

Reviewer

5.

Article is regarding retrospective study done (place and hospital/Institution not mentioned) to find out timing of phacoemulsification performed before, during and after PPV with ILM peeling for 43 eyes with full thickness macular holes.

Line 59

We report a retrospective study of 43 eyes in 43 patients who underwent PPV and ILM peeling for FTMH (stage 3 or 4) at the Vitreoretinal service of Barts Health NHS Trust, London, UK.

Authors describe the incidence of cystoids macular oedema in vitrectomized eyes. There are some difficulties in understanding the outcome of this retrospective study, nevertheless following are the reviewers comments that may help in revising the present study.

Abstract

1. The procedure runs in three groups but in the results section there are four groups with phakic group inclusion.

Line 82

We report a retrospective study of 43 eyes in 43 patients. All patients underwent vitrectomy and internal limiting membrane peeling for full-thickness macular hole. Patients were categorized according to their phakic status prior to vitrectomy. Group 1 remained phakic through the 12-month study, group 2 had combined surgery, group 3 were pseudophakic prior to vitrectomy and group 4 became pseudophakic subsequent to vitrectomy.

2. The age group and the place and duration of the study is not mentioned in the methods and materials section.

Line 82

The mean age of the 43 patients in this study was 68.1 ± 12.7 years.

Line 59

We report a retrospective study of 43 eyes in 43 patients who underwent PPV and ILM peeling for FTMH (stage 3 or 4) at the Vitreoretinal service of Barts Health NHS Trust, London, UK.

Line 65

All patients had OCT scans at 1, 3, 6, 9 and 12 months post PPV or PE.

3. Results are once again confusing with inclusion of phakic group (4th group). Demographic details regarding age, sex and laterality of the disease process lacking.

Line 82

The mean age of the 43 patients in this study was 68.1 ± 12.7 years. The mean stage of FTMH was 3.0 ± 0.6 . The FTMH was closed with a single procedure in 42/43 patients (98%). The remaining case resolved with a second procedure.

Group 3 had a mean 12.3 (± 11.1) months interval between procedures. The interval between procedures is not known for group 4, as their first procedures were performed in other units and the exact details were unavailable.

The OCT findings of a typical case are depicted in figure 1.

4. Three patients had CME recurrence resolved with topical regime, but they say two patients had first PPV ILM peeling followed by PE and one patient had first PE followed by PPV ILM peeling. What was the rationale for considering these three patients for surgical intervention once CME resolved with topical medication?

CME occurred after the last procedure in all cases. No procedures were performed on patients with CME or history of CME.

Introduction

1. Authors describe CME incidence in the introduction, can be enriched by inclusion of reference regarding how PE becomes a risk factor.

Line 37

Risk factors related to PE that predispose eyes to CME include factors at the time of surgery including vitreous loss, vitreous traction at incision sites, vitrectomy for retained lens fragments, iris trauma, posterior capsule rupture, intraocular lens (IOL) dislocation, early postoperative capsulotomy, and the use of iris-fixated or anterior chamber IOLs.[2,3]

Eyes with diabetic maculopathy,[4,5] previous uveitis [6] retinal vein occlusion (RVO), epiretinal membrane, and prostaglandin analogs use are all associated with a higher risk of developing CME following PE.[7]

2. What is the published incidence of CME for FTMH without PE

Line 145

This is the first paper to our knowledge, to report an incidence for CME post PPV/ILM peel alone (Table 1).

3. There are three groups according the purpose of the study, but four groups with inclusion of phakic group. Why phakic group included (8) whether for control or comparison. (Line no. 47-50)

Line 72

The group of 8 patients who were phakic and had PPV/ILM peel for FTMH (group 1) acted as a control group as they did not undergo PE at any stage. Group 2 patients had concurrent PE and PPV/ILM peel for FTMH. The group 3 patients had already undergone PE at other practices before presenting to our service with FTMH, the data from their first procedure is limited. Group 4 underwent PPV/ILM peel for FTMH under our care and we performed their subsequent PE.

Materials and methods

Although the article is submitted under short communication category, authors should describe in detail regarding the methods followed which are insufficient in the present study.

1. Age, sex distribution and place of study with ethical clearance from the institution should be described with how patients were categorised. Is it from case sheets in patient/out patient records

Line 82

The mean age of the 43 patients in this study was 68.1 ± 12.7 years. The mean stage of FTMH was 3.0 ± 0.6 . 67% of patients in this study were female.

Line 60

at the Vitreoretinal service of Barts Health NHS Trust, London, UK.

Line 78

Ethical approval was not required, given that the study was retrospective and all treatment was the standard of care. This study observed the tenets of the Declaration of Helsinki.

2. What were the inclusion criteria? Is hypertension not included?

Line 63

All adults who underwent PPV ILM peel for FTMH between 2008 and 2012 inclusively, with one year of follow up, were included.

Hypertensive patients were included.

3. What were the indication for using PPV with 20 and 23 gauge

This was during the period that the Trust switched from 20 to 23 guage surgery.

4. How long dexamethasone recommended

One month of four times daily topical dexamethasone 0.1%

Line 65

All patients received dexamethasone (0.1%) topical regime four times per day in the operated eye after every procedure for one month

5. What was the method followed to measure the CMT and complete details of the instrument should be stated. (please include 1 or 2 images showing OCT of post PE CME

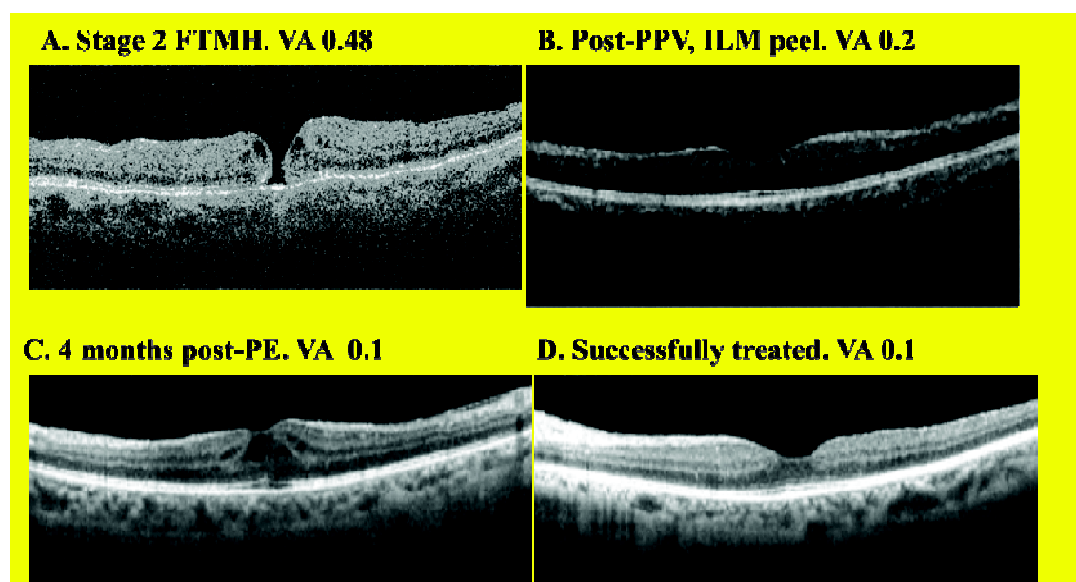
Line 68

Patients with CME had at least one cyst within the OCT field on, macular 256 scan, associated with increased central macular thickness (CMT > 250µm was taken as increased[12]) on spectral domain OCT (Cirrus HD-OCT, Carl Zeiss Meditec, Dublin, CA, USA).

Line 186

Figure 2. Case study

- A. Optical coherence tomography (OCT) scan, left macula of a 61 year old female with reduced vision and metamorphopsia of 3 weeks duration, showing a grade 4 full-thickness macular hole (FTMH). LogMAR best-corrected visual acuity (VA) of 0.48. This patient is from group 4.
- B. OCT scan of same eye 3 months post FTMH hole repair with pars plana vitrectomy and internal limiting membrane peel (PPV, ILM peel), showing a closed macular hole.
- C. OCT scan of same eye, 4 months post phacoemulsification (PE) demonstrating cystoid macular edema (CME).
- D. OCT scan of same eye 6 months post PE, after topical treatment with topical non-steroidal anti-inflammatories and topical steroids, showing resolution of CME.



6. How many phakic/pseudophakic/cataract eyes-please make it clear

Line 72

The group of 8 patients who were phakic and had PPV/ILM peel for FTMH (group 1) acted as a control group as they did not undergo PE at any stage. Group 2 patients had concurrent PE and PPV/ILM peel for FTMH. The group 3 patients had already undergone PE at other practices before presenting to our service with FTMH, the data from their first procedure is limited. Group 4 underwent PPV/ILM peel for FTMH under our care and we performed their subsequent PE.

Line 163

Table 1.

Summary of patients undergoing each procedure by number of cases of cystoid macular edema (CME). Total: The number of cases undergoing each procedure; OCT-evident CME: The number (and percentage) of cases with acute postoperative CME evident on ocular coherence tomography (OCT); CME Sympt: The number of cases who developed acute symptomatic postoperative CME; Late recurrence: The number of cases who developed acute postoperative

CME (all of which were symptomatic); PPV ILM-peel (phakic): Eyes that underwent pars plana vitrectomy (PPV) and internal limiting membrane (ILM) peel; Combined (PE +PPV ILM-peel): Eyes that underwent simultaneous phacoemulsification (PE) with PPV and ILM-peel; Sequential 1 (PE 1st then PPV ILM-peel): Eyes that underwent PE and then subsequently underwent PPV and ILM-peel; Sequential 2 (PPV ILM-peel 1st then PE): Eyes that underwent PPV and ILM-peel and subsequently underwent PE. P value. Result of ANOVA comparison between groups 2, 3 and 4 with group 1. P < 0.05 was taken as statistically significant.

Procedure	Total	OCT-evident CME	CME Sympt	Late recurrence	P value
PPV ILM-peel (phakic)	8	0 (0%)	0 (0%)	0 (0%)	
Group 1					
Combined (PE +PPV ILM-peel)	18	2 (11%)	1 (6%)	0 (0%)	0.853
Group 2					
PE 1 st then PPV ILM-peel	9	1 (11%)	1 (11%)	1 (11%)	0.876
Group 3					
PPV ILM-peel 1 st then PE	8	3 (38%)	2 (25%)	2 (25%)	0.173
Group 4					

Results

1. Once again, results section is weak due to missing of age, sex and laterality of the disease process. Categorisation of the groups should be clear.

Line 83

The mean age of the 43 patients in this study was 68.1 ± 12.7 years. The mean stage of FTMH was 3.0 ± 0.6. 67% of patients in this study were female.

Line 72

The group of 8 patients who were phakic and had PPV/ILM peel for FTMH (group 1) acted as a control group as they did not undergo PE at any stage. Group 2 patients had concurrent PE and PPV/ILM peel for FTMH. The group 3 patients had already undergone PE at other practices before presenting to our service with FTMH, the data from their first procedure is limited. Group 4 underwent PPV/ILM peel for FTMH under our care and we performed their subsequent PE.

2. In the methods, they say topical dexamethasone used for all patients but here NSAIDs ketorolac included. Did they use both agents (Line no. 67-69)-please make it clear

Line 67

Patients did not routinely receive prophylactic topical non-steroidal anti-inflammatories (NSAIDs) post-operatively.

Discussion

1. should be drawn from the results obtained in this retrospective study

Line 108

Our rates of symptomatic CME in the combined group (group 2) is comparable to that previously reported (1.9%[10]⁴ to 8.1%[11] compared to 6% in this study), which suggests our rate of OCT-evident CME approaches that in the population. The incidence of CME was highest group 4 relative to all the other groups, recurrent CME was also highest in this group. While our results did not reach statistical significance this trend warrants reporting, it is noteworthy that CME was observed more frequently if PE followed PPV than the reverse. A rate of 26.3% (5 of 19) OCT-evident CME was reported in eyes that under went PE subsequent to PPV/ILM peel (analogous to our group 4),[9] the rate of 38% in our study, while somewhat higher confirms the finding of Mylonas et al. They included a group of PE patients as controls as they wished to report the rate of CME if PPV/ILM peel was performed in pseudophakic eyes,[9] we were concerned about the timing, so we included patients who remained phakic as a control group as they did not undergo

PE at any stage, we looked at the incidence of CME if PE was performed prior to, with or subsequent to PPV/ILM peel for FTMH.

2. Describe how topical steroids/NSAI drugs help in CME resolution.

Line 139

The evidence that prophylactic topical NSAID regime reduces CME post PE is not easy to interpret due to other factors such as concurrent topical steroid use.[15] NSAIDs are routinely used to treat CME, it is postulated that intraocular inflammation drives CME formation and that NSAIDs better penetrate the blood ocular barrier than topical steroids, so may be more effective in CME.[15]

3. What factors are contributing to decreased incidence of CME in eyes underwent PE first?

Line 123

The interstitial pathway from the vitreous cavity to the subretinal space is formed by the external and internal limiting membranes. The junctions of the external limiting membrane (ELM) are not sealed and, consequently, can only partially limit the movement of large molecules. However, the ILM has no significant influence on water movement.[13] Thus, the balance between static and dynamic vitreous tractional forces determines whether CME forms a macular hole or becomes chronic. Whilst ILM peeling may have beneficial effects on CME because it removes tangential traction, increases retinal oxygenation, reduces VEGF production, and allows intraretinal fluid from the macula to reach the vitreous cavity, it also alters the inner retinal structure possibly resulting in greater responsiveness to inflammatory stimuli.[14] The beneficial effect of ILM peeling may therefore be lost in the setting of inflammation post PE, with increased risk of CME. It is possible that minute nuclear lenticular material may enter the vitreous cavity during uncomplicated PE via minute zonular gaps, and this material may have greater inflammatory potential in vitrectomised eyes than eyes where it is subsequently removed with the vitreous.

4. Discussion section needs improvement by inclusion of relevant references.

We agree and have complied.

Conclusion

1. How one can do PE in patients already underwent PPV ILM peeling without cataract formation (indications)
PE was performed if patients had symptomatic cataract.
2. Authors' advocated combined phacovitrectomy please explain (Line no. 99-100)

We have changed the conclusion

Line 158

In conclusion, we report a trend towards a higher incidence of CME in vitrectomized ILM-peeled eyes when PE is performed subsequently, than other sequences with PE.

References

1. Please improve with addition of relevant material
See references line 212

Minor

Although the paper needs major reorganisation of the protocol followed, authors attempted to find out the incidence of CME considering PE as a risk factor for 43 eyes before, during and after PPV ILM peeling for FTMH.

A prospective study would be more validated than retrospective study

We recommend such a study. This work justifies such a project.

Line 148

This limits our ability to extrapolate, however, this evidence justifies a large prospective randomized trial to elucidate the relative risk of the timing of phacoemulsification in such patients.

comment

Authors may utilise the journal criteria for the text (2500-3500 words) and references (15-20) under short communication that will enrich the article.

We have increased the volume of text and number of references significantly

Line 152

Our study is limited by sample size and retrospective design. This limits our ability to extrapolate, however, this evidence justifies a large prospective randomized trial to elucidate the relative risk of the timing of phacoemulsification in such patients.