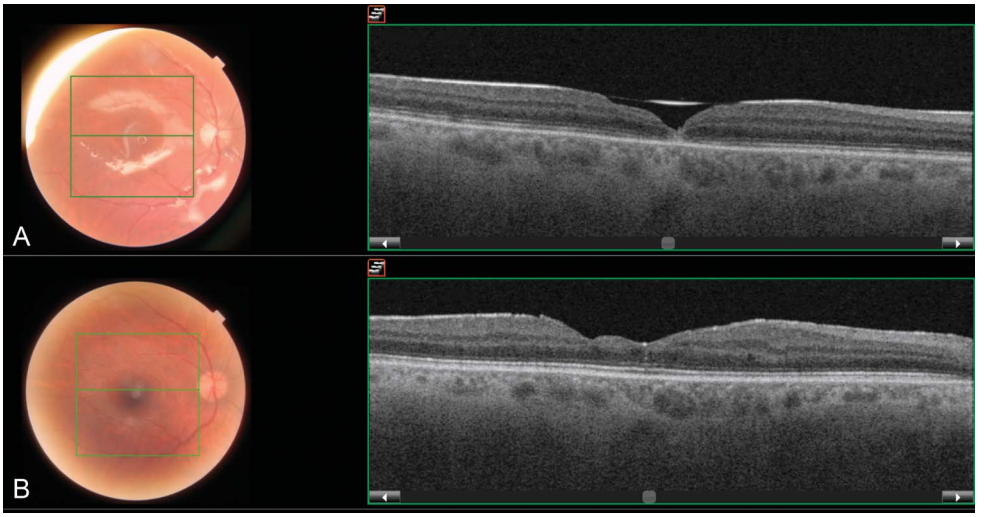

Fig. 2. Fundus photographs and OCT scans of Patient 5. The OCT scan shows a completely attached retina under silicon oil and the closure of the MH 1 month after the RD surgery (**A**). The same OCT scan 3 months after the removal of the silicon oil (7 months after RD surgery) showing a partial recovery of the normal macular profile.

detailed preoperative and postoperative values for each patient are presented in Table 1.

Discussion

In this study, we investigated the anatomical and functional outcomes of patients with MH coexistent with rhegmatogenous RD surgically treated with PPV and inverted ILM flap technique. In most of the patients (90%), we obtained a primary retinal reattachment, and we obtained a MH closure with improvement in visual acuity in all patients.

Although it may not be the primary cause of RD, the mere presence of an additional MH in the retina's most sensitive area represents a major complicating factor that heavily affects the patient's future visual prognosis and even the reoperation rate.[9,12] Although the retinal surgeon's primary focus will remain the treatment of all peripheral retinal breaks to reattach the retina,[13] achieving MH closure is obviously critical to improving postoperative visual recovery. The ILM flap technique is known to achieve MH closure rates higher than 90%,[14] and according to the literature, it seems to be the most effective procedure for the primary surgical approach of large idiopathic MH and secondary MH.[12] Multiple variants of the ILM flap technique have been proposed, but currently, there is no clear consensus on which technique should be routinely used.[15,16] In our case series, ILM flap insertion was performed as it might offer better MH closure rates, especially for bigger holes.[17]

However, creating the ILM flap is technically even more demanding in the presence of a detached retina which, by definition, is mobile. Such peeling of the internal limiting membrane may potentially lead to retinal tissue trauma and additional MH enlargement.

To gain a more in-depth understanding of the success of MH-RRD surgery, we performed a literature review on this topic. We identified 11 published studies reporting the outcomes of MH-RRD surgery mainly in highly myopic eyes. The success rates for retinal reattachment ranged from 85% to 100%. However, the MH closure rate varied greatly from 31% to 100%.[1–3,5,9,10,13,18–21] Although most patients undergo ILM peeling during the initial surgery, the role of ILM peeling remains controversial. Internal limiting membrane peeling in MH is primarily aimed to improve the surgical outcomes by removing any remaining tractional forces across the macular area. Despite increasing evidence suggesting that ILM peeling may lead to higher success rates of MH closure compared with no ILM peeling,[5,10] there are still reports that ILM peeling does not have an additional value.[7,8,19]

The inverted ILM flap technique has been recently introduced as an adjunct in the surgical repair of MH, particularly in cases of RD associated with high myopia.[15,22,23] A meta-analysis by Xu et al[8] showed

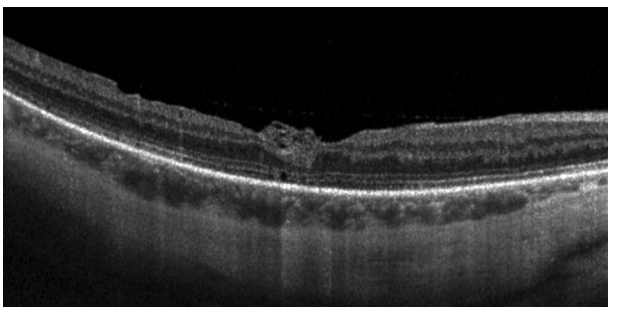

Fig. 3. Optical coherence tomography scan of Patient 11. The OCT scan shows a completely attached retina under silicon oil and the closure of the MH 3 months after the RD surgery. The remnant of the ILM flap filling the MH and creating a scaffold for the growth of the retinal layers is noticeable.

Table 2. Studies Reporting the Outcomes of Rhegmatogenous Retinal Detachment With Coexistent Macular Hole Surgery

First Author	Year	Study Population	Surgical Technique	Tamponade	Retina Attached	MH Closure	Postoperative BCVA, LogMAR (Snellen)	Comments
O'Driscoll[4]	2001	23	PPV + cryotherapy and scleral buckling	18 cases SF_6 5 cases SO	87%	31%	5 of 16 MH cases reach at least 0.8 (20/120)	ILM peeling in 6 cases; 16 cases available for MH closure assessment; 2 cases required reoperation for RD repair
Kiné[1]	2002	7	PPV	5 cases C_3F_8 1 case SF_6 1 case SO	85%	85%	Mean BCVA 0.72 ± 0.35	1 case required reoperation for RD repair After primary vitrectomy
Singh[15]	2009	12	20-G PV; 5 cases single surgery, 7 cases sequential (RD and MH) surgery	All cases gas (C_3F_8 or $SF_{6)}$	100%	91.6%	Single surgery mean BCVA 0.83 ± 0.03 Sequential surgery mean BCVA 0.66 ± 0.17	ILM peeling in 9 cases; 1 case declined MH surgery; 2 cases spontaneous closure of MH
Mennel[11]	2010	1	Scleral buckling	—	100%	100%	1 (20/200)	
Ryan[5]	2011	49	20-G PPV; additional scleral buckling in 44 cases	34 cases SF_6 15 cases C_3F_8	100%	85.7%	Mean BCVA 0.75 (20/120)	ILM peeling in 43 cases; 8 cases with macula-on RD; 2 cases required reoperation for RD repair
Cunningham[2]	2013	9	6 cases 20-G PPV; 3 cases 23-G PPV	7 cases C_3F_8 2 cases SO	100%	89%	Mean BCVA 1.23 ± 1.01	ILM peeling in 4 cases
Shukla[16]	2013	31	PPV	26 cases SO 5 cases C_3F_8	100%	87%	ILM peeling group: mean BCVA 1 ± 0.3 logMAR (20/200) No ILM peeling group: mean BCVA 0.6 ± 0.2 (20/80)	ILM peeling in 17 cases
Najafi[9]	2018	17	PPV; additional scleral buckling in 2 cases	15 cases gas (C_3F_8, or $SF_{6)}$; 2 cases SO	100%	71%	Mean BCVA 1.28 ± 0.76 (20/400)	ILM peeling 15 cases; 5 cases required reoperation for RD repair
Hsieh[3]	2019	2	PPV	Not reported	100%	100%	—	ILM peeling and flap coverage
Abouhussein[14]	2020	14	PPV	Silicon oil	100%	100%	Mean BCVA 0.67 ± 0.17	Use of amniotic membrane patch; no ILM peeling
Starr[17]	2020	43	Not reported	Not reported	86.1%	97.6%	Mean BCVA 0.87 ± 0.64	ILM peeling in 22 cases Single-surgery rates

C_3F_8, perfluoropropane; G, gauge; SF_6, sulfur hexafluoride; SO, silicon oil.

that compared with traditional ILM peeling, the inverted ILM flap technique achieves a higher MH closure rate. Under this technique, the ILM is centripetally peeled but not completely removed from the retina, leaving it attached to the edges of the MH. The presence of such a bridging tissue over the MH induces glial cell proliferation, which in turn may facilitate tissue adhesion by the proliferating cells and thus facilitate MH closure (Figures 2 and 3).[23–25]

Although ILM peeling has been reported to be beneficial in promoting MH closure in highly myopic eyes, no evidence thus far supports that this technique is effective in treating MH-RRD in eyes that are not highly myopic. Its influence on the resulting postoperative macular anatomy and, most importantly, its visual outcomes remains unclear.

To our best knowledge, this study is the first to investigate the outcomes of this technique in MH-RRD of non-highly myopic eyes. Interestingly, we observed an ultrastructural retinal remodeling on OCT during the postoperative period. This led to a visible restoration of the regular macular architecture combined with MH closure and final retinal reattachment rates of 100% on both counts. Regarding visual outcomes, all patients showed improvement from their preoperative BCVA, with 7 of the 11 patients (63%) achieving a BCVA of at least 20/80. The best visual acuity achieved was 20/25. We believe that such high visual acuities can be attributed to the restoration of central macular function after successful MH repair, and these cannot be obtained somehow "eccentrically." Considered as a group of macula-off detachments, the range of final visual outcomes of our study would be reasonable among a group of macula-off detachments that were not complicated by an MH.

In contrast, noncausal MH and RRD have been reported to result in significantly worse visual acuity outcomes than RRD without MH.[20] Moreover, our results were not inferior and, in most cases, better than the ones reported in literature without the use of the inverted flap (Table 2). For instance, in the more recent published case series by Najafi et al on 17 MH-RRD patients, 15 of whom underwent ILM peeling, only 24% of the patients reached a final BCVA of at least 20/80, and the final MH closure rate was 71%.[9] The corresponding rates in our study were 63% and 100%, respectively.

The limitations of our investigation were its retrospective nature, the absence of a control group, and the relatively small sample size. It is also important to highlight that our study reports the outcomes of a single-surgeon, single-center case series, which limits the generalizability of the results. However, given the rare occurrence of this condition in vitreoretinal practice, our outcomes provide additional evidence that can be helpful in the treatment of MH-RRDs as it could reinforce the awareness and encourage further reports of this condition.

In conclusion, ILM inverted flap PPV surgery not only achieves favorable anatomical retinal reattachment rates but also an encouraging recovery of central macular anatomy and visual function in patients with MH-RRD.

Key words: ILM, inverted flap, macular hole, rhegmatogenous retinal detachment, vitreous.

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