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Predictors of the presence of cystoid macular edema after idiopathic epiretinal membrane surgery

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ABSTRACT

Aim: To determine the predictors of the presence of cystoid macular edema (CME) after idiopathic epiretinal membrane surgery.

Material and methods: A two-center retrospective cohort study. A review of consecutive patients with ERM who underwent pars plana vitrectomy with ERM peeling. The study involved an analysis of a set of factors at baseline and during one-year follow-up, including best-corrected visual acuity (BCVA, LogMAR) and optical coherence tomography markers, surgical factors (posterior capsulotomy, steroid use, type of tamponade, ILM peeling). The statistical model utilized uni- and multivariate logistic regression analyses with final CME presence as a binary outcome.

Results: One-hundred twenty eight eyes (125 patients) were enrolled in the study. A significant improvement in BCVA was noted in both groups, but the improvement rate was faster in the non-CME group. Univariate analysis showed that young age (OR 0.9, CI: 0.84-0.96, $p = 0.02$), air tamponade (OR 8.62, CI: 1.92-38.73, $p = 0.005$), and silicone oil tamponade (OR 2.31, CI: 1.02-51.69, $p = 0.048$) represented risk factors for the presence of CME after PPV. Conversely, intraoperative posterior capsulotomy and intravitreal steroid administration were not associated with the incidence of CME. The risk factors for new postoperative CME included air tamponade (OR 3.80, CI: 1.62-8.92, $p = 0.002$) and increased preoperative central retinal thickness (OR 1.01, CI: 1.00-1.01, $p = 0.011$). However, in the multivariate analysis none of the evaluated parameters was found to be statistically significant.

Conclusions: The presence of cystoid macular edema is a negative prognostic factor after PPV in ERM patients. There is no link between an increased incidence of CME and the stage of ERM or intraoperative factors such as posterior capsulotomy, intraoperative steroid administration, ILM peeling, or the type of tamponade.

KEY WORDS: epiretinal membrane, optic coherence tomography, OCT, cystoid macular edema, CME, posterior capsulotomy.

INTRODUCTION

Epiretinal membrane (ERM) is a fibrocellular membrane containing extracellular matrix proteins and epiretinal cells of retinal and extraretinal origin. ERM may cause decreased visual acuity and other disturbances such as metamorphopsias and aniseikonia. The only effective treatment method for ERM is pars plana vitrectomy (PPV) with macular peeling, though it does not always result in full resolution of symptoms [1].

Postoperative cystoid macular edema (CME) is a relatively common cause of visual acuity deterioration after vitreoretinal surgery. It may complicate up to 45% of cases of ERM removal [2]. In most patients, CME is self-limiting, though refractory cases require treatment and may be associated with additional costs [3]. Two mechanisms are hypothesized to play a role in the development of macular edema in ERM [1, 4-6]. One involves biological factors/mechanical stress that can induce disruption of the blood-retinal barrier, leading to increased vascular permeability and CME formation [6, 7]. The other pathological mechanism is postulated to involve Müller cell degeneration [4, 5, 8].

Spectral-domain optical coherence tomography (SD-OCT) is a recognized, reliable and safe technique used to assess the severity of CME. Recent studies suggest that new markers of ERM severity, e.g. EIFL (ectopic inner foveal layer) may affect the incidence of CME [9]. This paper examines

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the impact of key OCT markers on postoperative CME rates and the prognostic role of macular edema in postoperative patient outcomes. In addition, the impact of different surgical procedures on CME was determined, including, for the first time, the potential effect of intraoperative posterior capsulotomy on the presence and risk of postoperative CME.

MATERIALS AND METHODS

Patients

This retrospective cohort study was based on the data pool of patients with idiopathic epiretinal membrane (ERM) who underwent vitrectomy with ERM peeling, with or without inner limiting membrane (ILM) peeling. To date, one paper relying on the data from that database has been published (Klinika Oczna 2022, 124 (3): 142-149). The procedures were performed between January 2017 and December 2019 in two university hospitals: 1) II Department of Ophthalmology, Pomeranian Medical University in Szczecin and 2) Independent Public Clinical Ophthalmology Hospital in Warsaw (Department of Ophthalmology, Medical University of Warsaw). The study was approved by the local ethics committee and conducted in accordance with the provisions of the Declaration of Helsinki.

The patients' preoperative and intraoperative assessment included a number of parameters: age, sex, endoillumination intensity, duration of procedure, ILM peeling, intraoperative posterior capsulotomy, type of tamponade, and intraoperative use of steroids. Best-corrected distance visual acuity (BCVA, logMAR) measurements and optical coherence tomography (OCT) scanning were performed at baseline and at 3, 6, and 12 months after vitrectomy.

The exclusion criteria included patients with secondary epiretinal membrane, history of retinal laser therapy and ophthalmic surgery (with the exception of uncomplicated cataract surgery) and patients with other retinal conditions (inflammatory diseases, diabetic macular edema, macular hole, vitreoretinal traction syndrome, central retinal vein occlusion, etc.).

The patients were divided into two groups based on the presence of postoperative cystoid macular edema (CME): 1) group with CME (CME group) 2) group without CME (non-CME group).

Optical coherence tomography

Optical coherence tomography (OCT) scanning was performed with the Zeiss Cirrus OCT system (Humphrey Instruments model 3000, Carl Zeiss Inc., Dublin, California). Each OCT scan was assessed by two independent investigators (MD and MP).

Cystoid macular edema (CME) was defined as the presence of any intraretinal fluid with concomitant central retinal thickening above reference values. The value of central macular thickness (CMT), corresponding to the innermost 1-mm wide circle of the ETDRS map, was automatically calculated from B-scans centered to the fovea. The thickness of the outer nuclear layer (ONL) was defined as the width of the outer dark-gray band between the ellipsoid zone (EZ) band beneath the present or presumed foveal depression and the outer plexiform layer/ONL boundary. It was measured manually using the caliper function in the Zeiss Cirrus system. The presence and thickness of the ectopic inner foveal layers (EIFL), defined as a continuous hypo- or hyperreflective inner retinal band spanning across the fovea, was assessed. In addition, SD-OCT B-scans were analyzed for damage to the ellipsoid zone/external limiting membrane (EZ/ELM), and the presence of the so-called 'cotton ball sign' defined as a round hyperreflective fuzzy thickening of the outer layers of the retina.

ERM stage was assessed using the classification proposed by Govetto [10] (stage 1 – mild ERM with preserved foveal depression and no anatomical distortions; stage 4 – advanced ERM, with EIFL, without foveal depression and with complete loss of macular segmentation).

Surgical procedure

Pars plana vitrectomy (PPV) was conducted through three 25G ports using the Constellation Vision System (Alcon, Fort Worth, TX). All procedures were performed in pseudophakic eyes. In some patients, intraoperative posterior capsulotomy was performed using a vitrectomy device (approx. 4 mm in width). The decision to carry out a capsulotomy was left to the surgeon's discretion. Central vitrectomy was performed at a cut rate of 4,000-10,000 cpm and aspiration rate of 400-650 mmHg. Posterior vitreous detachment was achieved without cutting, at an aspiration rate of 400-550 mmHg. In isolated cases, Diphrophos (betamethasone dipropionate + betamethasone sodium phosphate) was used to visualize the vitreous cortex. Xenon light intensity ranged from 30 to 50% (filter: 435 nm). For ERM/ILM staining, 0.3 ml of the following dyes were injected for 30-60 seconds: 1) ILM Blue, DORC International, Zuidland, the Netherlands: 0.025% Brilliant Blue G; 2) MembraneBlue-Dual, DORC International, Zuidland, the Netherlands: 0.15% Trypan Blue, 0.025% Brilliant Blue G. Visualization of the macula was done with the BIOS optical system. ERM/ILM peeling was performed using fine-tipped forceps (Alcon ILM forceps 25G). The internal limiting membrane was removed depending on the surgeon's discretion. Ocular tamponade was achieved with liquid, air, and less commonly with sulfur hexafluoride (SF6) or silicone oil. Sclerotomies were sutured (Vicryl 8.0) after the use of fluid or silicone oil, or in patients with wound leaks. At the end of the procedure, 0.2 ml of an antibiotic and a steroid were administered subconjunctivally.

Statistical analysis

The data collected in the study were presented using descriptive statistics, including means and SD (for quantitative variables), and counts and percentages (for qualitative variables). The assumption of normality of the distribution of continuous variables (BCVA, duration of surgery, CMT, ONL, EIFL) was checked using the Shapiro-Wilk W test. Parameter comparisons between the CME and non-CME groups were made using the Student's T or Mann-Whitney

Table I. Demographic and clinical characteristics of patients with idiopathic epiretinal membrane, broken down by the presence of cystoid macular edema (CME) after vitrectomy with ERM peeling

	All patients ($n = 128$)		Patients with CM ($n = 24$)		Patients without CM ($n = 104$)		p
	Mean	SD	Mean	SD	Mean	SD	
Age (years)	72.9	6.8	68.5	9.4	73.8	5.7	
	n	%	*n*	%	*n*	%	*p*
Sex							
Men	72	56.2	13	54.1	43	41.3	0.254
Women	56	43.8	11	45.9	61	58.7	
Preoperative BCVA (LogMAR)	0.50	0.2	0.52	0.1	0.47	0.2	0.041*
Surgical parameters							
	Mean	SD	Mean	SD	Mean	SD	*p*
Duration of procedure (min)	39.39	12.29	41.50	12.06	38.90	12.34	0.291
	n	%	*n*	%	*n*	%	*p*
Endoillumination							
30%	50	50.5	6	40.0	44	52.4	0.377
50%	49	49.5	9	60.0	40	47.6	
Tamponade type							
Air	77	60.2	21	87.5	56	53.8	0.008*
Fluid	48	37.5	2	8.3	46	44.2	
SF6	1	0.8	0	0	1	1.0	
Silicone oil	2	1.6	1	4.2	1	1.0	
ILM peeling	115	89.8	22	91.7	93	89.4	0.743
Intraoperative steroids	6	4.7	1	4.2	5	4.8	0.893
Posterior capsulotomy	27	21.1	5	20.8	22	21.2	0.972
OCT parameters							
	n	%	*n*	%	*n*	%	*p*
Stage of ERM							
1º	11	8.6	3	12.5	8	7.7	0.894
2º	37	28.9	7	29.2	30	28.8	
3º	74	57.8	13	54.2	61	58.7	
4º	6	4.7	1	4.2	5	4.8	
ELM/EZ damage	11	8.7	3	13.0	8	7.8	0.417
Cotton ball sign	42	33.3	5	20.8	37	36.3	0.149
	Mean	SD	Mean	SD	Mean	SD	*p*
CMT thickness (µm)	238.57	73.82	247.18	101.54	236.69	67.01	0.137
ONL thickness (µm)	449.30	67.46	470.10	61.43	444.44	68.19	0.873
EIFL thickness (µm)	79.81	88.76	72.10	99.99	81.70	86.37	0.554

** statistically significant*

BCVA – best-corrected distance visual acuity; CMT – central macular thickness; ELM – external limiting membrane; EIFL – ectopic inner foveal layer; ERM – epiretinal membrane; EZ – ellipsoid zone; ILM – internal limiting membrane; OCT – optical coherence tomography; ONL – outer nuclear layer; SD – standard deviation; SF6 – sulfur hexafluoride

U tests (for quantitative variables) or the χ^2 test (for qualitative variables). Comparisons of BCVA, CMT and ONL values between the four time points (pre-surgery, 3 months, 6 months, 12 months) were based on Friedman's ANOVA test. A univariate logistic regression analysis was performed with the development of CME as the dependent variable, and age, sex, and perioperative parameters as the explanatory variables. The odds ratio (OR) was calculated for each parameter separately. The results were considered statistically significant at $p < 0.05$.

RESULTS

Characteristics of study groups

The study involved a review of 128 eyes of 125 patients with a mean age of 72.9 ±6.88 years. The groups differed by age (68.5 vs. 73.8 years, $p = 0.029$) and preoperative BCVA (0.52 vs. 0.47, $p < 0.041$). In addition, air endotamponade was more commonly used during PPV in patients with preoperative CME (87.5% vs. 53.8%, $p = 0.008$). There were no statistically significant differences between the groups in terms of other surgical parameters, sex, and OCT characteristics ($p > 0.05$) (Table I).

Functional and anatomical outcomes after PPV with ERM peeling

The CME group had worse preoperative BCVA compared to the non-CME group. A significant improvement in BCVA was observed in both groups at one-year follow-up, but the increase in BCVA was more pronounced in the non-CME group (Table II). At six-month follow-up, better BCVA scores were observed in non-CME eyes, but the difference disappeared at 12 months of follow-up.

Both pre- and postoperative values of central macular thickness (CMT) were similar in both groups (Table II). A statistically significant reduction in CMT (Δ = 65 µm, p < 0.001) after PPV was observed only in the non-CME group. In the CME group, there was a trend towards lower CMT values at one-year follow-up, but without statistical significance. Furthermore, there were no significant differences in pre- and post-operative values of ONL thickness between the two groups.

Predictors of the presence of cystoid macular edema obrzęku plamki

Preoperatively, CME was present in 23 eyes. After PPV, it persisted in 15 eyes and resolved in eight eyes. New CME developed in nine eyes. In total, CME was observed in 24 eyes during the postoperative period (15 eyes – persistent CME, nine eyes – CME that emerged postoperatively).

Based on the univariate logistic regression analysis, young age of the patients (OR 0.9, CI: 0.84-0.96, $p = 0.02$), air tamponade (OR 8.62, CI: 1.92-38.73, $p = 0.005$), and silicone oil tamponade (OR 2.31, CI: 1.02-51.69, $p = 0.048$) represented risk factors for the presence of CME after macular peeling (Table III). Intraoperative posterior capsulotomy and intravitreal steroid administration were not found to be associated with the incidence of CME. Also, neither the ERM stage in Govetto's classification nor any other OCT parameters were found to correlate with the presence of CME. In the multivariate analysis, none of the evaluated parameters were revealed as statistically significant.

The subgroup of patients without preoperative CME was subjected to univariate logistic regression analysis in order to determine the risk of new CME after PPV surgery with macular peeling. The risk factors for new postoperative CME were found to include air tamponade (OR 3.80, CI: 1.62-8.92, $p = 0.002$) and increased preoperative central macular thickness (CMT) (OR 1.01, CI: 1.00-1.01, $p = 0,011$). The remaining demographic, surgical and anatomical parameters turned out to be statistically insignificant. In the multivariate analysis, none of the evaluated parameters was found to be statistically significant.

Table II. Changes in best-corrected distance visual acuity, central macular thickness, and outer nuclear layer thickness at one-year follow-up in patients after ERM peeling. Patient categorization was based on the presence of postoperative cystoid macular edema

	Best-corrected distance visual acuity (LogMAR)								
	Prior to surgery		3 months postoperatively		6 months postoperatively		12 months postoperatively		*p*
	Średnia	SD	Średnia	SD	Średnia	SD	Średnia	SD	
CME	0.52	0.12	0.40	0.31	0.33	0.20	0.28	0.15	0.004*
non-CME	0.47	0.21	0.33	0.25	0.22	0.16	0.19	0.14	0.001*
p	0.041*		0.505		0.008		0,058		
Central macular thickness (CMT) (µm)									
CME	470.10	61.43	429.88	58.85	442.88	97.08	392.62	87.14	0.215
non-CME	444.44	68.19	410.81	64.56	393.49	67.19	379.18	71.28	< 0.001*
p	0.137		0.220		0.077		0.856		
Outer nuclear layer (ONL) thickness (µm)									
CME	247.18	101.54	263.56	89.04	236.53	86.16	215.77	104.01	0.551
non-CME	236.69	67.01	206.90	79.98	204.59	62.72	188.13	57.18	0.053
p	0.873		0.008*		0.237		0.480		

** statistically significant*

BCVA – best-corrected distance visual acuity; CME – cystoid macular edema; ERM – epiretinal membrane; SD – standard deviation

Table III. Univariate logistic regression analysis of parameters associated with the presence or development of cystoid macular edema (CME) after vitrectomy (PPV) with epiretinal membrane (ERM) peeling. The odds ratio (OR) and 95% confidence interval (CI) are shown. In the multivariate analysis, none of the evaluated parameters were found to be statistically significant

		Risk of CME presence after PPV			Risk of new CME after PPV		
	Reference	OR	CI	*p*	OR	CI	*p*
Preoperative BCVA	–	3.52	0.41 29.90	0.249	1.48	0.24 8.97	0.669
Age (years)	–	0.90	0.84 0.96	0.002*	0.98	0.93 1.03	0.421
Sex	Men	1.68	0.69 4.09	0.257	1.48	0.72 3.07	0.287
Duration of procedure	–	1.02	0.98 1.05	0.351	1.00	0.97 1.03	0.786
Tamponade air	Fluid	8.62	1.92 38.73	0.005*	3.80	1.62 8.92	0.002*
Tamponade SF6	Fluid	0.00	0.00 0.00	0.998	0.00	0.00 0.00	0.998
Tamponade oil	Fluid	2.31	1.02 51.69	0.048*	0.00	0.00 0.00	0.998
ILM peeling	0	1.30	0.27 6.30	0.744	1.99	0.52 7.64	0.315
Posterior capsulotomy	0	0.98	0.33 2.92	0.972	0.44	0.16 1.17	0.100
Endoillumination 50%	30%	1.65	0.54 5.05	0.380	1.93	0.83 4.46	0.124
Intraoperative steroids	0	0.86	0.10 7.73	0.894	1.84	0.36 9.50	0.468
ERM classification in OCT 2	1	0.62	0.13 2.96	0.147	2.74	0.52 14.55	0.237
ERM classification in OCT 3	1	0.57	0.13 2.44	0.551	2.44	0.49 12.13	0.277
ERM classification in OCT 4	1	0.53	0.04 6.66	0.447	9.00	0.91 88.58	0.060
Preoperative ONL thickness (100 µm)°	–	1.00	0.99 1.01	0.594	1.01	1.00 1.01	0.088
Preoperative CMT thickness (100 µm)°	–	1.01	1.00 1.01	0.119	1.01	1.00 1.01	0.011*
Preoperative EIFL thickness (100 µm)°	–	1.00	0.99 1.00	0.664	1.00	1.00 1.01	0.668
Preoperative cotton ball sign	0	0.46	0.16 1.34	0.155	0.69	0.32 1.52	0.361
Preoperative ELM/EZ damage	0	1.78	0.43 7.31	0.423	3.41	0.94 12.36	0.062

** statistically significant in univariate analysis (no statistical significance in multivariate analysis); ° odds ratio of the presence of CME for every 100 µm of retinal layer thickness*

BCVA – best-corrected distance visual acuity; CMT – central macular thickness; ELM – external limiting membrane; EIFL – ectopic inner foveal layer; ERM – epiretinal membrane; EZ – ellipsoid zone; ILM – internal limiting membrane; OCT – optical coherence tomography; ONL – outer nuclear layer; HR – hazard ratio; CI – confidence interval

DISCUSSION

The reported study was conducted to retrospectively analyze patients undergoing PPV with ERM peeling with a focus on assessing the incidence of cystoid macular edema at one-year follow-up after PPV and determining the risk factors for CME. Even though improvements in visual acuity were achieved in all eyes, the outcomes were generally poorer in the eyes with CME after PPV compared to the eyes without CME. No evidence was found to indicate that preoperative OCT parameters and intraoperative factors (posterior capsu-

lotomy, ILM peeling, tamponade, etc.) had a significant impact on the development and progression of macular edema.

Macular edema is characterized by the accumulation of fluid in two retinal layers – the inner nuclear layer (INL) and the Henle fiber layer. It may be a morphological manifestation of various retinal diseases [11]. Macular edema is most typically defined as the coexistence of central retinal thickening > 250 μm with associated hyporeflective areas within the retina or intraretinal cysts (CME) [12]. However, different studies describe CME in various ways; the definition may be based on the presence of a leak on fluorescein angiography, a 10% increase in CMT [13] or CMT > 500 μm in cases of clinically significant CME [14]. These differences affect the incidence of CME in ERM, which ranges from 7.2% [15] to 45% [2]. In our study, the incidence of CME was 18.8%. Similarly to Fristina *et al.* [4], we observed that patients with CME had higher mean CMT scores and greater decreases in CMT at 12-month follow-up compared to patients without CME. It should be noted, though, that despite a clear trend towards lower CMT scores in the CME group in our study the results did not achieve statistical significance.

In our follow-up, preoperative CME persisted for many months after surgery in the majority of patients (15/23, 65%), which is a similar finding to that reported by other authors [4, 8, 15]. Even though fluid resolution potentially reverses macular dysfunction, irreversible retinal damage (i.e. thinning of the outer nuclear level, glial reaction) may occasionally occur as a result of chronic edema. In such cases, CME is poorly responsive or non-responsive to medical or surgical treatment. In two studies, patients with preoperative CME [16] and postoperative CME [4] showed no improvement in BCVA after surgery. In our study, preoperative CME reduced the benefits of the surgical intervention, but improvements in BCVA were nevertheless observed. The observation is in concordance with the majority of previous publications [4, 15, 17–21]. Only isolated case reports suggest that preoperative macular edema has no significant impact on postoperative BCVA [21, 22], or may even have a positive effect on visual acuity [23]. Do *et al.* [24], in their study assessing the influence of OCT on surgical decision-making, showed that the presence of CME was a factor prompting surgeons to advise patients with ERM to undergo PPV earlier. Our results support this approach and provide evidence that the presence of CME is a negative prognostic factor in ERM.

Many surgeons performing phaco-PPV or PPV in pseudophakic eyes face the dilemma of whether to carry out a posterior capsulotomy during the procedure. Posterior capsulotomy performed using a vitrectomy device (pars plana approach) allows complete removal of the anterior cortical vitreous and may improve visualization of the retina during macular surgery. Intraoperative capsulotomy is also used for the prophylaxis of posterior capsule opacification (PCO). Results of studies to date suggest that the PCO area may be greater in patients undergoing phaco-PPV than in those having cataract surgery alone, as the combined procedure may result in more severe postoperative inflammation [25, 26]. It has been suggested that pro-inflammatory cytokines including transforming growth factor β, interleukin-1 (IL-1), IL-6, IL-8, and fibroblast growth factor may play an important role in the proliferation of epithelial cells in the lens and the development of PCO [27]. In other words, the degree of postoperative inflammation appears to be linked to the development and severity of PCO [25]. At the same time, posterior capsulotomy has the potential to increase the level of pro-inflammatory cytokines in the posterior pole and affect CME. This appears to be a reasonable suspicion, as posterior capsule rupture during cataract surgery is associated with an increased risk of CME [12]. To the best of the authors' knowledge, this study is the first to evaluate the effects of posterior capsulotomy on the risk and incidence of CME after vitrectomy. We evaluated the impact of secondary posterior capsulotomy (when PPV was performed in pseudophakic eyes) and identified no correlation between this procedure and the incidence of CME. Similarly to Sato *et al*., we did not observe IOL translocation that could occur after PPV with simultaneous capsulotomy (especially when air/gas endotamponade was used) [28]. Our outcomes show that posterior capsulotomy performed with a vitrectomy device is a safe and effective technique preventing PCO in patients undergoing vitrectomy. In addition, the procedure is economically viable, as it does not require any special equipment, laser procedures or additional follow-ups.

The current treatment of choice for patients with ERM is PPV with macular peeling. Of note, the prevalence of ILM removal in the USA has increased from 30 to 70% over the past 15 years [29]. At the same time, some studies have shown that ILM peeling can cause traumatization of the underlying inner retinal layers [30, 31]. There is as yet no consensus as to whether ILM peeling improves postoperative visual acuity or reduces the risk of persistent postoperative CME [31]. Multiple studies corroborate the thesis that surgical removal of the ILM may result in disruption of the continuity of adjacent Müller cells, leading to the persistence and exacerbation of CME [4, 32, 33]. In the present study, no correlation was found between ILM peeling and the presence of macular edema or the development of new CME after surgery. Our findings are consistent with the results reported by Guber *et al.* [23] and Leisser *et al.* [15, 34]. Conversely, Geerts *et al.* [35] found that ILM peeling was a better surgical approach for CME reduction because of decreased epiretinal traction which resolved in 90% of patients (compared to 44% of patients who underwent ERM removal alone). In the study by Silva *et al*., removal of the ERM-ILM complex was also found to be a prognostic factor indicating protection against postoperative CME [36]. In conclusion, there is no unequivocal evidence for a correlation between ILM removal and postoperative CME in patients after ERM peeling.

Two mechanisms are hypothesized to play a role in the development of macular edema in ERM [1, 4-6]. One of them comprises biological factors (e.g. inflammatory cytokines, angiogenic factors) and mechanical stress, both of which can

lead to the disruption of the inner and outer blood-retinal barrier, resulting in increased vascular permeability (visible on angiography as leakage) and the development of CME [6, 7]. The mechanism is similar to the Irvine-Gass syndrome that can occur after any intraocular surgical procedure. The other hypothetical mechanism is based on Müller cell degeneration, with the determinants including ERM traction [4, 5], vitreous traction [37, 38], and retrograde transsynaptic degeneration of the internal retinal layers [39]. In this case, microcystic changes seen on OCT are fluid-filled voids replacing degenerated retinal cells (Müller cells) rather than actual leakage [4, 39]. Iuliano *et al*. determined that stage 4 ERM was associated with the greatest risk of CME development [9]. The authors concluded that the greater susceptibility of stage 4 ERM compared to other stages could be attributed to the pathogenesis of EIFL [9]. Ectopic inner foveal layers (EIFL) extend from the inner nuclear and plexiform layers of the retina across the entire foveal area, and are recognized as negative prognostic factors in patients with ERM [10, 21, 40]. The results of our study do not support the hypothesis put forth by Iuliano *et al*. about the mechanical tractive effect of EIFL on CME. We did not observe a relationship between the incidence of CME and EIFL (stage 3/4 according to Govetto's grading system) and EIFL thickness (Table III). Also, there was no identifiable correlation between the incidence of CME and any of the ERM stages in Govetto's classification. Further studies on the role of EIFL in the pathogenesis of CME are necessary, focusing in particular on fundal autofluorescence (to evaluate tangential traction) and fluorescein angiography (to visualize damage to the blood-retinal barrier).

Our study has several significant limitations. Because of the retrospective study design, we were unable to review data obtained from fluorescein angiography, as it was not routinely performed prior to PPV. These data could be used for a comprehensive assessment of the status of the blood-retinal barrier, resulting in accurate differentiation between the exudative (CME) and neurodegenerative (damage to Müller cells) etiology of edema. The absence of data explains the wide confidence intervals found for some of the variables under study. Other limitations of our study include the fact that different operators performed the surgical procedures and the size of the study sample was relatively small. Furthermore, as PPV is a rarely offered option at lower stages of ERM (1/2), the study could not detect relative differences compared to higher ERM stages (3/4). Finally, the resolution of currently available SD-OCT devices may result in false-positive diagnosis of EZ/ELM lesions due to OCT signal distortion because of the presence of massive CME. We attempted to reduce the risk of this error by having the OCT scans assessed by two independent specialists.

CONCLUSIONS

The study confirms that the presence of cystic macular edema is an important negative prognostic factor after PPV in patients with ERM. We found that a higher incidence of CME was not linked to the ERM stage or intraoperative factors such as posterior capsulotomy, intraoperative steroid administration, ILM peeling, and the type of tamponade.

DICLOSURE

The authors declare no conflict of interest.

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