Ophthalmologica

Research Article

Ophthalmologica 2025;248:29–39
DOI: 10.1159/000542770

Received: June 17, 2024
Accepted: November 13, 2024
Published online: November 25, 2024

# Anatomical, Functional, and Prognostic Results of Vitrectomy in Epiretinal Membranes Secondary to Retinal Vein Occlusions

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**Keywords**
Retinal vein occlusion · Secondary epiretinal membrane · Vitrectomy

**Abstract**

***Introduction:*** We investigated the anatomical and functional results of vitrectomy associated with the peeling of secondary epiretinal membranes (ERM) in patients with retinal vein occlusion (RVO) and determined the prognostic factors of surgical outcomes. ***Methods:*** This retrospective, multicenter, observational study included 50 patients with RVO who underwent vitrectomy with ERM removal between July 2012 and February 2021. Visual acuity (VA) and central macular thickness (CMT) were investigated up to 3 years. Univariate analysis identified the predictive factors associated with functional and anatomical outcomes. ***Results:*** Fifty eyes from 50 patients (62% with central RVO) were included. The mean VA of 0.9 ± 0.7 logMAR preoperatively improved to 0.5 ± 0.5 logMAR after 24 months ($p = 0.01$). Anatomically, the mean preoperative CMT was 501 ± 168 µm, decreasing to 348 ± 108 µm at month 24 ($p = 0.008$). By 36 months, VA had improved or stabilized in 90% of the eyes, whereas CMT had been reduced by at least 20% from baseline in 80% of the eyes. A lower number of intravitreal injections (IVI) were required after vitrectomy. Worse preoperative VA, absence of preoperative panretinal photocoagulation, and postoperative use of adjunctive IVI were associated with VA recovery. Higher baseline CMT and the use of preoperative dexamethasone injections were associated with an improvement in CMT. ***Conclusion:*** Vitrectomy for ERM secondary to RVO was effective in improving VA and recovering CMT for up to 3 years and reduced the number of IVIs.



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## Introduction

Epiretinal membranes (ERM) fall into two categories: idiopathic and secondary, based on the presence of baseline ocular morbidity [1]. Idiopathic ERM, accounting for around 80% of cases, develops without a specific pathological cause and is typically observed in individuals over 60 with posterior vitreous detachment (PVD) [2, 3]. Conversely, secondary ERM can be induced by various ocular pathologies such as retinal vein occlusion (RVO), diabetic retinopathy, inflammation, prior ocular surgery or trauma, and retinal photocoagulation [4–6]. These secondary ERMs are often thicker, associated with macular edema (ME), and less connected to PVD compared to idiopathic ERM [7, 8]. Both types can distort the macular structure, leading to visual impairment and metamorphopsia. Additionally, secondary ERMs may contribute to refractory ME that persists despite appropriately administered intravitreal injections (IVI) in eyes with vascular disorders.

The prevalence of ERM secondary to RVO is estimated at 14%–17% among all ERM cases [2, 9, 10], which may be an underestimate given RVO ranks as the second most common retinal disorder after diabetic retinopathy [11, 12]. Pars plana vitrectomy (PPV) with ERM peeling is a viable therapy for RVO cases complicated by secondary ERM. However, limited data exist on surgical outcomes for RVO eyes with secondary ERM [13–19]. Previous studies indicate that inducing PVD, along with ERM and internal limiting membrane (ILM) peeling, contributes to vision recovery and ME improvement [14–18]. One study demonstrated a 48.5% improvement in visual acuity (VA) for patients with ERM secondary to BRVO by vitrectomy with ILM peeling [13]. Nevertheless, most publications are small-sample studies with relatively short follow-up periods. Our objective was to present the anatomical and functional outcomes of PPV with ERM peeling in a larger sample and over a longer follow-up, aiming to identify the predictive factors for functional and anatomical recovery.

## Methods

*Design*

This retrospective multicenter observational study examined consecutive patients undergoing PPV with ERM peeling for RVO between July 2012 and February 2021. Patients' consent for the use of their retrospective and anonymized data was obtained prior to inclusion. The study adhered to the Declaration of Helsinki and was approved by the Institutional Review Board of the French Society of Ophthalmology (IRB No. 00008855). Participating hospitals included IRCCS San Raffaele Scientific Institute (Milan, Italy), University of Athens (Athens, Greece), Lariboisière University Hospital (Paris, France), and the Centre Hospitalier National Ophtalmologique des Quinze-Vingts Hospital (Paris, France).

The inclusion criteria were age >18 years, history of central retinal vein occlusion (CRVO) or BRVO in the operated eye, presence of a distorting ERM on preoperative OCT (with or without ME), the latter had to have developed mandatorily after the diagnosis of RVO, and availability of postoperative OCT scans within the first 3 months and up to 36 months after surgery. Vitrectomy with ERM removal was performed in all patients, while ILM peeling and tamponade were considered based on the surgeon's preference and occurrence of perioperative complications. Exclusions included patients with retinal pathologies other than RVO (e.g., diabetic retinopathy, age-related macular degeneration etc.), those undergoing surgery for idiopathic ERM, and individuals with prior retinal surgery or RVO complications causing visual loss (including retinal detachment and neovascular glaucoma).

*Data Collection*

Data were retrospectively reviewed from medical records at different time points, including before surgery (baseline) and 1, 3, 6, 12, 24, and 36 months after surgery. The following characteristics were collected: demographic data, medical and surgical history, details of the procedures performed along with PPV, ophthalmic data including VA, and OCT data using either Heidelberg Spectralis® (Heidelberg Engineering, Heidelberg, Germany) or Cirrus HD-OCT 5000® (Carl Zeiss Meditec, Jena, Germany). The same OCT device was used for each follow-up visit.

ME was diagnosed based on the presence of intraretinal cysts and/or subretinal fluid on OCT, excluding isolated macular thickening induced by ERM. Additionally, OCT images of a 1-mm-wide area centered on the fovea were analyzed for the presence of a disorganization of the retinal inner layers (DRIL), macular pseudohole, or alteration of the outer retinal layers, along with an automated measurement of the central macular thickness (CMT). DRIL was defined following Sun et al. [20], involving indistinguishable boundaries between the ganglion cell layer and inner plexiform layer complex, inner nuclear layer, and outer plexiform layer.

**Table 1.** Baseline characteristics of included patients

| Variables | *N* (%) or mean±SD |
|---|---|
| Demographic and preoperative characteristics | |
| Gender (female) | 15 (30) |
| Age at RVO diagnosis, years | 65±11 |
| Male | 62±10 |
| Female | 71±9 |
| Age at PPV, years | 69±11 |
| Male | 66±11 |
| Female | 74±9 |
| Interval between RVO and PPV, months | 43±45 |
| Follow-up period following PPV, months | 17±16 |
| Diabetes | 7 (14) |
| Hypertension | 33 (66) |
| Cardiovascular disorders | 36 (72) |
| Ocular characteristics | |
| Type of RVO (CRVO) | 31 (62) |
| Macular edema | 45 (90) |
| Glaucoma | 15 (30) |
| Uveitis | 5 (10) |
| Peripheral retinal ischemia | 20 (40) |
| Preoperative vitreous hemorrhage | 5 (10) |
| Preoperative PRP | 17 (34) |
| Preoperative IVIs of anti-VEGF and/or dexamethasone | 40 (80) |
| IVIs, *n* | 5.9±6.4 |
| Phakia | 32 (64) |
| Ellipsoid zone disruption | 27 (54) |
| DRIL | 33 (66) |
| Perioperative characteristics | |
| Combined with cataract surgery among phakic eyes | 14/32 (44) |
| PVD induction | 39 (78) |
| ILM peeling | 43 (86) |
| Tamponade | 25 (50) |
| Air | 16/25 (64) |
| $SF_6$ | 7/25 (28) |
| $C_2F_8$ | 1/25 (4) |
| Silicone | 1/25 (4) |
| Complications during surgery | 3 (6) |
| Posterior capsule rupture | 1 (33) |
| Perioperative retinal detachment | 2 (66) |

CRVO, central retinal vein occlusion; DRIL, disorganization of retinal inner layers; ILM, internal limiting membrane; IVI, intravitreal injections; N, number; PPV, pars plana vitrectomy; PVD, posterior vitreous detachment; RVO, retinal vein occlusion; SD, standard deviation; VEGF, vascular endothelial growth factor.

*Main Outcomes*

The study assessed VA and CMT outcomes of PPV for ERM secondary to RVO up to 36 months. Visual stability or improvement was defined as an unchanged or improved VA as compared to the preoperative VA value. Prognostic factors for visual stability, decreased CMT, ERM recurrence, and reduced postoperative IVI frequency were investigated. CMT reduction was defined as a ≥20% decrease from baseline.

*Statistical Analyses*

The R software (https://www.R-project.org) facilitated statistical analyses. Decimal VA data were logarithmically transformed into a logMAR scale, with corresponding values: counting fingers to 1.7, hand motion to 2.3, light perception to 2.4, and no light perception to 2.6. Descriptive statistics for quantitative variables included mean with standard deviation or median with range; categorical variables were expressed as absolute and

**Table 2.** Comparison of adjunctive treatments in the preoperative and postoperative periods

| Intravitreal agent | Preoperative | Postoperative | *p* value |
|---|---|---|---|
| Anti-VEGF | | | |
| Eyes, *n* (%) | 33 (66%) | 14 (28%) | <0.001* |
| IVI, *n* (mean±SD) | 4.9±6 | 0.54±1.1 | <0.001* |
| Median (range) | 4 (0–30) | 0 (0–5) | |
| Dexamethasone | | | |
| Eyes, *n* (%) | 22 (44%) | 14 (28%) | 0.140 |
| IVI, *n* (mean±SD) | 1±1.7 | 0.8±1.7 | 0.495 |
| Median (range) | 0 (0–8) | 0 (0–6) | |
| Anti-VEGF and/or dexamethasone | | | |
| Eyes, *n* (%) | 40 (80%) | 22 (44%) | <0.001* |
| IVI, *n* (mean±SD) | 5.9±6.4 | 1.4±2.3 | 0.093 |
| Median (range) | 4 (0–30) | 0 (0–11) | |

IVI, intravitreal injection; SD, standard deviation; VEGF, vascular endothelial growth factor. *$p$ value <0.05 comparing preoperative and postoperative values.

relative frequencies. Categorical variables were compared using $\chi^2$ and Fisher's exact tests, while quantitative variables were compared using the independent $t$ test or Mann-Whitney U test. Preoperative and postoperative values were compared using the paired $t$ test or Wilcoxon signed rank test. Univariate analyses, presented as odds ratios (ORs) with 95% confidence intervals, were performed using a generalized linear model. The significance level was set at $p < 0.05$.

## Results

### *Demographic and Ocular Characteristics*

This study comprised 50 patients with RVO who underwent ERM peeling. Table 1 summarizes their baseline characteristics. The average age at RVO diagnosis was 65 ± 11 years, increasing to 69 ± 11 years at the time of PPV. The mean follow-up period was 17 ± 16 months postoperatively.

Concerning ocular traits, 62% of eyes exhibited CRVO. Peripheral retinal ischemia occurred in 20 eyes (41%), with 85% undergoing panretinal photocoagulation (PRP) prior to surgery. Thirty-six percent of eyes were pseudophakic, and 90% presented with ME prior to PPV. Preoperative OCT revealed an interrupted EZ in 54% of eyes and DRIL in 66%. Eighty percent of eyes had received IVI of anti-vascular endothelial growth factor (VEGF) agents and/or dexamethasone implants, averaging 5.9 ± 6.4 injections per eye before surgery.

The mean interval between RVO diagnosis and PPV was 43 ± 45 months. Cataract surgery was performed along with PPV in 14 of 32 phakic eyes. PVD was induced in 78%, and ILM peeling in 86% of eyes. Tamponade was done in 50% of the eyes, mostly with air. Perioperative complications occurred in 3 eyes, including posterior lens capsule rupture and perioperative retinal detachment.

Postoperatively, ME prevalence decreased from 90% to 65% at 1 month and 59% at 12 months. Eyes requiring IVI significantly decreased from 80% preoperatively to 44% postoperatively ($p = 0.0004$). The mean postoperative IVI number decreased to 1.4 ± 2.3, compared to 5.9 ± 6.4 preoperatively (Table 2). The mean annualized number of anti-VEGF injections decreased after PPV (2.7 ± 5.3 [preoperatively] vs. 1.6 ± 5.2 [postoperatively], $p = 0.31$). Macular holes developed in 10% of eyes, and ocular hypertension in 8%. Cataract surgery was needed in 2 eyes within a year of surgery.

### *Functional Outcomes*

The mean VA improved from 0.90 ± 0.70 logMAR at baseline to 0.54 ± 0.47 after 24 months ($p = 0.01$) and to 0.42 ± 0.29 after 36 months ($p = 0.02$) (Table 3; Fig. 1a). After 24 months, 78% of eyes showed stable or improved VA, with 67% demonstrating ≥1-line improvement and 56% showing ≥2-line improvement. At the 36-month follow-up, 90% of eyes exhibited stable or improved VA, with 90% showing ≥1-line improvement and 80% showing ≥2-line improvement (Table 4).

Baseline VA was notably better in eyes without baseline EZ disruption, and improvement persisted in this subgroup during the follow-up compared to eyes with baseline EZ disruption (Fig. 2a). The presence of preoperative DRIL did not impact baseline VA; however, VA significantly improved up to 12 months in eyes without preoperative DRIL (Fig. 2b). No significant differences were seen in terms of VA improvement or VA loss between eyes with CRVO and BRVO at baseline (online suppl. Table 1; for all online suppl. material, see https://doi.org/10.1159/000542770).

### *Anatomical Outcomes*

Regarding anatomical features, baseline CMT was 501 ± 168 μm, showing a significant decrease at all follow-up time points (Table 3; Fig. 1b). Over 70% of eyes exhibited a ≥20% reduction in CMT at 24 and 36 months, compared to baseline values (Table 4).

Baseline CMT was thinner in eyes without EZ disruption (441 ± 91 vs. 556 ± 202 μm, $p = 0.01$), but its presence did not impact postoperative CMT values (online suppl. Table 2). In eyes with preexisting DRIL,

**Table 3.** Postoperative changes of VA and CMT from baseline

| Months | Patients, *n* | VA, logMAR | | CMT, µm | |
|---|---|---|---|---|---|
| | | mean±SD | *p* value | mean±SD | *p* value |
| Baseline | 50 | 0.90±0.70 | | 501±168 | |
| 1 | 43 | 0.87±0.69 | 0.70 | 435±182 | 0.02* |
| 3 | 31 | 0.90±0.73 | 0.60 | 409±169 | <0.0001* |
| 6 | 33 | 0.80±0.68 | 0.07 | 383±142 | <0.0001* |
| 12 | 28 | 0.73±0.62 | 0.12 | 443±188 | 0.03* |
| 24 | 18 | 0.54±0.47 | 0.01* | 348±108 | 0.008* |
| 36 | 10 | 0.42±0.29 | 0.02* | 358±94 | 0.08 |

CMT, central macular thickness; SD, standard deviation; VA, visual acuity. *$p$ value <0.05 compared to baseline values.

CMT was thicker at baseline without statistical significance (525 ± 189 vs. 452 ± 102 µm, $p = 0.1$). While the CMT was significantly thicker at 1-month post-surgery in eyes showing DRIL (466 ± 204 vs. 336 ± 96 µm, $p = 0.04$), the CMT difference was no longer significant after 3 months (all $p > 0.05$).

In terms of CMT improvement, no significant differences were seen between eyes with CRVO and BRVO at baseline (online suppl. Table 3). ERM recurred in 28% of eyes within a mean period of 47 ± 19 months, and reoperation was necessary in 9 eyes. ILM peeling did not reduce the risk of ERM recurrence (OR = 2.60, $p = 0.4$; online suppl. Table 4).

*Predictive Factors of Surgical Outcomes*

The predictive factors for VA stability or improvement included worse baseline VA (OR = 9.42 per logMAR unit, $p = 0.02$) and postoperative IVI use (OR = 6.47, $p = 0.03$; Table 5). Lack of visual improvement at the last follow-up was associated with the use of tamponade during PPV (OR = 0.20, $p = 0.03$) and a history of PRP (OR = 0.20, $p = 0.02$). Cataract surgery was not predictive of a stable or improved VA (OR = 2.64, $p = 0.25$).

In terms of CMT improvement, thicker baseline CMT (OR = 1.01 per micron, $p = 0.013$) and preoperative corticosteroid IVI use (OR = 5.57, $p = 0.02$) were associated with a ≥20% CMT decrease at the last follow-up (Table 5). Factors associated with a reduced need for postoperative IVI included a younger age at surgery (OR = 0.93 per year, $p = 0.04$), absence of glaucoma (OR = 6.6, $p = 0.01$), disrupted EZ in both the pre- and postoperative periods (OR = 4.50, $p = 0.03$), and the perioperative use of tamponade (OR = 4.52, $p = 0.04$) (online suppl. Table 5).

## Discussion

In this study, we examined cases of RVO that underwent PPV for contractile ERM. We showed that PPV with ERM removal resulted in a stable or improved vision up to 3 years, with an early postoperative improvement in CMT. ERM peeling correlated with reduced postoperative IVI requirements. Specific defects, like EZ disruption or DRIL, were linked to limited visual recovery but did not impact the long-term CMT changes.

This study included more CRVO cases than BRVO, in contrast to previous epidemiological data reporting BRVO as being four times more common than CRVO [12]. This discrepancy may stem from our inclusion criteria, which targeted RVO patients requiring PPV for secondary ERM. However, the type of RVO did not impact the anatomical and/or the visual outcomes in this study. Other demographic features and the proportion of eyes treated with IVI for ME were comparable to literature reports [13, 17, 21].

Regarding functional outcomes, ERM removal via PPV resulted in visual stability or improvement for up to 3 years post-surgery. Approximately 50% of patients gained more than one line at 1 year, mirroring the 48.5% rate reported by Kang et al. [13]. Notably, the proportion of >1-line gainers increased overtime, reaching almost 70% at 2 years and 90% at 3 years. The proportion of two-line gainers evolved similarly, reaching 80% of eyes at 3 years. Worse baseline VA and postoperative IVI correlated with visual stability or improvement. Patients with poorer preoperative vision exhibited greater potential for improvement, explaining our findings (ceiling effect). In cases of good baseline vision, the impact of ERM on visual function was limited, discouraging

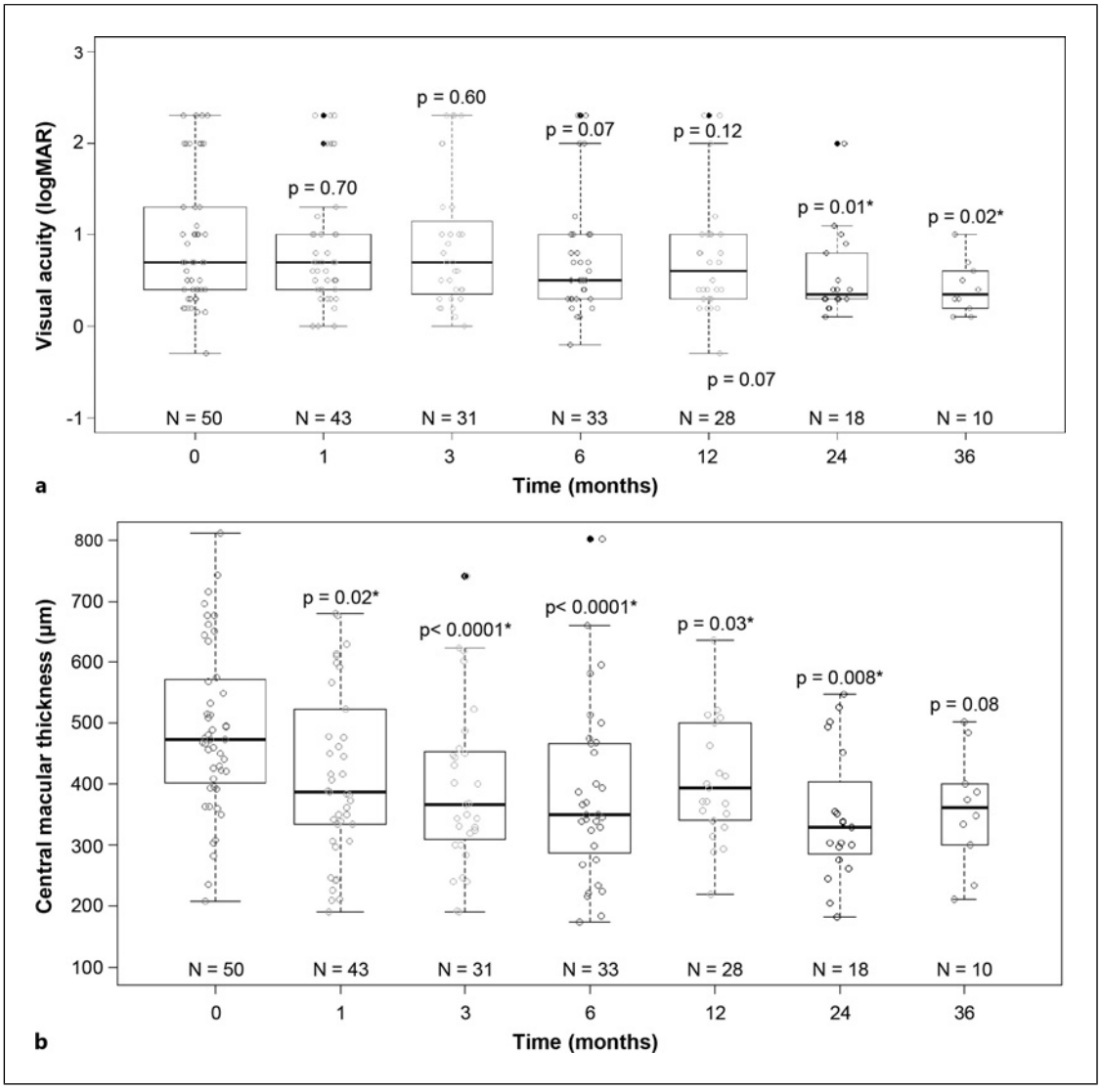


**Fig. 1.** Changes in VA and CMT post-vitrectomy with epiretinal membrane removal. Box plots illustrate the median and range of VA (**a**) and CMT (**b**). N, number of eyes at each time point. *$p$ value <0.05 compared to baseline values.

surgical intervention. The link between postoperative IVI and improved visual prognosis supports considering active adjuvant therapy for ME patients. Conversely, preoperative PRP was associated with a reduced likelihood of vision stabilization or improvement, possibly due to macular ischemia associated with the presence of peripheral ischemia [22, 23]. In terms of OCT findings, eyes without baseline EZ disruption or DRIL demonstrated better postoperative VA, aligning with prior studies on idiopathic ERM or other retinal pathologies [24–26]. Although statistically significant until 1 year, this difference became nonsignificant at 2 and 3 years, likely due to the limited sample size in longer follow-up periods.

Regarding anatomical outcomes, our study revealed that performing PPV with ERM removal led to a significant reduction in CMT at all observed time points. Our findings align with prior publications but extend the data to follow-ups exceeding 12 months, a less-explored timeframe [13]. Initial thicker CMT correlated with improved CMT at the final follow-up, and preoperative use of dexamethasone implants within 2 months of surgery was associated with CMT improvement. Utilizing dexamethasone implants preoperatively may create

**Table 4.** Proportions of eyes that showed functional and anatomical stability, improvement or worsening

| Months | VA, logMAR | | | CMT, μm | |
|---|---|---|---|---|---|
| | loss > 2 Snellen lines | stable or improved | gain ≥ 2 Snellen lines | generally reduced | reduction ≥20% |
| 1 | 5/43 (12%) | 29/43 (67%) | 12/43 (28%) | 32/41 (78%) | 16/41 (39%) |
| 3 | 7/31 (23%) | 24/31 (77%) | 8/31 (26%) | 25/31 (81%) | 17/31 (55%) |
| 6 | 5/33 (15%) | 27/33 (82%) | 11/33 (33%) | 30/31 (97%) | 17/31 (55%) |
| 12 | 5/28 (18%) | 23/28 (82%) | 11/28 (39%) | 18/24 (75%) | 10/24 (42%) |
| 24 | 1/18 (6%) | 14/18 (78%) | 10/18 (56%) | 14/18 (78%) | 13/18 (72%) |
| 36 | 0/10 (0%) | 9/10 (90%) | 8/10 (80%) | 7/9 (78%) | 7/9 (78%) |

CMT, central macular thickness; VA, visual acuity.

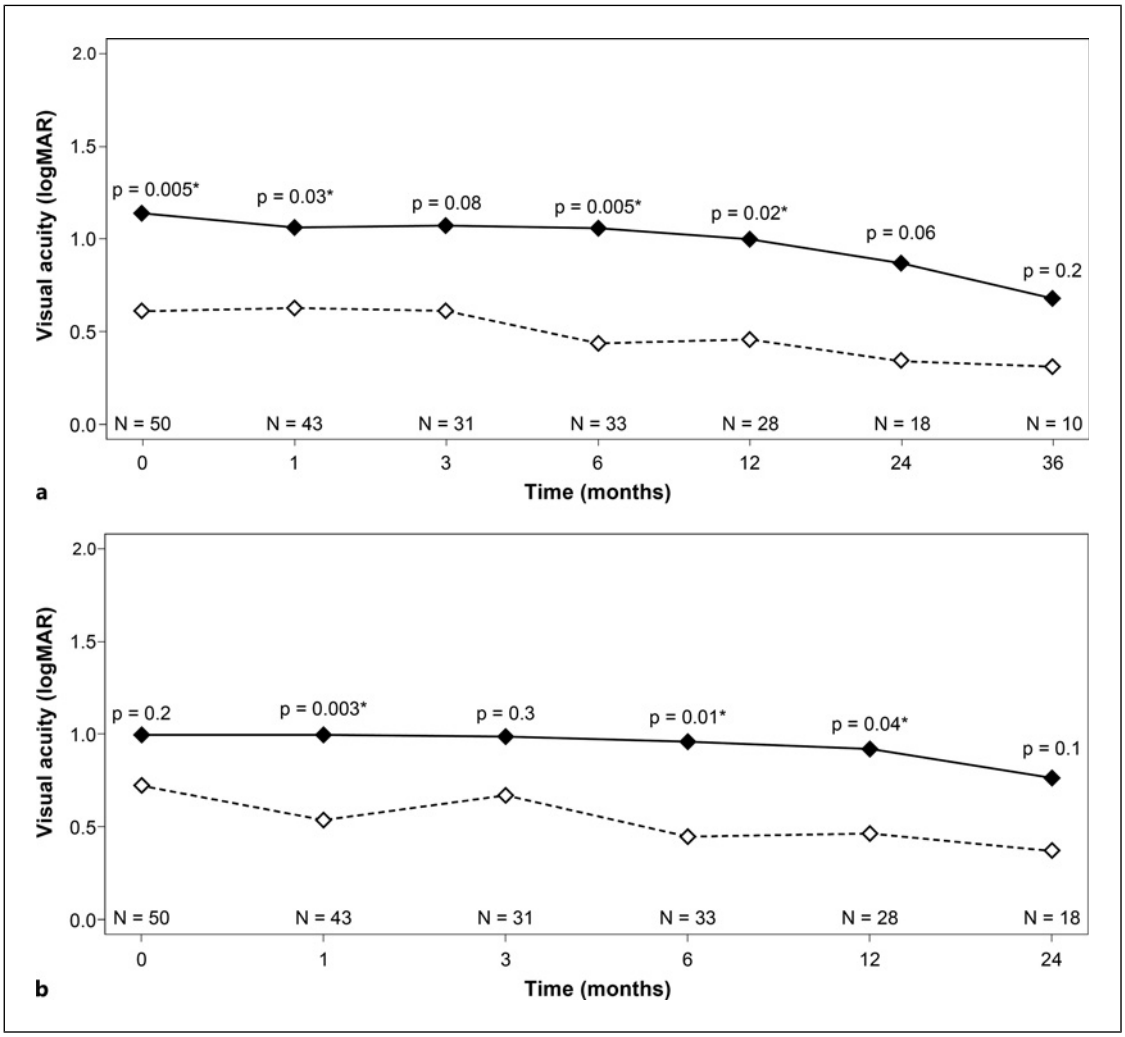


**Fig. 2.** Changes in VA post-vitrectomy with epiretinal membrane removal stratified by optical coherence tomographic findings. **a** Stratified by ellipsoid zone (EZ) disruption: the solid line represents EZ disruption, the dashed line indicates no EZ disruption. **b** Stratified by retinal inner layer (DRIL) disorganization: the solid line represents DRIL, the dashed line indicates no DRIL. N, number of eyes at each time point. *$p$ value <0.05, comparing groups with and without EZ disruption (for **a**) or DRIL (for **b**).

**Table 5.** Univariate analysis of the predictive factors of visual stability/improvement or CMT improvement at the last follow-up

| Variables | Stable or improved vision | | Improved CMT ≥20% | |
|---|---|---|---|---|
| | OR (95% CI) | *p* value | OR (95% CI) | *p* value |
| Age at PPV, years | 0.99 (0.93–1.05) | 0.780 | 0.99 (0.93–1.05) | 0.720 |
| Sex, male | 1.05 (0.24–4.01) | 0.944 | 0.73 (0.17–2.73) | 0.654 |
| Diabetes | 0.40 (0.08–2.33) | 0.238 | 0.20 (0.03–1.16) | 0.064 |
| Cardiovascular disorder | 0.38 (0.05–1.71) | 0.251 | 0.59 (0.12–2.39) | 0.482 |
| Hypertension | 0.27 (0.04–1.18) | 0.115 | 0.64 (0.115–2.34) | 0.511 |
| Glaucoma | 1.60 (0.40–8.11) | 0.529 | 0.28 (0.07–1.00) | 0.053 |
| Type of RVO branch | 0.41 (0.11–1.49) | 0.177 | 0.87 (0.25–3.15) | 0.831 |
| Bilateral involvement | 1.41 (0.115–31.05) | 0.780 | 0.14 (0.01–1.28) | 0.109 |
| Peripheral ischemia | 0.48 (0.13–1.75) | 0.269 | 0.93 (0.27–3.21) | 0.905 |
| Preoperative factor | | | | |
| Interval from RVO to PPV (per 12 M) | 1.02 (1.00–1.06) | 0.183 | 0.99 (0.98–1.01) | 0.415 |
| History of PRP | 0.20 (0.05–0.75) | 0.019* | 0.58 (0.17–2.05) | 0.395 |
| History of any IVI | 0.66 (0.09–3.16) | 0.630 | 4.20 (1.00–19.56) | 0.053 |
| History of IVI (anti-VEGF) | 1.30 (0.33–4.80) | 0.693 | 1.99 (0.56–7.08) | 0.282 |
| History of IVI (dexamethasone) | 2.13 (0.58–9.02) | 0.269 | 5.57 (1.46–27.89) | 0.019* |
| VA, logMAR | 9.42 (2.06–90.34) | 0.018* | 1.32 (0.55–3.51) | 0.549 |
| CMT, μm | 1.00 (1.00–1.00) | 0.587 | 1.01 (1.00–1.02) | 0.013* |
| Presence of ME | 2.06 (0.25–14.06) | 0.459 | 0.64 (0.03–5.54) | 0.714 |
| Pseudohole | 2.25 (0.30–46.42) | 0.487 | 0.40 (0.06–2.56) | 0.318 |
| Ellipsoid zone disruption | 1.01 (0.28–3.61) | 0.993 | 2.78 (0.82–10.09) | 0.106 |
| DRIL | 1.30 (0.33–4.80) | 0.693 | 0.87 (0.23–3.07) | 0.829 |
| Perioperative factor | | | | |
| Combined cataract surgery | 2.64 (0.59–18.83) | 0.251 | 1.00 (0.26–4.36) | 1.000 |
| PVD induction | 0.23 (0.01–1.38) | 0.177 | 0.37 (0.05–1.66) | 0.237 |
| ILM peeling | 0.43 (0.02–2.90) | 0.457 | 1.62 (0.28–8.39) | 0.565 |
| Tamponade | 0.20 (0.04–0.80) | 0.032* | 1.00 (0.30–3.36) | 1.000 |
| Postoperative factor | | | | |
| Any IVI | 6.47 (1.48–45.72) | 0.026* | 0.53 (0.15–1.78) | 0.308 |
| Ellipsoid zone disruption | 0.66 (0.17–2.36) | 0.527 | 1.88 (0.56–6.53) | 0.308 |
| DRIL | 0.52 (0.12–1.92) | 0.344 | 1.14 (0.33–3.84) | 0.836 |

CI, confidence interval; CMT, central macular thickness; DRIL, disorganization of retinal inner layers; ILM, internal limiting membrane; IVI, intravitreal injection; M, months; ME, macular edema; OR, odds ratio; PPV, pars plana vitrectomy; PRP, panretinal photocoagulation; PVD, posterior vitreous detachment; RVO, retinal vein occlusion; VEGF, vascular endothelial growth factor. *$p$ value <0.05 by generalized linear model.

optimal inflammation-free conditions during PPV, thereby minimizing postoperative macular thickening risks [27]. Notably, the postoperative CMT remained unaffected by EZ disruption or DRIL at most time points. While DRIL is recognized as a marker of macular ischemia in RVO [28], the impact of DRIL on CMT may warrant further investigation during longer follow-ups to assess the potential occurrence of macular thinning and atrophy.

The recurrence rate was higher than reported in the literature [29]; however, it is worth noting that most publications investigated the idiopathic and not the secondary forms of ERMs. Besides, our described rate matches what has been reported in diabetic retinopathy, with a recurrence rate reaching 13–38% [30, 31]. Although the surgical procedure for secondary ERMs is not different from that used in idiopathic ERM, the underlying etiology may affect the recurrence rate [32].

In fact, secondary ERM are thought to be mostly associated with an inflammatory component, which may affect the recurrence rate, especially when the ILM is not peeled [33, 34]. On the other hand, not all recurrent ERMs required surgery. Only 9 eyes were reoperated because of an impact of the recurrent ERM on visual function.

The postoperative period witnessed a decline in both the number of eyes subjected to IVI of anti-VEGF agents and the overall IVI frequency. Younger age at PPV correlated with a diminished IVI requirement, likely due to enhanced retinal plasticity and the absence of systemic factors perpetuating vasogenic or inflammatory aspects of ME in younger patients. Conversely, the presence of glaucoma, defined by intraocular pressure exceeding 21 mm Hg with the use of anti-glaucoma medications, was associated with an increased postoperative IVI need. This elevation could be attributed to potential interference between anti-glaucomatous medications and the bioavailability of anti-VEGF agents, especially in vitrectomized eyes [35], or the heightened likelihood of glaucoma in severe RVO cases necessitating repeated IVI [36]. A reduced postoperative IVI requirement in cases of disrupted EZ might stem from physicians' hesitancy to prescribe IVI for patients with altered outer retinas. Interestingly, the use of tamponade during PPV (surgeon's preference, or because of the occurrence of complications) correlated with a diminished postoperative IVI frequency. Intravitreal tamponade with air, gas, or silicone was noted to lower proinflammatory cytokine concentrations in the vitreous cavity, leading potentially to less frequent occurrence or persistence of ME [37]. In terms of ERM recurrence, our study did not identify ILM peeling as a significant predictive factor, aligning with findings in other publications [38]. However, surgeons may overestimate the rate of spontaneous ILM peeling (i.e., occurring simultaneously to ERM peeling), which can induce a bias limiting the impact of ILM peeling on the recurrence rate.

This study is constrained by its retrospective design, limited sample size, and lack of a control group. Patient heterogeneity in a multicenter setup should be acknowledged, as well as treatment preferences regarding the use of postoperative IVI to treat ME. The significant rate of follow-up losses overtime might be associated with the composition of participating university hospitals as many patients were followed-up by their local ophthalmologists after a certain postoperative period. The study did not explore specific OCT features, including continuous ectopic inner foveal layers, which can impact the prognosis [39]. Additionally, prognostic factors were analyzed only through univariate analysis due to the impracticality of multivariate analysis with the available sample size.

In conclusion, removing secondary ERM in RVO patients yielded improved vision and reduced CMT for up to 3 years post-surgery, lowering the need for postoperative IVIs. Favorable prognostic factors for functional and anatomical outcomes included poorer baseline VA and CMT, preoperative dexamethasone implant use, and use of postoperative IVIs. Younger age at surgery and tamponade use predicted reduced postoperative IVI needs, while ILM peeling conferred no additional benefits. Nonetheless, prospective studies are essential to validate these findings.

## Statement of Ethics

This study protocol was reviewed and approved by the Institutional Review Board of the French Society of Ophthalmology (IRB No. 00008855). Informed consent was waived by the Institutional Review Board of the French Society of Ophthalmology, due to the retrospective nature of the study.

## Conflict of Interest Statement

The authors have no conflicts of interest to declare.


## Funding Sources

This study was not supported by any sponsor or funder.


## Author Contributions

Conceptualization: Sara Touhami. Data curation: Irini Chatziralli, Anissa Smaoui, Bahram Bodaghi, Michel Paques, Ramin Tadayoni, and Maria Vittoria Cicinelli. Data analysis: Yoo-Ri Chung, Adam Mainguy, Irini Chatziralli, Maria Vittoria Cicinelli, and Sara Touhami. Writing – original draft: Yoo-Ri Chung, Adam Mainguy, and Sara Touhami. Writing – review and editing and final approval of the manuscript: all authors.

## Data Availability Statement

All data generated and analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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