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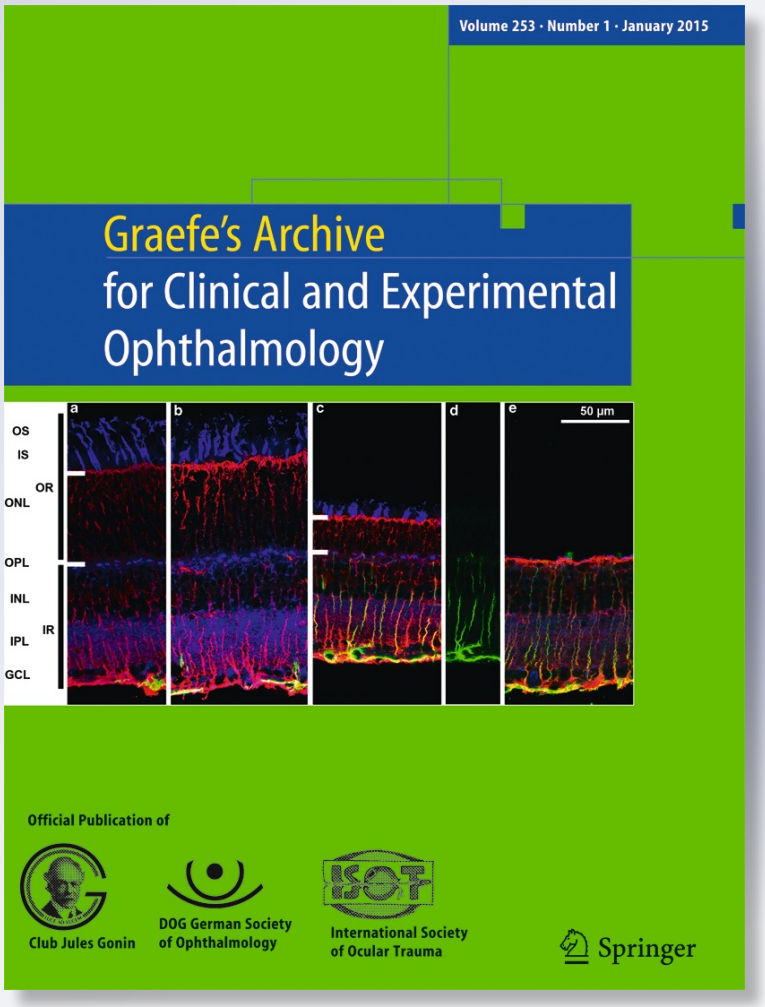

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RETINAL DISORDERS

Cystoid macular edema after pars plana vitrectomy for idiopathic epiretinal membrane

Rino Frisina · Sajish J. Pinackatt · Mauro Sartore · Alessandro Monfardini · Andrea Baldi · Bruno Mario Cesana · Francesco Semeraro · Adriana Bratu · Barbara Parolini

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Abstract
Background To evaluate the incidence of cystoid macular edema (CME) after 23-gauge pars plana vitrectomy (PPV) with or without combined cataract surgery for the treatment of idiopathic epiretinal membrane (ERM).
Methods Retrospective, non-comparative, interventional case series. Data included patient age, indication for surgery, and intra- and post-operative complications. The follow-up lasted 1 year. Best-corrected visual acuity (BCVA logMAR), central foveal thickness (CFT micron-μ) and the incidence of intra-retinal cysts were evaluated.

CME was defined as post-operative observation of intra-retinal cysts at optical coherence tomography, preventing improvement or causing reduction of BCVA when compared to the pre-operative value. Statistical analysis was performed to identify the risk factors of CME.
Results Two hundred and forty two eyes of 242 patients underwent PPV for the treatment of idiopathic ERM. Statistical analysis showed that the presence of preoperative intra-retinal cysts were associated with persistent CME following surgery (odds ratio 3.89; 95%CI: 1.63–9.28, P= 0.0004). However, postoperative CME occurred in 10 % of eyes that did not show preoperative CME. In addition, there was a significant correlation between the baseline value of CFT and the values of CFT at each time point during the follow up (p<0.0001), with greater values of the pre-operative thickness correlating to greater values of post-operative thickness.
Conclusions Persistent or new CME following surgery for idiopathic ERM are frequently identified after PPV for ERM. The statistical results of the current study suggest that intraretinal cysts and increased preoperative CFT are associated with reduced visual acuity after surgery.

Keywords Pars plana vitrectomy · Internal limiting membrane · Central foveal thickness · Cystoid macular edema · Epiretinal membrane · Intraretinal cyst

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Introduction

Cystoid macular edema (CME) is a well-known complication of anterior segment surgery, and is commonly referred to as Irvine–Gass Syndrome. The pathogenesis of CME after surgery is attributed to the breakdown of the blood–aqueous barrier due to an exaggerated inflammatory reaction and to the release of cytokine [1–6].

Many articles have been written on macular edema following ocular surgery. CME is observed after various types of intraocular surgery procedures. CME could be a post-operative complication after glaucoma surgery, penetrating keratoplasty, scleral buckling, and anterior vitrectomy [7, 8]. Nonetheless, there are few articles describing the occurrence of this complication after pars plana vitrectomy (PPV). Some cases, however, do occur and have been noticed in recent years.

This is a retrospective study to evaluate the incidence of CME in a non-homogenous series of eyes that underwent PPV

or PPV combined with phacoemulsification and implant of intraocular lens (Phaco IOL) for the treatment of idiopathic epiretinal membrane (ERM) .

Materials and methods

All subjects signed an informed consent document before surgery. IRB approval was not required, since this is a retrospective study and standard surgery was performed for a standard indication. The study included all surgical cases of idiopathic ERM consecutively operated with 23-gauge system. Cases of ERM secondary to other pathologies (retinal and choroid inflammation, vascular occlusion, ocular trauma, diabetes mellitus, retinal detachment, severe myopia with posterior staphiloma, uveitis, and glaucoma) were excluded from the study.

In addition to the exclusion criteria above mentioned, there were two exclusion criteria for surgical treatment of ERM that were assessed by fluorescein angiography (FA) and optical coherence tomography (OCT). The first was the presence of CME associated with the ERM with vascular leakage, the second was the defect of the photoreceptors line in the foveal region that could affect the functional recovery after a successful surgery.

The patients included in the study underwent surgery from May 2005 to July 2012. PPV cases were retrospectively identified through a search of the computerized database of hospital surgical records. The data that we abstracted from these charts included:

a. Demographic characteristics: patient age, sex, eye (right or left)
b. Baseline pre-operative clinical data: best-corrected visual acuity (BCVA) in logMAR, central foveal thickness (CFT) and the presence of pre-operative CME associated with ERM, assessed by OCT.
c. Surgical report: intra-operative complications, combination with Phaco IOL
d. Post-operative data: BCVA, CFT, at months 1, 3, 6, and 12; new appearance or persistence of CME during the follow up, assessed by OCT and FA.

Spectral OCT scanning laser ophthalmoscopy (SLO) (OPKO OTI Miami, FL), choosing six radial line scans centered on the fovea, was performed in all cases

The patients underwent PPV with or without Phaco IOL. The decision of combining Phaco IOL to PPV was up to the surgeon, in the presence of cataract of any level of severity. Therefore, two subgroups were identified as follows: PPV group, PPV+Phaco IOL group.

CME was defined as observation of intra-retinal cysts by OCT. Eyes with CME were evaluated for possible risk factors and outcome of BCVA.

Surgical technique

The surgical procedure was the same for every case. Four surgeons performed the operations in two hospitals (Sant'Anna Clinical Institute, Brescia – Sacrocuore Hospital, Verona).

The anesthesia procedure and the preliminary preparation of the patients are described elsewhere (Parolini et al.) [9].

Central and extended peripheral vitrectomy was performed for each case.

Peripheral laser treatment was performed by applying two or three rows of laser spots on the retinal side of the vitreous base around the sclerotomy sites, with the aim to prevent secondary retinal detachment.

The ERM was removed with forceps. The internal limiting membrane (ILM) was removed routinely. The ILM staining could be Brilliant Peel, Infracianine green or Membrane Dual.

If phacoemulsification had been planned, it was performed after the central vitrectomy and the surgical maneuvers on the posterior pole, prior to the peripheral vitrectomy and laser photocoagulation.

Dutch Ophthalmic Research Corporation (DORC, Zuidland, The Netherlands), Oertli (Berneck, Switzerland) or the Stellaris PC (Bausch and Lomb, Rochester, USA) instrumentation were randomly used for all surgical procedures. An incomplete fluid–air exchange was performed in every case.

Statistical methods

Descriptive statistics are absolute and relative frequencies for qualitative variables and means, standard deviation, median for quantitative variables. The two surgical procedures were compared by means of the Student's *t*-test (or its non-parametric equivalent the Wilcoxon signed-rank test) for quantitative variables and by means of the χ^2 test for the qualitative ones. The relationships between the presence of CME and the baseline variables were assessed by means of the Student's *t* test (or its non-parametric equivalent the Wilcoxon signed-rank test) for quantitative variables and by means of the χ^2 test for the qualitative ones. Furthermore, the prognostic relevance of the baseline characteristics on the CME was assessed by means of multiple logistic regression, according to a backward procedure. Goodness of fitting was assessed by means of Hosmer and Lemeshow's test.

Finally, the analysis of the repeated measurements (BCVA and CFT) was carried out according to a mixed factorial covariance analysis with sex and surgical procedure as two qualitative fixed factors (together with their interaction), and age and baseline value as covariates were carried out for the analysis of repeated measurements. For this analysis, the non-monotonic missing values, owing to a visit missed at the

scheduled time, were filled by carrying forward the value recorded at the previous visit; furthermore, monotonic missingness pattern of the last two assessments, owing to the loss of view of the patient, was filled according to the last observation carried forward (LOCF) method. In the case of a statistically significant result between the visits, multiple pairwise comparisons between the visits were carried out according to the Bonferroni's correction. In the case of a statistically significant result of the interaction treatment by visit, multiple pairwise comparisons of the interaction terms were carried out.

Statistical significance was set at 0.05 (two-tailed); statistical analyses were performed by using SAS®, 9.2 release.

Results

Two hundred and forty-two eyes of 242 patients underwent PPV for treatment of idiopathic ERM. One hundred and twenty-four eyes of 124 patients underwent PPV (PPV group), while 118 eyes of 118 patients underwent PPV and Phaco IOL (PPV+Phaco IOL group).

The demographic characteristics (age, sex, eye) were comparable in the PPV group and in the PPV+Phaco IOL group.

The baseline clinical characteristics (BCVA, CFT, pre-operative CME) were similar in the PPV group and in the PPV+Phaco IOL group (Table 1), and the statistical analysis did not show significant differences between the two surgical groups

The mean pre-operative BCVA was 0.4±0.2 (0.2–0.9) logMAR in the PPV group, and 0.5±0.2 (0.2–1.0) logMAR in PPV+Phaco IOL group (Table 1), without a statistically significant difference between the two surgical groups (P=0.0853).

The mean pre-operative CFT was 460.5±110.3 in the PPV group and 410.1±97.1 in the PPV+Phaco IOL group, with a statistically significant difference between the two surgical groups (P=0.0022).

The prevalence of pre-operative CME in the whole group was 13.63 % (33/242). The prevalence of pre-operative CME in each group of surgical treatment was respectively: 16.94 % (21 eyes) in the PPV group and 10.17 % (12 eyes) in the PPV+Phaco IOL group, without a statistically significant difference between the two surgical groups (P=0.1229).

Role of pre-operative CME as a complication of previous cataract surgery

In order to investigate the occurrence of pre-operative CME as a possible complications of previous cataract surgery, the PPV group was further divided into two subgroups: phakic patients (phakic group) and patients with previous cataract surgery (pseudophakic group).

The prevalence of pre-operative CME in the PPV group was 11.21 % in the subgroup of phakic patients and 6.03 % in the subgroup of pseudo-phakic patients. The statistical analysis did not show a significant difference in the distribution of pre-operative CME between the two subgroups of the PPV group (P=0.9574).

Post-operative CME

The prevalence of postoperative CME in the total group of 242 eyes was 12.8 % (31 eyes).

Table 1 Clinical characteristics of the patients

Pre-operative data			
Variable	Group		*P* value
Type of surgery	PPV (n=124)	PPV+PHACO IOL (n=118)	
Age (years)	74.7±8.86; (40–91)	72.1±7.7; (43–90)	0.0149[a]
Sex male/female	52/72	60/58	0.2596[b]
Eye right/left	61/63	68/50	0.1884[b]
Pre-operative BCVA LogMAR	0.4±0.2; (0.2–0.9)	0.5±0.2; (0.2–1.0)	0.0853[a]
Pre-operative CFT (μ)	460.05±110.3; (230–795)	410.1±97.1; (190–755)	0.0022[a*]
Pre-operative CME n. (%)	21 (16.94)	12 (10.17)	0.1229[b]

mean±SD (min–max)

*statistically significant

PPV: pars plana vitrectomy

PPV+PHACO IOL: pars plana vitrectomy+phacoemulsification intraocular lens; SD: standard deviation; BCVA: best- corrected visual acuity; LogMAR: logarithm of the minimal angle of resolution; CFT: central foveal thickness; IrC pre-op: intraretinal cysts pre-operatively

[a] *Student's t*-test

[b] χ^2 test

The prevalence of postoperative CME in the PPV group was 10.48 % (13/124 eyes). The eyes with CME had not encountered intra-operative complications.

The prevalence of post-operative CME in the PPV+Phaco IOL group was 15.25 % (18/118 eyes). Also, in this group the eyes with CME had not encountered intra-operative complications and the IOL was in the bag.

In this study, the prevalence of post-operative CME was higher in the PPV+Phaco IOL group compared to the PPV group. However, this difference was not statistically significant (P=0.2665); therefore, the combination of cataract surgery to PPV did not significantly increase the risk of CME. The incidence of post-operative CME was similar for both surgical teams. Respectively, the incidence of post-operative CME was 10.34 % (6/58) for surgeons of the Sant'Anna Clinical Institute, Brescia and 13.58 % (21/184) for surgeons of the Sacrocuore Hospital; the difference was non statistically significant (P=0.3426).

In order to identify the prognostic factors of developing CME, the relationships between the pre-operative data and CME was assessed.

The statistical analysis showed a statistically significant correlation with pre-operative CME (odds ratio 3.89; 95%CI: 1.63–9.28, p=0.0004). Among the 33 patients with pre-operative CME, 10 (30.30 %) developed post-operative CME while among the 209 without the pre-operative CME, 21 (10.04 %) developed postoperative CME.

Among the 13 eyes in the PPV group that developed postoperative CME, seven (53.8 %) did not present pre-operative CME, and six (46 %) already had CME pre-operatively. Among the 18 eyes of the PPV+Phaco IOL group that developed postoperative CME, 14 (77.7 %) did not present pre-operative CME, while four (22.2 %) eyes had CME pre-operatively.

Role of the status of the lens as a risk factor for the development of postoperative CME in the PPV group

The prevalence of post-operative CME was 6.03 % in the subgroup of phakic patients and 5.17 % in the subgroup of pseudo-phakic patients. The statistical analysis did not show a statistically significant difference in the distribution of postoperative CME in the two subgroups (P=0.3562)

Best-corrected visual acuity

Table 2 shows the changes in BCVA, in both groups of treatment, at different time points during the follow-up. The mixed factorial ANOVA for repeated measurements did not show a statistically significant difference between the two surgical groups (interaction time by surgical group: P=0.3260) and between the different time points during the follow-up (P=0.8042). However, there was a strong correlation (P<0.0001) between the baseline mean value of visual acuity and the trend of BCVA at each time point during the follow-up. In particular, from linear regression analyses with the baseline as the independent variable and each post-operative time point as the dependent one, for each increment of one unity of baseline BCVA there was an increase of postoperative BCVA of 0.53 at the 1stmonth (P<0.0001), 0.34 at the 3rdmonth (P=0.0002), 0.17 at the 6thmonth (P=0.1845), and 0.19 at the 12thmonth (P=0.0505).

Central foveal thickness

Table 3 shows a constant reduction in CFT in the two groups of surgical treatment during the entire follow-up. The mixed factorial ANOVA for repeated measurements did not show a statistically difference between the two surgical groups (interaction time by surgical group: P=0.2237). There was a statistically significant difference among the different time points of the follow-up (P<0.0001), with a CFT reduction between the baseline value and the 12th month of 16.4 % (P<0.0001), and between the 1rd postoperative month (P=0.0015) and the 12th month of 13.8 %.

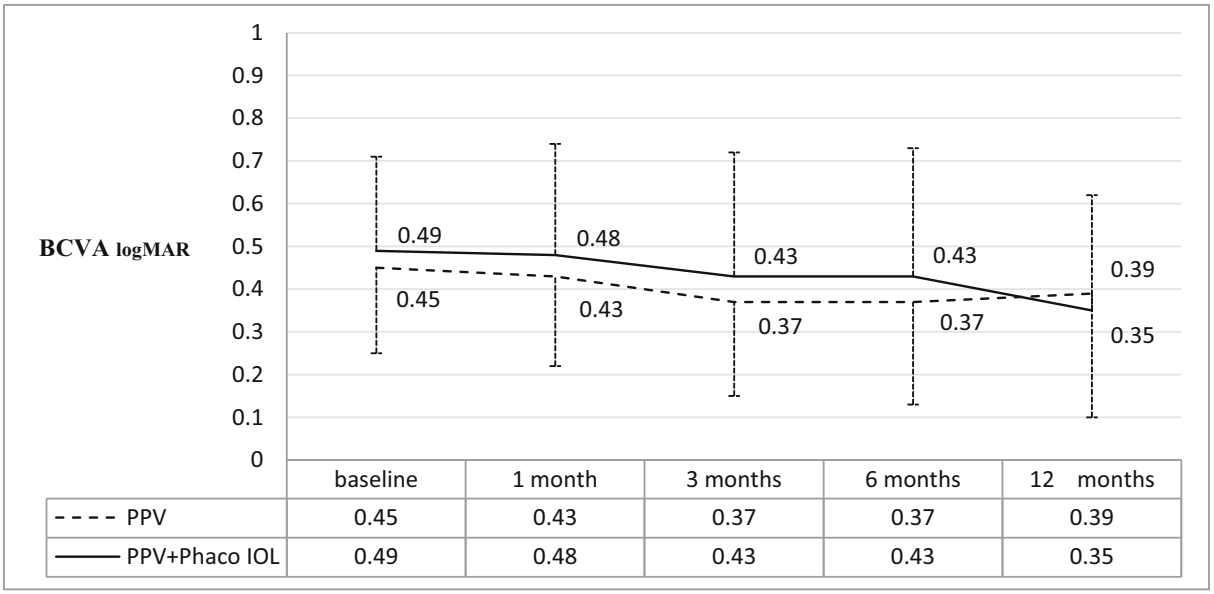
In addition, there was a significant correlation between the baseline value of CFT and the CFT values at the time points during the follow-up (P<0.0001); particularly, from linear regression analyses with the baseline as the independent variable and each postoperative time point as the dependent one, for each increment of one unity of baseline CFT there was an increase of postoperative CFT of 0.80 at the 1stmonth (P<0.0001), 0.30 at the 3rd month (P=0.0011), 0.28 at the 6th month (p=0.0020), and 0.24 at the 12th month (p=0.0036).

Patients with or without post-operative CME

Although it cannot be analyzed how the CME can influence the post-operative evolution of BCVA and the values of CFT, due to the fact that the occurrence of CME is a time-dependent variable, only for illustrative purposes we divided "a posteriori" all the patients in two subgroups with postoperative CME or without. The pattern of BCVA and CFT during the follow-up time points was shown respectively in graph 3 and graph 4. It is possible to see that patients with CME during the 12 months follow-up have a lower mean value of BCVA and a greater mean value of CFT than patients without CME.

Furthermore, BCVA in the patients with postoperative CME did not change during follow up, being 0.51±0.23 logMAR at baseline and 0.51±0.29 logMAR at 12 months (Table 4).

Table 2 Pattern of best-corrected visual acuity mean (BCVA logMAR) at baseline and in the postoperative period, in both surgical treatment groups (PPV and PPV+Phaco IOL)



	baseline	1 month	3 months	6 months	12 months
PPV	0.45	0.43	0.37	0.37	0.39
PPV+Phaco IOL	0.49	0.48	0.43	0.43	0.35

BCVA: best corrected visual acuity

PPV: pars plana vitrectomy

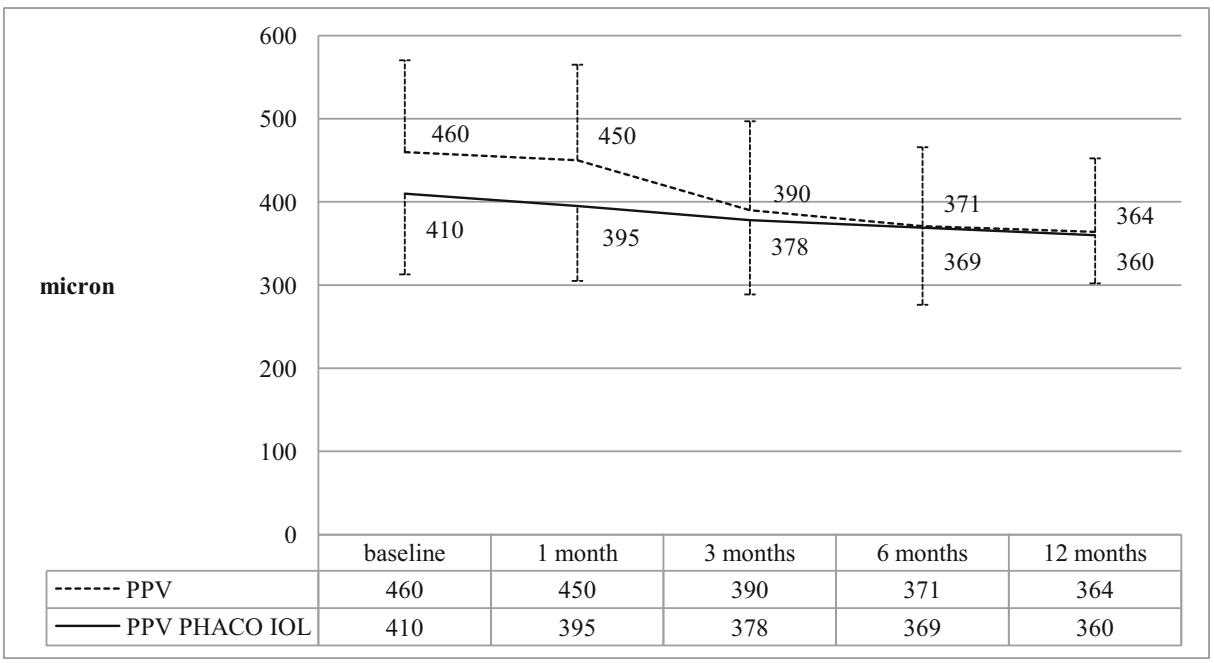
PPV+PHACO IOL: pars plana vitrectomy+phacoemulsification intraocular lens

In addition, mean CFT in the subgroup of patients with post-operative CME decreased by 7.9 % (479.1 μ at baseline and 422.45 μ at 12 months), against a decrease of 15.4 % in eyes that did not develop post-operative CME (431.36 μ at baseline and 364.94 μ at 12 months), as shown in Table 5.

Conclusions

The incidence of macular edema after PPV for ERM peeling was of 12.8 % in this study, confirming that CME is a serious complication after posterior segment surgery as well.

Table 3 Pattern of central foveal thickness mean (micron) at baseline and in the postoperative period, in both surgical treatment groups (PPV and PPV+Phaco IOL)

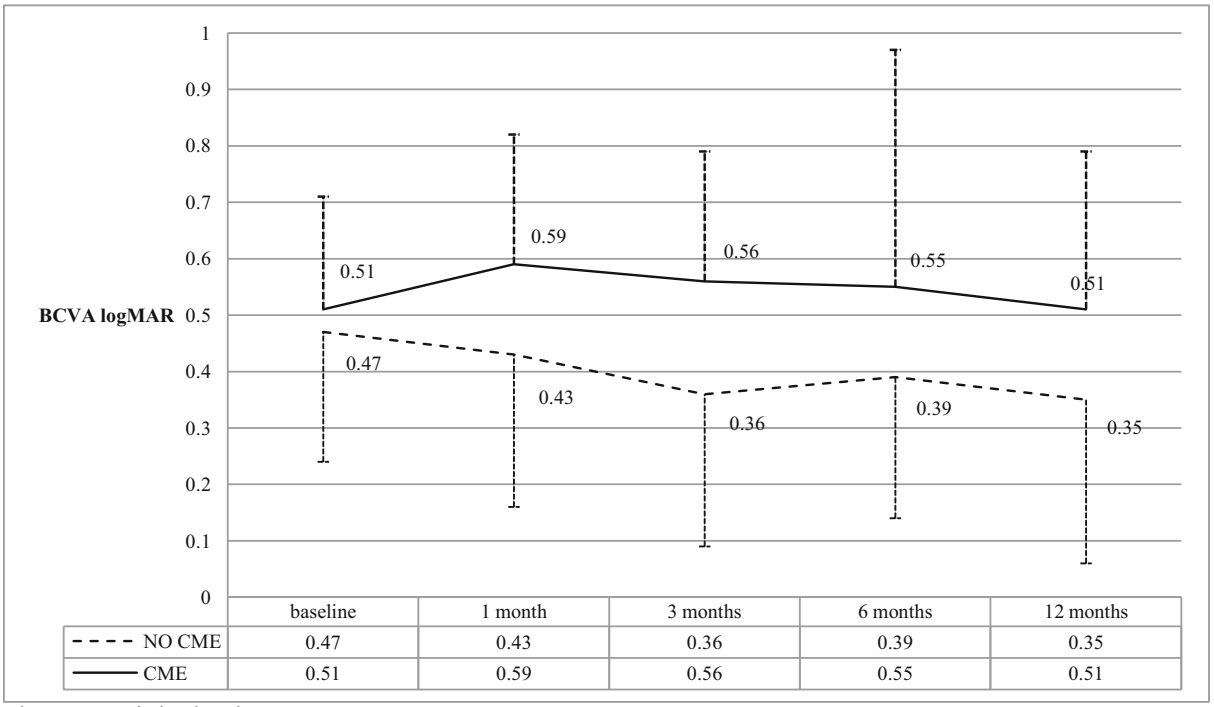


	baseline	1 month	3 months	6 months	12 months
PPV	460	450	390	371	364
PPV PHACO IOL	410	395	378	369	360

PPV: pars plana vitrectomy

PPV+PHACO IOL: pars plana vitrectomy+phacoemulsification intraocular lens

Table 4 Pattern of best corrected visual acuity mean (BCVA logMAR) at baseline and in the postoperative period, in CME group and No CME group



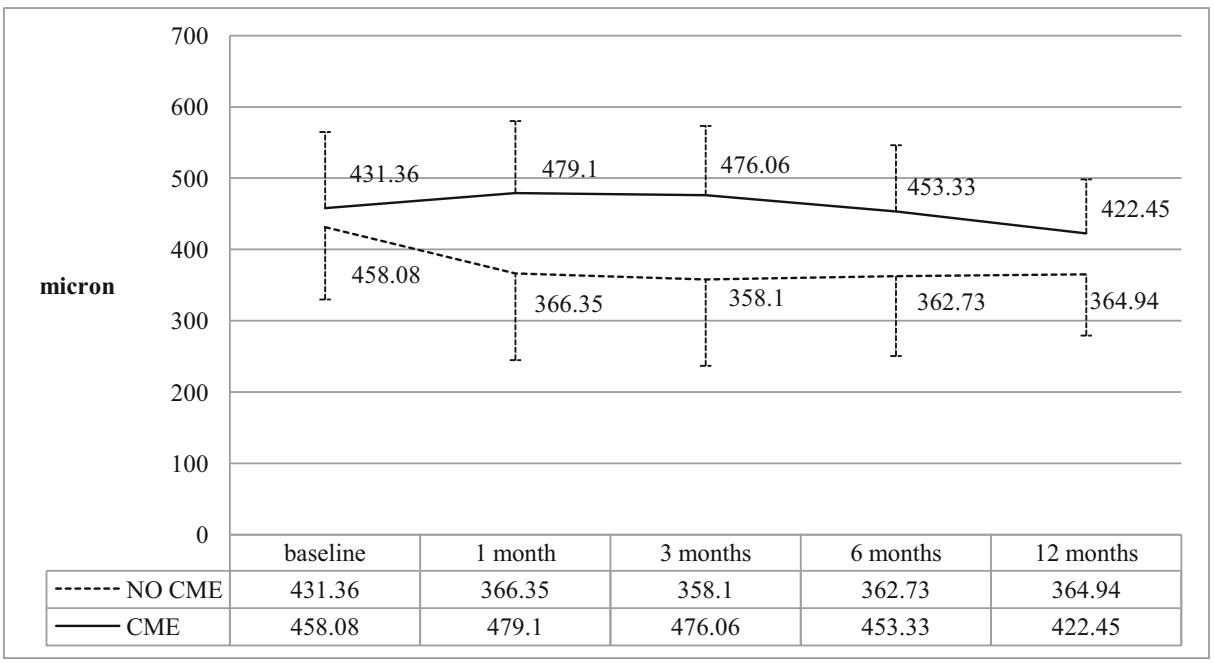
	baseline	1 month	3 months	6 months	12 months
NO CME	0.47	0.43	0.36	0.39	0.35
CME	0.51	0.59	0.56	0.55	0.51

BCVA: best corrected visual acuity

NO CME: No cystoid macular edema

CME: cystoid macular edema

Table 5 Pattern of central foveal thickness mean (micron) at baseline and in the postoperative period in CME group and No CME group



	baseline	1 month	3 months	6 months	12 months
NO CME	431.36	366.35	358.1	362.73	364.94
CME	458.08	479.1	476.06	453.33	422.45

NO CME: No cystoid macular edema

CME: cystoid macular edema

The authors have investigated the role of cataract surgery in the development of CME and tried to answer three important questions:

1) Could cataract surgery combined with PPV increase the risk of developing postoperative CME?
2) Could pseudophakic eyes be at higher risk of developing postoperative CME when compared to phakic eyes, in eye undergoing only PPV?
3) Could the pre-operative CME be a consequence of previous cataract surgery?

It is well-known that the incidence of CME is higher when surgical procedures are combined in a single operation [10]. The authors divided the whole group of patients into two subgroups, the PPV group and the PPV+Phaco IOL group, to assess whether the combination of cataract surgery with PPV could increase the incidence of postoperative CME. The occurrence of postoperative CME had a higher prevalence in the group where PPV was combined with Phaco+IOL implantation, but the statistical analysis did not show significant correlation between the combined surgery and the incidence of CME. Among the 13 eyes with postoperative CME in the PPV group, 7 eyes (53.8 %) did not present CME preoperatively. Among the 18 eyes with postoperative CME in the PPV+Phaco IOL group, 14 eyes (77.7 %) did not present CME preoperatively. Although even this difference is not statistically significant (P=0.2469 at a bilateral Fisher's exact test), it is noticeable that there is a tendency for a higher incidence of newly formed CME in the combined group.

To answer the second question, the role of previous cataract surgery in the development of CME was evaluated. The cataract surgery could release pro-inflammatory mediators (cytokines, prostaglandins, and other mediators) and induce subsequent development of CME (Irvine–Gass Syndrome). Consequently, postoperative CME after ERM peeling could be due to the previous cataract surgery and not, or not only, due to the following vitrectomy. To investigate if pseudophakic eyes were at higher risk of developing CME, the prevalence of postoperative CME was evaluated in the phakic and pseudophakic patients undergoing only PPV. The statistical analysis did not show any significant correlation between the lens status and the incidence of postoperative CME.

To answer the third question, the authors assessed the prevalence of pre-operative CME in phakic and pseudophakic eyes. The incidence of pre-operative CME was not statistically different in phakic and pseudophakic. The authors then assumed that the pre-operative CME was not related to the previous cataract surgery, but to the morphological changes due to the ERM evolution.

Although the influence of cataract remains debatable, it could be advisable to remove cataract first and then perform vitrectomy a few months later, since it is easier to perform vitrectomy in pseudophakic patients, and since it is not known which is the sequence of surgeries that would guarantee the lowest incidence of postoperative CME.

Kim et al. published a paper where macular edema was defined as an absolute value of postoperative macular thickness equal to or more than 272 μm, and it was studied at 1 month after surgery; therefore, it was considered an immediate postoperative reaction to vitrectomy performed for different indications. The degree of postoperative inflammation and the addition of intraoperative epinephrine were described as possible risk factors [11]. However, it is a common experience that a deviation from the normal CFT in idiopathic ERM does not always negatively impact vision. Therefore, rather than focusing on the value of CFT, the authors decided to look for the occurrence of intraretinal cysts, because these abnormal features were associated with lack of visual improvement or decrease in postoperative vision compared to the pre-operative BCVA value. In the present study, intraocular epinephrine was not used. The degree of early bulbar postoperative inflammation, assessed by slit-lamp biomicroscopy was not significant, and in accordance with the standard post-operative evolution of minimally invasive techniques.

CME was noticed to occur even 3 months after surgery; therefore, the authors are convinced that the follow-up in the studies of this complication should be extended to 1 year.

Several articles have attempted to identify the prognostic factors for the success of ERM surgery [12, 13]. Although in the current paper CME appears to be correlated significantly only to the presence of intraretinal cysts (odds ratio 3.893, P= 0.00037), the high incidence of CME among eyes without pre-operative CME suggest that this topic needs further investigation.

Many articles have reported a not statistically significant correlation between the pre-operative CME and the postoperative visual acuity [14, 15]. On the other hand, other studies showed a statistically significant correlation between CME and morphological alterations of the retina [15]. In fact, Inoue et al. noticed the presence of intraretinal cysts associated with irregularity of inner segment/outer segment junctions in seven of 11 patients [16]. Trese et al. described an opaque membrane associated with intraretinal cysts [17].

The development of interstitial spaces around the fovea can be seen by OCT. The cystoid spaces are predominantly located in two retinal layers, the inner nuclear layer and the Henle fibers layer (Fig. 1). There are some studies suggesting that degenerating Muller cells may contribute to the formation and persistence of intra-retinal cysts. Moreover, surgical removal of ERM and ILM may cause detachment and disruption of adhering Muller cell end-feet, and subsequent persistence and increase of CME [18, 19].

In a recent retrospective study of 768 eyes, published by Sigler et al. [20], the occurrence of CME after PPV was investigated in eyes with ERM but without pre-operative CME. A 1 % incidence of post-operative cysts into the inner

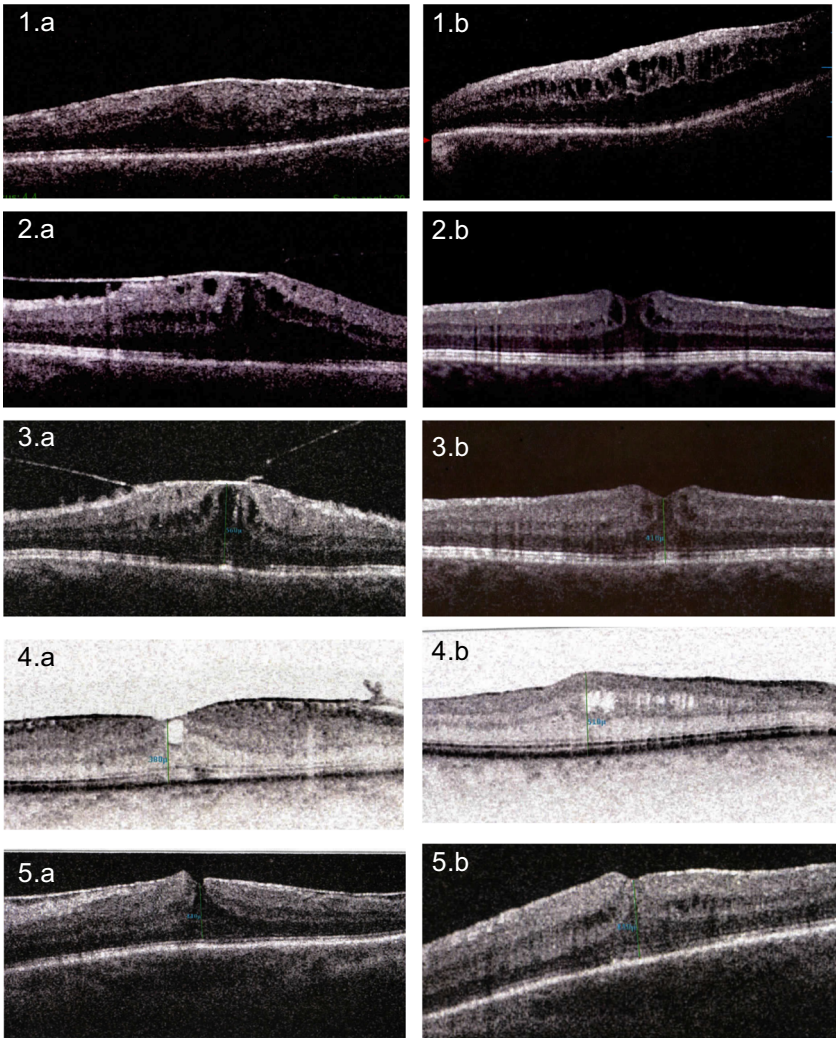


Fig. 1 Tomographic characteristics of cases with ERM that developing intraretinal postoperatively: 1) ERM without pre-operative CME [1.**a**] that developed postoperative CME [1.**b**]. 2–3) ERM with pre-operative CME [2.**a**-3.**a**]. After surgery, intra-retinal cysts persisted [2.**b**–3.**b**]. 4–5) ERM with pre-operative intra-retinal cysts [4.**a**–5.**a**]. After surgery, intraretinal cysts appeared More marked compared to pre-operative period [4.**b**–5.**b**]

nuclear layer was found. This incidence is 10 times lower than the 10.04 % incidence reported in our study. Understanding the cause of this different result becomes therefore crucial. The differences in the methodology are the use of the 23-G vitrectomy system instead of the 25-G vitrectomy system, the application of peripheral laser, and the use of more than one method staining (ICG, brilliant peel, membrane dual) in our study. Therefore it may be hypothesized whether these different techniques could stimulate an inflammatory reaction in the macula. The reason to apply peripheral laser was to prevent the development of post-operative sclerotomy-related retinal detachment [21]. On the other hand, it is well-known that endolaser treatment, especially when extended to the peripheral retina, releases pro-inflammatory mediators that could induce the development of CME.

To understand the mechanisms of the development of CME, the authors studied the FA features of the 31 patients with post-operative CME. FA showed no vascular leakage phenomena in correspondence of intra-retinal cysts in 25 cases, confirming what was highlighted in a study of Sigler et al. However, in six cases, five without pre-operative CME and one with pre-operative CME, FA showed fluorescein pooling and late vascular leakage (Fig. 2).

The authors hypothesize two different pathogenic mechanisms of development of postoperative CME.

The first mechanism concerns the cases with post-operative CME without vascular leakage. The hypothesized mechanisms are based on the iatrogenic damage of the Muller cells secondary to the removal of ERM and peeling of ILM. In these cases, the weakening of the Muller cells due to the evolution of ERM could lead to the formation of intraretinal cysts. The absence of leakage during fluorescein angiography could confirm that the intra-retinal cysts are not related to the breakdown of the blood–retinal barrier but are related to a structural damage of the retina. ERM with intra-retinal cysts could exert great force on the underlying retina including the photoreceptor layer, and promote inner segment/outer segment (IS/OS) junction disruption. Therefore, the authors recommend that vitrectomy should be performed before the occurrence of intraretinal cysts, and as soon as possible

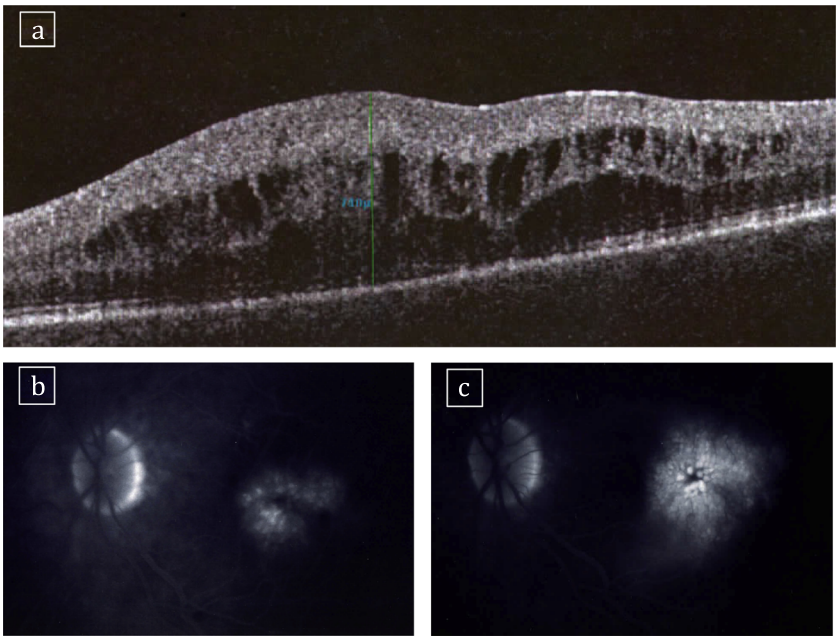


Fig. 2 Postoperative CME. OCT showed CME with intraretinal cysts in inner retinal layers with intact photoreceptors line and retinal pigment epithelium (a). FA showed the fluorescein pooling (**b**) and late leakage (**c**)

in patients with pre-operative intra-retinal cysts, even if they have an intact IS/OS junction.

The second mechanism concerns the occurrence of post-operative CME, with leakage highlighted by fluorescein angiography. The postoperative CME could be due to an inflammatory process due to a breakdown of the blood–retinal barrier, similar to the one known as "Irvine–Gass syndrome", that occurs after any type of intraocular surgery.

Eyes with preoperative intraretinal cysts have a probability to develop postoperative CME with any kind of surgery. Eyes without preoperative intraretinal cysts have a tendency to develop postoperative CME with combined surgery.

CME is a collection of fluid in both plexiform and inner layers of the retina. It has a characteristic pattern of development of cystoid spaces in the foveal area due to perifoveal capillary bed changes. These changes disrupt the blood–retinal barrier allowing fluid to enter, thus thickening the area. Also in these cases, the degenerating Muller cells may contribute to the formation of retinal cysts.

The exact cause of inflammatory post-operative CME is unknown. We acknowledge the fact that peripheral laser at the sclerotomy site is not a standard procedure, and could influence the rate of postoperative inflammation. The authors also think that there could be a factor related to the patient in the development of CME. In fact, there were two patients with bilateral ERM; developing CME in one eye tended to develop postoperative CME also in the other eye

A larger amount of pre-operative data should be collected, such as gauge system vitrectomy, relation to staining methods, phototoxicity, duration of surgery, duration of ERM, and ILM peeling. The role of metamorphopsia was not evaluated due to the retrospective analysis. Therefore, it is not known whether this symptom was improved by surgery, even in cases of postoperative CME.

Moreover, the efficacy of different regimens of postoperative therapy should be consideredm with the aim of limiting and preventing the incidence of this vision-threatening complication.

Conflict of interest No conflicting relationship exists for any author.

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