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Management of optic disc pit maculopathy: the European VitreoRetinal society optic pit study

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ABSTRACT.
Purpose: **To evaluate a variety of techniques, and their anatomical and functional results, for the treatment of optic disc pit maculopathy (ODP-M). A secondary aim was to report on results of secondary procedures in cases of initial failure or recurrence.**
Methods: **Multicentre retrospective study of 95 eyes with ODP-M, treated by 25 surgeons from 12 countries. Primary outcomes were anatomical resolution of subretinal fluid (SRF), intraretinal fluid (IRF) and visual acuity (VA) at 12 months.**
Results: **Higher rates of SRF and IRF resorption were achieved in eyes treated with pars plana vitrectomy (PPV) compared to external laser with or without tamponade: 64/72 (88.9%) versus 8/14 (57.1%) for SRF (p = 0.003), and 50/59 (84.7%) versus 3/10 (30%) for IRF (p = 0.002). The addition of juxtapapillary laser or internal limiting membrane (ILM) peel during PPV did not improve SRF or IRF resolution. Pars plana vitrectomy (PPV) with tamponade and PPV with tamponade plus endolaser were associated with significant visual gain. In the former group, VA improved from a mean of logMAR 0.91 (20/162), to a mean of logMAR 0.52 (20/66) at 12 months; in the latter group, VA improved from a mean of logMAR 0.82 (20/132) to a mean of logMAR 0.47 (20/59) at 12 months. Retreatments were performed in 14 eyes (15.7%), only enhancing anatomical outcomes.**
Conclusion: **Vitrectomy with tamponade had better final outcomes than external laser treatment with or without gas tamponade. Laser endophotocoagulation and ILM peel provided no additional benefit. A secondary treatment resulted in anatomical but not functional improvement.**

Key words: gas tamponade – internal limiting membrane peeling – optic disc pit maculopathy – optic nerve pit maculopathy – pars plana vitrectomy – retreatment

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Introduction

Optic disc pit maculopathy (ODP-M) may be present in 25%–75% of eyes with optic disc pit (ODP) (Kranengurg 1960; Brown et al. 1980; Jain & Johnson 2014; Shah et al. 2014). It usually appears between the second and fourth decade of life and is characterized by the presence of intraretinal or subretinal fluid. Although the pathophysiology is not completely understood, it is proposed that the fluid responsible for the ODP-M may have a double source of origin: vitreal and cerebrospinal (Michalewski et al. 2014). In most cases, the fluid follows a pattern described by Lincoff (Lincoff et al. 1988), in which it first creates a schisis-like separation of the inner retina and then reaches to the subretinal space creating a macular neuroepithelial detachment.

This fluid accumulation seen on optical coherence tomography (OCT) may have variable presentations. It can produce a schisis-like separation of retinal layers, more frequently outer layers, or be present only as subretinal fluid. Many cases have both, intraretinal and subretinal fluid in variable configurations. Sometimes, fluid may also present in multiple retinal layers and the occurrence of an outer lamellar macular hole is also possible (Tzu et al. 2013; Michalewski et al. 2014; Wehrmann et al. 2018; Wachtlin et al. 2019). Untreated, ODP-M usually leads to a progressive deterioration of the macular structure and visual loss. It is of note that while spontaneous reabsorption of fluid may occur in up to 25% of cases according to Gass (Gass 1969), relapses are frequent.

Multiple treatment options have been considered for ODP-M. Historically, bed rest combined with ocular patching was advised, followed by laser photocoagulation to the juxtapapillary region in an attempt to induce resolution of the retinal detachment (Annesley et al. 1987). Later, macular buckling (Theodossiadis 1996) and pneumatic displacement were proposed (Lincoff & Kreissig 1998), in some cases combined with laser photocoagulation to the temporal side of the disc (Lei et al. 2015). Currently, pars plana vitrectomy (PPV) is the most common therapeutic approach, either alone or combined with gas tamponade and/or laser photocoagulation (Moisseiev et al. 2015; Chatziralli et al. 2018; Steel et al. 2018; Uzel & Karacorlu 2019). Different authors have proposed several modifications of the vitrectomy technique so as to improve visual outcomes (Mohammed & Pai 2013; Ooto et al. 2014). Among these, inner retina fenestration was proposed by Spaide et al. to redirect the intraretinal fluid into the vitreous cavity (Spaide et al. 2006).

There is paucity of literature on the outcome of ODP-M. Due to the low prevalence of the disease, most studies are limited to case series that seldom exceed 20 cases, originating from single centres, and thus, definite conclusions are difficult to draw (Monin et al. 1994; Garcia Arumi et al. 2004; Hirakata et al. 2005; Sandali et al. 2011; Teke & Citirik 2015). Also, the usefulness of some surgical manoeuvres during vitrectomy surgery, such as peeling of the internal limiting membrane (ILM) or laser photocoagulation to the temporal side of the disc, remain controversial. Further, even in the studies with larger numbers of cases, the management of initial failures and recurrences were not discussed (Abouammoh et al. 2016; Steel et al. 2018).

We conducted this large multicentre study, to analyse common treatment techniques used for ODP-M and to evaluate their anatomical and functional results at 12 months. Additionally, we aimed to investigate OCT features that correlated with treatment success and to report the results of secondary procedures in cases of initial failure or recurrence.

Methods

Data extraction

The EVRS Optic Disc Pit study was a nonrandomized, retrospective, multicentre study. The EVRS Scientific Committee sent a datasheet to all EVRS members in order to collect data on the management of ODP-M. Completed data sets from participant physicians were returned to EVRS scientific committee for analysis.

To be eligible for the study, patients were required to have ODP with maculopathy and a follow-up history of at least 12 months. Data pertaining to gender, age, year of diagnosis of ODP, lens status, visual acuity (VA), OCT features, signs of posterior vitreous detachment (PVD), duration of initial observation and year of treatment were collected by each physician.

Additionally, data on OCT features, including the presence of subretinal fluid (SRF) and/or intraretinal fluid (IRF), the extent of serous detachment and the presence of an outer lamellar hole, were collected. The study was performed in multiple countries with various regulations and institutional review board requirements. Thus, each physician was responsible for following the rules and regulations of their own institution. The EVRS committees also approved the design and ethical aspects of the study.

Data categorization and exclusion criteria

Treatment was part of routine clinical care, and treatment decisions were therefore subject to physicians' discretion. For the purpose of the analysis, we divided the treatment strategies into 4 groups comprising: (A) PPV + tamponade + endolaser; (B) PPV + tamponade; (C) laser treatment with or without gas tamponade; and (D) observation.

We excluded from the analysis data of 35 eyes: 30 eyes with missing operative data and 5 eyes treated with different surgical techniques that did not meet the treatment classifications (PPV alone: 3 eyes, and intravitreal injection of anti-VEGF or autologous plasmin: 2 eyes).

Anatomical and functional responses to treatment for primary and repeat treatment were determined based on OCT and VA. Follow-up was divided into 5 time periods: 1 month, 3 months, 6 months (3–8 months), 1 year (9–17 months), 2 years (18–29 months) and 3 years (≥30 months).

Statistical analysis

Statistical analysis was conducted using SPSS statistical software version 24 (SPSS Inc, Chicago, Illinois, USA). We analysed categorical variables using Fisher's exact test and fitted a multivariate linear regression model in order to study the effect of different treatment modalities on visual acuity. Predictor variables included patient's age, preoperative VA, pretreatment retinal fluid on OCT, pretreatment outer lamellar hole on OCT and treatment method. To test whether the modality of treatment modifies the relation between preoperative and postoperative vision, we included the interaction between preoperative vision and the modality of treatment in the linear regression model.

Results

Baseline characteristics

There were 95 eyes of 95 patients with ODP-M eligible for the analysis (contributed by 25 surgeons from 12 countries). The mean age was 42.7 ± 19.7 years (range, 10–89 years), and 51/95 patients (53.6%) were female. None of the reported cases was bilateral. At the time of diagnosis, 88 eyes were phakic (92.6%) and 7 were pseudophakic (7.4%). The mean baseline logMAR visual acuity was 0.81 ± 0.50. Pretreatment clinical signs of PVD were recorded only in 4 eyes (4.2%), and the remaining had attached posterior hyaloid. The mean waiting time before treatment was 6.4 ± 11.6 months (range, 2–48 months). At baseline, SRF was present in OCT scans in 88 eyes (92.6%) and the remaining 7 eyes (7.4%) did not show evidence of SRF. In the cases with SRF in OCT scans, it involved the fovea in 87 eyes (98.9%) and did not involve the fovea in 1 eye

(1.1%). Intraretinal fluid (IRF) was present in 74 eyes (77.9%), while the remaining did not show any IRF in OCT scans. Outer lamellar hole was recorded in 71 cases (74.7%).

Treatment allocation

During the course of the study, 5 eyes (5.3%) were only observed as they were asymptomatic with minimal IRF and/or SRF on OCT scans. Intervention was undertaken in 90 (94.7%) eyes. This included PPV combined with endolaser and gas tamponade in 47 (49.4%) eyes; PPV with gas tamponade in 28 (29.5%) eyes; and external retinal laser with (13 eyes) or without (2 eyes) gas tamponade, in 15 (15.8%) eyes.

For eyes that underwent treatment, mean time of observation before treatment was 4.9 months (range: 0–19 months). Regarding the details of PPV surgery, PVD induction was performed in 65/75 eyes (86.6%). In the remaining eyes, PVD was present at the time of surgery. Internal limiting membrane (ILM) peeling was performed in 47/75 eyes (62.6%). The 'ILM flap technique' was employed in 4 eyes by one participating physician, and the flap was introduced into the optic nerve pit. Juxtapapillary laser during PPV was applied to the temporal side of the disc in 47/75 eyes (62.6%). A tamponade was used in all PPV cases: air tamponade in 13 eyes (17.3%), gas tamponade in 60 eyes (80%) (SF_6 in 37 eyes (49.3%), C_3F_8 in 18 eyes (24%), C_2F_6 in 5 eyes (6.7%) and silicone oil tamponade in 2 eyes (2.7%).

Observation periods after treatment were as follows: For group A (47 eyes) 19.61 ± 6.62 months, for group B (28 eyes) 19.72 ± 7.24 months, for group C (15 eyes) 18.32 ± 4.74 months and for group D (5 eyes) 24.60 ± 17.52 months.

Anatomical outcomes

Subretinal fluid

Of the 88 eyes with SRF, we found an anatomical improvement in 73 eyes (82.9%) by 12 months after treatment. Complete resorption occurred in 49/73 (67.2%) eyes and partial resorption in 24/73 (32.8%). Initial resorption was followed by recurrence in 6 eyes (6.8%), and no change in SRF was reported in 8 eyes (9.1%). Subretinal fluid (SRF) increased in one eye (1.1%). The mean time for complete resorption was 9.7 ± 1.1 months.

Table 1 shows the changes in SRF at 12 months with different treatment strategies. We observed a higher rate of SRF resolution in eyes treated by PPV (64/72, 88.9%) compared to external laser with or without tamponade (8/14, 57.1%) ($p = 0.003$).

For eyes treated with PPV, the addition of endolaser was not associated with better anatomical outcomes. Resorption of SRF was seen in 24 of 26 eyes (92.3%) with PPV and in 40 of 46 eyes (86.9%) with PPV + endolaser ($p = 0.48$) (Table 1). We did not observe significant differences in proportions of eyes that had SRF resolution between those that underwent PPV with ILM peeling (40/45 eyes, 88.9%) and those in which ILM was not peeled (24/27 eyes, 88.9%). Subretinal fluid (SRF) was present in 3 of 4 eyes where inverted ILM flap was performed and improved in all eyes.

Intraretinal fluid

Of the 74 eyes where IRF was present, we observed resorption in 54 eyes (73%). Of these, 34(63%) had complete resorption and 20(37%) partial reabsorption. No change or initial resorption followed by recurrence developed in 17 eyes (22.9%) and worsening in 3 eyes (4.1%). For 34 eyes that had complete resolution of intraretinal fluid, this occurred at a mean time of 4.50 ± 1.50 months. Table 2 shows the changes in IRF at 12 months with different treatment strategies.

We found a higher rate of IRF resolution in eyes treated with PPV (50/59, 84.7%) compared to external laser with or without tamponade (3/10, 30%) ($p = 0.002$). Resorption of IRF was seen in 21 of 23 eyes (91.3%) with PPV and in 29 of 36 eyes (80.6%) with PPV + endolaser ($p = 0.27$) (Table 2). In eyes that underwent PPV (60 eyes), we did not observe significant differences in resolution of IRF between those in which ILM was peeled (38/43 eyes, 88.3%) and those in which it was not (13/17 eyes, 76.5%). Intraretinal fluid was present in 2/4 eyes where inverted ILM flap was performed and improved in 1 eye.

Functional outcomes

We observed gradual improvement of vision in the entire cohort with a baseline logMAR VA of 0.82 (±0.50),

Table 1. Subretinal fluid (SRF) evolution at 12 months with different treatment strategies

	Total (*n*)	Observation	Vitrectomy + laser + tamponade	Vitrectomy + tamponade	Laser ± tamponade
N (%)	95	5	47	28	15
SRF present	88	2/5	46/47	26/28	14/15
Evolution of SRF					
Better	73 (82.9)	1 (50%)	40 (86.9)	24 (92.3)	8 (57.1)
Same/ recurrent	14 (15.9%)	1 (50%)	5 (10.9%)	2 (7.7%)	6 (42.9%)
Worse	1 (1.2%)	0	1 (2.9%)	0	0

N = number, SRF = subretinal fluid.

Table 2. Intraretinal fluid (IRF) evolution at 12 months with different treatment strategies

	Total (n)	Observation	Vitrectomy + laser + tamponade	Vitrectomy + tamponade	Laser ± tamponade
N (%)	95 (100%)	5 (5.3%)	47 (49.4%)	28 (29.5%)	15 (15.8%)
Eyes with IRF	74	5/5	36/47	23/28	10/15
Evolution of IRF					
Better	54/74 (73.0%)	1 (20%)	29 (80.6%)	21 (91.3%)	3 (30%)
Same/ recurrent	17/74 (22.9%)	3 (60%)	6 (16.6%)	2 (8.7%)	6 (60%)
Worse	3/74 (11.8%)	11 (20%)	1 (2.7%)	0	1 (10%)

N = number, IRF = intraretinal fluid.

Table 3. Linear regression model for the magnitude of postoperative logMAR visual acuity at 12 months

	Estimate	p	95% confidence interval	
Age	−0.00111	0.512	−0.00445	0.002234
Male gender	0.024529	0.69	−0.09748	0.146539
Preoperative LogMAR VA	1.802689	<0.0001	0.892869	2.712509
Intraretinal fluid presence	0.022207	0.772	−0.13007	0.174487
Subretinal fluid presence	−0.48794	0.004	−0.8109	−0.16498
Outer lamellar hole on OCT	0.219906	0.004	0.072826	0.366985
Treatment strategy:				
PPV + laser + tamponade	0.770238	0.001	0.313324	1.227151
PPV + tamponade	0.570143	0.011	0.134541	1.005744
Laser ± tamponade	0.421291	0.27	−0.33409	1.176671
Treatment strategy * Preoperative VA:				
PPV + laser + tamponade * Preoperative VA	−1.35691	0.005	−2.2902	−0.42363
PPV + tamponade * Preoperative VA	−1.17192	0.013	−2.09116	−0.25268
Laser ± tamponade * Preoperative VA	−0.99712	0.094	−2.16916	0.174923

LogMAR = logarithm minimum angle of resolution; PPV = pars plana vitrectomy; VA = visual acuity.

* Refers to the interaction between the specified treatment modality and preoperative vision.

0.57 (±0.40) at 3 months, 0.57 (±0.40) at 6 months and 0.45 (±0.43) at 12 months. We modelled the effect of the different techniques on logMAR VA at the 12-month time point using a multivariate linear regression model (Table 3). We found preoperative VA (estimate = 1.80), the presence of SRF (estimate = −0.49) and the presence of outer lamellar hole (estimate = 0.2) predicted postoperative VA at 12 months. Age and the presence of intraretinal fluid at baseline did not have a predictive effect on postoperative logMAR VA.

We included the interaction between preoperative vision and the modality of treatment in the linear regression model and their effect on postoperative vision in the model (Table 3 and Fig. 1). We found that treatment modality techniques had an effect on VA gain, and their effect also depended on baseline VA level. With preoperative vision taken in account, both vitrectomy groups (with or without endolaser) were associated with significant visual gain as compared to observation ($p = 0.005$ and $p = 0.013$). However, external laser alone or with tamponade was not significantly different from observation.

Retreatments

Out of the 90 eyes that underwent treatment, 14 (15.6%) were retreated: with external laser in 4 eyes and with PPV in 10 eyes. In the retreated-PPV group, 7 eyes had ILM peeling. Air was used as a tamponade in 1 eye, SF_6 in 7 eyes, and silicone oil in 2 eyes. Subretinal drainage of fluid through a retinotomy was performed in 2 eyes, and juxtapapillary endolaser was applied in 7 eyes. One eye also received preoperative external laser treatment before PPV.

Information on the timing of retreatment was available for 9 of 14 (64.2%) eyes. The mean time for retreatment was 13.8 months after the first treatment. Six eyes (42.8%) were retreated for recurrence of fluid after 24 months, and the remaining 8 eyes (57.2%) were retreated due to persistence fluid after 7.6 months. Resorption of SRF after retreatment was observed in 8 of 9 eyes (88.9%) of which 5 had complete reabsorption and 3 exhibited partial resorption. Intraretinal fluid (IRF) resorption was complete in 6 of 9 eyes (66.7%). Regarding VA changes with retreatment, there was no significant difference in mean VA pretreatment (0.70 logMAR) and post retreatment at 1 year (0.76 logMAR) nor at 2 years (0.68 logMAR).

Complications

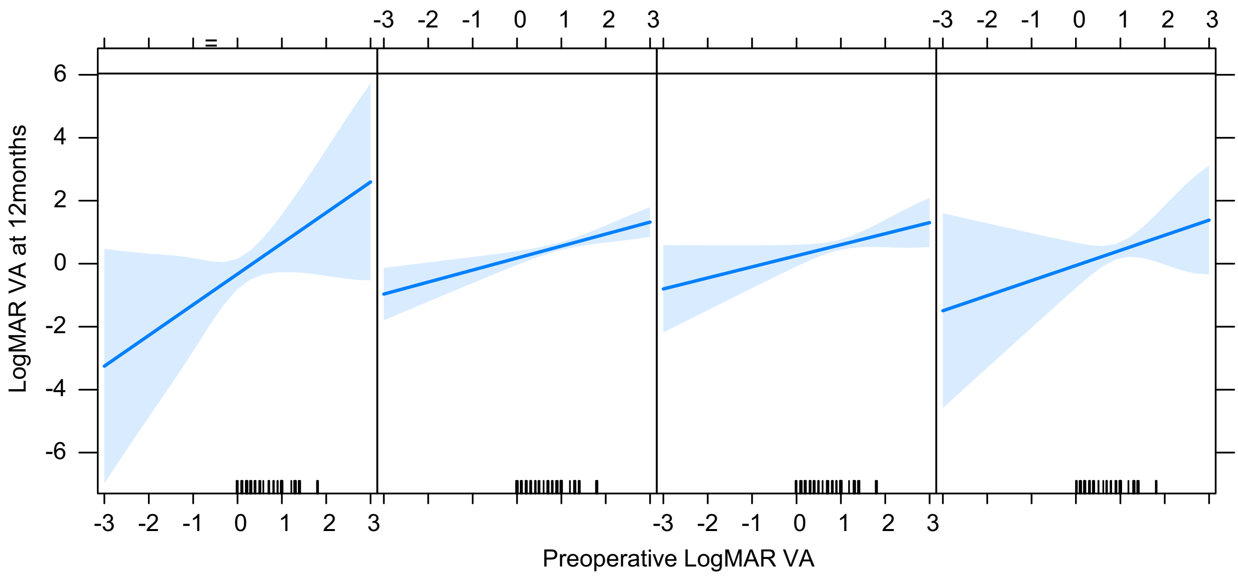
Postoperative complications were reported in 7 of 90 eyes that underwent treatment (7.8%). Four eyes (4.4%) developed a macular hole; of these, 3 eyes had ILM peeling during PPV. Two eyes (2.2%) had a retinal tear, and one eye developed postoperative uveitis that resolved with topical steroids.

Discussion

This multicentre study looked at the treatment outcomes of ODP-M. We found vitrectomy with gas tamponade to be associated with a high likelihood of better anatomical and functional outcomes. Addition of juxtapapillary laser and ILM peeling during PPV provided no additional benefit. Retreatment of persistent or recurrent cases of ODP-M was required in 15% of eyes improving anatomical but not functional results.

Our analysis of treatment modality has also shown that vitrectomy and gas tamponade with or without laser photocoagulation adjacent to the pit was superior to observation, for SRF and IRF resorption, highlighting the important role of vitrectomy and gas tamponade. Laser photocoagulation alone was found to be the least effective treatment modality for achieving resorption of SRF. This concurs with previous findings by Gass (1969), and Monin (Monin et al. 1994), who reported minimal or no anatomical improvement with laser photocoagulation only.

It has been suggested that the release of vitreous traction with vitrectomy and the induction of a complete PVD is essential for achieving success (Schatz & McDonald 1988; Bartz-Schmidt et al. 1996). Nevertheless, theories supporting vitreous traction as the main cause of the disease have limitations, due to the lack of OCT-observable vitreous traction over the pit membrane in some cases and also the reappearance of retinal fluid in previously vitrectomized eyes (Doyle et al. 2009; Imamura et al. 2010; Gregory-Roberts et al. 2013). These observations may suggest that the beneficial effect of vitrectomy is not limited to the release of traction but may involve other mechanisms such as altering pressure gradients or removing incarcerated vitreous that maintains a fluid channel and stimulates scarring within the disc pit (Jain & Johnson 2014). In 2018, Steel and colleagues (Steel et al. 2018), reported an anatomical rate of success of 75% with surgical approaches involving PPV combined with gas tamponade and a variety of other procedures, including laser and ILM peeling. Our results are in line with their report, with around 83% of patients achieving reduction or total



	Observation	PPV + laser + tamponade	PPV + tamponade	Laser +/- tamponade
Estimate	Reference	0.770	0.570	0.42
p-value	N/A	0.001 *	0.011 *	0.27

LogMAR= logarithm minimum angle of resolution; PPV = pars plana vitrectomy; VA = visual acuity

Fig. 1. Effect plot for treatment strategies and preoperative visual acuity on the postoperative visual acuity at 12 months. A less steep slope indicates a smaller postoperative logMAR VA (i.e. better VA) for a given preoperative logMAR VA measure. LogMAR = logarithm minimum angle of resolution, PPV = pars plana vitrectomy, VA = visual acuity.

absorption of SRF with VA improvement at 12 months.

Similar to our series, the use of gas tamponade in combination with vitrectomy surgery has been described in most of the published studies of ODP-M (Todokoro & Kishi 2000; Garcia-Arumi et al. 2004; Hirakata et al. 2005; Sandali et al. 2011; Abouammoh et al. 2016). Intraocular gas may serve as a temporary barrier between the vitreous cavity and ODP, and it could enhance the resorption of fluid. Moreover, there are reports of vitrectomy without gas tamponade that failed to show resorption of intraretinal or subretinal fluid; however, when gas tamponade was performed in a second procedure, the fluid resolved (Hotta 2004; Pichi et al. 2012).

Laser photocoagulation adjacent to the optic nerve pit during vitrectomy surgery for ODP-M has been a common practice. In our study, this was undertaken in nearly two thirds (62.6%) of the eyes that underwent PPV. The rationale is to create a scar in the area of the fluid passage from the pit to intraretinal tissue. Most of the published reports that included laser treatment in addition to vitrectomy and gas tamponade have demonstrated good anatomical and functional results (Monin et al. 1994; Sanghi et al. 2014; Rayat et al. 2015; Teke & Citirik 2015). However, it has also been suggested that juxtapapillary photocoagulation adds no benefit to treatment and may result in visual field defects due to damage of the papillomacular nerve bundle (Abouammoh et al. 2016). We found the combination of PPV and gas tamponade with juxtapapillary laser not to be superior to PPV and tamponade alone with respect to SRF or IRF resolution. Because the present study did not include any visual field or microperimetry testing, we are not able to draw conclusions as to whether juxtapapillary laser treatment has any negative effect of on visual function.

As shown in previous reports (Hirakata et al. 2005; Sandali et al. 2011; Abouammoh et al. 2016; Steel et al. 2018), anatomical resolution of retinal changes was gradual and slow. This pattern of slow and late improvement, which occurred not only in anatomical but also in functional results, deserves special attention and should be considered before retreatment is contemplated (Fig. 2). As in other macular pathologies, preoperative ellipsoid zone disruption has also been recognized as an ominous predictor for VA gain in ODP-M (Sanghi et al. 2014; Sisk & Toygar 2016). In agreement, we found the presence of a preoperative outer lamellar hole (estimate = 0.2) to be associated with poor postoperative VA recovery in our series.

The usefulness of ILM peeling in ODP-M remains controversial. In the present study, 62% of the eyes treated with vitrectomy received ILM peeling. No anatomical or functional advantage was found with the addition of this surgical step. However, as previously reported (Rayat et al. 2015), we observed an association between ILM peeling and the appearance of a

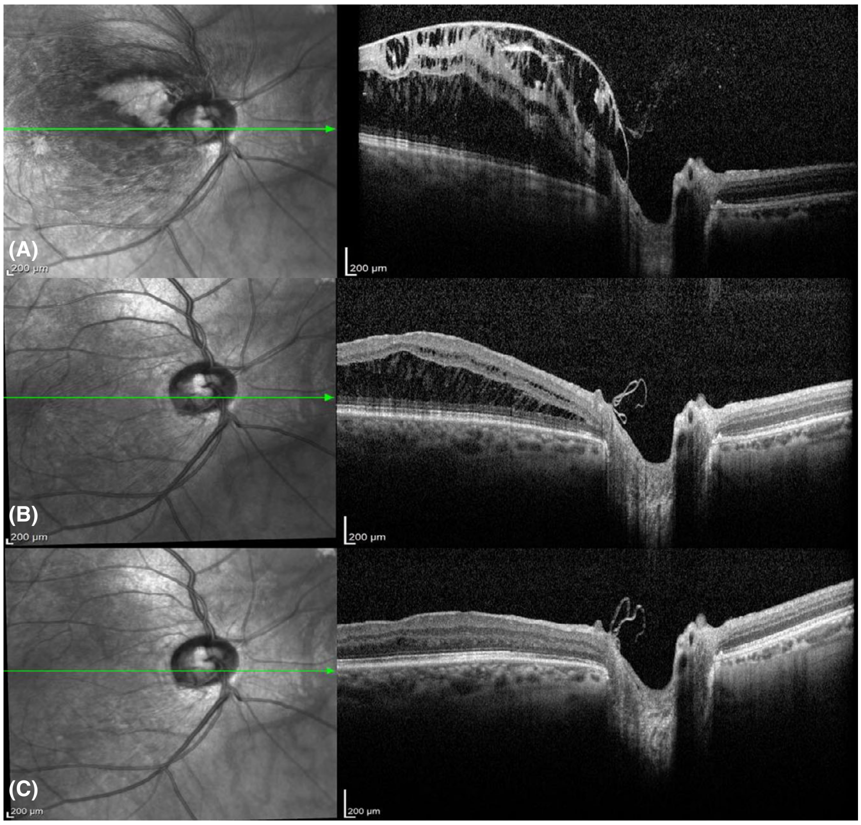


Fig. 2. Postoperative fluid evolution over time. (A) Preoperative optical coherence tomography scan showing severe schisis with multilayered fluid accumulation due to optic disc pit maculopathy. No subretinal fluid is detected in this case. (B) Postoperative scans at month 4 show partial fluid reabsorption with residual fluid more evident in the outer plexiform layer. (C) Postoperative scans at month 14 show complete fluid reabsorption.

postsurgical macular hole; 3 of 4 eyes (75%) that developed post-treatment macular hole have had ILM peeling. As such, our data suggest that ILM peeling may not be necessary and may pose an increased risk of macular hole formation in ODP-M.

Another related technique used in some of our patients was ILM flap over or inside the pit. Pastor-Idoate (Pastor-Idoate et al. 2019) has reported good anatomical and functional results with either translocation or pit plugging with autologous ILM or fovea sparing ILM flap. In contrast, Nawrocki et al., (2016) and Babu et al. (2020) reported superior results when ILM was stuffed into the pit. In the present study, resolution of IRF and SRF occurred in nearly all eyes where ILM flap was performed, but the number of eyes was too small to draw a firm conclusion.

Retreatments for ODP-M, to our knowledge, have not been evaluated previously. Two factors may trigger retreatment: the persistence or the recurrence of IRF and SRF. Fourteen out of 90 eyes (15.6%) were retreated in the present study. Although there was complete resolution of IRF/SRF in 2/3 of these retreated cases, VA did not improve. The mean time interval between initial and retreatment was about 6 months for persistent cases and 2 years for recurrent cases. As previously shown (Steel et al. 2018; Hirakata et al. 2005; Sandali et al. 2011; Abouammoh et al. 2016), anatomical and functional response to treatment may take more than 1 year to be effective. It is therefore possible that at least a proportion of these eyes may have recovered spontaneously, without a secondary procedure. While it is difficult to draw firm conclusions on the effectiveness of retreatment, because of the small number of eyes in this cohort, our results suggest that secondary interventions may improve the anatomical recovery but not visual function in ODP-M.

This study has a number of limitations. First, the nonrandomized, retrospective design makes it subject to selection bias if some physicians only selected the cases they wanted to contribute. However, because treatment techniques are presented in comparison with each other, rather than as an individual result in the study, the effect of such bias should have a comparative effect across groups. In addition, having a large number of physicians contributing to this study further minimizes the effect of this bias. Second, some baseline and follow-up data were missing (as often noted in other database studies), which can affect the quality of the results. Third, as the study was multicentre, cases were collected from different centres with the potential of differently guided demographics and physician-guided indications for treatment and retreatment that may have introduced bias. Further, while we used multiple regression analysis statistic in analysing the effect of treatment modality on the VA, to potentially adjust for confounding variables, this was not possible with other outcomes such as the effect of ILM removal technique on the VA or macular hole development due to a smaller sample size. Finally, potential confounding factors such as concomitant retinal pathology, refractive errors or cataracts were not excluded as would be the case in a trial setting.

Despite these limitations, our study has strengths. While a prospective randomized controlled study represents the gold-standard level of evidence, the low prevalence of ODP-M makes the conducting of such a study difficult and expensive, with mainly only small studies being currently available. As such, our study represents an important level of evidence that is relevant to clinical practice. Considering that a large number of physicians from different countries participated in this study, makes the data representative of retinal physicians' real-world practice as compared to small studies originating from single or selected institutions.

In conclusion, our data suggest that PPV combined with gas tamponade is associated with good anatomical and functional results for ODP-M. The addition of juxtapapillary laser to PPV does not result in additional anatomical or functional benefit. Internal limiting membrane (ILM) peeling is not mandatory and may pose an increased risk of postoperative macular hole formation. Finally, retreatment of persistent or recurrent cases of ODP-M may enhance anatomical success but this may not translate into better vision.

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APPENDIX A

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