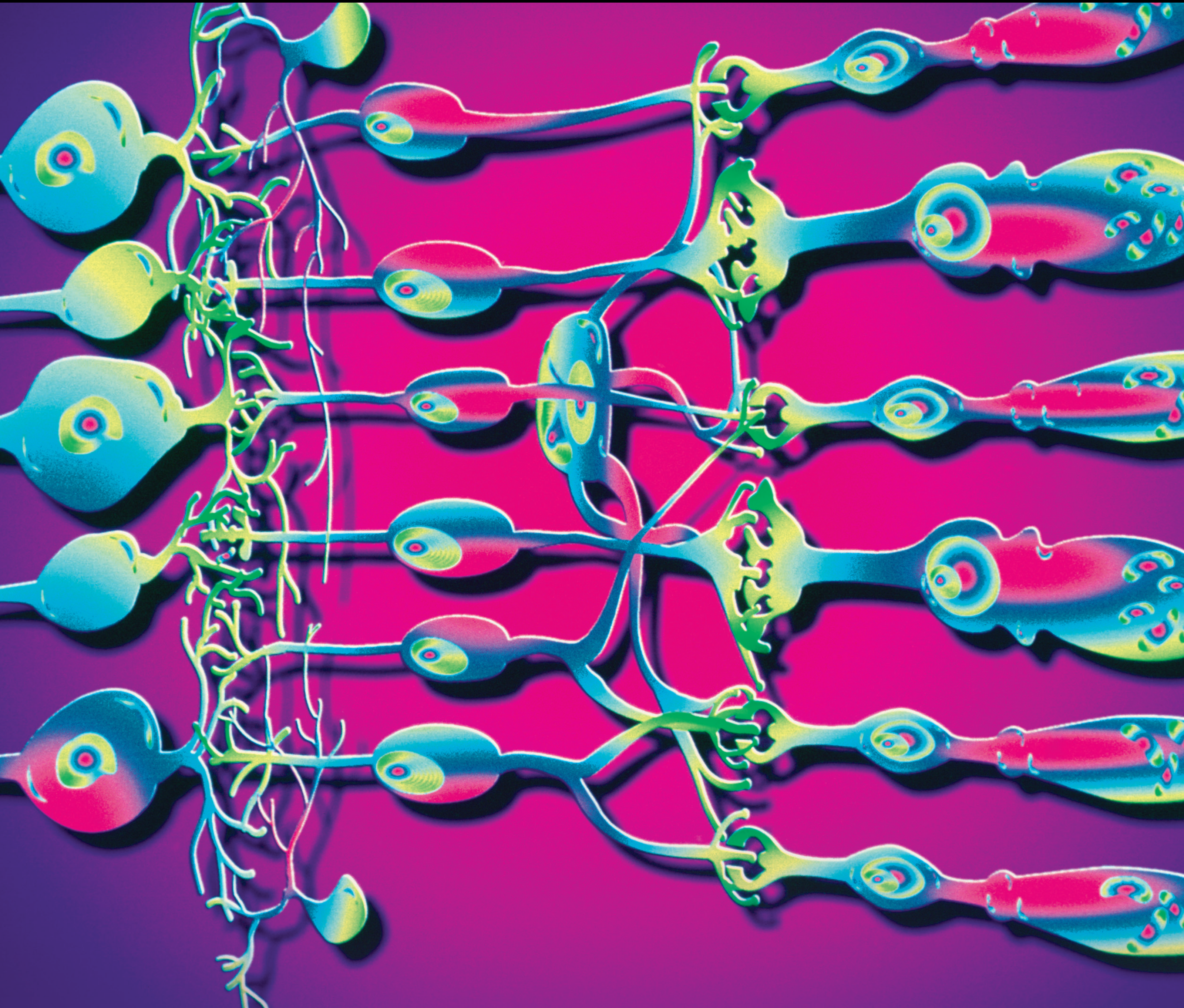
Journal of Ophthalmology

Advances in Vitreoretinal Interface Disorders

Lead Guest Editor: Irini Chatziralli
Guest Editors: Panagiotis Theodossiadis, Luke Nicholson, and David Steel



Advances in Vitreoretinal Interface Disorders

Journal of Ophthalmology

Advances in Vitreoretinal Interface Disorders

Lead Guest Editor: Irini Chatziralli
Guest Editors: Panagiotis Theodossiadis, Luke Nicholson, and David Steel

Editorial Board

Contents

Hindawi
Journal of Ophthalmology
Volume 2017, Article ID 7612712, 2 pages
https://doi.org/10.1155/2017/7612712

Editorial

Advances in Vitreoretinal Interface Disorders

Irini Chatziralli,[1] Panagiotis Theodossiadis,[1] Luke Nicholson,[2] and David Steel[3,4]

[1] *2nd Department of Ophthalmology, Attikon Hospital, University of Athens, Athens, Greece*
[2] *National Institute for Health Research, Moorfields Biomedical Research Centre and University College London Institute of Ophthalmology, London, UK*
[3] *Sunderland Eye Infirmary, Queen Alexandra Road, Sunderland, UK*
[4] *Institute of Genetic Medicine, Newcastle University, Newcastle upon Tyne, UK*

Correspondence should be addressed to Irini Chatziralli; eirchat@yahoo.gr

Received 28 May 2017; Accepted 29 May 2017; Published 2 July 2017

In recent years, there have been a variety of advances in vitreoretinal interface (VRI) disorders. Multimodal imaging, such as spectral domain and swept source optical coherence tomography (OCT), allows for enhanced visualization of vitreous evolution and leads to a better understanding of VRI diseases in terms of both their diagnosis and management. However, the role of vitreous per se in these diseases has been neglected. Q. Ghadiali et al. tried to evaluate the impact of the vitreous body and the extent of its degeneration in eyes with vitreomacular traction (VMT) and macular hole (MH), showing that the eyes with VMT and MH demonstrated earlier stages of vitreous degeneration when compared to the control eyes, despite significantly greater age. The authors concluded that VRI diseases are more often associated with a formed vitreous and an intact premacular bursa. They hypothesized that the state of the vitreous itself may play a role in the aetiology of VMT, in addition to the strength of vitreoretinal adhesion, contrary to previous assumptions implicating degeneration of vitreous as a precipitating factor of VRI disease when in conjunction with abnormal vitreomacular separation.

Additionally, posterior vitreous detachment (PVD) can act as a protecting factor in cases with endogenous endophthalmitis. K. Umazume et al. retrospectively studied ten patients with endogenous endophthalmitis and found that despite an advanced age during the vitrectomy, PVD was absent in 80%, 50% of which showed retinal necrosis, supporting that the state of vitreous attachment may be related to the occurrence of endogenous endophthalmitis. In fact, the authors suggested that the contact between the retina and the vitreous body may be associated with severe disease and proposed that the gel-like vitreous body may play the role as a growth medium for the causative microorganisms.

On the other hand, there have also been many advances in surgical techniques for the treatment of VRI diseases. U. Soiberman et al. in a retrospective study of 74 eyes compared the outcome of MH surgery with that of ILM peeling using two different vital dyes, namely, membrane blue and membrane blue dual. They concluded that membrane blue dual led to better visual results probably due to better staining and lesser toxicity, while there was no difference in MH closure rate between the two dyes. Furthermore, A. Bedda et al. reported the anatomic and visual results of a new sutureless illuminated macular buckle designed for patients with the complex clinical situation of MH retinal detachment related to high myopia with an axial length of >30 mm. They achieved a MH closure rate of 40% postoperatively with a significant increase of visual acuity from 0.11 to 0.21 (decimal) without complications in the 20 studied eyes.

Nevertheless, although the majority of surgical techniques have been found to be safe and effective for VRI disease management, transient or permanent postoperative complications have been reported. K. Ohta et al. supported that the postoperative retinal nerve fiber layer (RNFL) was thicker in all but the nasal-inferior sector for at least 12 months after combined phacoemulsification and pars plana vitrectomy (PPV) with

ILM peeling for patients with MH. This prolonged increase of the RNFL thickness may indicate damage or mild edema of the RNFL.

Finally, P. Stavrakas et al. in their retrospective study evaluated the anatomic and functional outcomes of patients with rhegmatogenous retinal detachment primarily treated with PPV based on the location of the retinal breaks. The authors found that there was no statistically significant difference between patients with superior and inferior breaks with regard to primary retinal reattachment, mean visual acuity change, and complication rate. Therefore, PPV alone can be used to treat uncomplicated rhegmatogenous retinal detachment irrespective to the location of the breaks, suggesting that inferior breaks do not constitute an independent risk factor for worse anatomic or functional outcome.

Irini Chatziralli
Panagiotis Theodossiadis
Luke Nicholson
David Steel

Hindawi
Journal of Ophthalmology
Volume 2017, Article ID 2565249, 7 pages
https://doi.org/10.1155/2017/2565249

Clinical Study

Anatomical and Functional Results Following 23-Gauge Primary Pars Plana Vitrectomy for Rhegmatogenous Retinal Detachment: Superior versus Inferior Breaks

Panagiotis Stavrakas,[1] Paris Tranos,[2] Angeliki Androu,[1] Paraskevi Xanthopoulou,[3] Dimitrios Tsoukanas,[1] Polixeni Stamatiou,[1] and Panagiotis Theodossiadis[1]

[1]*2nd Department of Ophthalmology, University of Athens Medical School, Attikon University General Hospital, Athens, Greece*
[2]*Ophthalmica Clinic, Thessaloniki, Greece*
[3]*Ophthalmology Department, 401 Military Hospital, Athens, Greece*

Correspondence should be addressed to Panagiotis Theodossiadis; bofthalmologiki@attikonhospital.gr

Received 15 November 2016; Revised 24 January 2017; Accepted 1 February 2017; Published 4 June 2017

Academic Editor: Tamer A. Macky

Purpose. In this retrospective study, we evaluated the anatomical and functional outcomes of patients with rhegmatogenous retinal detachment primarily treated with pars plana vitrectomy in regard to the location of the breaks. Methods. 160 eyes were enrolled in this study, divided into two groups based on break location: the superior break group (115 eyes) and the inferior break group (45 eyes). The main endpoint of our study was the anatomical success at 3 months following surgery. *Results*. Primary retinal reattachment was achieved in 96.5% of patients in group A and in 93.3% in group B (no statistically significant difference, OR 1.98, 95% CI: 0.4, 7.7). Mean BCVA change and intraoperative complication rate were also not statistically significantly different between the two groups ($p > 0.05$, OR: 1.0, 95% CI: 0.9, 1.01, resp.). Statistical analyses showed that macula status, age, and preoperative BCVA had a significant effect on mean BCVA change ($p = 0.0001$, $p = 0.005$, and $p = 0.001$, resp.). *Conclusion*. This study supports that acceptable reattachment rates can be achieved using PPV for uncomplicated RRD irrespective of the breaks location and inferior breaks do not constitute an independent risk factor for worse anatomical or functional outcome.

1. Introduction

The primary use of pars plana vitrectomy (PPV) for the treatment of rhegmatogenous retinal detachment (RRD) has gained increasing popularity over the last few years as vitreoretinal surgeons become more familiar with this technique and recent technological advances contributed to improved anatomical and functional outcomes [1–14]. There are several advantages of PPV over scleral buckling (SB) technique including better visualization of the retina facilitating effective identification and treatment of all retinal breaks. In addition, adopting an internal approach makes it feasible to completely remove vitreoretinal traction and manage preretinal or subretinal proliferative vitreoretinopathy (PVR). Furthermore, the introduction of the new small-gauge transconjuctival sutureless systems is associated with less inflammation and patient discomfort as well as shorter recovery time [15–17].

However, RRD cases with inferior breaks may occasionally be challenging especially for phakic patients, in terms of completely removing the inferior vitreous and producing an effective endotamponading effect. In order to overcome the above shortcomings, a combined PPV and scleral buckling technique is often carried out to support the inferior retina, thus avoiding inconvenient posturing. However, this procedure is time-consuming and technically demanding, produces an increased risk of choroidal hemorrhage, and bears the risks of all the complications associated with SB,

Table 1: Distribution of preoperative variables in superior and inferior groups.

Characteristics	Superior break group	Inferior break group	p value
Age (y) [mean (SD)]	64 (±12)	66 (±12)	0.6[b]
Male/female (%)	74/40 (65/35)	33/9 (79/21)	0.12[a]
Presurgery visual acuity (logMAR)	1.2 (0.7)	1.37 (0.9)	0.8[b]
IOL status (yes/no) (%)	57/58 (50/50)	24/21 (53/47)	0.7[a]
Macula status (on/off) (%)	26/89 (23/77)	12/33 (27/73)	0.36[a]

[a]p value obtained using Fisher's exact test; [b]p value obtained using the Mann–Whitney–Wilcoxon test.

including refractive change, diplopia, explant erosion or infection, possible decreased retinal flow, and risk of anterior segment ischaemia [18–23].

During the last few years, an expanding published literature suggests that the adjuvant buckling procedure for RRDs with inferior breaks does not provide any statistically significant benefit as far as anatomical or functional success is concerned [24–28] and that the inferior location of the retinal break does not constitute a risk factor for anatomical failure [2, 29–31]. Additionally, it has been reported that small-gauge systems used for the repair of RRDs with inferior breaks are equally efficient to conventional 20 G techniques, despite the possible disadvantages of the increased flexibility of the instrumentation and the consequent insufficient peripheral vitreous removal and incomplete gas filling [32, 33]. On the other hand, there is a significant number of studies identifying the presence of an inferior break as a risk factor for anatomical failure [1, 11, 34–36] so that the initial surgical approach for RRD with inferior breaks remains a controversy.

The aim of our study is to compare the anatomical success rate and functional outcomes of patients with RRD primarily treated with PPV alone in regard to the location of the retinal breaks.

2. Materials and Methods

A retrospective computer- and intraoperative chart-based review of patients who were referred to the vitreoretinal service of the 2nd Department of Ophthalmology, University of Athens, was carried out. The institution's vitreoretinal database was used to select all consecutive patients who underwent vitrectomy for primary repair of RRD associated with superior or inferior breaks between January 2013 and March 2015. All consecutive patients with a RRD associated with superior or inferior breaks were included in the study.

Exclusion criteria were giant retinal tears, proliferative vitreoretinopathy (PVR) grade C or greater as defined by the Retina Society Terminology Committee [37], history of penetrating ocular trauma, retinal dialysis, previous ocular surgery excluding noncomplicated cataract extraction, and significant ocular comorbidities such as uveitis and glaucoma. Cases of concomitant presence of both superior and inferior breaks associated with RRD were also excluded.

Once suitable patients were identified, they were further subdivided into two groups. Group A consisted of patients with RRD associated with superior breaks, and group B consisted of patients with RRD associated with inferior breaks. A superior break was defined as a retinal break or hole present between 9 and 3 o'clock meridian whereas an inferior break was defined as a break or hole present between 4 and 8 o'clock meridian. Localization of breaks was ascertained on the basis of intraoperative findings instead of preoperative examinations, as indicated by a postsurgery report.

Preoperative evaluation consisted of a thorough examination including demographics, preoperative best-corrected visual acuity (BCVA), axial length, lens and macular status, and clinical features of retinal detachment including number and distribution of all retinal breaks and holes. Although preoperative retinal mapping is routinely performed for every case of retinal detachment for reasons of surgical planning, only data deriving from the postsurgery report were used for the purposes of this study, as mentioned above. Snellen VA was converted to the negative logarithm of minimal angle resolution (logMAR) for statistical analysis and comparison. Patient data are demonstrated in Table 1.

All patients underwent surgery by a single vitreoretinal surgeon (P.S.) under peribulbar anesthesia. A standard three-port 23 G pars plana vitrectomy was carried out using the Alcon Accurus (Alcon, Forth Worth, TX, USA) under a wide-angle viewing system (OCCULUS BIOM, Wetzlar, Germany). Phacoemulsification was only performed if the lens opacity was impairing the view during surgery. Core vitrectomy and peripheral shaving were carried out, and care was taken to relieve vitreous traction on all retinal breaks and suspicious degeneration areas. In all cases, cut rates ranged from 2200 to 2500 cpm to remove central vitreous and a fixed cut rate at 2500 cpm was used to remove peripheral vitreous. Following vitrectomy, an internal search was carried out with 360-degree indentation. All retinal breaks or holes as well as suspicious peripheral retinal degeneration areas were treated with either transscleral cryoretinopexy or endolaser depending on their position. A fluid/air exchange was subsequently performed via the most accessible retinal break. If there was no appropriate safe drainage site, a retinotomy was performed. Perfluorocarbon liquids were not routinely used as adjuncts to surgery. All patients underwent an air/gas exchange with either 20% sulfur hexafluoride (SF6) for group A or 14% octafluoropropane (C3F8) for group B as endotamponade agents. All patients were instructed to position their heads according to the localization of the breaks for only 24 hours postoperatively to encourage tamponade of retinal breaks and prompt absorption of subretinal fluid. No head positioning was advised to the patients after the first 24 hours postsurgery regardless of break location. No adjuvant SB procedure was used in either group. The follow-up varied from a minimum of 3 months to a maximum of one year.

The main endpoint of our study was the anatomical success as defined by complete retinal reattachment in the absence of any tamponade agent at 3 months following surgery. Functional outcome and intraoperative complications, namely, retinal incarceration, hemorrhage, crystalline lens touch, and inadvertent retina touch, were also recorded and analyzed. Further comparisons were made depending on lens status (superior phakic versus inferior phakic and superior pseudophakic versus inferior pseudophakic) as well as macula status (superior macula on versus inferior macula on and superior macula off versus inferior macula off). All combined cases were included in pseudophakic groups for statistical analysis, since the combined approach does not seem to influence the final anatomical result, which constitutes the main endpoint of our study [38].

Visual acuity measurements with Snellen charts were converted to a logarithm of the minimal angle of resolution (logMAR) for statistical analysis (counting fingers was converted to 1.40 logMAR and hand movements were converted to 2.70 logMAR [39]). We compared categorical variables using the chi-square test and continuous variables using the Mann–Whitney U test. Univariate and multivariable logistic regression analyses were performed to identify potential risk factors for anatomical restoration. Analyses were performed using SPSS v16.0 (SPSS Inc. Released 2007. SPSS for Windows, Version 16.0. Chicago, SPSS Inc.).

Institutional review board approval was obtained for this retrospective study by the local Ethics Committee. The research adhered to the tenets of the Declaration of Helsinki.

3. Results

One hundred and sixty eyes of 160 patients were included in this study. The mean age (SD) of the patients was 64.3 (11.7) years, and the male-to-female ratio was 3 : 2. Patients were divided into two groups according to the type of retinal detachment. Group A consisted of 115 eyes with retinal detachment caused by a superior break (superior break group), and group B consisted of 45 eyes with retinal detachment caused by an inferior break (inferior break group). The preoperative characteristics are shown in Table 1. The majority of the patients had a macula-off RD (89 out of 115 eyes in group A and 33 out of 45 eyes in group B). There were 79 phakic and 81 pseudophakic eyes in both groups. The mean number of breaks found intraoperatively was 1.62 ± 0.91 (range 1 to 4) for group A and 1.64 ± 0.93 (range 1 to 4) for group B. Only 5 patients from group A and 2 patients from group B received a combined phacoemulsification and intraocular lens procedure at the time of retinal detachment repair. There was no statistically significant difference between the 2 groups in terms of age, sex, preoperative visual acuity, macula status (on/off), intraocular lens status, and number of retinal breaks.

3.1. Primary Outcome Measures. Primary complete retinal reattachment following 23-gauge vitrectomy, retinopexy, and intraocular gas was achieved in 96.5% of patients in group A and in 93.3% of patients in group B. No statistically significant difference between the 2 groups was noted (Mann–Whitney U test; odds ratio 1.98, 95% CI: 0.4, 7.7).

Best-corrected visual acuity (BCVA) improved from 0.7 logMAR preoperatively to 0.4 postoperatively in group A and from 0.9 preoperatively to 0.3 postoperatively in group B. Comparing the mean change of preoperative and postoperative logMAR BCVA, there was no statistically significant difference between the two groups (Mann–Whitney U test, $p > 0.05$). Similarly, the patients in both groups presented no significant difference in an intraoperative complication rate (1.7% and 0.0% complication rates in group A and group B, resp.; odds ratio: 1.0, 95% CI: 0.9, 1.01).

3.2. Risk Factor Analysis for Anatomical Failure. Separate univariate analyses were performed to determine potential risk factors for anatomical failure (redetachment). The variables tested included the following: break location, age, sex, lens status (phakic/pseudophakic), intraoperative complications (yes/no), macular status before surgery (macula on/macula off), preoperative BCVA, and BCVA mean difference pre- and postsurgery. None of the variables was statistically significant (p value > 0.5). Univariate and multivariable logistic regression analyses were also performed to identify potential risk factors for retinal redetachment. However, due to the limited number of redetachments, the logistic regression models included only two predictors: break location and one of the following variables (age, sex, lens status (phakic/pseudophakic), intraoperative complications (yes/no), macular status before surgery (macula on/macula off), preoperative BCVA, and BCVA mean difference pre- and postsurgery), as well as the respective interaction term. There was no alteration in the statistical significance of the univariate analysis (Table 2).

3.3. Factors Affecting Mean Difference in BCVA Pre- and Postsurgery. Statistical analyses were performed using the Mann–Whitney U test to determine factors [anatomical restoration (yes/no), age, lens status (phakic/pseudophakic), intraoperative complications (yes/no), macular status before surgery (macula on/macula off), and BCVA before surgery] associated with mean change in BCVA following surgery. A 3-month period follow-up was used in order to reduce the possible bias caused by subsequent cataract development. Results showed that macula status, age, and preoperative BCVA had a significant effect on mean change in BCVA following PPV ($p = 0.0001$, $p = 0.005$, and $p = 0.001$, resp.). More precisely, younger patients with macula on retinal detachment and better presurgery BCVA had a more favorable outcome concerning mean change of BCVA following PPV (Table 3).

4. Discussion

This study constitutes, to our knowledge, one of the largest to date published series of uncomplicated rhegmatogenous

Table 2

Categorical variables		Restoration Yes	Restoration No	p value
Sex	Male ($n = 107$)	102	5	0.6[a]
	Female ($n = 49$)	47	2	
Macula status	On ($n = 38$)	36	2	0.6[a]
	Off ($n = 117$)	111	5	
Intraoperative complications	Yes ($n = 2$)	2	0	0.7[a]
	No ($n = 157$)	151	7	
Phakic status	IOL ($n = 81$)	78	3	0.7[a]
	CL ($n = 79$)	75	4	
Break location	Superior ($n = 113$)	108	3	0.41[a]
	Inferior ($n = 40$)	37	3	
Categorical variables		Restoration Yes	Restoration No	p value
Age		64 ± 11	67 ± 10	0.4[c]
Presurgery BCVA (logMAR)		1.2 ± 0.8	1.6 ± 0.95	0.1[b]

[a] p value obtained using Fisher's exact test; [b] p value obtained using the Mann–Whitney–Wilcoxon test; [c] correlation is significant at the 0.05 level (2-tailed).

Table 3

Categorical variables		BCVA Mean difference (SD)	p value
Macula status	On ($n = 38$)	0.25 ± 0.5	0.0001[a]
	Off ($n = 117$)	0.86 ± 0.65	
Intraoperative complications	Yes ($n = 2$)	0.6 ± 0.6	0.5[a]
	No ($n = 157$)	0.7 ± 0.7	
Phakic status	IOL ($n = 81$)	0.7 ± 0.7	0.3[a]
	CL ($n = 79$)	0.6 ± 0.66	
Break location	Superior($n = 113$)	0.6 ± 0.5	0.2[a]
	Inferior ($n = 40$)	0.9 ± 0.9	
Restoration	Yes ($n = 145$)	0.68 ± 0.66	0.75[a]
	No ($n = 8$)	0.9 ± 1.0	
Categorical variables		BCVA Mean difference (SD)	p value[b]
Age		0.273	0.005
Presurgery BCVA		0.85	<0.001

[a] p value obtained using the Mann–Whitney–Wilcoxon; [b] correlation is significant at the 0.05 level (2-tailed).

retinal detachment treated with PPV and gas alone focusing on retinal break location. Results showed no significant difference in the final anatomical and functional outcomes between patients treated with vitrectomy for RRD with superior or inferior breaks. Similarly, break location did not affect intra- and postoperative complication rates. Interestingly, in our series, lens and macular status did not show any correlation with the anatomical outcomes, suggesting that the primary reattachment rate was independent on the extent of retinal detachment.

Up until recently, the presence of an inferior break would favor a combined PPV and SB procedure in order to support the inferior retina and thus increase the final success rate. However, the current study revealed a high reattachment rate with PPV alone, implying that undergoing a potentially more traumatic combined procedure might be unnecessary [5–14, 18–23].

At present, there is little published literature on the outcomes of vitrectomy and gas alone focusing exclusively on retinal break location. In addition, results of such studies are contradictory. In 1996, Heimann et al. [11] published a retrospective study of 53 patients studying the final outcome of PPV without adjuvant scleral buckle for RRD, stating that the final attachment rate for PPV alone for RRD associated with inferior breaks was 50%, which would clearly suggest a poor outcome for this group. However, the number of patients in the inferior break group was too small to draw any firm conclusions (6 patients). In 2009, Von Fricken et al. [34] studied the outcomes of vitrectomy for the repair of RRD using either 20 G or 25 G instrumentation in 125 eyes. They concluded that the success rate for inferior breaks was three times lower as opposed to that of superior breaks. Moreover, Abu El-Asram et al. [35] studied a consecutive series of 115 eyes with bullous RD treated with vitrectomy, concluding that the presence of inferior retinal breaks was significantly associated with a higher primary redetachment rate ($p = 0.0156$). However, perfluorocarbon liquids were routinely used during surgery, and encircling scleral bands were placed in all cases, rendering the procedure much more traumatic than PPV alone. In 2013, Goto et al. [36] compared the anatomical success rate of PPV alone for RRD with superior and inferior breaks of 82 eyes. The authors concluded that the primary anatomical success rate in the inferior group was significantly lower than that in the superior group ($p = 0.012$). However, only 20 of 82 eyes were associated with inferior breaks and 20% SF6 was used as an endotamponade agent in all cases irrespective of the localization of the breaks.

On the other hand, in 2011, Wickham et al. [29] produced a simplified formula to estimate the risk of failure and PVR following primary RRD repair by vitrectomy, where the localization of the breaks was not identified as a risk factor for anatomical failure. Sharma et al. [31] in a series of 48 eyes also concluded that there was no significant difference regarding anatomical and functional outcome between RRD associated with superior and inferior breaks treated with PPV alone. Similarly, Senn et al. [2], in 2002, while studying the role of PPV for pseudophakic RD, reported that the localization of the breaks had no influence on the anatomical or functional outcomes of 129 eyes included in their study.

In our study, we analyzed 160 consecutive eyes with a 96.5% success rate after primary vitrectomy in eyes with RRD associated with superior breaks and 93% success rate in eyes with RRD associated with inferior breaks and the difference in the reattachment rate proved to be nonsignificant. Our success rate is consistent with the high anatomical reattachment rates published in recent years in patients undergoing PPV for RRD [27, 30]. More importantly, our results further support the impression that inferior breaks do not represent a risk factor for retinal redetachment. Additionally, the phakic or pseudophakic status of the patient did not influence the final success rate either on the superior break group (group A) or on the inferior break group (group B). As far as the functional outcome is concerned, our analysis showed that macula status (macula on versus macula off), age, and baseline visual acuity were significantly related to the final BCVA.

The notion that PPV alone without scleral buckle may be enough in order to tamponade effectively the inferior retinal pathology seems to be increasingly adopted in published data over the last few years. Furthermore, acceptable rates of anatomical success using this method are being increasingly published: 89% for Wickham et al. [24] as well as for Tanner et al. [30], 81.82–92.68% for Dell'Omo et al. [32], 93.3% for Martinez-Castillo et al. [40], and 83.3–89.6% for Coyler et al. [33] and even in cases with PVR present (87.5% for Sheng et al. [41]) or even without postoperative head posturing (90% for Martinez-Castillo et al. [42]).

It is well known that retinal reattachment requires relief of traction, alteration of intravitreal currents, and chorioretinal adhesion [43]. A combined PPV-SB procedure does effectively address all three issues and, over the last few years, given the technological advances of PPV, the introduction of new small-gauge transconjuctival systems and panoramic viewing systems, and surgeons' growing confidence, so does PPV procedure alone. Relief of vitreous traction can be achieved with PPV alone for inferior retinal pathology, even for phakic patients, using new enhanced panoramic viewing systems in combination with scleral indentation bihanded approaches. This is also the case for addressing the issue of alteration of intraocular currents within the eye, since an almost complete vitreous clearance almost guarantees an adequate gas fill. The development of longer-acting gases and the elucidation of their physical properties have also contributed to PPV's high success rates, even for treating inferior retinal pathologies. Finally, chorioretinal adhesion is sufficiently addressed by the complete intraoperative subretinal fluid drainage in combination with retinopexy techniques.

There is a number of limitations in this study, including its retrospective nature as well as the lack of a control group of RRDs treated with combined procedure. However, already published data sufficiently address the issue of success and complication rates of the combined approach and since we have been applying our findings to our everyday practice over the last years, only a very limited number of combined procedures would have been available for statistical analysis. The uneven number of eyes with superior and inferior breaks is also a shortcoming; however, the consecutive nature of our data collection and analysis showed a prevalence of superior break RRDs compared to that of inferior break RRDs and any attempt to collect an equal number of eyes between the 2 groups would have generated bias to the statistical analysis.

We also excluded cases of concomitant superior and inferior breaks because the study set-up was to compare superior versus inferior breaks; thus, a third group of patients including both the main compared parameters would need a completely different study design.

The type of retinopexy used may also need clarification. We routinely use cryotherapy as retinopexy of choice in the presence of anterior breaks, regardless of their location. The advantages are simplicity of the procedure, since retinopexy can be applied even in the extreme periphery of phakic patients without a need for bimanual scleral indentation. In addition, cryotherapy can be applied in the presence of residual subretinal fluid as we avoid the routine use of perfluorocarbon liquids. However, in some of the cases of inferior breaks, endolaser was used instead of cryopexy. This was based on the assumption that endolaser creates chorioretinal scar in a shorter time compared to cryopexy; therefore, it would hold an advantage for breaks in the inferior quadrants that benefit from the endotamponade effects for a shorter postoperative period. We also used endolaser in cases of large inferior retinal breaks or breaks within areas of extended lattice degenerations that would otherwise require extended applications of cryopexy, thus causing a significant amount of inflammation.

In conclusion, this study provides further evidence that acceptable rates can be achieved using PPV alone to treat uncomplicated RRD irrespective of the location of the breaks. In this context, we suggest that additional SB procedure may be unnecessary even for eyes undergoing PPV for RRD caused by inferior breaks, since the latter does not constitute an independent risk factor for worse anatomical or functional outcome.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

References

[1] H. Heimann, X. Zou, C. Jandeck et al., "Primary vitrectomy for rhegmatogenous retinal detachment: an analysis of 512 cases," *Graefe's Archive for Clinical and Experimental Ophthalmology*, vol. 244, no. 1, pp. 69–78, 2006.

[2] P. Senn, M. K. Schmid, O. Job, A. Hürlimann, and I. Schipper, "Pars plana vitrectomy for pseudophakic retinal detachment," *Klinische Monatsblätter für Augenheilkunde*, vol. 219, no. 4, pp. 226–230, 2002.

[3] H. Gerding and A. Hersener, "Anatomical and functional results of primary pars plana vitrectomy in rhegmatogenous retinal detachment," *Klinische Monatsblätter für Augenheilkunde*, vol. 230, no. 4, pp. 409–412, 2013.

[4] E. Mendrinos, N. P. Dang-Burgener, A. N. Stangos, J. Sommerhalder, and C. J. Pournaras, "Primary vitrectomy for pseudophakic rhegmatogenous retinal detachment," *American Journal of Ophthalmology*, vol. 145, no. 6, pp. 1063–1070, 2008.

[5] D. M. Miller, C. D. Riemann, R. E. Foster, and M. R. Petersen, "Primary repair of retinal detachment with 25-gauge pars plana vitrectomy," *Retina*, vol. 28, no. 7, pp. 931–936, 2008.

[6] K. N. Hakin, M. J. Lavin, and P. K. Leaver, "Primary vitrectomy for rhegmatogenous retinal detachment," *Graefe's Archive for Clinical and Experimental Ophthalmology*, vol. 231, no. 6, pp. 344–346, 1993.

[7] D. K. Newmann and R. L. Burton, "Primary vitrectomy for pseudophakic and aphakic retinal detachments," *Eye (London, England)*, vol. 13, Part 5, pp. 635–639, 1999.

[8] Y. Oshima, K. Emi, M. Motokura, and S. Yamanishi, “Survey of surgical indications and results of primary pars plana vitrectomy for rhegmatogenous retinal detachments,” *Japanese Journal of Ophthalmology*, vol. 43, no. 2, pp. 120–126, 1999.

[9] E. W. Schneider, R. L. Geraets, and M. W. Johnson, “Pars plana vitrectomy without adjuvant procedures for repair of primary rhegmatogenous retinal detachment,” *Retina*, vol. 32, no. 2, pp. 213–219, 2012.

[10] M. S. Figueroa, C. López-Caballero, and I. Contreras, “Anatomical and functional outcomes for the treatment of pseudophakic rhegmatogenous retinal detachment,” *Archivos de la Sociedad Española de Oftalmología*, vol. 85, no. 2, pp. 59–63, 2010.

[11] H. Heimann, N. Bornfeld, W. Friedrichs et al., “Primary vitrectomy without sclera buckling for rhegmatogenous retinal detachment,” *Graefe's Archive for Clinical and Experimental Ophthalmology*, vol. 234, no. 9, pp. 561–568, 1996.

[12] R. F. Escoffery, R. J. Olk, M. G. Grand, and I. Boniuk, “Vitrectomy without scleral buckling for primary rhegmatogenous retinal detachment,” *American Journal of Ophthalmology*, vol. 99, no. 3, pp. 275–281, 1985.

[13] R. V. Campo, J. O. Sipperley, S. R. Sneed et al., “Pars plana vitrectomy without scleral buckle for pseudophakic retinal detachments,” *Ophthalmology*, vol. 106, no. 9, pp. 1811–1815, 1999.

[14] D. S. Gartry, A. H. Chignell, W. A. Franks, and D. Wong, “Pars plana vitrectomy for the treatment of rhegmatogenous retinal detachment uncomplicated by advanced proliferative vitreoretinopathy,” *The British Journal of Ophthalmology*, vol. 77, no. 4, pp. 199–203, 1993.

[15] G. Y. Fujii, E. De Juan Jr, M. S. Humajun et al., “A new 25-gauge instrument system for transconjuctival sutureless vitrectomy surgery,” *Ophthalmology*, vol. 109, no. 10, pp. 1807–1812, 2002.

[16] G. Y. Fujii, E. De Juan Jr, M. S. Humajun et al., “Initial experience using the transconjuctival sutureless vitrectomy system for vitreoretinal surgery,” *Ophthalmology*, vol. 109, no. 10, pp. 1814–1820, 2002.

[17] L. Kellner, B. Wimpissinger, U. Stolba, W. Brannath, and S. Binder, “25-gauge versus 20-gauge system for pars plana vitrectomy: a prospective randomized clinical trial,” *The British Journal of Ophthalmology*, vol. 91, no. 7, pp. 945–948, 2007.

[18] R. J. Flindall, E. W. Norton, V. T. Curtin, and J. D. Gass, “Reduction of extrusion and infection following episcleral silicone implants and cryopexy in retinal detachment surgery,” *American Journal of Ophthalmology*, vol. 71, no. 4, pp. 835–837, 1971.

[19] H. Hayashi, K. Hayashi, F. Nakao, and F. Hayashi, “Corneal shape changes after scleral buckling surgery,” *Ophthalmology*, vol. 104, no. 5, pp. 831–837, 1997.

[20] Y. Domniz, M. Cahana, and I. Avni, “Corneal surface changes after pars plana vitrectomy and scleral buckling surgery,” *Journal of Cataract and Refractive Surgery*, vol. 27, no. 6, pp. 868–872, 2001.

[21] P. N. Fison and A. H. Chignell, “Diplopia after retinal detachment surgery,” *The British Journal of Ophthalmology*, vol. 71, no. 7, pp. 521–525, 1987.

[22] J. Kwartz, S. Charles, P. McCormack, A. Jackson, and M. Lavin, “Anterior segment ischaemia following segmental scleral buckling,” *The British Journal of Ophthalmology*, vol. 78, no. 5, pp. 409–410, 1994.

[23] A. Yoshida, G. T. Feke, G. J. Green et al., “Retinal circulatory changes after scleral buckling procedures,” *American Journal of Ophthalmology*, vol. 95, no. 2, pp. 182–188, 1983.

[24] L. Wickham, M. Connor, and G. W. Aylward, “Vitrectomy and gas for inferior break retinal detachments: are the results comparable to vitrectomy, gas and scleral buckle?” *The British Journal of Ophthalmology*, vol. 88, no. 11, pp. 1376–1379, 2004.

[25] R. B. Rush, M. P. Simunovic, S. Sheth, A. Kratz, and A. P. Hunyor, “Pars plana vitrectomy versus combined pars plana vitrectomy-scleral buckle for secondary repair of retinal detachment,” *Ophthalmic Surg Lasers Imaging. Retina.*, vol. 44, no. 4, pp. 374–379, 2013.

[26] E. D. Weichel, A. Martidis, M. S. Fineman et al., “Pars plana vitrectomy versus combined pars plana vitrectomy-scleral buckle for primary repair of pseudophakic retinal detachment,” *Ophthalmology*, vol. 113, no. 11, pp. 2033–2040, 2006.

[27] S. Mehta, K. J. Blinder, G. K. Shah, and M. G. Grand, “Pars plana vitrectomy versus combined pars plana vitrectomy and scleral buckle for primary repair of rhegmatogenous retinal detachment,” *Canadian Journal of Ophthalmology*, vol. 46, no. 3, pp. 237–241, 2011.

[28] M. Kinori, E. Moisseiev, N. Shoshany et al., “Comparison of pars plana vitrectomy with and without scleral buckle for the repair of primary rhegmatogenous retinal detachment,” *American Journal of Ophthalmology*, vol. 152, no. 2, pp. 291–297, 2011.

[29] L. Wickham, G. O. Ho-Yen, C. Bunce, D. Wong, and D. G. Charteris, “Surgical failure following primary retinal detachment by vitrectomy: risk factors and functional outcomes,” *The British Journal of Ophthalmology*, vol. 95, no. 9, pp. 1234–1238, 2011.

[30] V. Tanner, M. Minihan, and T. Williamson, “Management of inferior retinal breaks during pars plana vitrectomy for retinal detachment,” *The British Journal of Ophthalmology*, vol. 85, no. 4, pp. 480–482, 2001.

[31] A. Sharma, V. Grigoropoulos, and T. H. Williamson, “Management of primary rhegmatogenous retinal detachment with inferior breaks,” *The British Journal of Ophthalmology*, vol. 88, no. 11, pp. 1372–1375, 2004.

[32] R. Dell'Omo, F. Barca, H. S. Tan, H. M. Bijl, S. Y. Lesnik Oberstein, and M. Mura, “Pars plana vitrectomy for the repair of primary, inferior rhegmatogenous retinal detachment associated to inferior breaks. A comparison of a 25-gauge versus a 20-gauge system,” *Graefe's Archive for Clinical and Experimental Ophthalmology*, vol. 251, no. 2, pp. 485–490, 2013.

[33] M. H. Coyler, M. K. Barazi, and M. A. von Fricken, “Retrospective comparison of 25-gauge transconjuctival sutureless vitrectomy to 20-gauge vitrectomy for the repair of pseudophakic primary inferior rhegmatogenous retinal detachment,” *Retina*, vol. 30, no. 10, pp. 1678–1684, 2010.

[34] M. Von Fricken, N. Kunjukunju, C. Weber, and G. Ko, “25 gauge sutureless vitrectomy versus 20 gauge vitrectomy for the repair of primary rhegmatogenous retinal detachment,” *Retina*, vol. 29, no. 4, pp. 444–450, 2009.

[35] A. M. Abu El-Asram, H. F. Al-Kwikbi, and D. Kangave, “Prognostic factors after primary pars plana vitrectomy and perfluorocarbon liquids for bullous rhegmatogenous retinal detachment,” *European Journal of Ophthalmology*, vol. 19, no. 1, pp. 107–117, 2009.

[36] T. Goto, T. Nakagomi, and H. Ijima, “A comparison of the anatomic successes of primary vitrectomy for rhegmatogenous retinal detachment with superior and inferior breaks,” *Acta Ophthalmologica*, vol. 91, no. 6, pp. 552–556, 2013.

[37] R. Machemer, T. M. Aaberg, H. M. Freeman, A. R. Irvine, J. S. Lean, and R. M. Michels, "An updated classification of retinal detachment with proliferative vitreoretinopathy," *American Journal of Ophthalmology.*, vol. 112, no. 2, pp. 159–165, 1991.

[38] G. M. Tosi, A. Balestrazzi, S. Baiocchi et al., "Previtrectomy phacoemulsification versus combined phacovitrectomy," *Retina*, vol. 74, no. 4, pp. 630–636, 2017, [Epub ahead of print].

[39] H. S. Tan, M. Mura, S. Y. Lesnik Oberstein, and H. M. Bijl, "Safety of vitrectomy for floaters," *American Journal of Ophthalmology*, vol. 151, no. 6, pp. 995–998, 2011.

[40] V. Martinez-Castillo, A. Verdugo, A. Boixadera, J. Garcia-Arumi, and B. Corcostegui, "Management of inferior breaks in pseudophakic rhegmatogenous retinal detachment with pars plana vitrectomy and air," *Archives of Ophthalmology*, vol. 123, no. 8, pp. 1078–1081, 2005.

[41] Y. Sheng, W. Sun, B. Mo, Y. J. Yu, Y. S. Gu, and W. Liu, "Non-buckled vitrectomy for retinal detachment with inferior breaks and proliferative vitreoretinophathy," *Int J Ophthalmol.*, vol. 5, no. 5, pp. 591–595, 2012.

[42] V. Martinez-Castillo, A. Boixadera, A. Verdugo, and J. Garcia-Arumi, "Pars plana vitrectomy alone for the management of inferior breaks in pseudophakic retinal detachment without facedown position," *Opthalmology*, vol. 112, no. 7, pp. 1226–1226, 2005.

[43] R. Machemer, "The importance of fluid absorption, traction, intraocular currents and chorioretinal scars in the therapy of rhegmatogenous retinal detachments," *American Journal of Ophthalmology*, vol. 98, no. 6, pp. 681–693, 1984.

Hindawi
Journal of Ophthalmology
Volume 2017, Article ID 6742164, 7 pages
https://doi.org/10.1155/2017/6742164

Clinical Study

A New Sutureless Illuminated Macular Buckle Designed for Myopic Macular Hole Retinal Detachment

Ahmed M. Bedda,[1] Ahmed M. Abdel Hadi,[1] Mohamed Lolah,[1] and Muhammad S. Abd Al Shafy[2]

[1] *Ophthalmology Department, Faculty of Medicine, Alexandria University, Alexandria 21526, Egypt*
[2] *General Ophthalmology Hospital of Alexandria, Alexandria 21547, Egypt*

Correspondence should be addressed to Ahmed M. Abdel Hadi; aabdelhadi2010@gmail.com

Received 21 October 2016; Revised 28 November 2016; Accepted 5 December 2016; Published 16 March 2017

Academic Editor: David Steel

Purpose. To report the anatomic and visual results of a new sutureless illuminated macular buckle designed for patients with macular hole retinal detachment related to high myopia (MMHRD). *Design*. Prospective nonrandomized comparative interventional trial. *Methods*. Twenty myopic eyes of 20 patients (mean age, 51.4 years; range, 35–65 years) presenting with MMHRD with a posterior staphyloma, in whom the new buckle was used, were evaluated. The buckle used was assembled from a 5 mm wide sponge and a 7 mm wide silicone tire; it was fixed utilizing the sterile topical adhesive Histoacryl Blue (B Braun, TS1050044FP) which polymerizes in seconds upon being exposed to water-containing substances. The primary outcomes measured included aided visual acuity (BCVA) and optical coherence tomography (OCT) findings. The mean follow-up period was 6 months. *Results*. Postoperatively, the MH closure was identified by OCT in 8 (40%) eyes. The mean BCVA increased from 0.11 to 0.21 ($p < 0.005$). The axial length of the eyes included decreased from 30.5 mm preoperatively to 29.8 mm ($p = 0.002$) postoperatively. *Conclusion*. Preparation of the new sutureless macular buckle is simple and easy. Illumination of the terminal part of the buckle ensures proper placement. Histoacryl Blue is effective in fixing the buckle in its place for at least 6 months with no reported intra- or postoperative complications.

1. Introduction

Progressive myopia is a relatively frequent condition affecting all ocular structures, including the vitreous, the retina, the choroid, and the sclera. Globe elongation with subsequent development of posterior staphyloma represents the hallmark of the disease and can be complicated by myopic foveoschisis and myopic macular hole with secondary retinal detachment [1].

Other factors implicated in the pathogenesis are anteroposterior traction caused by the vitreous cortex, tangential forces due to the epiretinal membranes (ERMs) or the internal limiting membrane (ILM), and the stretched retinal arteries [2].

With the revival of macular buckling as a noninvasive surgical solution for these cases, several published reports describe a success rate comparable to or even higher than that of pars plana vitrectomy which was considered the preferred surgical procedure for this relatively complicated type of detachment [3, 4].

Difficulties with EMB prevented its establishment as the gold standard treatment for myopic macular hole detachment; such difficulties include accurate placement under the macular hole, with a sufficient indentation height to alleviate the stretched macular area [5].

Fibre-optic-guided Ando plombe was used few years back [5], which improved the success rate of such surgery.

Despite the 100% and 40% rates of retinal reattachment and MH closure, respectively, using the fibre-optic-guided Ando plombe, scleral perforation occurred in 15% of the cases, which was significantly higher than that of the vitrectomy group operated by the same surgeon in a recent study published during 2015 [4].

Consequently, to avoid any damage during buckle fixation and to enhance visualization, we propose the use of a new sutureless fibre-optic-guided macular buckle, which allows better visualization of the indenting heel, as well as placing it correctly under the centre of the fovea.

2. Patients

Recruitment of cases took place between February 2015 and August 2015. MH was defined as the presence of a foveal full thickness based on the fundus examination. Twenty myopic eyes from 20 patients with a high degree of myopic error, defined as eyes with axial length of >30 mm or greater (measured by the calliper during a B-scan US), with macular hole retinal detachment were selected to be included in the study. Additional inclusion criteria were the absence of any stage of proliferative vitreoretinopathy; no history of posterior segment eye surgery; intraocular pressure lower than 20 mmHg; absence of any systemic disease that might confound the visual function, for example, diabetes; and absence of history of ocular trauma.

3. Methods

This was a prospective, interventional case series conducted at a tertiary referral centre in Alexandria, Egypt. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. This research protocol and its amendments were approved by the Ophthalmology Department of the Alexandria University Institutional Review Boards and Ethics Committees. Explanation about the procedure and its duration was given to the subject of the research in clear, understandable words. Each patient was informed about the liable reasonable risk. All patients provided written informed consent. Confidentiality was assured.

In all cases, the following examinations were performed preoperatively.

Best-corrected visual acuity (BCVA) was assessed by using Snellen testing. Applanation tonometry was carried out. Dilated indirect binocular ophthalmoscopy with scleral depression was performed to exclude the presence of peripheral tear. Slit lamp examination supplemented with a plus 90-D lens to confirm the diagnosis was done. Fundus photograph was taken; axial length was measured utilizing the A/B scan vector method to avoid fallacies in the myopic eyes with detached retinas by means of a 10 MHz probe (Echoscan US 4000, Nidek Inc., Fremont, CA); and optical coherence tomography (OCT; Cirrus HD-OCT 4000, version 5.0, Carl Zeiss Meditec) before operation was performed whenever feasible.

In certain cases, OCT was not useful or even possible to perform either due to vitreous opacities obscuring the view of the macula or due to a bullous central retinal detachment with no useful data obtained as the area which might contain the hole was out of range of the machine used. Postoperatively at 1 day, 15 days, and 1, 3, and 6 months, patients were examined. Slit lamp examination was done; fundus examination was attempted in all patients on day 1 to assess the condition of the retina, and thereafter during all postoperative visits. Fundus photography and OCT were ordered when needed.

4. Surgical Technique

The surgical technique was used in 20 patients with high myopia and central retinal detachment who were referred to an Alexandria vitreoretinal centre in Alexandria, Egypt (See Supplemental Video available online at https://doi.org/10.1155/2017/6742164). All operations were performed by the same surgeon (AMB).

The buckle used was assembled from a sponge (width, 5 mm) and a silicone tire (width, 7 mm) readily available in the vitreoretinal operating room. A 9 mm segment from the tire was cut; a 6 mm segment from the sponge was split into two halves and sutured to the tire so that the convex part is made facing the sclera (Figure 1).

Before starting the operation, a track is prepared for a fiber-optic light. A disposable chandelier fibre (25 gauge/0.5 mm) (Geuder AG, Heidelberg, Germany) was inserted in the indenting head (Figure 1).

The surgical steps included performing a superotemporal conjunctival peritomy, careful exposure of the superior and inferior oblique muscles so as to identify the posterior edge of the inferior oblique insertion marking the exact position of the transverse long posterior ciliary artery (TLPCA).

Subretinal fluid evacuation was attempted in cases where RD was so extensive to reach the peripheral retina. In those cases, with shallow retinal detachment limited to the posterior pole, a paracentesis was done instead as posterior drainage was too risky to perform and very difficult without muscle disinsertion. This was done to allow for adequate indentation of the tire at the macular area.

Preliminary place the buckle along the prementioned vessel course. Turn on the fiber-optic light previuosly fixed to the buckle when the buckle head was thought to be accurately placed. With the aid of the binocular indirect ophthalmomicroscopy (Oculus BIOM5, OCULUS Optikgeräte GmbH) system (BIOM), the glowing head position could be seen easily (Figure 2).

Now, the macular buckle was fixed in place by utilizing the sterile topical adhesive Histoacryl Blue (B Braun TS1050044FP). This is a sterile liquid topical adhesive composed of n-butyl-2-cyanoacrylate monomer. Histoacryl Blue—supplied in 0.5 ml single-use ampoules—is colored with the dye D&C Violet #2 in order to easily see the thickness of its applied layer. The tissue adhesive polymerizes in seconds upon being exposed to water or water-containing substances like a human tissue. The buckle's head could still be adjusted and positioned under the fovea before the tissue adhesive fixes it in place.

At the completion of the surgery, filtered air was injected in cases where subretinal fluid drainage was done to restore normal IOP. Sutureless macular buckling with

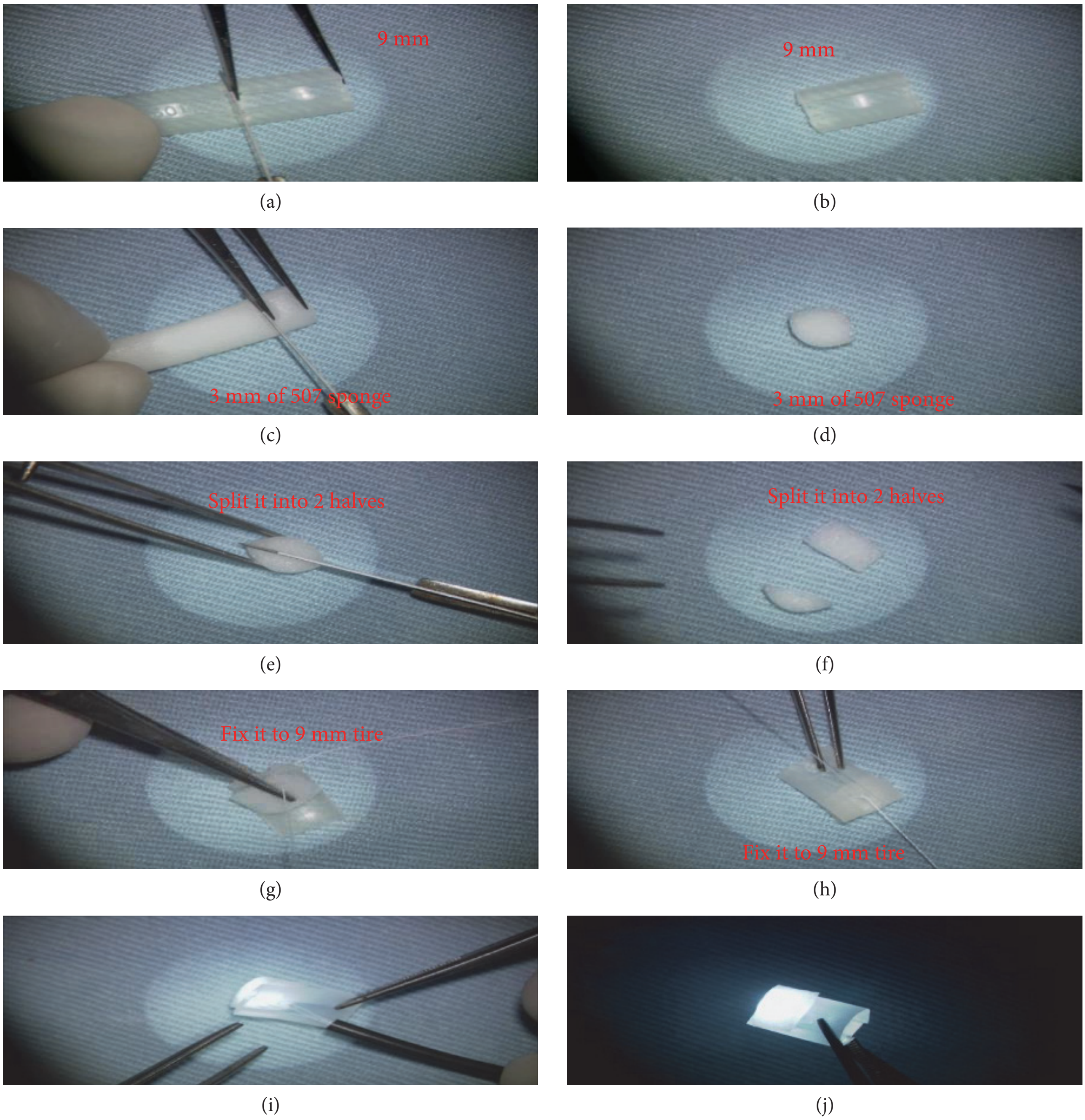


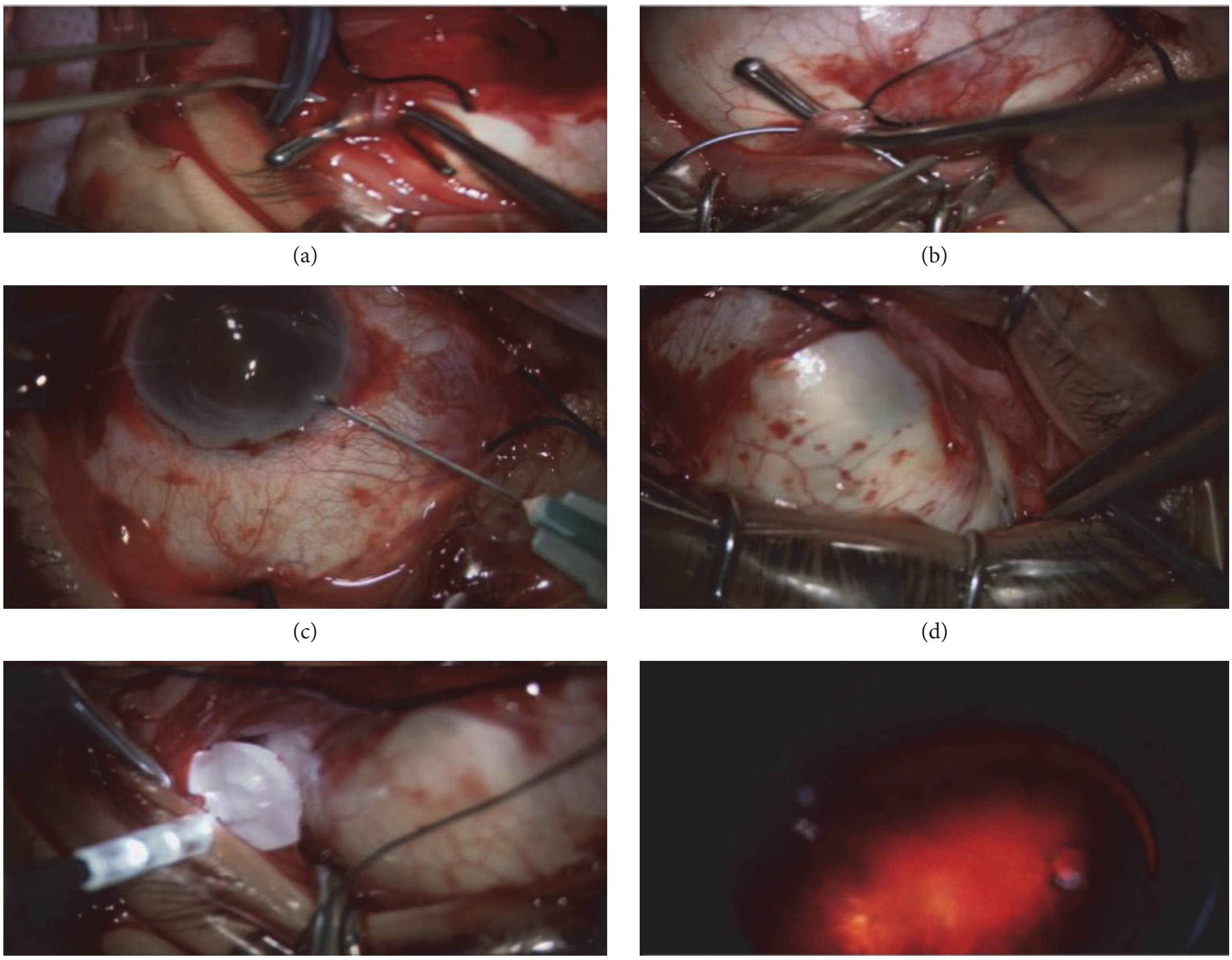
Figure 1: (a–f) Macular buckle assembled from a 5 mm wide sponge and a 7 mm wide silicone tire. A 9 mm segment from the tire was cut; a 6 mm segment from the sponge was split into two halves. (g, h) Both were sutured together so that the convex part is made facing the sclera. (i, j) Before starting the operation, a track is prepared for a fibre-optic light in which a disposable 25 g chandelier was inserted in the indenting head.

fibre-optic-guided episcleral buckle insertion was the only procedure performed in all patients.

5. Results

The study included 20 highly myopic eyes from 20 patients attending a specialized vitreoretinal centre in Alexandria, Egypt. Demographic data and the axial lengths, before and after surgery of the eyes as measured by B-scan US, are shown in Table 1.

The study sample included 20 eyes from 20 high myopia patients (mean age, 51.4 years; range, 35–65 years). Nine were males (45%) with a mean age of 48 years, while 11 were females with a mean age of 54.2 years. Fundus photography showed retinal reattachment in all eyes. OCT showed a convex configuration of the posterior pole with foveal reattachment in all eyes (Figures 3 and 4).



(a) (b) (c) (d) (e) (f)

Figure 2: Surgical steps: (a) exposure and hanging of the inferior oblique; (b) exposure and hanging of the superior oblique; (c) paracentesis or evacuation of subretinal fluid was attempted; (d) identification of the transverse long posterior ciliary artery; (e) temporary placement of the macular buckle along the vessel course; (f) confirmation of the position of the buckle head by the aid of binocular indirect ophthalmomicroscopy.

Table 1: Demographic data, axial length, BCVA, and macular hole closure rate.

Number	Sex		Axial length (mm), $p = 0.002^*$		BCVA (decimal), $p < 0.005^*$		Macular hole closure
	Male	Female	Preop	Postop	Preop	Postop	
20	9 (45%)	11 (55%)	30.55	29.8	0.11	0.21	8 eyes closed (40%)

*Statistically significant at $p \leq 0.05$.

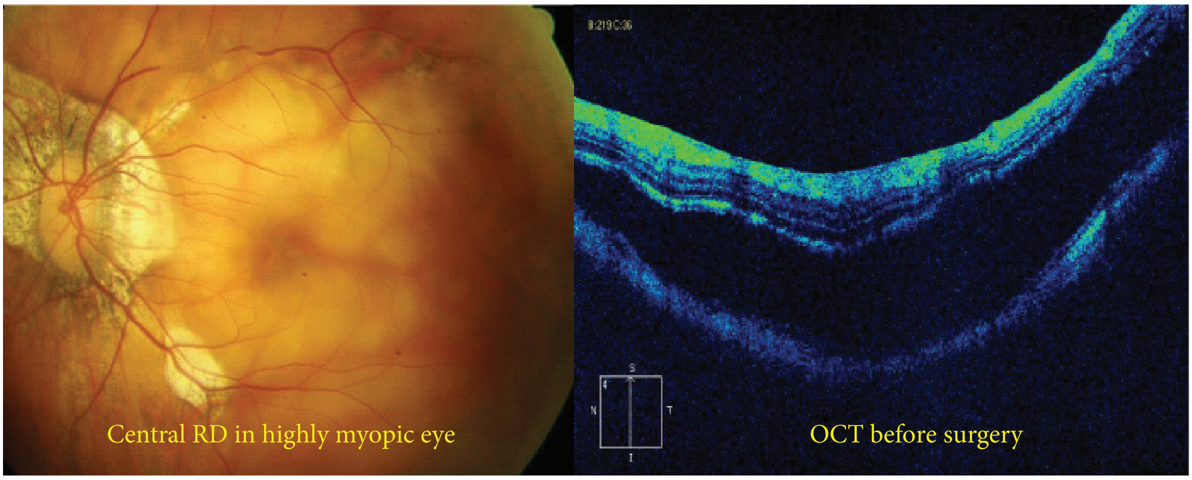
There was a statistically significant difference in axial length before (30.5 mm) and after (29.8 mm) the procedure in the studied eyes, $p = 0.002$. Likewise, the BCVA after the surgery (0.21) was statistically better than the BCVA before the surgery (0.11), $p < 0.005$.

At the end of the six-month follow-up period, normal foveal contour and architecture were evident on OCT and macular hole closure occurred in 8 (40%) cases.

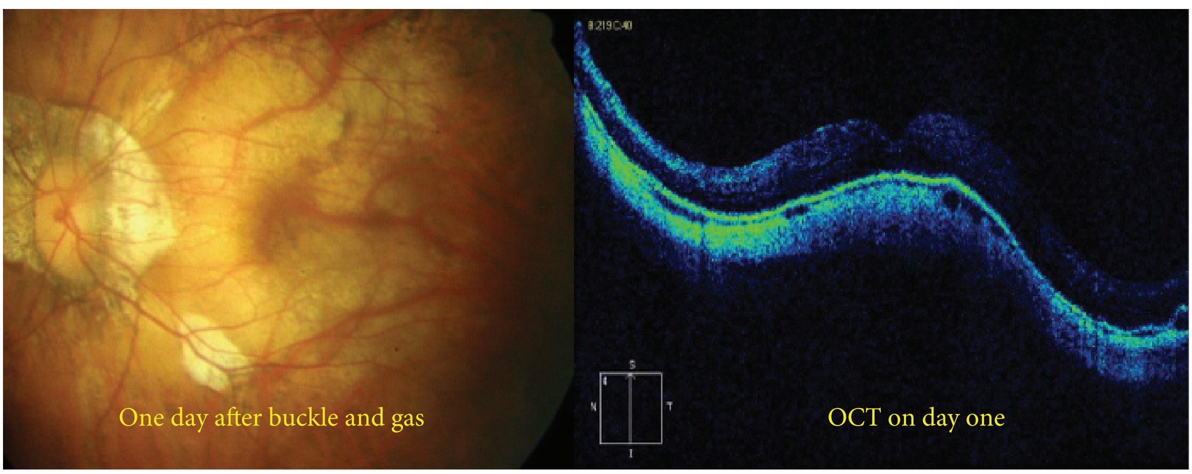
The mean BCVA of the eyes where the holes have closed was 0.28 versus a mean BCVA of 0.16 in the eyes with persistent opened holes.

6. Discussion

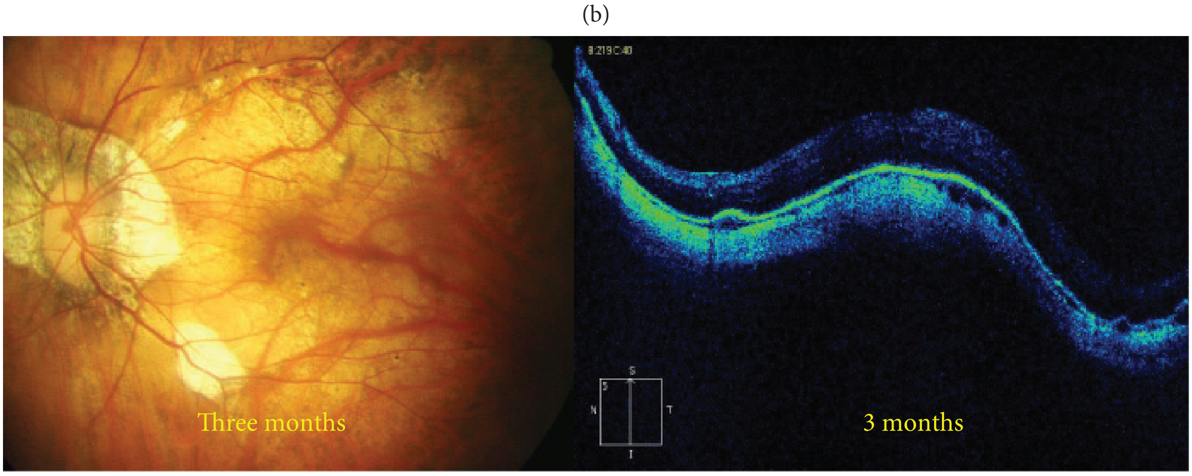
The presence of a marked posterior staphyloma in high myopia patients clearly affects the surgical outcomes of MHRD



(a)



(b)



(c)

Figure 3: (a) Fundus photograph of a highly myopic eye with central macular detachment; the corresponding preoperative OCT was unable to detect the macular hole, in spite of being detected by high-magnification contact biomicroscopy, probably due to vitreous opacities preventing a detailed OCT examination of the area harboring the hole. (b) Only one day after the buckle, the fluid is gone and the retina is attached; this was confirmed by OCT. (c) Three months later, the fundus photograph shows the retina completely in place with no recurrence of detachment; also OCT shows attachment of the macula with a convex configuration of the posterior pole.

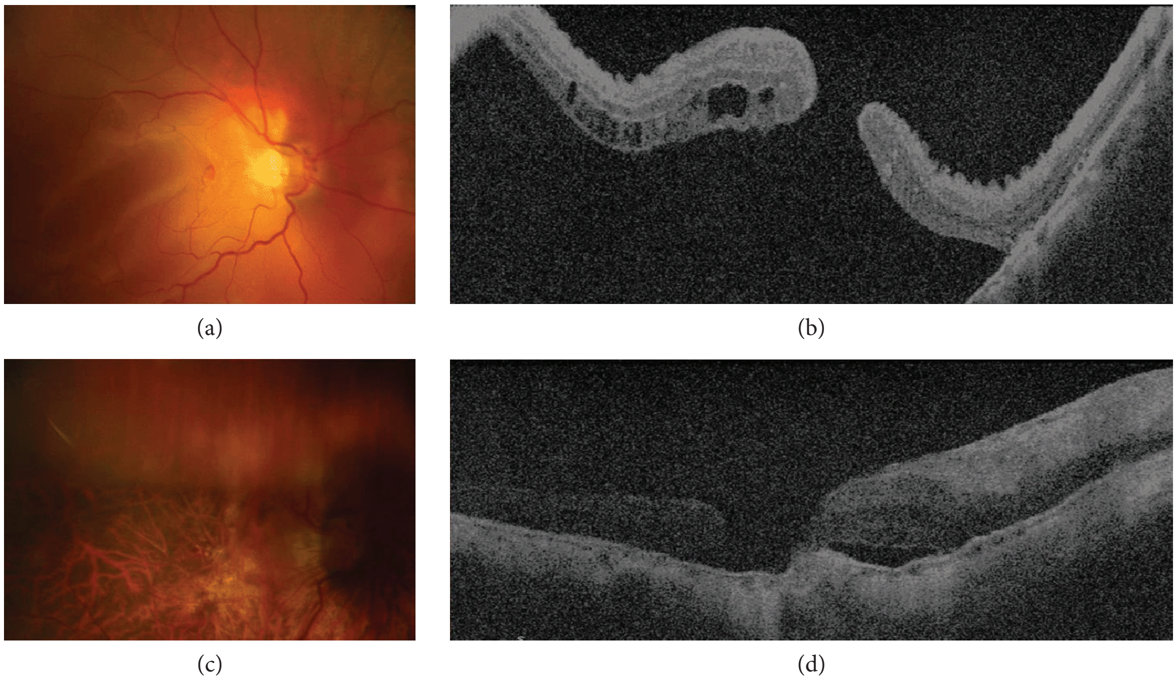


Figure 4: (a) Fundus photograph showing an eye with macular hole retinal detachment, confirmed by OCT (b). (c) Only 3 days after surgery, the retina was totally attached, which was confirmed by OCT (d).

surgeries. This observation paved the way for the resurrection of the macular buckling, which primarily addresses the posterior scleral elongation caused by the staphyloma.

Nowadays, OCT allows detailed imaging of myopic foveoschisis, myopic macular hole, and even early retinal detachment, a diagnosis difficult to be given for sure by fundus examination [6, 7]. The prevalence of foveoschisis in highly myopic eyes ranges from 9% to 34% depending on the series [8–10].

The use of macular buckling in MHRD was proven to have many advantages over vitrectomy like avoiding cataract progression and iatrogenic breaks, which are common risks of vitrectomy [11].

In the present study, the macular buckle used was prepared from materials readily available in the vitreoretinal operation room. This buckle has the same advantages as the Ando plombe (production discontinued) of the safe placement on the sclera without extraocular muscle disinsertion, reducing the potential damage of the nerves and vessels in the posterior pole. It has a much shorter length of 9 mm in comparison to the 21–29 mm length range of the Ando plombe. Moreover, accurate placement over the region of the fovea containing the hole externally was guaranteed by the use of fibre-optic light [4].

The development of a sutureless buckle was the natural next step in the evolution of the fibre-optic-guided macular buckle because of the high rate (15%) of scleral perforation in the macular buckle group in the original series performed by the authors [4].

In the present study, foveal reattachment was achieved in all patients as confirmed by fundus examination postoperatively and optical coherence tomography. Moreover, all patients had an improvement in their BCVA, which was statistically significant ($p < 0.005$). The axial length decreased from 30.5 mm preoperatively to 29.8 mm postoperatively, which was again statistically significant. This was due to the indenting effect of the buckle. In all cases, the macular buckle was easily positioned without the need for subsequent procedures such as repositioning or replacement. Extraocular muscle cutting which was a mandatory step in the macular buckle developed by Siam et al. was not needed [12]. The surgical technique described in their study involved cutting the superior oblique as well as placing two posterior sutures as close as possible to the optic nerve without causing damage to the posterior ciliary vessels.

There were no intraoperative or postoperative complications in any of the 20 eyes operated; consequently, the new proposed tissue adhesive was successful in fixing the buckle in its place with no reported migration of any of the buckle still at the end of the follow-up period.

The macular hole closure was identified by OCT in 8 (40%) eyes. This was similar to the macular hole closure rate in the original series, where it was suggested that even applying the macular Ando plombe alone was probably enough to counteract the anteroposterior traction exerted by the staphyloma. By changing the posterior eyewall from a concave into a convex shape, the retina tends to reattach to the underlying RPE, thus also facilitating the MH closure in some cases [4].

In spite of the aforementioned advantages of the sutureless macular buckles, several studies reported the effectiveness of a primary combined surgery which includes both PPV and the episcleral approach. In the series by Alkabes et al. [13], postoperative results in previously untreated MHRD cases (group 1, 21 eyes) were compared to those obtained in recurrent cases (group 2, 21 eyes). Final retinal reattachment and

MH closure rates in previously untreated MHRDs were 100% and 81%, respectively. However, the same rates were slightly lower in case of recurrent MHRDs, reaching 90.5% and 57%, respectively. Based on these results, the authors suggested that PPV combined with MB might be considered as the first surgical approach especially in naïve MHRD cases.

The eyes where the hole closed achieved a mean BCVA of 0.28 versus a mean BCVA of 0.16 in the eyes with persistent opened hole; this was statistically significant ($p < 0.005$). This finding was highlighted in many other studies [11, 13].

7. Conclusion

Preparation of the new sutureless macular buckle is simple and easy. Moreover, illumination helps to ensure proper placement. The tissue adhesive (Histoacryl Blue) is effective in fixing the buckle in its place for at least 6 months with no reported intra- or postoperative complications in the 20 eyes studied.

Conflicts of Interest

The authors declared that there is no conflict of interest.

References

[1] C. B. Sun, Z. Liu, A. Q. Xue, and K. Yao, "Natural evolution from macular retinoschisis to full-thickness macular hole in highly myopic eyes," *Eye (London, England)*, vol. 24, no. 12, pp. 1787–1791, 2010.

[2] B. Ward, "Degenerative myopia: myopic macular schysis and the posterior pole buckle," *Retina*, vol. 3, no. 1, pp. 224–231, 2013.

[3] F. Ando, N. Ohba, K. Touura, and H. Hirose, "Anatomical and visual outcomes after episcleral macular buckling compared with those after pars plana vitrectomy for retinal detachment caused by macular hole in highly myopic eyes," *Retina*, vol. 27, no. 1, pp. 37–44, 2007.

[4] A. M. Bedda, A. M. Abdel Hadi, and M. S. Abd Al Shafy, "A comparative study between vitrectomy with internal tamponade and a new modified fiber optic illuminated Ando plombe for cases of macular hole retinal detachment in myopic eyes," *Journal of Ophthalmology*, vol. 2015, Article ID 841925, 7 pages, 2015.

[5] C. Mateo, M. Dutra Medeiros, M. Alkabes, A. Bur'es-Jelstrup, M. Postorino, and B. Corc'ostegui, "Illuminated Ando plombe for optimal positioning in highly myopic eyes with vitreoretinal diseases secondary to posterior staphyloma," *JAMA Ophthalmology*, vol. 131, no. 10, pp. 1359–1362, 2013.

[6] M. Ip, C. Garza-Karren, J. S. Duker et al., "Differentiation of degenerative retinoschisis from retinal detachment using optical coherence tomography," *Ophthalmology*, vol. 106, no. 3, pp. 600–605, 1999.

[7] Z. Zhu, J. Xueying, J. Zhang, and G. Ke, "Posterior scleral reinforcement in the treatment of macular retinoschisis in highly myopic patients," *Clinical and Experimental Ophthalmology*, vol. 37, no. 7, pp. 660–663, 2009.

[8] J. Akiba, S. Konno, E. Sato, and A. Yoshida, "Retinal detachment and retinoschisis detected by optical coherence tomography in a myopic eye with a macular hole," *Ophthalmic Surgery and Lasers*, vol. 31, no. 3, pp. 240–242, 2000.

[9] T. Baba, K. Ohno-Matsui, S. Futagami et al., "Prevalence and characteristics of foveal retinal detachment without macular hole in high myopia," *American Journal of Ophthalmology*, vol. 135, no. 3, pp. 338–342, 2003.

[10] G. Panozzo and A. Mercanti, "Optical coherence tomography findings in myopic traction maculopathy," *Archives of Ophthalmology*, vol. 122, no. 10, pp. 1455–1460, 2004.

[11] G. Ripandelli, A. M. Copp'e, R. Fedeli, V. Parisi, D. J. D'Amico, and M. Stirpe, "Evaluation of primary surgical procedures for retinal detachment with macular hole in highly myopic eyes: a randomized comparison of vitrectomy versus posterior episcleral buckling surgery," *Ophthalmology*, vol. 108, no. 12, pp. 2258–2264, 2001.

[12] A. L. Siam, T. A. El Maamoun, and M. H. Ali, "Macular buckling for myopic macular hole retinal detachment: a new approach," *Retina*, vol. 32, no. 4, pp. 748–753, 2012.

[13] M. Alkabes, A. Bur'es-Jelstrup, C. Salinas et al., "Macular buckling for previously untreated and recurrent retinal detachment due to high myopic macular hole: a 12-month comparative study," *Graefe's Archive for Clinical and Experimental Ophthalmology*, vol. 252, no. 4, pp. 571–581, 2014.

Hindawi
Journal of Ophthalmology
Volume 2017, Article ID 6834692, 6 pages
https://doi.org/10.1155/2017/6834692

Research Article

An Assessment of Vitreous Degeneration in Eyes with Vitreomacular Traction and Macular Holes

Quraish Ghadiali,[1,2,3] Sarwar Zahid,[1,3] Rosa Dolz-Marco,[1,2] Anna Tan,[1,2,4] and Michael Engelbert[1,2,3]

[1] *Department of Ophthalmology, Manhattan Eye Ear and Throat Hospital of Northwell Health, 210 East 64th Street, New York, NY 10021, USA*
[2] *Vitreous Retina Macula Consultants of New York, 460 Park Avenue, New York, NY 10022, USA*
[3] *Department of Ophthalmology, New York University Langone Medical Center, 462 1st Avenue, New York, NY 10016, USA*
[4] *Singapore National Eye Center and Singapore Eye Research Institute, The Academia, 20 College Road, Discovery Tower Level 6, Singapore 169856*

Correspondence should be addressed to Michael Engelbert; michael.engelbert@gmail.com

Received 20 September 2016; Accepted 13 December 2016; Published 4 January 2017

Academic Editor: Luke Nicholson

Purpose. To compare the stages of vitreous degeneration in patients with vitreomacular traction (VMT) and macular holes (MH). *Methods*. A retrospective study was performed analyzing stages of vitreous degeneration of eyes with VMT or MH using swept-source optical coherence tomography (SS-OCT) and spectral-domain optical coherence tomography (SD-OCT). An analogous review was performed on a control group of eyes with contralateral posterior vitreous detachments. Thirty-four eyes with VMT/MH and 39 control eyes were reviewed. *Results*. Twenty-seven VMT/MH eyes and 31 control eyes were included. Eyes with VMT/MH demonstrated significantly earlier stages of vitreous degeneration when compared to the control group ($p = 0.048$) despite significantly greater age ($p = 0.032$). *Conclusions*. Vitreoretinal interface disease is more often associated with a formed vitreous and an intact premacular bursa. This is contrary to previous assumptions implicating degeneration of vitreous as a precipitating factor of interface disease when in conjunction with abnormal vitreomacular separation.

1. Introduction

Multimodal imaging has promoted a better understanding of vitreoretinal interface disease. Visualization of the structural alterations of the retina and the vitreoretinal interface has changed both the diagnosis and management of vitreomacular traction (VMT) and macular holes (MH). However, our understanding of the role of the vitreous body itself in this spectrum of disease has been neglected. As a result, it is typically accepted that progression of vitreous degeneration may be responsible for disease in an eye with a pathologically adherent cortical vitreous [1]. However, this theory has not been substantiated by in vivo imaging modalities.

The idea that vitreous degeneration may not, in fact, be positively correlated with vitreoretinal interface disease originated from the authors' anecdotal observations during VMT and MH repair by pars plana vitrectomy. During manipulation of the posterior vitreous, it was noted that it generally appeared to be elastic, formed, and gel-like rather than exhibiting the mobility and displacement one would expect in degenerated vitreous that may be encountered during detachment repair in patients of similar age. This was further observed on optical coherence tomography imaging leading to further investigation.

The purpose of this study was to analyze the vitreous body and its grade of degeneration in eyes with VMT and MH.

2. Materials and Methods

This retrospective observational case series was conducted at Vitreous Retina Macula Consultants of New York. The study complied with the Health Insurance Portability and Accountability Act and adhered to the tenets of the Declaration of Helsinki. The Western Institutional Review Board ruled that approval was not required for this retrospective study.

2.1. Subjects. A retrospective chart review was performed on patients who presented with VMT or MH as a manifestation of an anomalous PVD to a single physician (ME) between February 2013 and November 2015 (VMT/MH group). The diagnosis of VMT or MH was based on fundus examination and either SS-OCT or SD-OCT imaging.

A second analogous retrospective chart review was also performed to establish a control group consisting of patients presenting with an uneventful, "normal," unilateral posterior vitreous detachment (PVD) and an attached vitreous in the contralateral eye. These contralateral eyes without a PVD were placed in the control group. Patients with pathologic myopia, lamellar holes, and neovascular disease were excluded. Furthermore, eyes with a history of vitreoretinal surgery were also excluded.

2.2. Data Collection. Our current understanding of posterior vitreous anatomy has recently been augmented by swept-source optical coherence tomography (SS-OCT) which allows an enhanced depth of field [2–4]. Furthermore, manipulation of image capture using standard spectral-domain optical coherence tomography (SD-OCT) allows for improved visualization of structures within the posterior vitreous [5, 6]. We previously described the anatomical features seen within the posterior vitreous and proposed a grading scheme for vitreous degeneration based on the state of the premacular bursa and its relationship to the various lacunae and degenerative cleavage planes within the vitreous body [2]. The study defined grade 0 as having an intact premacular bursa with no connections to more anterior spaces within the vitreous. Grade 1 identified anterior cleavage planes with speckled hyperreflectivity without connection to the premacular bursa. More advanced vitreous degeneration was seen in grade 2, which was characterized by connections between these spaces and the premacular bursa. Finally, grade 3 degeneration displayed connections between the premacular bursa and larger anterior lacunae.

All eyes underwent a complete ophthalmic examination as well as either structural SD-OCT or SS-OCT macular scans using the Heidelberg Spectralis (Heidelberg Engineering, Heidelberg, Germany) or the DRI OCT-1 Atlantis SS-OCT (Topcon Medical Systems, Oakland, NJ), respectively, using protocols described by our group previously [2, 7]. Briefly, radial scans of the vitreous were taken with SD-OCT using defocus, scan-tilt, and automatic real-time averaging. SS-OCT scans were completed using 5-line cross-scan patterns focused on the vitreous and contrast adjusted using the viewing software to enhance visualization of vitreous structures. Scans were excluded if the premacular bursa was not readily visible. For each eye, all B-scans through the central macula from both the VMT/MH and control groups were exported. A single nonblinded evaluator (QG) familiar with the hypothesis of the study graded each eye based on the previously described grading scheme established by our group. The exported B-scans from both study groups were then randomized and two additional blinded evaluators (RDM, AT), who were not aware of the hypothesis of the study, graded each eye.

Eyes were excluded from the data analysis if there was disagreement in grading between all three evaluators and/or scan quality did not allow unequivocal grading. If two or more evaluators were in agreement, the eye was assigned the corresponding grade and was included in the data analysis. Therefore, disagreement by only the nonblinded grader would not exclude an eye from the final analysis.

2.3. Statistical Analysis. Average ages between the control groups were compared using a two-tailed heteroscedastic t-test. The distributions of vitreous grades between the control and VMT/MH groups were compared using a Fisher exact test of a 4 by 2 contingency table. Statistical analyses were performed using SPSS v.22.0 (IBM Corp., Armonk, NY, USA). A p value less than 0.05 was considered statistically significant.

3. Results

A total of 34 eyes in the VMT/MH group and 39 eyes in the control group were reviewed for the study. After excluding eyes with disagreement between evaluators, 27 eyes were included in the VMT/MH group and 31 eyes in the control group. Average age in the VMT/MH group (68.2 years, range: 45–93) was higher than the control group (63.4, range: 50–77) ($p = 0.0137$, t-test). Regarding eyes with a previous history of cataract surgery, the two groups were not significantly different (VMT/MH = 5 eyes, control = 2 eyes, $p = 0.2332$, Fisher exact test).

Of the 27 eyes in the VMT/MH group, 7 had MH and 20 had VMT. Table 1 displays patient characteristics for each eye and their respective vitreous degeneration grading while Figure 1 demonstrates the distribution of vitreous degeneration grades within each group. Both groups exhibited varying degrees of degeneration with grade 0 representing the highest frequency in both groups. The levels of vitreous degeneration demonstrated in the VMT/MH group were 19 grade 0 (70.4%), 5 grade 1 (18.5%), and 3 grade 3 (11.1%). Grade 2 vitreous degeneration was not seen in this group. The levels of vitreous degeneration demonstrated in the control group were 15 grade 0 (48.4%), 3 grade 1 (9.7%), 4 grade 2 (12.9%), and 9 grade 3 (29.0%). Examples of each grade within the control and VMT/MH group are pictured in Figures 2 and 3, respectively.

A Fisher exact test showed a statistically significant difference between the VMT/MH and control groups ($p = 0.048$) demonstrating earlier stages of vitreous degeneration within the VMT/MH group.

4. Discussion

In this study, we assessed the stages of vitreous degeneration in patients with VMT and MH. When compared to a control group, eyes with VMT and MH demonstrated a statistically significant deviation toward earlier stages of vitreous

Table 1: Patient characteristics and vitreous degeneration grading for individual eyes.

(a) VMT/MH group

Age	Gender	Diagnosis	Grade
73	F	VMT	0
61	M	VMT	0
68	M	VMT	0
65	F	MH	0
59	F	VMT	0
69	F	VMT	0
79	M	VMT	0
68	F	VMT	0
93	F	VMT	0
81	F	VMT	0
63	F	MH	0
78	F	MH	0
65	M	VMT	0
62	F	VMT	0
69	M	VMT	0
66	M	MH	0
74*	F	VMT	0
68	F	MH	0
73	F	VMT	0
56	M	VMT	1
73	F	VMT	1
66	F	VMT	1
45	F	MH	1
67	F	VMT	1
75	F	VMT	3
73	F	MH	3
74*	F	VMT	3

VMT: vitreomacular traction.
MH: macular hole.
M: male; F: female.
*Both eyes included from a single patient.

(b) Control group

Age	Gender	Grade
68	F	0
69	F	0
61	F	0
71	F	0
57	M	0
77	M	0
70	F	0
54	F	0
62	F	0
68	M	0
51	F	0
61	F	0
73	M	0
61	M	0
64	F	0
71	F	1
67	F	1
73	M	1
63	F	2
63	F	2
68	M	2
57	F	2
65	F	3
59	M	3
75	F	3
61	M	3
50	M	3
68	F	3
58	M	3
58	M	3
60	M	3

M: male; F: female.

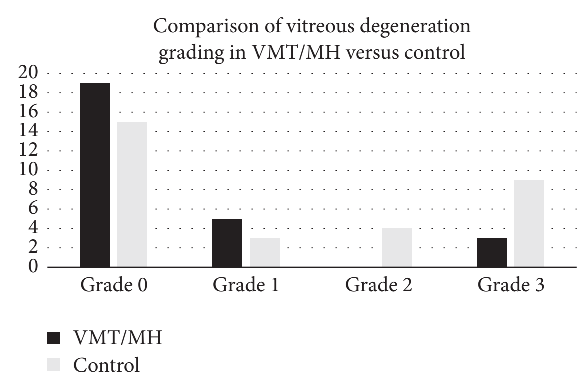


Figure 1: Distribution of vitreous grades in vitreomacular traction/macular hole (VMT/MH) eyes and control eyes. The VMT/MH eyes demonstrated significantly earlier degrees of vitreous degeneration when compared to the control group ($p = 0.048$).

degeneration. As the VMT/MH group was significantly older than the control group, this correlation is unlikely to be confounded by vitreous degeneration related to age. Our data reveal that grade 0 has highest prevalence in both groups but the latter stages of degeneration vary considerably.

While an abnormally strong adhesion of the posterior cortical vitreous to the macula is thought to play an important role in VMT/MH formation, the above findings suggest that a relatively formed vitreous anteriorly may also be involved in the pathogenesis of MH and VMT. Although seemingly counterintuitive and contrary to previous thinking [1], the pathogenesis involved may be substantiated by existing mechanical models. While it is known that rotation of the eye results in shearing forces on the retina transmitted from the vitreous gel, saccadic movements also cause a secondary motion of the vitreous itself directed inward to the axis of

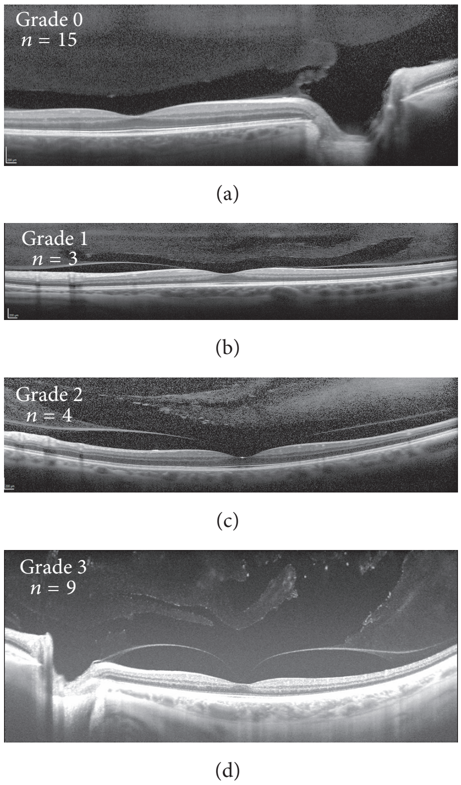


Figure 2: Examples of vitreous grading in eyes from patients with a posterior vitreous detachment in the contralateral eye. Spectral-domain optical coherence tomography (a to c) and swept-source optical coherence tomography (d) examples of grade 0 (a), 1 (b), 2 (c), and 3 (d) vitreous degeneration. Number of eyes demonstrating each vitreous grade included in respective panels.

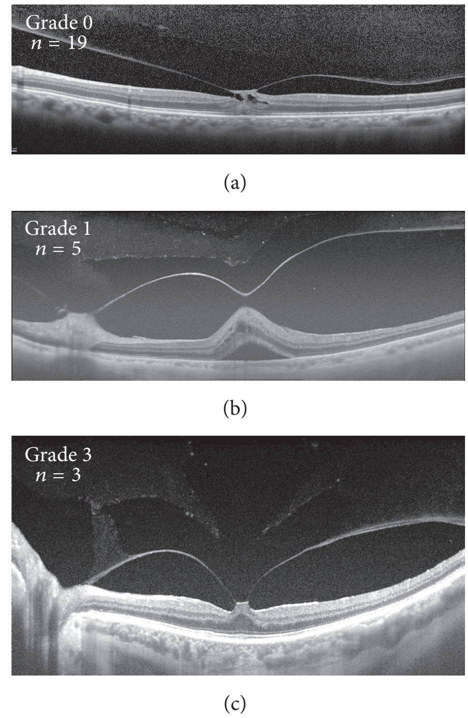


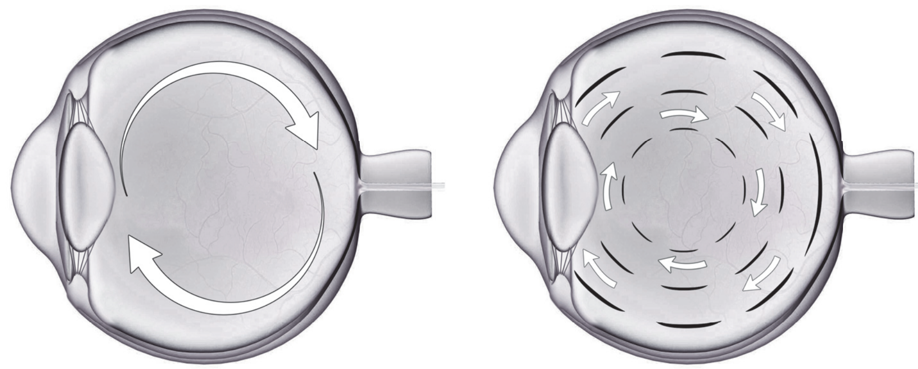
Figure 3: Examples of vitreous grading in eyes from patients with vitreomacular traction/macular hole (VMT/MH). Spectral-domain optical coherence tomography (a) and swept-source optical coherence tomography (b and c) examples of grade 0 (a), 1 (b), and 3 (c) vitreous degeneration. Number of eyes demonstrating each vitreous grade included in respective panels. Note that no patient in the VMT/MH group demonstrated grade 2 vitreous degeneration.

rotation. This force is in a direction opposite to the pull of the extraocular muscles exerting inertia counterforce at the vitreoretinal interface (Figure 4(a)) [8, 9]. Therefore, degeneration and compartmentalization of the vitreous gel may buffer or interrupt transmission of inertia counterforce exerted by the more central vitreous (Figure 4(b)). Spaide first suggested that the preexisting liquid spaces in the vitreous may function as a buffer, but since they are universally present, this would not explain why some eyes develop VMT or MH, while others do not [10]. As demonstrated in this study, vitreous degeneration is variable. The observation that a more formed vitreous is present in eyes affected by VMT or MH as observed during pars plana vitrectomy repair by the senior author and the OCT correlation presented in this study support the notion that vitreous degeneration or rather a lack thereof is implicated in vitreoretinal interface disorders.

Several of the limitations of this study stem from its retrospective nature and small sample size. A stratified analysis of VMT and MH did not demonstrate a statistically significant difference compared to controls, likely secondary to limited subject numbers in each respective disease group. In addition, one observer was familiar with the observations that lead to the study hypothesis and may have introduced unintentional bias. However, disagreement by the two additional blinded graders would likely negate this bias. Finally, while eyes with previous vitreous surgery were excluded, other intraocular surgeries such as cataract extraction may have disturbed the vitreous architecture leading to an altered state of the vitreous. Given that the proportion of pseudophakic patients was not significantly different between groups, this would be an unlikely confounder.

It is probable that a constellation of factors contribute to disease at the vitreoretinal interface. While the data presented show a significant correlation between interface disease and formed vitreous, three eyes demonstrated advanced vitreous degeneration. Since MH can occur when only residual cortex is present as seen in eyes after pars plana vitrectomy or in myopic macular holes with a preexisting PVD, it is clear that the forces generated to create MH and VMT are not derived exclusively from the vitreous body [11].

However, this study suggests that progression of vitreous degeneration is not a causative factor in vitreoretinal interface disease but may in fact be preventative. The implications of this theory may alter the way we think about not only the pathogenesis but also future treatment paradigms of VMT-MH spectrum disorders. It may be possible that enzymatic mechanisms used to advance vitreous degeneration may slow or halt the progression of vitreoretinal interface disease. Conceivably, the degree of vitreous degeneration is a currently



(a) (b)

Figure 4: Vitreous degeneration force diagram: Shown is a schematic horizontal section of an eye with early stages of vitreous degeneration with formed vitreous (a). The forces are transmitted to the vitreoretinal interface by more central, formed vitreous without buffering from compartmentalization. Advanced vitreous degeneration with compartmentalization of the formed vitreous by liquid spaces may buffer the transmission of these forces (b).

overlooked prognostic factor in spontaneous resolution of VMT and MH with persistently attached vitreous, or in the success of enzymatic vitreolysis. This may be translated even further to consider prophylactic advancement of vitreous degeneration in the contralateral vitreous of a diseased eye. In the same vein, the state of vitreous degeneration may alter the rate of enzymatic vitreolysis and consequently guide treatment strategies for VMT and MH. Future prospective investigations may allow us to understand the unfolding of vitreous degeneration in patients with vitreoretinal interface disease.

5. Conclusions

Multiple factors are likely to contribute to the pathogenesis of vitreoretinal interface disturbance along the VMT-MH spectrum. Modern imaging methods such as SD-OCT and SS-OCT allow for enhanced visualization of vitreous evolution and will continue to broaden our understanding of retinal disease.

This study is the first to support the novel hypothesis that the state of the vitreous itself may play a role in addition to the strength of vitreoretinal adhesion.

Disclosure

This paper was previously presented at the Association for Research and Vision and Ophthalmology, Seattle, WA, USA, May 2016. The funding organization had no role in the design or conduct of this research.

Competing Interests

No conflicting relationship exists for any author.

Acknowledgments

This paper was financially supported by the Macula Foundation, Inc.

References

[1] J. Sebag, "Anomalous posterior vitreous detachment: a unifying concept in vitreo-retinal disease," *Graefe's Archive for Clinical and Experimental Ophthalmology*, vol. 242, no. 8, pp. 690–698, 2004.

[2] K. B. Schaal, C. E. Pang, M. C. Pozzoni, and M. Engelbert, "The premacular bursa's shape revealed in vivo by swept-source optical coherence tomography," *Ophthalmology*, vol. 121, no. 5, pp. 1020–1028, 2014.

[3] H. Itakura, S. Kishi, D. Li, and H. Akiyama, "Observation of posterior precortical vitreous pocket using swept-source optical coherence tomography," *Investigative Ophthalmology and Visual Science*, vol. 54, no. 5, pp. 3102–3107, 2013.

[4] C. E. Pang, K. B. Schaal, and M. Engelbert, "Association of prevascular vitreous fissures and cisterns with vitreous degeneration as assessed by swept source optical coherence tomography," *Retina*, vol. 35, no. 9, pp. 1875–1882, 2015.

[5] G. Barteselli, D.-U. Bartsch, S. El-Emam et al., "Combined depth imaging technique on spectral-domain optical coherence tomography," *American Journal of Ophthalmology*, vol. 155, no. 4, pp. 727.e1–732.e1, 2013.

[6] H. Itakura and S. Kishi, "Aging changes of vitreomacular interface," *Retina*, vol. 31, no. 7, pp. 1400–1404, 2011.

[7] C. E. Pang, K. B. Freund, and M. Engelbert, "Enhanced vitreous imaging technique with spectral-domain optical coherence tomography for evaluation of posterior vitreous detachment," *JAMA Ophthalmology*, vol. 132, no. 9, pp. 1148–1150, 2014.

[8] R. Repetto, "An analytical model of the dynamics of the liquefied vitreous induced by saccadic eye movements," *Meccanica*, vol. 41, no. 1, pp. 101–117, 2006.

[9] T. David, S. Smye, T. Dabbs, and T. James, "A model for the fluid motion of vitreous humour of the human eye during saccadic movement," *Physics in Medicine and Biology*, vol. 43, no. 6, pp. 1385–1399, 1998.

[10] R. F. Spaide, "Visualization of the posterior vitreous with dynamic focusing and windowed averaging swept source optical coherence tomography," *American Journal of Ophthalmology*, vol. 158, no. 6, pp. 1267–1274, 2014.

[11] S. Kishi, N. Hagimura, and K. Shimizu, "The role of the premacular liquefied pocket and premacular vitreous cortex in idiopathic macular hole development," *American Journal of Ophthalmology*, vol. 122, no. 5, pp. 622–628, 1996.

Hindawi Publishing Corporation
Journal of Ophthalmology
Volume 2016, Article ID 1292735, 6 pages
http://dx.doi.org/10.1155/2016/1292735

Research Article

Macular Hole Surgery with Internal Limiting Membrane Peeling Facilitated by Membrane-Blue® versus Membrane-Blue-Dual®: A Retrospective Comparative Study

Uri Soiberman, Daniel Shai, Anat Loewenstein, and Adiel Barak

Department of Ophthalmology, Tel Aviv Medical Center and the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Correspondence should be addressed to Adiel Barak; adielbarak@gmail.com

Received 2 September 2016; Accepted 6 November 2016

Academic Editor: Luke Nicholson

Background. This study aims to compare the outcome of macular hole (MH) surgery with internal limiting membrane (ILM) peeling facilitated by two different vital dyes. *Methods*. This was a retrospective chart review. The group designated "group-MB" underwent pars plana vitrectomy with ILM peeling facilitated by Membrane-Blue (MB), whereas in "group-MBD," the vital dye used was Membrane-Blue-Dual (MBD). *Results*. Seventy-four eyes comprised the study population: 53 in group-MB and 21 in group-MBD. There was no difference in the rate of macular hole closure in group-MB or group-MBD: 71.2% closed MHs compared to 66.7%, respectively ($p = 0.7$). Postoperative visual improvement was of a higher magnitude in the MBD group compared to the MB group: -0.34 ± 0.81 logMAR versus 0.01 ± 0.06 logMAR, respectively ($p = 0.003$). *Conclusions*. In this study, MBD led to better visual results that may be related to better staining characteristics or lesser toxicity compared to MB.

1. Introduction

Macular hole surgery (MHS) is currently the mainstay for treatment of large full-thickness macular holes (FTMH) [1]. This procedure has evolved significantly since Kelly and Wendel initially reported a 58% anatomical closure rate [2]. Modern surgery includes pars plana vitrectomy (PPV) with or without internal limiting membrane (ILM) peeling and intraocular air/gas tamponade and leads to anatomical closure rates of 90% or more, especially when FTMH smaller than 400 μm are treated [3]. The role of internal limiting membrane (ILM) peeling in the primary surgical treatment of this pathology is still controversial, but a growing number of surgeons employ this technique during the primary intervention in order to maximize the closure rate of the FTMH [4].

ILM peeling is a technically challenging procedure: the membrane is translucent and has a relatively low visibility. Many vital dyes have been suggested to facilitate the visualization of the ILM, such as indocyanine-green (ICG), trypan blue, and brilliant blue G® (BBG) [5–7]. In the past few years, two additional vital dyes have been introduced in clinical practice: Membrane-Blue (MB) and Membrane-Blue-Dual (MBD). MB consists of trypan blue 0.15%. It is commonly used in vitrectomy surgery to stain epiretinal membranes (ERMs), as well as the ILM. Prior studies with trypan blue or MB demonstrated macular hole closure rates exceeding 85% and a mean visual acuity improvement of at least two Snellen lines [6, 8, 9]. Other comparative studies of trypan blue or MB mostly demonstrated that when compared to ICG, both vital dyes led to similar macular hole closure rates (at least 84%) [10–15]. As for the visual acuity improvement, the results were inconclusive, with some studies reporting a better outcome with trypan blue/MB.

MBD consists of a combination of trypan blue (0.15%), brilliant blue G (0.025%), and 4% polyethylene glycol (PEG). This dye stains the ILM as well as other membranes (ERMs and proliferative vitreoretinopathy membranes), and it does not require an air-fluid exchange prior to dye injection because of its heavier molecular weight. A previous study comparing MBD to ILM-Blue®, another vital dye containing PEG that does not necessitate air-fluid exchange, has shown that there was no difference in visual outcome in eyes undergoing macular surgery with ILM peeling using either one of the aforementioned dyes [16]. However, macular hole was not the most common indication for surgery in that study.

MB and MBD were not compared directly in previous studies. This study aims to compare the outcome of MHS with ILM removal using MB versus MBD.

2. Materials and Methods

This was a retrospective study that was approved by the institutional review board (IRB) and was in accordance with the Helsinki Declaration of 1975, as revised in 2000. Since this study was retrospective, informed consent was waived by the IRB committee. All cases were identified from the operating-room log book in a tertiary referral academic medical center in the period between January 2010 and April 2013. All consecutive eyes that underwent pars plana vitrectomy with MB- or MBD-assisted ILM peeling for idiopathic FTMH were included. All patients were 18 years or older at the time of surgery. This study did not include eyes with a history of uveitis, endophthalmitis, or retinal detachment, nor eyes with other vision limiting pathologies. Cases of idiopathic FTMH in pregnant women were also excluded.

All operations were performed by one of two senior vitreoretinal surgeons (AL, AB). All PPVs were performed using a 23G transconjunctival trocar system and included a surgical induction of posterior vitreous detachment, a near-complete vitrectomy, a complete tamponade with C_3F_8, and postoperative head-down positioning for one week. Two groups were included in this study: group-MB—Membrane-Blue (DORC International, The Netherlands); group-MBD—Membrane-Blue-Dual (DORC International, The Netherlands). Both groups underwent similar surgeries, as stated above; however the MB group underwent air-fluid exchange prior to dye injection.

Study parameters included demographic data, lens status, and intraocular pressure (IOP). Additional parameters included presence of systemic hypertension and laterality (right or left eye). Best-corrected visual acuity (BCVA) was transformed from the Snellen acuity scale to logMAR. No light perception was set at logMAR 2.9, light perception at 2.6, hand motion at 2.3, and counting fingers at 1.85 [17, 18].

Surgical data included the type of vital dye used and noted cases in which PPV was combined with phacoemulsification and intraocular lens implantation. Postoperative data included the duration of follow-up, final BCVA and improvement in BCVA, BCVA at 6 months following surgery (when available), postoperative lens status, and IOP. Complications were also documented, especially, glaucoma, retinal detachment, residual subretinal fluid, reoperation, posterior capsular opacification, choroidal neovascularization (CNV), and reinjection of gas.

Spectral-domain optical coherence tomography (SD-OCT) was performed with Heidelberg Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany). All measurements were performed by one skilled ophthalmologist (US). First available preoperative scans were compared with last available postoperative scans. Central macular thickness was calculated using the Heidelberg Spectralis module. The macular holes' transverse dimensions were assessed at the center of the holes: both basal diameter and the aperture diameter were measured. Other data included the attenuation of foveal retinal pigment epithelium (RPE), defined as focal or diffuse discontinuation of the sub- or perifoval RPE layer, focal retinal nerve fiber layer (RNFL) defects, defined as focal or diffuse breaks or absence of the inner retinal layers, intraretinal cysts, defined as intraretinal hyporeflective spaces, and misalignment in the retinal layers surrounding the location of the hole and closure of the macular hole. The latter was defined as misalignment of the hyper- or hyporeflective bands normally observed to be continuous when imaged with OCT.

Postoperative scans were examined specifically for the existence of foveolar vertical planes of separation. A vertical plane of separation was defined as a hyperreflective axial line present in the foveola and extending from the retinal nerve fiber layer to Bruch's membrane (Figure 1).

Statistical Analysis. Statistical analysis was performed using SPSS software version 19.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were examined for normal distribution by the Kolmogorov-Smirnov test, Q-Q plot, and histogram. Normally distributing parameters were described by mean and standard deviation, and the rest were described by median and range. A univariate analysis of the FTMH closure and categorical predictors was performed using Chi-square or Fisher's exact test. A t-test was performed for continuous, normally distributing parameters; the rest were tested with Mann–Whitney. Change in lens status between the two groups was assessed with McNemar's test. Visual acuity improvement analysis was performed with repeated measures ANOVA. A multivariate analysis for the outcomes was performed with a forward logistic regression with adjustment to universal confounders (age and gender with additional block). All tests were two-sided. A p value ≤ 0.05 was considered statistically significant; $0.05 < p \leq 0.1$ was considered a trend, due to the small size of the sample.

3. Results

Seventy-four eyes of 74 patients were included in this study: 53 in group-MB and 21 in group-MBD. Both groups had similar baseline characteristics, except for duration of the follow-up period, as illustrated in Table 1.

Information on the closure of the macular hole was available for 73 patients (data was missing for one patient in group-MB). Thirty-seven (71.2%) patients in group-MB had a closed macular hole by the end of follow-up compared with 14 (66.7%) in group-MBD ($p = 0.7$).

There was no baseline difference in BCVA between the MB and MBD groups (Table 1): 0.89 ± 0.54 logMAR (mean ± standard deviation; Snellen equivalent ~20/155) and 1.1 ± 0.67 logMAR (Snellen equivalent ~20/250, $p = 0.17$), respectively. When all study participants were included, BCVA improved from 0.95 ± 0.67 logMAR (Snellen: ~20/178) at baseline to 0.86 ± 0.55 logMAR (Snellen: ~20/145) at the last postoperative visit ($p < 0.001$). Visual improvement (the difference in mean postoperative BCVA at the last follow-up visit and preoperative BCVA) in the MBD group was greater

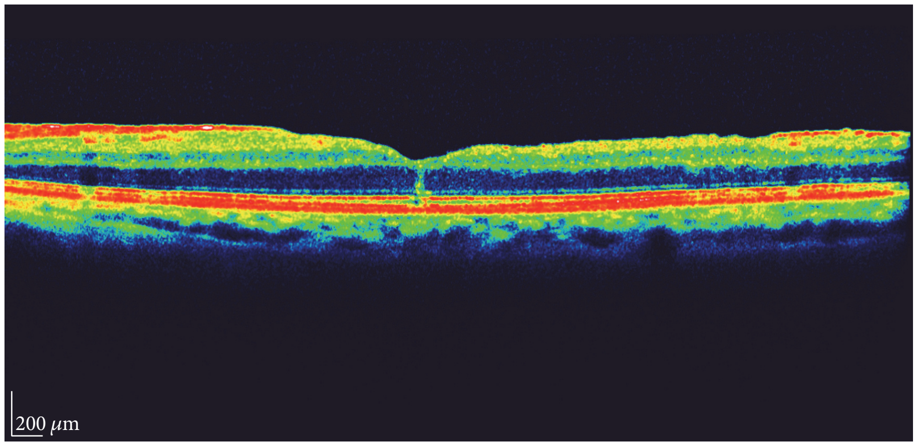


Figure 1: A vertical plane of separation is depicted anteriorly to the foveola in this spectral-domain OCT scan.

Table 1: Demographical and baseline characteristics.

Criteria	Membrane-Blue [n]	Membrane-Blue-Dual [n]	p value
Age (years)	66.83 ± 8.46 [53]	66.71 ± 5.62 [21]	0.95
Preop CMT (μm)	405.08 ± 88.79 [40]	393.5 ± 72.39 [16]	0.64
Preop IOP (mmHg)	15.19 ± 2.45 [53]	14.1 ± 2.59 [21]	0.09
BCVA (logMAR)	0.89 ± 0.54 [53]	1.1 ± 0.67 [21]	0.17
MH aperture diameter (μm)	403.82 ± 191.71 (range: 0–769) [44]	424.21 ± 128.08 (range: 230–637) [19]	0.62
MH base diameter (μm)	958.07 ± 347.1 (range: 247–1981) [42]	1012.93 ± 226.4 (range: 739–1421) [15]	0.57
Duration of macular hole (months)	6.69 ± 7.34 [49]	5.4 ± 5.02 [20]	0.77
Duration of FU (days)	352.96 ± 364.66 (8–2327) [53]	95.05 ± 63.57 (9–211) [21]	<0.001

All data presented as mean ± standard deviation (range was also presented for duration of follow-up). Values within square brackets refer to the number of eyes with available data for analysis. CMT: central macular thickness; IOP: intraocular pressure; BCVA: best-corrected visual acuity; MH aperture diameter: the diameter at the narrowest point; MH base diameter: the base diameter of the macular hole; FU: follow-up.

than that of the MB group: −0.34 ± 0.81 logMAR versus 0.01 ± 0.06, respectively ($p = 0.003$). A similar trend was observed at 6 months postoperatively: −0.54 ± 0.63 logMAR for group-MBD ($n = 17$) versus 0.08 ± 0.33 logMAR ($n = 45$) for group-MB ($p < 0.001$).

Most of the study's participants did not undergo combined cataract extraction and vitrectomy—the procedure was only used on 4 eyes (all in group-MB). Nevertheless, at the end of follow-up there were 29 pseudophakic eyes in the MB group and 11 in the MBD group and a total of 24 eyes became pseudophakic during the follow-up period: 18 in the MB group and 6 in the MBD group ($p = 0.6$). The improvement in BCVA did not correlate with lens status exchange from phakic to pseudophakic during the study follow-up period ($p = 0.26$) nor with the final postoperative BCVA ($p = 0.47$).

The OCT findings differed between the two studied groups: a vertical plane of separation was evident in 19/53 (35.8%) eyes in group-MB and in 3/21 (14.3%) eyes in group-MBD ($p = 0.07$). Postoperative foveal RPE attenuation was detected in 34/53 (64.2%) eyes in group-MB and 9/21 (42.9%) eyes in group-MBD ($p = 0.09$). RPE attenuation was associated with the existence of systemic hypertension (OR 7.24, 95% CI 1.23–42.74, $p = 0.03$) and with laterality (right eye OR 0.12, 95% CI 0.02–0.56, $p = 0.007$). The compared groups did not vary in other studied parameters or complications (see Tables 2 and 3).

4. Discussion

The results of this study show that there was no difference in the rate of macular hole closure regardless of whether MB or MBD were used to facilitate ILM visualization during PPV and ILM peeling. Overall, there was a significant improvement in visual acuity, with the MBD group experiencing a higher magnitude of change. There was a trend for a vertical plane of separation in the MB group ($p = 0.07$), although the significance of the finding is unclear. A trend for postoperative foveal RPE attenuation was also detected in the MB group ($p = 0.09$). Associated risk factors were systemic hypertension and laterality, with the left eye being more affected (both surgeons in this study were right-handed).

The role of ILM peeling in macular hole surgery is still controversial. A recent meta-analysis failed to demonstrate a substantial benefit associated with ILM peeling: there was no difference in best-corrected distance visual acuity at 6 or 12 months postoperatively whether ILM peeling was performed or not [19]. The findings demonstrated that ILM peeling may be associated with primary hole closure after a single

Table 2: Postoperative parameters.

Criteria	Membrane-Blue	Membrane-Blue-Dual	p value
CMT (μm)	287.4 ± 89.03 [45]	290.67 ± 59.34 [15]	0.18
IOP (mmHg)	14.45 ± 3.18 [52]	14.5 ± 3.14 [20]	0.9
Final BCVA (logMAR)	0.9 ± 0.56 [53]	0.76 ± 0.55 [21]	0.22
In eyes with an open macular hole postoperatively:			
MH aperture diameter (μm)	582.5 ± 275.52 [10]	507 [1]	0.75
MH base diameter (μm)	1136.3 ± 358.25 [10]	979 [1]	0.75

All data presented as mean ± standard deviation. Values within square brackets refer to the number of eyes with available data for analysis. CMT: central macular thickness; IOP: intraocular pressure; BCVA: best-corrected visual acuity; MH aperture diameter: the diameter at the narrowest point; MH base diameter: the base diameter of the macular hole.

Table 3: Postoperative OCT findings and complications.

Type of postop complication	Membrane-Blue n (%)	Membrane-Blue-Dual n (%)	p value
OCT parameters			
Vertical plane of separation	19 (35.8%)	3 (14.3%)	0.07
RPE attenuation	34 (64.2%)	9 (42.9%)	0.09
Misalignment of retinal layers	4 (7.5%)	1 (4.8%)	1
RNFL defects	34 (64.2%)	11 (52.4%)	0.35
Intraretinal cysts	12 (22.6%)	4 (19%)	1
Clinical complications			
Glaucoma	2 (3.8%)	1 (4.8%)	1
Retinal detachment	1 (1.9%)	0	1
Residual subretinal fluid	1 (1.9%)	1 (4.8%)	0.49
Reoperation	7 (13.2%)	1 (4.8%)	0.43
Posterior capsular opacity	1 (1.9%)	1 (4.8%)	0.49
Choroidal neovascularization	1 (1.9%)	0	1
Reinjection of gas	2 (3.8%)	0	1

OCT: optical coherence tomography; RPE: retinal pigment epithelium; RNFL: retinal nerve fiber layer.

surgical intervention for macular hole stages 2–4 and also that fewer eyes with macular holes stages 2-3 necessitated repeat surgery if ILM peeling was performed. There was no difference between groups in the rate of intraoperative or postoperative complications. The findings suggest that ILM peeling should be reserved for eyes with prognostic factors for nonclosure. However, the meta-analysis did not specifically compare the outcomes for MBD versus MB.

If ILM peeling is to be performed, the optimal choice of vital dye remains in question. There is no data directly comparing all of the vital dyes commercially available, but many studies have compared some of them to ICG. A meta-analysis assessing the role of ICG in ILM peeling demonstrated that there was no significant difference between groups in anatomical outcomes (rate of primary, secondary, or final closure) whether or not ICG was used to stain the ILM [20]. However, visual acuity results were worse in the first 12 postoperative months in the ICG group. There was no difference in postoperative complications.

Another study comparing the results of MHS with ILM peeling using either BBG or ICG demonstrated that the mean BCVA and central (2°) retinal sensitivity were significantly better in the BBG group at 3 and 6 months postoperatively [21]. In the current study, eyes that had MBD staining had better visual results than eyes with MB staining. MBD contains BBG and TB; therefore the results support the findings of the previous report; however, the present study did not compare MBD to ICG.

A study comparing BBG, trypan blue, and ICG showed that, in eyes with macular holes stages 3-4, there was no statistically significant difference in anatomical closure rates [13]. At 6 months postoperatively, there were significantly more eyes in the combined BBG and TB group that had visual improvement in comparison to the ICG group. Also, visual acuity deterioration was significantly more common in the ICG group. That study reported that the participating surgeons described better ILM staining with BBG compared to TB, as well as easier ILM removal. Those results are also in compliance with the results of the current study, since MBD contains BBG and TB, and MB contains TB.

While the aforementioned studies suggest that ICG may lead to unfavorable surgical results, another study that compared BBG with ICG did not demonstrate a significant difference in postoperative BCVA between the two groups at 3 and 6 months [22]. Those results are contradictory to the current study's findings, where the MBD group had a better visual outcome.

A study comparing two heavy dyes, MBD and ILM-Blue, failed to demonstrate a difference in postoperative BCVA between the two groups at 1 month postoperatively;

however, unlike the current study, macular holes were not the indication for surgery in the majority of the eyes included [16]. The lack of a difference between the two dyes may be the result of the incorporated PEG in both formulations. Our study compared a PEG-containing dye (MBD) to a non-PEG formulation (MB), which is the likely reason for the difference in visual outcome.

Dye toxicity becomes a substantial clinical consideration in ocular surgery, particularly when the toxicity surpasses efficacy. Trypan blue was previously reported to be toxic to the RPE: one case report suggested that reapplication of trypan blue caused progressive atrophy of the RPE in an eye that underwent MHS with ILM peeling [23]. Another case report associated trypan blue, light toxicity, or both with postoperative RPE atrophy [24]. Recent in vitro studies reported that trypan blue is nontoxic to the RPE [25, 26]. The present study demonstrated postoperative foveal RPE abnormalities that were more common (but not statistically significant) in the MB group. Considering the latest literature on trypan blue toxicity, these RPE abnormalities may be the product of increased dye concentration resulting from the air-fluid exchange, or they could even be the product of the air-fluid exchange itself.

This study has some limitations because of its retrospective nature. Additionally, the lack of substantial visual acuity improvement in the MB group and the low macular hole closure rate in both groups were disappointing. A recent study reported anatomical closure rates of approximately 90%; however all persistent macular holes were larger than 400 μm [3]. That study failed to specify just how large the holes were. Another study assessing the risk factors for nonclosure following PPV and ILM peeling reported that the closure rate for Gass stage 4 idiopathic macular holes was 78.7%, and that those with a basal hole diameter of 800 μm or above were 4 times more likely to persist [27]. The macular holes included in the current study had a wide range of basal diameter, as illustrated in Table 1, and some had very large diameters (>1000 μm). Their mean basal diameters were $958.07 \pm 347.1\,\mu$m and $1012.93 \pm 226.4\,\mu$m for the MB and MBD groups, respectively; therefore the relatively low closure rates and lack of improvement in BCVA in the MB group may have been the result of selection bias.

In this retrospective study, eyes that underwent MHS with MBD-assisted ILM peeling had greater improvement in BCVA when compared with eyes that underwent MB-assisted ILM peeling. The difference between the two studied dyes may be attributed to higher contrast staining, which is usually associated with the use of MBD versus MB alone. This higher contrast may have resulted in more efficient ILM peeling, leading to better visual improvement; however there was no difference in hole closure rates between the two groups. The greater improvement in BCVA in the MBD group may also suggest that MB is more toxic to the retina than MBD.

5. Conclusions

In this study, MBD led to better visual results that may be related to better staining characteristics or lesser toxicity compared to MB.

Competing Interests

The authors declare no competing interests or proprietary interests.

References

[1] D. H. W. Steel and A. J. Lotery, "Idiopathic vitreomacular traction and macular hole: a comprehensive review of pathophysiology, diagnosis, and treatment," *Eye*, vol. 27, supplement 1, pp. S1–S21, 2013.

[2] N. E. Kelly and R. T. Wendel, "Vitreous surgery for idiopathic macular holes: results of a pilot study," *Archives of Ophthalmology*, vol. 109, no. 5, pp. 654–659, 1991.

[3] S. P. Shah, V. Manjunath, A. H. Rogers, C. R. Baumal, E. Reichel, and J. S. Duker, "Optical coherence tomography-guided facedown positioning for macular hole surgery," *Retina*, vol. 33, no. 2, pp. 356–362, 2013.

[4] N. Lois, J. Burr, J. Norrie et al., "Internal limiting membrane peeling versus no peeling for idiopathic full-thickness macular hole: a pragmatic randomized controlled trial," *Investigative Ophthalmology and Visual Science*, vol. 52, no. 3, pp. 1586–1592, 2011.

[5] S. E. Burk, A. P. Da Mata, M. E. Snyder, R. H. Rosa Jr., and R. E. Foster, "Indocyanine green-assisted peeling of the retinal internal limiting membrane," *Ophthalmology*, vol. 107, no. 11, pp. 2010–2014, 2000.

[6] F. Aguilera Teba, A. Mohr, C. Eckardt et al., "Trypan blue staining in vitreoretinal surgery," *Ophthalmology*, vol. 110, no. 12, pp. 2409–2412, 2003.

[7] H. Enaida, T. Hisatomi, Y. Hata et al., "Brilliant blue G selectively stains the internal limiting membrane/brilliant blue G-assisted membrane peeling," *Retina*, vol. 26, no. 6, pp. 631–636, 2006.

[8] E. A. Abdelkader, V. A. McBain, M. Anand, N. W. Scott, M. A. R. Siddiqui, and N. Lois, "In vivo safety of trypan blue use in vitreoretinal surgery," *Retina*, vol. 31, no. 6, pp. 1122–1127, 2011.

[9] K. Li, D. Wong, P. Hiscott, P. Stanga, C. Groenewald, and J. McGalliard, "Trypan blue staining of internal limiting membrane and epiretinal membrane during vitrectomy: visual results and histopathological findings," *British Journal of Ophthalmology*, vol. 87, no. 2, pp. 216–219, 2003.

[10] K. E. Schmid-Kubista, P. D. Lamar, A. Schenk, U. Stolba, and S. Binder, "Comparison of macular function and visual fields after membrane blue or infracyanine green staining in vitreoretinal surgery," *Graefe's Archive for Clinical and Experimental Ophthalmology*, vol. 248, no. 3, pp. 381–388, 2010.

[11] U. C. Christensen, K. Krøyer, B. Sander et al., "Value of internal limiting membrane peeling in surgery for idiopathic macular hole stage 2 and 3: a randomised clinical trial," *British Journal of Ophthalmology*, vol. 93, no. 8, pp. 1005–1015, 2009.

[12] J. Beutel, G. Dahmen, A. Ziegler, and H. Hoerauf, "Internal limiting membrane peeling with indocyanine green or trypan blue in macular hole surgery: a randomized trial," *Archives of Ophthalmology*, vol. 125, no. 3, pp. 326–332, 2007.

[13] D. Shukla, J. Kalliath, N. Neelakantan, K. B. Naresh, and K. Ramasamy, "A comparison of brilliant blue g, trypan blue, and indocyanine green dyes to assist internal limiting membrane peeling during macular hole surgery," *Retina*, vol. 31, no. 10, pp. 2021–2025, 2011.

[14] C. Bellerive, B. Cinq-Mars, M. Louis et al., "Retinal function assessment of trypan blue versus indocyanine green assisted

internal limiting membrane peeling during macular hole surgery," *Canadian Journal of Ophthalmology*, vol. 48, no. 2, pp. 104–109, 2013.

[15] K. L. Lee, S. Dean, and S. Guest, "A comparison of outcomes after indocyanine green and trypan blue assisted internal limiting membrane peeling during macular hole surgery," *British Journal of Ophthalmology*, vol. 89, no. 4, pp. 420–424, 2005.

[16] M. Veckeneer, A. Mohr, E. Alharthi et al., "Novel 'heavy' dyes for retinal membrane staining during macular surgery: multicenter clinical assessment," *Acta Ophthalmologica*, vol. 92, no. 4, pp. 339–344, 2014.

[17] J. T. Holladay, "Proper method for calculating average visual acuity," *Journal of Refractive Surgery*, vol. 13, no. 4, pp. 388–391, 1997.

[18] K. Schulze-Bonsel, N. Feltgen, H. Burau, L. Hansen, and M. Bach, "Visual acuities 'hand motion' and 'counting fingers' can be quantified with the Freiburg Visual Acuity Test," *Investigative Ophthalmology and Visual Science*, vol. 47, no. 3, pp. 1236–1240, 2006.

[19] K. Spiteri Cornish, N. Lois, N. W. Scott et al., "Vitrectomy with internal limiting membrane peeling versus No peeling for idiopathic full-thickness macular hole," *Ophthalmology*, vol. 121, no. 3, pp. 649–655, 2014.

[20] Y. Wu, W. Zhu, D. Xu et al., "Indocyanine green-assisted internal limiting membrane peeling in macular hole surgery: a meta-analysis," *PLoS ONE*, vol. 7, no. 11, Article ID e48405, 2012.

[21] T. Baba, A. Hagiwara, E. Sato, M. Arai, T. Oshitari, and S. Yamamoto, "Comparison of vitrectomy with brilliant blue G or indocyanine green on retinal microstructure and function of eyes with macular hole," *Ophthalmology*, vol. 119, no. 12, pp. 2609–2615, 2012.

[22] K. Kadonosono, A. Arakawa, M. Inoue et al., "Internal limiting membrane contrast after staining with indocyanine green and brilliant blue G during macular surgery," *Retina*, vol. 33, no. 4, pp. 812–817, 2013.

[23] S. Jain, K. Kishore, and Y. Sharma, "Progressive atrophy of retinal pigment epithelium after trypan-blue-assisted ILM peeling for macular hole surgery," *Indian Journal of Ophthalmology*, vol. 61, no. 5, pp. 235–237, 2013.

[24] M. U. Saeed and H. Heimann, "Atrophy of the retinal pigment epithelium following vitrectomy with trypan blue," *International Ophthalmology*, vol. 29, no. 4, pp. 239–241, 2009.

[25] C. Arndt, I. Meunier, O. Rebollo, C. Martinenq, C. Hamel, and L.-O. Hattenbach, "Electrophysiological retinal pigment epithelium changes observed with indocyanine green, trypan blue and triamcinolone," *Ophthalmic Research*, vol. 44, no. 1, pp. 17–23, 2010.

[26] E. F. Costa, N. M. T. Barros, L. P. Coppini et al., "Effects of light exposure, pH, osmolarity, and solvent on the retinal pigment epithelial toxicity of vital dyes," *American Journal of Ophthalmology*, vol. 155, no. 4, pp. 705–712, 2013.

[27] T. Brockmann, C. Steger, M. Weger, A. Wedrich, and A. Haas, "Risk assessment of idiopathic macular holes undergoing vitrectomy with dye-assisted internal limiting membrane peeling," *Retina*, vol. 33, no. 6, pp. 1132–1136, 2013.

Hindawi Publishing Corporation
Journal of Ophthalmology
Volume 2016, Article ID 5903452, 6 pages
http://dx.doi.org/10.1155/2016/5903452

Clinical Study

Transient Increase of Retinal Nerve Fiber Layer Thickness after Vitrectomy with ILM Peeling for Idiopathic Macular Hole

Kouichi Ohta, Atsuko Sato, Nami Senda, and Emi Fukui

Department of Ophthalmology, Matsumoto Dental University, Nagano Prefecture, Japan

Correspondence should be addressed to Kouichi Ohta; ohta@po.mdu.ac.jp

Received 9 May 2016; Accepted 19 September 2016

Academic Editor: Irini Chatziralli

Purpose. The purpose of this study was to determine the long-term changes in the circumpapillary retinal nerve fiber layer (RNFL) thickness following macular hole surgery with internal limiting membrane (ILM) peeling combined with phacoemulsification. *Methods*. Thirty-eight eyes of 37 patients who had pars plana vitrectomy ($n = 36$) between 2010 and 2014 were studied. The average thicknesses of the global and the six sectors of the RNFL were determined before and at 1, 3, 6, 12, and 24 ($n = 22$) months (M) after the surgery by spectral-domain optical coherent tomography. The postoperative mean RNFL thickness at each time was compared to that before the surgery by paired t-tests. *Results*. The RNFL of the operated eyes was significantly thicker at 1 month (1 M) and 3 M in all but the inferior-nasal sectors. The significant increase remained until 12 M in the superior-temporal and superior-nasal sectors. In addition, the RNFL was also significantly thicker in the temporal-inferior sector at 12 M based on the findings in 38 eyes. *Conclusions*. The postoperative RNFL was thicker in all but the nasal-inferior sector for at least 12 M after surgery. This prolonged increase of the RNFL thickness may indicate damage and mild edema of the RNFL.

1. Introduction

Kelly and Wendel reported that idiopathic macular holes (MHs) can be closed by pars plana vitrectomy (PPV) with fluid-gas exchange [1, 2]. Thereafter, the surgical techniques for closing a MH have been modified by removing the internal limiting membrane (ILM) which increased the anatomic success rates and improved the functional results [3–5]. Despite the increased success rates with ILM peeling, it is still debated whether ILM peeling is completely safe for the retina. It has been reported that there is an early transient swelling of the arcuate retinal nerve fiber layer (RNFL) and a later development of a dissociated optic nerve fiber layer (DONFL) appearance after ILM peeling [6, 7]. Although the DONFL appearance may not influence visual recovery or decrease the retinal sensitivity [6–9], the indocyanine green G (ICG) dye used to make the ILM more visible may do so [10–12].

The circumpapillary RNFL thickness can be measured by optical coherence tomography (OCT). A thinning of the RNFL and defects of the corresponding visual fields have been reported in MH patients who had undergone ICG-assisted ILM peeling [12]. Time-domain- (TD-) OCT was used to measure the thickness of the RNFL in these earlier studies, but the recently developed spectral-domain- (SD-) OCT processes data 50 times faster, is more sensitive, and can obtain higher resolution images. Quantification of the SD-OCT images showed a transient increase of the RNFL thickness 1 month after the ILM peeling [13–16]. However, the follow-up period was relatively short at 6 to 12 months.

At present, a prospective retinal and optic nerve vitrectomy evaluation (PROVE) study is on-going [17, 18]. However, the subjects being studied are not only those with a MH but also epiretinal membrane (ERM) and other retinal diseases. The published report was the results of only the 12-month findings [18].

The purpose of this study was to determine the long-term changes in the cpRNFL thickness in eyes with a MH that had undergone vitrectomy with ILM peeling. To accomplish this, we used SD-OCT with an eye tracking system to evaluate the changes in the cpRNFL thickness for 24 months in patients who underwent pars plana vitrectomy (PPV) with TA-assisted ILM peeling.

Table 1: Demographics of study population.

Number of eyes	38
Number of patients	37
Age, (yrs)	67.2 ± 6.4 (51–76)
Sex (men/women)	17/20
Axial length, mm	23.78 ± 0.89 (22.64–25.61)
Macular hole stage	Stage 2; 16, stage 3; 16, stage 4; 6
Mean macular hole size, μm	376.3 ± 152.1 (160–674)
Mean visual acuity, log MAR unit	
Preoperative	0.472 ± 0.256
Postoperative	−0.003 ± 0.169
ILM staining	
TA only	29
TA + BBG	9
MIVS	23G; 3, 25G; 35
Combined with PEA/IOL/pseudophakia	36/2

BBG = brilliant blue G; MIVS = microincision vitreous surgery; PEA/IOL = phacoemulsification and intraocular lens implantation; TA = triamcinolone acetonide.
Data are the mean ± standard deviation.

2. Methods

2.1. Patients. The medical charts of 38 eyes of 37 Japanese patients (17 men and 20 women) with a full-thickness MH who had undergone vitrectomy with triamcinolone acetonide- (TA-) assisted ILM peeling at the Matsumoto Dental University Hospital between February 2010 and July 2014 were reviewed (Table 1). Eyes with a MH duration >6 months or with a MH >1,000 μm in diameter were excluded. Patients with other ocular diseases, such as those with an epiretinal membrane (ERM), macular edema, rhegmatogenous retinal detachment, glaucoma, diabetic retinopathy, uveitis, and high pathological myopia were also excluded.

All of the procedures adhered to the tenets of the Declaration of Helsinki. The protocol of this study was approved by the Institutional Review Board and Ethics Committee of Matsumoto Dental University, and a written informed consent for the examination and surgery was obtained from all of the patients.

2.2. Surgical Procedures. The vitreoretinal surgery was performed with standard 23-gauge (23G; $n = 3$) or 25G ($n = 35$) instruments by a single surgeon (KO). After core vitrectomy, a posterior vitreous detachment (PVD) was created by suction with the vitrectomy cutter after TA (Kenakolt-A; Bristol Pharmaceuticals KK, Tokyo, Japan or MaQaid, Wakamoto Pharmaceuticals Co., Ltd., Tokyo, Japan) was injected into the vitreous cavity [19, 20]. A PVD already existed in 6 eyes with stage 4 MH. Because nuclear cataracts can develop after PPV, 36 eyes underwent PPV combined with phacoemulsification and aspiration (PEA) with implantation of an intraocular lens [21]. Two of the 38 eyes were already pseudophakic. In the end, all 38 eyes were pseudophakic after the PPV.

During the MH surgery, the ILM of all eyes was made more visible with TA. The ILM was additionally stained with brilliant blue G (Brilliant Peel®, Geuder, Heidelberg, Germany) in 9 eyes. The ILM was grasped at the temporal raphe to avoid damaging the retinal nerve fiber layer in the thicker nasal, superior, and inferior areas. The size of the peeled area was measured with the ImageJ software in the video images recorded during the surgery. Then fluid-air exchange was performed with the air pressure set at 35 mmHg. At the completion of the surgery, 20% sulfur hexafluoride (SF_6) was injected for a gas tamponade. The patients were instructed to remain in a prone position for at least 7 days.

2.3. Spectral-Domain Optical Coherence Tomography (SD-OCT). SD-OCT examinations were performed with the Spectralis HRA + OCT (Heidelberg Engineering, Heidelberg, Germany) before and at 1, 3, 6, 12, and 24 months after the PPV. The horizontal and vertical images centered on the fovea in the cross-hair mode (30°) were evaluated. Circular scans of 1.8 mm radius centered on the optic disc were recorded to measure the RNFL thickness. Each OCT image was obtained along a 360-degree path around the optic disc. The mean RNFL thickness of the 1,536 measured points was called the mean global thickness. The mean RNFL thickness of the temporal-superior (1° to 45°), temporal (46° to 135°), temporal-inferior (136° to 180°), nasal-inferior (181° to 225°), nasal (226° to 315°), and nasal-superior (316° to 360°) sectors was obtained for the sector analyses. During the follow-up visits, the baseline circumpapillary scan was set as the reference scan, and the same peripapillary region was scanned with the eye tracking system functioning.

2.4. Statistical Analyses. The results are expressed as the means ± standard deviations (SDs). The best-corrected visual acuity (BCVA) was measured with a Landolt C chart, and the decimal values were converted to logarithm of the minimal angle of resolution (log MAR) units. Data were analyzed with the SPSS for Windows software (version 11.0J, SPSS, Chicago, IL). The significance of differences in the pre- and postoperative values was determined by paired t-tests. The significance of differences between the eyes with a closed MH and the fellow eyes in 36 unilateral cases was determined by unpaired t-tests. A difference was considered to be statistically significant when the P was <0.05.

3. Results

3.1. Demographics and Best-Corrected Visual Acuity of All Eyes. The clinical characteristics of all of the eyes are summarized in Table 1. The MH was closed in all of the eyes after the first operation. The postoperative BCVA was −0.003 ± 0.169 log MAR units which was significantly better than the preoperative BCVA at 0.472 ± 0.256 log MAR units ($P < 0.00001$). During the follow-up period, an aftercataract developed in three eyes of 3 patients, and neodymium:yttrium aluminum-garnet (Nd:YAG) laser capsulotomy was performed.

Table 2: Comparison of circumpapillary global and sectoral RNFL thickness (μm) in affected and fellow eyes ($n = 36$).

Sector	Affected eye	Fellow eye	P^*
Global	95.0 ± 10.4	92.6 ± 11.5	0.36
Temporal-superior	127.0 ± 15.3	121.6 ± 22.8	0.24
Temporal	70.5 ± 10.3	69.1 ± 9.4	0.57
Temporal-inferior	137.6 ± 17.4	140.8 ± 13.6	0.39
Nasal-superior	102.1 ± 19.5	103.8 ± 22.4	0.73
Nasal	70.0 ± 17.9	66.3 ± 19.1	0.40
Nasal-inferior	109.6 ± 25.7	103.5 ± 21.7	0.28

Data are the mean ± standard deviation.
*Unpaired t-test.

3.2. Comparisons of Preoperative Global and Sectoral RNFL Thicknesses of Operated and Fellow Eyes. The preoperative peripapillary global and sectoral RNFL thicknesses of the experimental and fellow eyes are shown in Table 2. Two eyes were excluded because a MH was present bilaterally. The mean RNFL thickness in the MH eyes was thicker than that of the fellow eyes in the temporal-superior and nasal-inferior sectors (127.0 ± 15.3 μm versus 121.6 ± 22.8 μm and 109.6 ± 25.7 μm versus 103.5 ± 21.7 μm, resp.). However, the differences were not significant. The preoperative global and sectoral RNFL thicknesses were not significantly different between the operated and fellow eyes.

3.3. Longitudinal Changes in Global and Sectoral RNFL Thicknesses. The global and sectoral RNFL thicknesses of the preoperative and 1, 3, 6, 12, and 24 months after MH surgery are shown in Table 3. Unfortunately, some patients did not visit at all times except at 12 months. Thus, the number of examined eyes was only twenty-two. The mean global RNFL was significantly thicker at 1 month (101.1 ± 11.2 μm, $P < 0.0001$), 3 months (98.4 ± 11.3 μm, $P < 0.01$), and 6 months (97.1 ± 10.4 μm, $P < 0.05$) than the preoperative value (93.9 ± 9.1 μm). At 12 and 24 months, the global RNFL thickness was not significantly different from the preoperative thickness (95.2 ± 10.9 μm and 93.4 ± 11.4 μm, resp.).

The mean RNFL of the temporal-superior and temporal-inferior sectors were significantly thicker at 1 month ($P < 0.0001$, $P < 0.0001$, resp.), 3 months ($P < 0.0001$, $P < 0.001$, resp.), and 6 months ($P < 0.0001$, $P < 0.01$, resp.) than the preoperative thickness. In addition, the mean RNFL thickness of the temporal-superior sector was still significantly thicker at 12 months ($P < 0.05$).

The mean RNFL of the nasal-superior sector was significantly thicker at 1 month ($P < 0.0001$), 3 months ($P < 0.01$), 6 months ($P < 0.05$), and 12 months ($P < 0.05$). These findings were similar to that for the temporal-superior sector.

The mean RNFL of the temporal and nasal sectors was significantly thicker at 1 month ($P < 0.001$) and 3 months ($P < 0.001$, $P < 0.05$, resp.) after the MH surgery. The mean RNFL thickness did not differ significantly at 6, 12, and 24 months from baseline thickness.

In contrast to these findings, the mean RNFL thickness of the nasal-inferior sector did not change significantly at 1, 3, and 6 months from that of the preoperative thickness. On the other hand, the mean RNFL was thinner at 12 and 24 months although the difference was not significant. The thicknesses of the global and all of the sectors were not significantly decreased at 24 months.

The mean intraocular pressure (IOP) at each time point is presented in Table 3. The IOP was significantly lower at 6 and 12 months after the MH surgery. On the other hand, the IOP was not significantly changed at 1 and 3 months when the global and sectoral RNFL were significantly thicker.

3.4. RNFL Thicknesses at 12 Months after MH Surgery. The RNFL thickness of 36 eyes was measured at 12 months after surgery (Table 4). The mean RNFL was significantly thicker at the temporal-superior, temporal-inferior, and nasal-superior sectors than the preoperative thicknesses of the corresponding sectors (130.7 ± 17.2 μm versus 126.9 ± 17.6 μm, $P < 0.01$; 141.1 ± 19.8 μm versus 136.3 ± 18.1 μm, $P < 0.01$; and 104.1 ± 22.3 μm versus 101.1 ± 19.5 μm, $P < 0.05$; paired t-tests). Only the mean RNFL in the nasal-inferior sector was thinner than the preoperative thickness although the difference was not significant.

4. Discussion

Our results showed that the RNFL was significantly thicker in all sectors but the nasal-inferior sector at 1 and 3 months after PPV with TA-assisted ILM peeling. The increase was still present at 6 months postoperatively except in the temporal and nasal sectors. At 12 months, the increase in the thickness in the temporal-superior and nasal-superior or temporal-inferior sectors was still present.

Kurimoto et al. reported that the temporal quadrant was significantly thinner in MH eyes especially in eyes with stage 3 MH [22], but it has been reported that there were no changes in the RNFL thickness in long standing MHs such as those at stage 4 [23]. Our results showed that there were no significant differences in the RNFL thicknesses between the eyes with MH and fellow eyes preoperatively. In the earlier reports, the RNFL thickness was measured by scanning laser polarimeter and not by SD-OCT. The RNFL thickness was measured within a 10-pixel-wide ellipse that was concentric with the optic disc and was 1.5 disc diameter in size [22]. On the other hand, circular scans of 1.8 mm radius were performed by SD-OCT in this study. This difference of scan area may explain the discrepancies between the previous report and our results.

It has been reported that the RNFL was thicker in the temporal sector at the baseline in eyes with an ERM and was thinner after successful surgery [24]. However, the RNFL thickness was evaluated in not only MH eyes but also some eyes with a MH and ERM in some studies [16, 18, 25–27]. We believe it is important to show that there was no significant difference in the preoperative RNFL thickness between the eyes with a MH and the fellow eyes.

A transient increase of the RNFL thickness after MH surgery was recently reported [14–16]. The global or mean overall thickness was increased at 1 month, and it returned to preoperative values at 3 or 6 months [14–16]. An increase at 1 month is in agreement with our results. However, a residual increase at not only 3 months but also 6 and 12 months in

Table 3: Comparison of circumpapillary global and sectoral RNFL thickness (μm) and intraocular pressure (mmHg) during 24-month follow-up period ($n = 22$).

Sector	Preoperative	Postoperative				
		1 month	3 months	6 months	12 months	24 months
Global	93.9 ± 9.1	101.1 ± 11.2§	98.4 ± 11.3†	97.1 ± 10.4*	95.2 ± 10.9	93.4 ± 11.4
TS	125.1 ± 17.1	135.2 ± 17.5§	132.1 ± 16.9§	131.2 ± 15.1§	129.7 ± 17.5*	126.7 ± 17.5
T	70.7 ± 11.3	78.3 ± 10.5‡	76.2 ± 9.0‡	73.6 ± 10.6	71.3 ± 18.6	72.1 ± 11.0
TI	137.7 ± 16.0	148.6 ± 19.1§	144.0 ± 17.0‡	143.1 ± 16.3†	141.1 ± 18.3	136.6 ± 18.7
NS	99.1 ± 20.7	107.1 ± 23.8§	105.0 ± 24.1†	104.3 ± 24.4*	103.3 ± 24.8*	99.8 ± 25.8
N	68.5 ± 14.6	74.1 ± 18.9‡	72.2 ± 17.6*	71.1 ± 16.8	69.4 ± 17.1	67.4 ± 17.6
NI	107.4 ± 20.7	112.0 ± 19.9	107.7 ± 20.0	107.2 ± 18.6	105.0 ± 18.5	103.5 ± 19.9
Mean IOP	14.7 ± 2.4	14.0 ± 2.9	13.6 ± 2.4	13.7 ± 2.3*	13.6 ± 1.8†	14.7 ± 2.5

TS = temporal-superior; T = temporal; TI = temporal-inferior; NI = nasal-inferior; N = nasal; NS = nasal-superior.
IOP = intraocular pressure.
Data are the mean ± standard deviation.
$^{*}P < 0.05$.
$^{\dagger}P < 0.01$.
$^{\ddagger}P < 0.001$.
$^{\S}P < 0.0001$.
Paired t-test compared with preoperative value.

Table 4: Comparison of circumpapillary global and sectoral RNFL thickness (μm) at 12 months after surgery ($n = 38$).

Sector	Before operation	12 months postoperatively	P^{*}
Global	96.4 ± 13.3	96.3 ± 11.3	0.97
Temporal/superior	126.9 ± 17.6	130.7 ± 17.2	0.0049
Temporal	70.7 ± 12.2	72.6 ± 12.2	0.12
Temporal/inferior	136.3 ± 18.1	141.1 ± 19.8	0.0035
Nasal/superior	101.1 ± 19.5	104.1 ± 22.3	0.044
Nasal	68.6 ± 17.8	69.6 ± 17.9	0.41
Nasal/inferior	107.6 ± 25.4	105.1 ± 21.5	0.36

Data are the mean ± standard deviation.
*Paired t-test.

some sectors was the only change in our study. In contrast, it has been reported that the global RNFL thickness was significantly decreased at 6 months [16] which is contrary to the findings in our patients. There are several possible reasons for this discrepancy. First, 23 of the 30 patients in the earlier study had an ERM and 6 had a MH [16]. In eyes with an ERM, the RNFL in the temporal quadrant was significantly thicker at the baseline although the global thickness was not significantly thicker than that of the fellow eyes [24]. The RNFL in the temporal pathological area of eyes with an ERM was significantly thinner at 3, 6, and 12 months postoperatively. The longitudinal changes in the RNFL thickness compared to the preoperative values after ERM surgery must differ from that in eyes with a MH. In contrast, the RNFL thickness of only MH cases was measured by Toba and Hibi. They found no significant decrease in temporal sector after MH surgery. Instead, an increase in the RNFL thickness in the nasal quadrant or a decrease in the nasal-inferior sector was observed [14, 15].

The second possible reason for the discrepancy is the differences in the SD-OCT instruments used. In recent studies, the SD-OCT instruments used for RNFL thickness measurements were the Cirrus OCT (Carl Zeiss Medlitec, Dublin, CA) [14, 17, 18] or Spectralis HRA + OCT [15, 16]. The reproducibility of the RNFL thickness measurements with the Spectralis SD-OCT with the eye tracking system is excellent for the follow-up measurements [28, 29]. Thus, smaller changes in the RNFL thickness can be detected by Spectralis SD-OCT compared to the Cirrus OCT. We believe that the eye tracking system was not present in the Cirrus OCT at that time [14, 17, 18]. This may account for the discrepancies.

Third, phacovitrectomy may contribute to the significant increases in the RNFL thicknesses at 6 and 12 months. When cataract surgery is not performed during the PPV, cataract surgery was needed in 6 of 13 MH eyes within a year [18] or all 8 eyes by 2 years [27]. The development of cataract may have some influence on the measurements of RNFL thickness. In contrast, all 38 eyes were pseudophakic during follow-up period in our study. Thus, our measurements of the RNFL thickness were probably more reliable.

Toba et al. measured the RNFL thickness by the same type of SD-OCT instrument, the Spectralis HRA + OCT, as we did [15]. The surgical procedures were also similar to our procedures. They compared the effects of ICG-, BBG-, and TA-assisted ILM peeling on the RNFL thickness. In spite of the use of these agents, the changes in the RNFL thickness did not differ from what we found for up to 12 months, for example, the postoperative increase of the global and sectorial thicknesses except the nasal-inferior thickness at only 1 month after surgery. Because the mean RNFL thicknesses were not given in their text, it was difficult to compare the absolute values to ours. However, the pattern of longitudinal changes was similar to our results. There were no significant differences at 3, 6, and 12 months after surgery in our study, and the changes in their RNFL thicknesses appeared similar to ours.

The RNFL sectors that increased or decreased postoperatively differed in the different studies. At 6 months, the nasal RNFL was significantly thicker in only the study by Hibi et al. [14]. On the other hand, the inferior RNFL was reduced at 12 months as reported by Lalezary et al. [18] or at 24 months by Thinda et al. [27]. The inferior sector is the 226–315° quadrant with the Cirrus OCT. When Spectralis OCT was used, this sector can be divided into the nasal-inferior and temporal sectors. A significant decrease at 6 and 12 months after surgery in the temporal-inferior sector was reported by Toba et al. [15]. We similarly found that the RNFL thickness in only the temporal-inferior sector did not increase even at 1 and 3 months. In addition, it decreased at 12 and 24 months but the decrease was not significant.

The exact mechanism causing the transient increase in the RNFL thickness after MH surgery has been investigated. There are many studies that suggest that indocyanine green (ICG), which was used to make the ILM more visible, has a toxic effect on the inner retina [10, 30, 31]. However, there was no significant decrease of the RNFL thickness in the ICG group when the ICG concentration was low and was washed out quickly [15]. In our cases, we can exclude the toxic effect of ICG because we did not use it.

Another possible mechanism for the transient increase in the RNFL thickness was the retinal damage induced during the infusion of saline and/or the air that were directed against the retinal surface from the cannula during vitrectomy [14]. They used 20G instruments in 17 of 20 eyes while we used only 23G or 25G instruments. In the 20G system, the infusion cannula is usually placed at the temporal-inferior region and is aimed toward the optic disc or nasal side of the retina. With the 23G or 25G instruments, the infusion cannula is generally placed obliquely, and the area of the retina where the saline or air is directed must be different. This difference may be associated with the sector that is increased or decreased.

We cannot explain why the RNFL thickness in only the nasal-inferior sector decreased [15] or did not increase in our patients. More recently, a thinning of the inferior RNFL was observed at 12 months, and they suggested that this was due to early glaucomatous damage [18]. However, we did not find such a decrease or elevation of the IOP in this study. Instead, we believe that the surgical procedures, such as creating the posterior vitreous detachment, grasping the ILM with forceps, or making an incision by microknife, and attachment to the retina during ILM peeling must differ. So these surgical factors may be related to the changes of the RNFL thickness by the loss of retinal ganglion cell.

There are several limitations to this study. First, this was a retrospective study and the number of patients studied was small which may have affected the reliability of the statistical analyses. Second, a single surgeon performed all of the surgeries which may limit any broad conclusions. Third, functional analysis such as visual field analysis, microperimetry, and electroretinography were not performed. Further prospective studies will be necessary to confirm our results.

In conclusion, the RNFL thickness in all but the nasal-inferior sector increased significantly at 1, 3, 6, and 12 months after MH surgery combined with cataract surgery. The transient increase in the RNFL thickness may be due to a mild edema of the inner retinal layer cause by the procedures used in the MH surgery. However, the exact mechanism was not definitively determined. Further studies including a functional analysis are needed.

Ethical Approval

Ethical approval was provided by the Institutional Review Board of the Matsumoto Dental University, Shiojiri, Japan.

Competing Interests

The authors declare no conflict of interests.

Acknowledgments

The authors thank Professor Duco Hamasaki of the Bascom Palmer Eye Institute for editing the manuscript.

References

[1] N. E. Kelly and R. T. Wendel, "Vitreous surgery for idiopathic macular holes: results of a pilot study," *Archives of Ophthalmology*, vol. 109, no. 5, pp. 654–659, 1991.

[2] R. T. Wendel, A. C. Patel, N. E. Kelly, T. C. Salzano, J. W. Wells, and G. D. Novack, "Vitreous surgery for macular holes," *Ophthalmology*, vol. 100, no. 11, pp. 1671–1676, 1993.

[3] H. L. Brooks Jr., "Macular hole surgery with and without internal limiting membrane peeling," *Ophthalmology*, vol. 107, no. 10, pp. 1939–1949, 2000.

[4] U. C. Christensen, K. Krøyer, B. Sander et al., "Value of internal limiting membrane peeling in surgery for idiopathic macular hole stage 2 and 3: a randomised clinical trial," *British Journal of Ophthalmology*, vol. 93, no. 8, pp. 1005–1015, 2009.

[5] N. Lois, J. Burr, J. Norrie et al., "Internal limiting membrane peeling versus no peeling for idiopathic full-thickness macular hole: a pragmatic randomized controlled trial," *Investigative Ophthalmology & Visual Science*, vol. 52, no. 3, pp. 1586–1592, 2011.

[6] R. Tadayoni, M. Paques, P. Massin, S. Mouki-Benani, J. Mikol, and A. Gaudric, "Dissociated optic nerve fiber layer appearance of the fundus after idiopathic epiretinal membrane removal," *Ophthalmology*, vol. 108, no. 12, pp. 2279–2283, 2001.

[7] Y. Mitamura and K. Ohtsuka, "Relationship of dissociated optic nerve fiber layer appearance to internal limiting membrane peeling," *Ophthalmology*, vol. 112, no. 10, pp. 1766–1770, 2005.

[8] Y. Ito, H. Terasaki, A. Takahashi, T. Yamakoshi, M. Kondo, and M. Nakamura, "Dissociated optic nerve fiber layer appearance

after internal limiting membrane peeling for idiopathic macular holes," *Ophthalmology*, vol. 112, no. 8, pp. 1415–1420, 2005.

[9] H. Imai and K. Ohta, "Microperimetric determination of retinal sensitivity in areas of dissociated optic nerve fiber layer following internal limiting membrane peeling," *Japanese Journal of Ophthalmology*, vol. 54, no. 5, pp. 435–440, 2010.

[10] C. Haritoglou, A. Gandorfer, C. A. Gass, M. Schaumberger, M. W. Ulbig, and A. Kampik, "Indocyanine green-assisted peeling of the internal limiting membrane in macular hole surgery affects visual outcome: a clinicopathologic correlation," *American Journal of Ophthalmology*, vol. 134, no. 6, pp. 836–841, 2002.

[11] S. Kanda, A. Uemura, T. Yamashita, H. Kita, K. Yamakiri, and T. Sakamoto, "Visual field defects after intravitreous administration of indocyanine green in macular hole surgery," *Archives of Ophthalmology*, vol. 122, no. 10, pp. 1447–1451, 2004.

[12] T. Yamashita, A. Uemura, H. Kita, and T. Sakamoto, "Analysis of the retinal nerve fiber layer after indocyanine green-assisted vitrectomy for idiopathic macular holes," *Ophthalmology*, vol. 113, no. 2, pp. 280–284, 2006.

[13] A. Clark, N. Balducci, F. Pichi et al., "Swelling of the arcuate nerve fiber layer after internal limiting membrane peeling," *Retina*, vol. 32, no. 8, pp. 1608–1613, 2012.

[14] N. Hibi, M. Kondo, K. Ishikawa, S. Ueno, K. Komeima, and H. Terasaki, "Transient increase of retinal nerve fiber layer thickness after macular hole surgery," *International Ophthalmology*, vol. 34, no. 3, pp. 575–581, 2014.

[15] Y. Toba, S. Machida, and D. Kurosaka, "Comparisons of retinal nerve fiber layer thickness after indocyanine green, brilliant blue g, or triamcinolone acetonide-assisted macular hole surgery," *Journal of Ophthalmology*, vol. 2014, Article ID 187308, 8 pages, 2014.

[16] N. Balducci, M. Morara, C. Veronese, C. Torrazza, F. Pichi, and A. P. Ciardella, "Retinal nerve fiber layer thickness modification after internal limiting membrane peeling," *Retina*, vol. 34, no. 4, pp. 655–663, 2014.

[17] R. K. Reddy, M. Lalezary, S. J. Kim et al., "Prospective retinal and optic nerve vitrectomy evaluation (PROVE) study: findings at 3 months," *Clinical Ophthalmology*, vol. 7, pp. 1761–1769, 2013.

[18] M. Lalezary, R. J. Shah, R. K. Reddy et al., "Prospective Retinal and Optic Nerve Vitrectomy Evaluation (PROVE) study: twelve-month findings," *Ophthalmology*, vol. 121, no. 10, pp. 1983–1989, 2014.

[19] K. Ohta, A. Sato, and E. Fukui, "Asymmetrical thickness of parafoveal retina around surgically closed macular hole," *British Journal of Ophthalmology*, vol. 94, no. 11, pp. 1545–1546, 2010.

[20] K. Ohta, A. Sato, and E. Fukui, "Retinal thickness in eyes with idiopathic macular hole after vitrectomy with internal limiting membrane peeling," *Graefe's Archive for Clinical and Experimental Ophthalmology*, vol. 251, no. 5, pp. 1273–1279, 2013.

[21] Y. Ogura, T. Takanashi, H. Ishigooka, and N. Ogino, "Quantitative analysis of lens changes after vitrectomy by fluorophotometry," *American Journal of Ophthalmology*, vol. 111, no. 2, pp. 179–183, 1991.

[22] Y. Kurimoto, Y. Kaneko, K. Matsuno, M. Akimoto, and N. Yoshimura, "Evaluation of the retinal nerve fiber layer thickness in eyes with idiopathic macular holes," *American Journal of Ophthalmology*, vol. 131, no. 6, pp. 756–760, 2001.

[23] A. Assi, P. Watts, and J. McAllister, "Estimation of the retinal nerve fibre layer thickness in the papillomacular area of long standing stage IV macular holes," *British Journal of Ophthalmology*, vol. 83, no. 5, pp. 573–576, 1999.

[24] S.-B. Lee, Y.-I. Shin, Y.-J. Jo, and J.-Y. Kim, "Longitudinal changes in retinal nerve fiber layer thickness after vitrectomy for epiretinal membrane," *Investigative Ophthalmology & Visual Science*, vol. 55, no. 10, pp. 6607–6611, 2014.

[25] P. D. Brazitikos, J. M. Katsimpris, E. Tsironi, and S. Androudi, "Retinal nerve fiber layer thickness evaluation after trypan blue-assisted macular surgery," *Retina*, vol. 30, no. 4, pp. 640–647, 2010.

[26] K. Y. Kim, S.-Y. Yu, M. S. Kim, E. S. Kim, and H. W. Kwak, "Changes of parafoveal retinal nerve fiber layer thickness analyzed by spectral-domain optical coherence tomography after pars plana vitrectomy," *Retina*, vol. 33, no. 4, pp. 776–784, 2013.

[27] S. Thinda, R. J. Shah, and S. J. Kim, "Two-year anatomical and functional outcomes after macular hole surgery: A Prospective, Controlled Study," *Ophthalmic Surgery Lasers and Imaging Retina*, vol. 46, no. 9, pp. 926–934, 2015.

[28] S. J. Langenegger, J. Funk, and M. Töteberg-Harms, "Reproducibility of retinal nerve fiber layer thickness measurements using the eye tracker and the retest function of spectralis SD-OCT in glaucomatous and healthy control eyes," *Investigative Ophthalmology and Visual Science*, vol. 52, no. 6, pp. 3338–3344, 2011.

[29] A. M. C. Costa, R. A. Costa, L. A. S. Melo Jr., D. Calucci, J. L. Orefice, and S. Cronemberger, "Influence of the eye-tracking-based follow-up function in retinal nerve fiber layer thickness using fourier- domain optical coherence tomography," *Investigative Ophthalmology and Visual Science*, vol. 54, no. 3, pp. 1958–1963, 2013.

[30] A. Gandorfer, C. Haritoglou, C. A. Gass, M. W. Ulbig, and A. Kampik, "Indocyanine green-assisted peeling of the internal limiting membrane may cause retinal damage," *American Journal of Ophthalmology*, vol. 132, no. 3, pp. 431–433, 2001.

[31] N. Horio and M. Horiguchi, "Effect on visual outcome after macular hole surgery when staining the internal limiting membrane with indocyanine green dye," *Archives of Ophthalmology*, vol. 122, no. 7, pp. 992–996, 2004.

Hindawi Publishing Corporation
Journal of Ophthalmology
Volume 2016, Article ID 8561379, 4 pages
http://dx.doi.org/10.1155/2016/8561379

Research Article

Possible Relation between Lack of Posterior Vitreous Detachment and Severe Endogenous Endophthalmitis

Kazuhiko Umazume, Jun Suzuki, Yoshihiko Usui, Yoshihiro Wakabayashi, and Hiroshi Goto

Department of Ophthalmology and Visual Sciences, Tokyo Medical University, Tokyo, Japan

Correspondence should be addressed to Kazuhiko Umazume; kazuhikouma@me.com

Received 29 July 2016; Accepted 7 September 2016

Academic Editor: Irini Chatziralli

Purpose. Endogenous endophthalmitis (EE) is a rare ocular disease caused by bacterial or fungal infection of intraocular spaces by hematogenous spread of pathogens from distant infectious loci in the body. We investigated the clinical characteristics and management of eyes with EE in ten consecutive patients. *Methods*. Ten patients (10 eyes) with EE treated at Tokyo Medical University Hospital in 2014 were reviewed. We retrospectively studied the causative organisms, systemic complications, pre/postoperative mean best-corrected visual acuity (BCVA), and status of posterior vitreous detachment (PVD). *Results*. The 10 patients comprised 8 males and 2 females, with mean age of 71.2 years. The causative organisms were bacteria in 6 eyes and fungi in 4 eyes. Systemic complications included septicemia or disseminated intravascular coagulation in 5 patients and diabetes mellitus in 4 patients. Postoperative BCVA was improved by 0.2 log MAR or greater in 4 eyes and decreased in 4 eyes. Vitrectomy was performed in all eyes, and 4 required multiple surgeries. During vitrectomy, PVD was absent in 8 eyes, 4 of which showed retinal necrosis. The mean age of patients with no PVD was 71.2 years. *Conclusion*. Despite an advanced age, PVD was absent in the majority of patients with EE. PVD may be related to the pathogenesis and aggravation of EE.

1. Introduction

Metastatic endogenous endophthalmitis is a potentially sight-threatening intraocular infection resulting from hematogenous spread of microorganisms from a distant infective source within the body. The incidence of endogenous endophthalmitis is far lower than that of exogenous endophthalmitis including postoperative endophthalmitis, accounting for only 2 to 8% of all endophthalmitis cases [1, 2]. The causative microorganisms are divided into bacteria and fungi, most commonly *Candida* species. Among bacteria, Gram-positive bacteria are common in developing countries, while Gram-negative bacteria have been reported in East Asia region [3–5]. Compared to fungal infections, bacterial infections spread rapidly to intraocular tissues and require urgent management.

Basic local treatments for endogenous endophthalmitis include intravitreal injection of antibacterial or antifungal agents against the causative microorganisms as well as vitrectomy. In the case of phakic eyes, lens extraction is conducted simultaneously, and in the case of eyes with implanted intraocular lens, extraction of the intraocular lens should be considered as the situation demands. In addition, frequent instillation of ceftazidime and vancomycin eye drops after surgery is an accepted treatment for bacterial endophthalmitis [6, 7] and should be started as soon as possible after operation.

The predisposing risk factors for metastatic endogenous endophthalmitis include urinary tract infection, diabetes, HIV infection, intravenous hyperalimentation, liver abscess, and infectious endocarditis, while long-term hospitalization that has increased with the progression of population aging is also an important risk factor [5, 6, 8, 9]. Furthermore, the association of posterior vitreous detachment (PVD) with retinal disease has attracted attention, accompanying the advent of optical coherence tomography [10, 11]. The relationship between PVD and the pathogenesis or severity of endogenous endophthalmitis has not been reported. In the present study, we examined PVD pre- and intraoperatively in patients with endogenous endophthalmitis and correlated the presence of absence of PVD with clinical features.

Recently, the aging society has become an issue mainly in industrial countries, and the increase of endogenous endophthalmitis accompanying aging has been a concern. In this report, we describe the clinical characteristics, surgical methods, and outcomes of 10 cases of endogenous endophthalmitis treated in our department during the previous one year.

2. Methods

Ten consecutive patients (10 eyes; 4 left eyes and 6 right eyes) diagnosed with metastatic endogenous endophthalmitis at the Tokyo Medical University Hospital between April 2014 and March 2015 were studied. The patients comprised 8 males and 2 females, with mean age of 71.2 ± 10.5 years. All patients underwent 25-gauge vitrectomy using the Constellation Vision System (Alcon Laboratories Inc., Fort Worth). Ceftazidime and vancomycin were added to Balanced Salt Solution (BSS) to obtain final concentrations of 20 mg/mL and 1 mg/mL, respectively, and used as intraocular irrigation solution. During surgery, vitreous fluid sample was collected for culture, smear, and microscopic examination to identify the causative microorganism. Blood culture was also performed before surgery.

The parameters analyzed were causative microorganism, clinical findings, pre- and postoperative visual acuity, surgical method, systemic disease, and PVD. Clinical findings focused on chemosis, keratic precipitates, fibrin deposition in anterior chamber, hypopyon, and fundus visibility. Posterior vitreous detachment was assessed by B mode ultrasonography before surgery and by microscopic observation during surgery.

Preoperative and postoperative visual acuity were compared by Student's t-test. Statistical analyses were performed using MedCalc version 12.1.1 (Mariakerke, Belgium). P values less than 0.05 were considered significantly different.

3. Results

The causative microorganisms isolated from vitreous fluid samples collected during surgery and from blood cultures were bacteria in 6 eyes and fungi in 4 eyes. The bacterial species isolated were *Klebsiella* species in 2 eyes, *Escherichia coli* in 1 eye, *Nocardia* species in 1 eye, and unidentified Gram-negative bacteria in 2 eyes. The fungal species isolated were *Candida* species in 3 eyes and *Cryptococcus* in 1 eye (Table 1).

Preoperative clinical findings in all 10 eyes (Table 2) included chemosis in 7 eyes, keratic precipitates in 9 eyes, fibrin deposition in 8 eyes, hypopyon in 6 eyes, and invisible fundus in 5 eyes. Among the 4 eyes with fungal endophthalmitis, the fundus was visible in 3 eyes and difficult to observe in only 1 eye. Hence, fungal endophthalmitis appears to show slower progression of inflammation clinically compared to bacterial endophthalmitis.

Table 1: Cultures results.

Species	Number of eyes
Bacteria	
Klebsiella pneumonia	2
Escherichia coli	1
Nocardia	1
Gram-negative bacteria (detail unknown)	2
Fungus	
Candia albicans	3
Cryptococcus	1

Table 2: Clinical features.

Symptoms	Number of eyes	Number of eyes (fungal)
Chemosis	7	2
Keratic precipitates	9	4
Fibrin	8	3
Hypopyon	6	3
Indistinct of fundus	5	1

When improvement in visual acuity was defined as gain of more than 0.2 log MAR, postoperative visual acuity was improved in 4 eyes, unchanged in 2 eyes, and deteriorated in 4 eyes (Figure 1). In this analysis, the logMAR equivalent for counting fingers was 1.85, hand motion was 2.3, light perception was 2.8, and no light perception was 2.9 [12]. Four eyes (40%) were able to avoid becoming socially blind (>0.7 log MAR). Comparison of final visual acuity between bacterial endophthalmitis and fungal endophthalmitis showed that visual acuity tended to be slightly better in fungal endophthalmitis (1.03 ± 1.24) compared to bacterial endophthalmitis (2.24 ± 1.18), although there was no significant difference between two groups. Three eyes lost light perception after surgery. All three had bacterial endophthalmitis, caused by *Klebsiella* species, *Escherichia coli*, and *Nocardia* species in 1 eye each.

The risk factors in the 10 patients in the present study were diabetes in 4 patients, anastomotic leakage after colon cancer surgery in 2 patients, ruptured liver abscess in 1 patient, aspiration pneumonia in 1 patient, and long-term oral steroid therapy in 1 patient. Serious systemic complications consisted of septicemia in 1 patient and disseminated intravascular coagulation in 4 patients.

Regarding treatment method, all 10 eyes underwent vitrectomy, and 4 (40%) required multiple surgeries before inflammation was resolved. In only one eye with severe pain and loss of light perception, eyeball enucleation was eventually conducted. In 2 eyes that had been implanted with intraocular lens before surgery, the intraocular lenses were extracted in both eyes.

Posterior vitreous detachment was absent in 8 eyes (80%) before surgery. In these eyes, PVD was induced intentionally during surgery. In this series, a high frequency of the absence of PVD was observed (Figure 2).

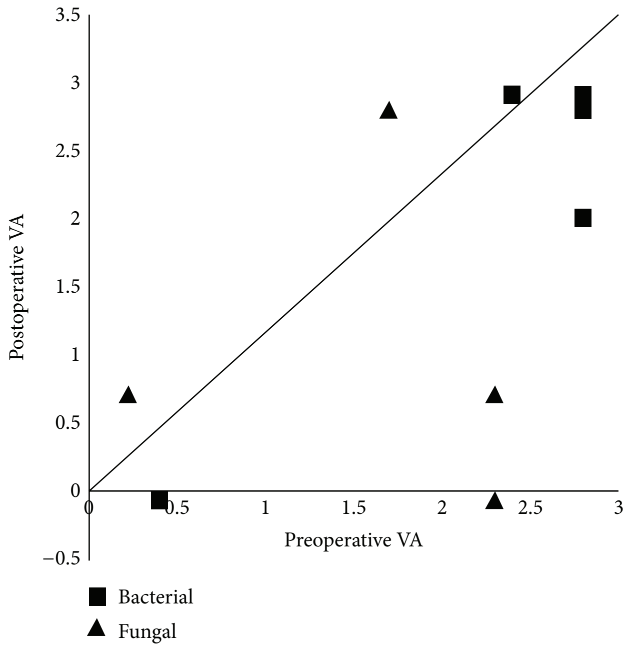


FIGURE 1: Comparison of pre- and postoperative visual acuity in 10 eyes treated for endogenous endophthalmitis. VA: visual acuity.

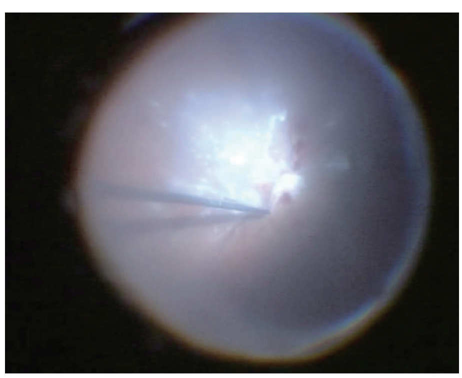


FIGURE 2: Fundus image shows induction of posterior vitreous detachment.

4. Discussion

According to an epidemiological survey of intraocular inflammations in Japan conducted in 2007, endogenous endophthalmitis accounted for 1 to 2% of intraocular inflammations [13]. Despite being a relatively rare intraocular disease, we observe a trend of increase at the Tokyo Medical University Hospital. While we treated a total of 13 cases between 2006 and 2013, we encountered 10 cases during one year in 2014. Regarding the age of disease onset, the patients with acute anterior uveitis (m = 147), which is differential diagnosis of endogenous endophthalmitis, were 43.2 ± 14.8 years old. On the other hands, the patient with endogenous endophthalmitis in this series was 71.2 ± 10.5 years old. With the progression of population aging, the increase in endogenous endophthalmitis in the future is a concern.

The clinical picture of endogenous endophthalmitis is diverse. The misdiagnosis rates at presentation ranged from 16 to 63% [3, 14]. The early clinical symptoms include pain, hyperemia, floaters, and decreased vision. However, since some patients are not capable of complaining about the symptoms due to poor general condition, many patients are diagnosed in a serious state. In the present series, high rates of severe inflammatory findings were observed: fibrin deposition in 8 patients (80%) and hypopyon in 6 patients (60%). Furthermore, many patients with bacterial endophthalmitis had invisible fundus, probably as a result of rapid exacerbation of inflammation.

In the present study, all 10 eyes underwent vitrectomy. When inflammation spreads to the vitreous, prompt dissection of the vitreous is necessary. Although whether the causative organisms are bacteria or fungi can only be identified after performing culture of vitreous samples, we conducted surgery using an intraocular irrigation solution containing a mixture of vancomycin (1 mg/mL) and ceftazidime (20 mg/mL), as reported previously [15]. Although the vitreous body has to be dissected as much as possible, induction of an iatrogenic retinal break should be avoided, because this may affect retinal reattachment. In principle, we replaced the vitreous cavity with the intraocular irrigation solution containing antibiotics, but we used silicon oil when retinal tear was observed during surgery. In 4 patients (40%), the first vitrectomy failed to resolve inflammation and multiple surgeries were required. In one patient with bacterial endophthalmitis, loss of light perception and uncontrolled pain eventually led to enucleation. Patients with endogenous endophthalmitis usually present with pain, and due to the high risk of expulsive hemorrhage during surgery, conducting surgery under general anesthesia is recommended if the general condition of the patient can tolerate anesthesia [16, 17].

The present study also examined the relation between PVD and endogenous endophthalmitis. Posterior vitreous detachment was not found before surgery in 8 eyes (80%), and PVD was induced during surgery in these eyes. The patients with no PVD had a mean age of 73.4 ± 8.4 years, which was older than the mean age of 54 to 57 years reported for the occurrence of PVD [18]. Furthermore, retinal necrosis is known to occur secondary to severe inflammation in endogenous endophthalmitis. In the present study, retinal necrosis was observed in 4 eyes (40%), all of which had no PVD before surgery. These findings suggest that contact between the retina and the vitreous body may be associated with severe disease. A possible reason is that the gel-like vitreous body plays the role as a growth medium for the causative microorganisms. *In vitro* study has shown that the vitreous is associated with cell proliferation [19]; the same phenomenon may occur also *in vivo*. Currently, the use of ocriplasmin for vitreolysis has attracted interest [20, 21], and use of this agent may also prevent aggravation of endogenous endophthalmitis.

Although the causative microorganisms have not changed compared to past reports, endogenous endophthalmitis remains a disease with poor visual outcome despite the advances in vitreous surgery. With the continuous progression of population aging, the number of cases is expected to increase in the future, and appropriate management including early diagnosis is required.

Competing Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

References

[1] S.-P. Chee and A. Jap, "Endogenous endophthalmitis," *Current Opinion in Ophthalmology*, vol. 12, no. 6, pp. 464–470, 2001.

[2] A. V. Rachitskaya, H. W. Flynn Jr., and J. L. Davis, "Endogenous endophthalmitis caused by *Salmonella* serotype B in an immunocompetent 12-year-old child," *Archives of Ophthalmology*, vol. 130, no. 6, pp. 802–804, 2012.

[3] T. L. Jackson, S. J. Eykyn, E. M. Graham, and M. R. Stanford, "Endogenous bacterial endophthalmitis: a 17-year prospective series and review of 267 reported cases," *Survey of Ophthalmology*, vol. 48, no. 4, pp. 403–423, 2003.

[4] V. Schiedler, I. U. Scott, H. W. Flynn Jr., J. L. Davis, M. S. Benz, and D. Miller, "Culture-proven endogenous endophthalmitis: clinical features and visual acuity outcomes," *American Journal of Ophthalmology*, vol. 137, no. 4, pp. 725–731, 2004.

[5] A. Lingappan, C. C. Wykoff, T. A. Albini et al., "Endogenous fungal endophthalmitis: causative organisms, management strategies, and visual acuity outcomes," *American Journal of Ophthalmology*, vol. 153, no. 1, pp. 162–e1, 2012.

[6] A. S. H. Tsai, S. Y. Lee, and A. H. E. Jap, "An unusual case of recurrent endogenous *Klebsiella* endophthalmitis," *Eye*, vol. 24, no. 10, pp. 1630–1631, 2010.

[7] M. Ang, A. Jap, and S.-P. Chee, "Prognostic factors and outcomes in endogenous *Klebsiella pneumoniae* endophthalmitis," *American Journal of Ophthalmology*, vol. 151, no. 2, pp. 338–344.e2, 2011.

[8] V. Ho, L. Y. Ho, T. M. Ranchod, K. A. Drenser, G. A. Williams, and B. R. Garretson, "Endogenous methicillin-resistant *Staphylococcus aureus* endophthalmitis," *Retina*, vol. 31, no. 3, pp. 596–601, 2011.

[9] J. Sridhar, H. W. Flynn Jr., A. E. Kuriyan, D. Miller, and T. Albini, "Endogenous fungal endophthalmitis: risk factors, clinical features, and treatment outcomes in mold and yeast infections," *Journal of Ophthalmic Inflammation and Infection*, vol. 3, no. 1, article 60, 2013.

[10] D. Gaucher, R. Tadayoni, A. Erginay, B. Haouchine, A. Gaudric, and P. Massin, "Optical coherence tomography assessment of the vitreoretinal relationship in diabetic macular edema," *American Journal of Ophthalmology*, vol. 139, no. 5, pp. 807–813, 2005.

[11] P. Carpineto and L. Mastropasqua, "Incomplete posterior vitreoschisis and vitreomacular traction," *American Journal of Ophthalmology*, vol. 140, no. 4, pp. 765–766, 2005.

[12] K. Schulze-Bonsel, N. Feltgen, H. Burau, L. Hansen, and M. Bach, "Visual acuities 'hand motion' and 'counting fingers' can be quantified with the freiburg visual acuity test," *Investigative Ophthalmology & Visual Science*, vol. 47, no. 3, pp. 1236–1240, 2006.

[13] H. Goto, M. Mochizuki, K. Yamaki, S. Kotake, M. Usui, and S. Ohno, "Epidemiological survey of intraocular inflammation in Japan," *Japanese Journal of Ophthalmology*, vol. 51, no. 1, pp. 41–44, 2007.

[14] M. I. Binder, J. Chua, P. K. Kaiser, G. W. Procop, and C. M. Isada, "Endogenous endophthalmitis an 18-year review of culture-positive cases at a tertiary care center," *Medicine*, vol. 82, no. 2, pp. 97–105, 2003.

[15] Y. Yonekawa, R. V. Paul Chan, A. K. Reddy, C. G. Pieroni, T. C. Lee, and S. Lee, "Early intravitreal treatment of endogenous bacterial endophthalmitis," *Clinical and Experimental Ophthalmology*, vol. 39, no. 8, pp. 771–778, 2011.

[16] Y.-Q. Zhang and W.-J. Wang, "Treatment outcomes after pars plana vitrectomy for endogenous endophthalmitis," *Retina*, vol. 25, no. 6, pp. 746–750, 2005.

[17] S. Jalali, N. Pehere, P. K. Rani et al., "Treatment outcomes and clinicomicrobiological characteristics of a protocol-based approach for neonatal endogenous endophthalmitis," *European Journal of Ophthalmology*, vol. 24, no. 3, pp. 424–436, 2014.

[18] J. Yonemoto, H. Ideta, K. Sasaki, S. Tanaka, A. Hirose, and C. Oka, "The age of oneset of posterior vitreous detachment," *Graefe's Archive for Clinical and Experimental Ophthalmology*, vol. 232, no. 2, pp. 67–70, 1994.

[19] D. Meitinger, D. M. Hunt, D.-T. Shih, J. C. Fox, and R. C. Hunt, "Vitreous-induced modulation of integrins in retinal pigment epithelial cells: effects of fibroblast growth factor-2," *Experimental Eye Research*, vol. 73, no. 5, pp. 681–692, 2001.

[20] J. A. Haller, P. Stalmans, M. S. Benz et al., "Efficacy of intravitreal ocriplasmin for treatment of vitreomacular adhesion: subgroup analyses from two randomized trials," *Ophthalmology*, vol. 122, no. 1, pp. 117–122, 2015.

[21] P. Stalmans and A. Girach, "Vitreous levels of active ocriplasmin following intravitreal injection: results of an ascending exposure trial," *Investigative Ophthalmology and Visual Science*, vol. 54, no. 10, pp. 6620–6627, 2013.