EJO
ISSN 1120-6721

Eur J Ophthalmol 2017; 00 (00): 000-000
DOI: 10.5301/ejo.5001040

ORIGINAL RESEARCH ARTICLE

Comparison of inverted flap and subretinal aspiration technique in full-thickness macular hole surgery: a randomized controlled study

Claudio Iovino[1], Giulia Caminiti[1], Mario Miccoli[2], Francesco Nasini[3], Giamberto Casini[3], Enrico Peiretti[1]

[1] Eye Clinic, Department of Surgical Science, University of Cagliari, Cagliari - Italy
[2] Department of Clinical and Experimental Medicine, University of Pisa, Pisa - Italy
[3] Department of Surgical, Medical, Molecular and Critical Area Pathology, University of Pisa, Pisa - Italy

ABSTRACT

Purpose: To compare the inverted flap and the subretinal aspiration technique for full-thickness macular hole (FTMH) surgery.

Methods: Forty consecutive eyes with a stage IV FTMH were randomly assigned into 2 treatment groups. After core vitrectomy and perimacular internal limiting membrane (ILM) peeling, in group A, the subretinal remnant macular fluid was aspirated with a 41-G cannula after the air-fluid exchange procedure, while in group B, the technique of an inverted ILM flap was completed. Differences in postoperative best-corrected visual acuity (BCVA) and occurrence of intraoperative or postoperative complications between the 2 groups were evaluated.

Results: All FTMHs were closed after the first surgery with no intraoperative or postoperative complications. In group A, 16 patients (80%) showed improvement of BCVA and 4 (20%) showed stabilization. In group B, 12 patients (60%) had improved BCVA, while 6 (30%) remained stable and 2 (10%) worsened. Postoperative BCVA for group A was significantly better than for group B (p = 0.022).

Conclusions: The surgical techniques had similar rates of closure of FTMH, although BCVA outcomes were significantly better in the subretinal aspiration group.

Keywords: Inverted internal limiting membrane flap, Macular hole surgery, Pars plana vitrectomy, Subretinal aspiration

Introduction

Macular hole (MH) is a common, often unilateral, retinal disease more frequently affecting elderly women (1-4). The majority of these gaps that open up at the center of the retina are idiopathic, but they can also follow an ocular trauma or could be a complication in highly myopic eyes (5). Full-thickness MHs (FTMHs) progress in a condition where there is a failure of normal age-related separation of the vitreous cortex from the posterior pole and can result in an anomalous and persistent adhesion to the fovea. Full-thickness MHs represent an important cause of blurred and distorted central vision and the treatment is vitreous surgery, first described by Kelly and Wendel (6) in 1991. In the most recent International Vitreomacular Traction Study Group Classification (7), large FTMH with no vitreomacular traction corresponds to stage IV MH with a diameter of 400 µm or more and posterior vitreous detachment, as described in the Gass MH classification (8, 9). Several optical coherence tomography (OCT) parameters have been used to predict functional and anatomic results in MH repair (10-13) including MH index, hole form factor, diameter hole index, tractional hole index, and recently MH angle (14). Advances in diagnostic tools and surgical techniques have enabled an improvement in MH surgery outcomes; nevertheless, complete surgical closure is still an important challenge in longstanding large MHs (15). The standard approach to FTMHs is a surgical procedure by pars plana vitrectomy (PPV) and peeling, infusion of long- or short-acting gas, and positioning after surgery. During recent years, various surgical techniques have been introduced to improve postoperative outcomes (16, 17), including the inverted internal limiting membrane (ILM) flap technique described by Michalewska et al (18), with encouraging results. In this method, a part of the ILM is not completely removed, then is inverted on the margin of the FTMH and gently laid over it until complete coverage is achieved. Although many authors reported good anatomic results with the different surgical

Accepted: September 3, 2017
Published online: September 18, 2017

Corresponding author:
Enrico Peiretti, MD
Eye Clinic
University of Cagliari
Via Ospedale 48
09124 Cagliari, Italy
enripei@hotmail.com

techniques, flat borders with bare retinal pigment epithelium associated with worse functional results were observed in 19% to 39% of large MHs postoperatively (19-21), but this percentage was significantly decreased after the introduction of the inverted flap technique. As described by Michalewska et al (18), conventional vitrectomy with ILM peeling has a closure rate of 88%, compared with 98% if the inverted ILM flap technique is performed. The current study reports a comparison between the inverted flap maneuver and a different surgical technique, which consists of subretinal active aspiration of the fluid in the hole after the air-fluid exchange procedure.

Methods

This was a randomized controlled interventional study following the guidelines of the Declaration of Helsinki and it was approved by the 2 local institutional review boards. Forty patients (40 eyes) underwent surgery for FTMHs at the Retina Center of the Eye Clinic University of Cagliari and at the Department of Surgical, Medical, Molecular, and Critical Area Pathology, University of Pisa, between January 2015 and June 2016. Only pseudophakic patients with stage IV FTMHs defined on the basis of OCT scan with macular hole diameter exceeding 400 µm were enrolled. Exclusion criteria included severe myopia (>6 D), proliferative diabetic retinopathy, retinal detachment, exudative age-related maculopathy, and ocular trauma history. Written consent was obtained and patients were randomly assigned into group A (subretinal aspiration technique) or group B (inverted flap technique) of 20 patients each, using a computer-generation randomization list. They were operated on by 2 retinal surgery specialists (E.P. and G.C.) under local anesthesia with retrobulbar lidocaine injection. All patients underwent a standard sutureless 25-G PPV using the Constellation machine (Alcon Laboratories) and an intraoperative posterior capsulotomy with vitrectomy cutter in order to avoid any posterior visualization disturbance during the surgery. After core vitrectomy and a posterior vitreous detachment induction if needed using the vitrectomy cutter in the suction mode, a meticulous peripheral vitrectomy with indentation was performed, and ILM until the vascular arcades and any epiretinal membrane were peeled after Blue Dual (Dorc) coloration. In group A, the subretinal remnant macular fluid was delicately aspirated with a 41-G de Juan cannula after the air-fluid exchange procedure and in group B the classical inverted ILM technique was performed according to the report by Michalewska et al (18). In this technique, during a perimacular peeling, a fragment of the peeled-off ILM anchored on the hole edges was left and inverted/inserted into the hole using an ILM microforceps. In both groups, a meticulous examination of the periphery was performed during surgery and any retinal defect (holes or peripheral retinal degenerations) was treated by cryotherapy or endolaser therapy. At the end of the surgery, a mix of air and 20% SF_6 long-acting gas was injected into the eye and the patients were instructed to keep a face-down position for 5 days after the operation. Before and after surgery (1 day, 1 month, 3 and 6 months), all patients underwent a complete ocular evaluation including best-corrected visual acuity (BCVA), dilated fundus examination, color fundus photography, infrared reflectance, and spectral-domain OCT. The day after the operation, general ophthalmic examination, intraocular pressure measurement, and fundus examination without dilation were performed.

TABLE I - Baseline characteristics

	Group A (20 eyes)	Group B (20 eyes)	p value
Age, y, mean ± SD (range)	69 ± 10.4 (49-88)	71 ± 8.77 (54-83)	0.526
Sex, n (%)			
Male	7 (35)	9 (45)	0.747
Female	13 (65)	11 (55)	0.747
Initial BCVA, logMAR, mean ± SD	1.3 ± 1.7	1.2 ± 1.4	0.848
Minimum FTMH diameter, µm, mean ± SD	664.6 ± 71.1	666.95 ± 63.7	0.753
Epiretinal membrane, n (%)	3 (15%)	2 (10%)	0.990

BCVA = best-corrected visual acuity; FTMH = full-thickness macular hole.

Spectral-domain OCT

The SD-OCT scans were obtained with HRA (Heidelberg Engineering) with radial scan protocol after pupil dilation with 1% tropicamide. The scan with the minimum MH diameter was considered for the hole staging.

Statistical analysis

The Shapiro-Wilk test was performed to verify the normality of distributions of the study variables. Best-corrected visual acuity and minimum MH diameter were not normally distributed, thus nonparametric Mann-Whitney U test was used to compare the groups. t Test was carried out to compare the age of the groups. Categorical variables were studied using the Fisher exact test or chi-square test with Yates correction (depending on the frequencies). The correlation between postoperative BCVA and the other variables was estimated with the Pearson coefficient or Mann-Whitney test. Multivariate regression was not performed because only the surgical technique turned out to be statistically significant. The analysis was undertaken using SPSS version 17.0.1.

Results

The study included 40 patients (40 eyes) and baseline characteristics are summarized in Table I. All patients were examined at baseline and at 1, 3, and 6 months after surgery. The preoperative characteristics of the MHs and their dimensions were evaluated but no statistical difference was noted (p = 0.75) (Tab. I). Before the surgical procedure ,the average BCVA (±SD) was similar in the 2 groups of patients (p = 0.85). No intraoperative or postoperative complications were reported; only mild hyperemia and some swelling of the conjunctiva was observed in the first week after surgery. In all patients of group A (100%), FTMHs closed after the first surgery, of which 16 patients (80%) showed improvement of

TABLE II - Defects of retinal layers during consecutive follow-up visits

	1 Month, %		3 Months, %		6 Months, %	
	Group A	**Group B**	**Group A**	**Group B**	**Group A**	**Group B**
Ellipsoid zone defects	100	100	50	75	35	65
External limiting membrane defects	95	100	35	50	15	45

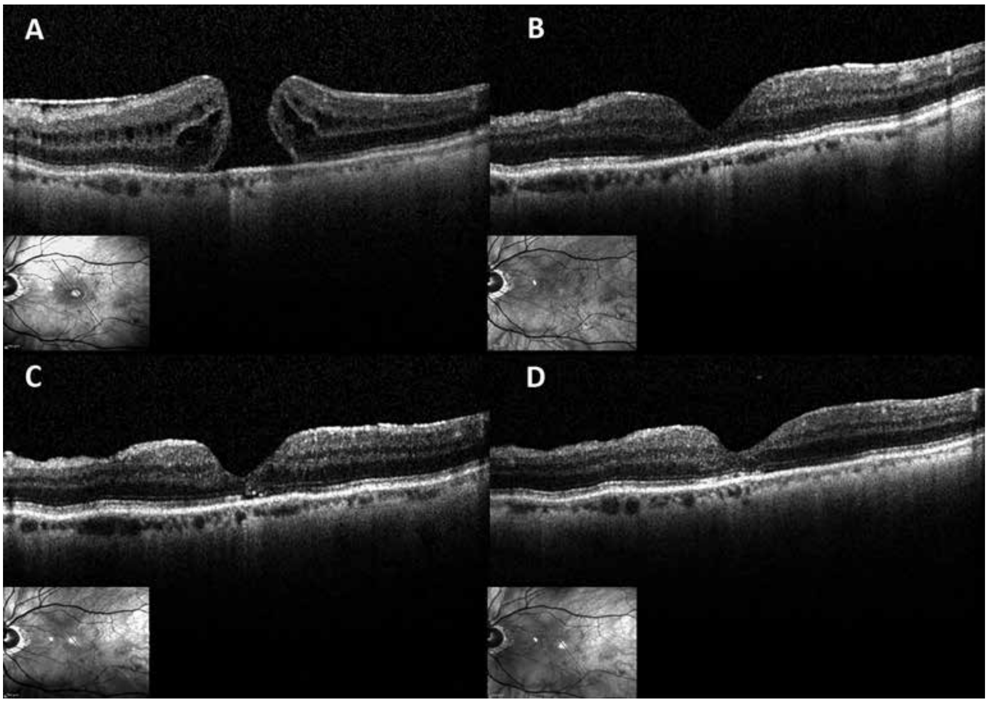

Fig. 1 - Serial optical coherence tomography (OCT) images of an eye with full-thickness macular hole (group A). (**A**) Preoperative scan demonstrating a stage 4 full-thickness macular hole. (**B**) One month after surgery, complete macular hole closure is achieved and an ellipsoid zone and external limiting membrane alteration is present in the foveal region. (**C**) Three months after surgery, the outer retinal layers restoration process is taking place. (**D**) Six months after surgery, the ellipsoid zone repopulation is completed and external limiting membrane is restored, resulting in improved best-corrected visual acuity.

BCVA and the other 4 (20%) showed stabilization. The mean BCVA at baseline was 1.3 ± 1.7 logMAR and at 6 months follow-up was 0.2 ± 0.6 logMAR. In group B (100%), FTMHs closed after the first surgery and 12 patients (60%) improved their BCVA, while 6 (30%) remained stable and 2 (10%) worsened. In this group, the mean BCVA at baseline was 1.2 ± 1.4 logMAR and at the end of the follow-up was 0.4 ± 0.6 logMAR. Postoperative BCVA for group A was significantly better than in group B (p = 0.022). Ellipsoid zone (EZ) and external limiting membrane (ELM) integrity was evaluated by 2 retina specialists masked to surgical technique at each follow-up visit by SD-OCT scans and defects such as interruptions or disruptions were noted in nearly 100% of cases at the 1-month postoperative visit (Tab. II). By 6 months after surgery, EZ defects decreased to 35% in group A and 65% in group B (p = 0.01), whereas ELM defects decreased to 15% and 45%, respectively, in groups A and B (p = 0.01), as documented by SD-OCT (Figs. 1 and 2).

Discussion

Macular hole surgery represents an important challenge for vitreoretinal surgeons and vitrectomy is still the gold standard since its first description by Kelly and Wendel (6) in 1991. In recent years, new surgical approaches have been described and most authors nowadays achieve a closure success rate >90% (22-24). The postoperative closure of idiopathic MHs is related to MH diameter measured preoperatively by OCT (25) and in MHs exceeding 500 µm reoperations are needed in some cases (26).

Despite surgical success, patients can have limited visual acuity due to incomplete restoration of retinal anatomy. After the introduction of the inverted flap technique for MH closure, the number of cases with flat MH margins with bare retinal pigment epithelium (RPE) seems to be drastically reduced (18). In group A, after core and peripheral vitrectomy and perimacular ILM peeling, the subretinal remnant macular fluid was delicately aspirated with a 41-G de Juan cannula, a very thin needle, to obtain a vacuum shrinking of the MH center and to minimally reduce the iatrogenic damage at the RPE layer. Although MH endodrainage has been used by several authors (27-31), it is not universally practiced because anatomic and functional outcomes are uncertain. The subretinal fluid contains cellular elements including cell bodies of photoreceptor elements, RPE cells, lymphocytes, and macrophages (31); Shimada et al (30) defined the fluid inside the MH as a sticky liquid with high viscosity. In group B, the part of ILM initially adherent to the retina was, after being inverted, oriented to the vitreous cavity, whereas the other part, primarily faced toward vitreous cavity, is made touching

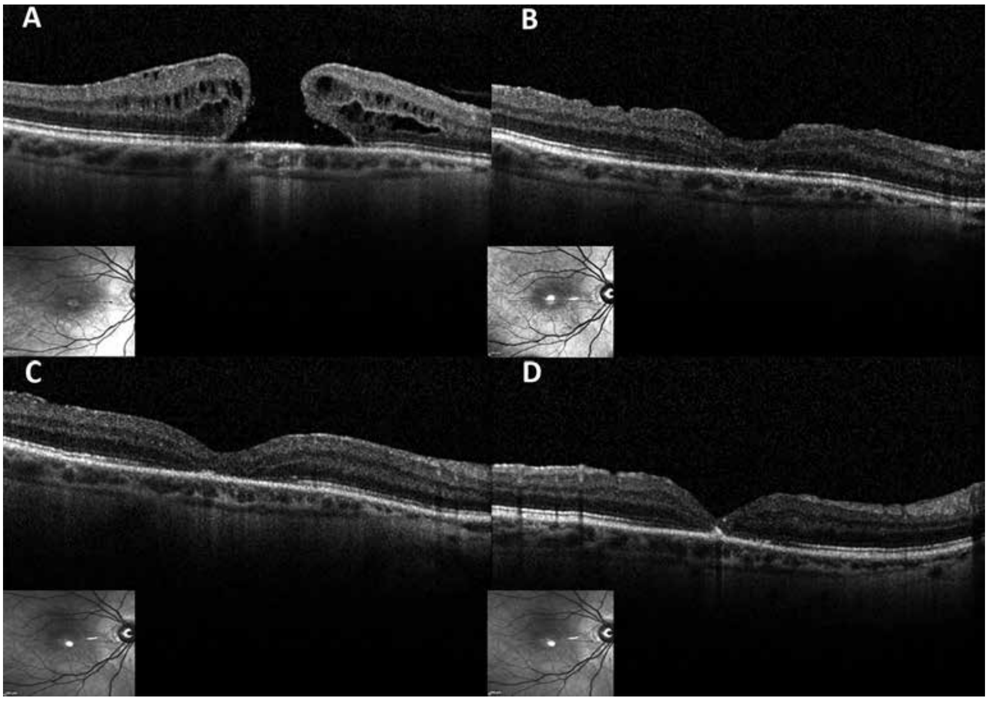

Fig. 2 - Serial optical coherence tomography (OCT) images of an eye with full-thickness macular hole (group B). (**A**) Preoperative scan demonstrating a stage 4 full-thickness macular hole. (**B**) One month after surgery, macular hole is closed and a disruption of external retinal layers is visible. (**C**) Three months after surgery, macular retinal profile is more regular, but the ellipsoid zone and external limiting membrane are interrupted in the foveal area. (**D**) Six months after surgery, a subfoveal epithelium pigment accumulation and some hyperreflective intraretinal points are present, with no signs of ellipsoid zone restoration process, matching with poor visual acuity recovery.

the RPE. The ILM can act as a scaffold for glial cells proliferation promoting hole closure, although sometimes fibrosis can occur, disrupting this process. In our study, the closure rate was 100% in both groups and no reoperation was necessary, although BCVA outcomes seemed to be better in the subretinal aspiration group. Functional outcomes may depend on the restoration of outer retinal layers after the operation, which generally increase over time. Analyzing OCT images, group A showed a better repopulation of the EZ and of the ELM, which seems to be correlated with better visual acuity outcomes (Fig. 1). It can be speculated that the presence of the sticky subretinal fluid inside the hole could play a role in the delay of the outer retina layers restoring process. Indeed, even if with the standard vitrectomy with ILM peeling and gas tamponade the subretinal fluid is usually reabsorbed by itself within a few days after surgery owing to the RPE pump activity (32), the active aspiration with a de Juan cannula at the end of surgery causes a vacuum shrinking of the MH margins, helping the fovea regain normal contour earlier. The role of MH surgery is to remove the causes that led to the gap formation and vitrectomy with ILM peeling seems to be able to remove the tangential forces in order to improve the closure rate success. In this study, the vitrectomy technique with fluid aspiration with a thin cannula from the bottom of the hole induced an intraoperative flattening of the MH edges. This procedure seems to cause less fibrotic changes in the healing process of the hole based on OCT scan, while the inverted flap technique group showed more hyperreflective material at the level of EZ (Fig. 2), and these results matched BCVA outcomes. Furthermore, some authors have also reported an extension of the RPE atrophy when the inverted flap technique is performed, possibly secondary to fibrogenic stimulation of glial cells (33). One limitation of this study is the small number of patients, although our data show significant differences between the 2 groups, which can be further explored in larger studies; moreover, the 2 techniques could also be combined in the treatment of larger MHs.

Disclosures

Financial support: No financial support was received for this submission.
Conflict of interest: None of the authors has conflict of interest with this submission.

References

1. Aaberg TM, Blair CJ, Gass JD. Macular holes. Am J Ophthalmol. 1970;69(4):555-562.
2. Morgan CM, Schatz H. Idiopathic macular holes. Am J Ophthalmol. 1985;99(4):437-444.
3. Lewis ML, Cohen SM, Smiddy WE, Gass JD. Bilaterality of idiopathic macular holes. Graefes Arch Clin Exp Ophthalmol. 1996;234(4):241-245.
4. Kang HK, Chang AA, Beaumont PE. The macular hole: report of an Australian surgical series and meta-analysis of the literature. Clin Exp Ophthalmol. 2000;28(4):298-308.
5. la Cour M, Friis J. Macular holes: classification, epidemiology, natural history and treatment. Acta Ophthalmol Scand. 2002;80(6):579-587.
6. Kelly NE, Wendel RT. Vitreous surgery for idiopathic macular holes. Results of a pilot study. Arch Ophthalmol. 1991;109(5):654-659.
7. Duker JS, Kaiser PK, Binder S, et al. The International Vitreomacular Traction Study Group classification of vitreomacular adhesion, traction, and macular hole. Ophthalmology. 2013;120(12):2611-2619. Published online September 17, 2013.
8. Gass JD. Idiopathic senile macular hole. Its early stages and pathogenesis. Arch Ophthalmol. 1988;106(5):629-639.

9. Gass JD. Reappraisal of biomicroscopic classification of stages of development of a macular hole. Am J Ophthalmol. 1995; 119(6):752-759.
10. Wakely L, Rahman R, Stephenson J. A comparison of several methods of macular hole measurement using optical coherence tomography, and their value in predicting anatomical and visual outcomes. Br J Ophthalmol. 2012;96(7):1003-1007.
11. Kusuhara S, Teraoka Escaño MF, Fujii S, et al. Prediction of postoperative visual outcome based on hole configuration by optical coherence tomography in eyes with idiopathic macular holes. Am J Ophthalmol. 2004;138(5):709-716.
12. Ullrich S, Haritoglou C, Gass C, Schaumberger M, Ulbig MW, Kampik A. Macular hole size as a prognostic factor in macular hole surgery. Br J Ophthalmol. 2002;86(4):390-393.
13. Ruiz-Moreno JM, Staicu C, Piñero DP, Montero J, Lugo F, Amat P. Optical coherence tomography predictive factors for macular hole surgery outcome. Br J Ophthalmol. 2008;92(5):640-644.
14. Chhablani J, Khodani M, Hussein A, et al. Role of macular hole angle in macular hole closure. Br J Ophthalmol. 2015;99(12):1634-1638.
15. Salter AB, Folgar FA, Weissbrot J, Wald KJ. Macular hole surgery prognostic success rates based on macular hole size. Ophthalmic Surg Lasers Imaging. 2012;43(3):184-189.
16. Alpatov S, Shchuko A, Malyshev V. A new method of treating macular holes. Eur J Ophthalmol. 2007;17(2):246-252.
17. Couvillion SS, Smiddy WE, Flynn HW Jr, Eifrig CW, Gregori G. Outcomes of surgery for idiopathic macular hole: a case-control study comparing silicone oil with gas tamponade. Ophthalmic Surg Lasers Imaging. 2005;36(5):365-371.
18. Michalewska Z, Michalewski J, Adelman RA, Nawrocki J. Inverted internal limiting membrane flap technique for large macular holes. Ophthalmology. 2010;117(10):2018-2025.
19. Imai M, Iijima H, Gotoh T, Tsukahara S. Optical coherence tomography of successfully repaired idiopathic macular holes. Am J Ophthalmol. 1999;128(5):621-627.
20. Kang SW, Ahn K, Ham DI. Types of macular hole closure and their clinical implications. Br J Ophthalmol. 2003;87(8):1015-1019.
21. Michalewska Z, Michalewski J, Cisiecki S, Adelman R, Nawrocki J. Correlation between foveal structure and visual outcome following macular hole surgery: a spectral optical coherence tomography study. Graefes Arch Clin Exp Ophthalmol. 2008;246(6): 823-830.
22. Ando F, Sasano K, Ohba N, Hirose H, Yasui O. Anatomic and visual outcomes after indocyanine green-assisted peeling of the retinal internal limiting membrane in idiopathic macular hole surgery. Am J Ophthalmol. 2004;137(4):609-614.
23. Beutel J, Dahmen G, Ziegler A, Hoerauf H. Internal limiting membrane peeling with indocyanine green or trypan blue in macular hole surgery: a randomized trial. Arch Ophthalmol. 2007;125(3):326-332.
24. Krishnan R, Tossounis C, Fung Yang Y. 20-gauge and 23-gauge phacovitrectomy for idiopathic macular holes: comparison of complications and long-term outcomes. Eye (Lond). 2013;27(1):72-77.
25. Ip MS, Baker BJ, Duker JS, et al. Anatomical outcomes of surgery for idiopathic macular hole as determined by optical coherence tomography. Arch Ophthalmol. 2002;120(1): 29-35.
26. Michalewska Z, Michalewski J, Nawrocki J. [Diagnosis and evaluation of macular hole with the HRT 2 retina module]. Ophthalmologe. 2007;104(10):881-888.
27. Wells JA, Gregor ZJ. Surgical treatment of full-thickness macular holes using autologous serum. Eye (Lond). 1996;10 (Pt 5):593-599.
28. Van De Moere A, Stalmans P. Anatomical and visual outcome of macular hole surgery with infracyanine green-assisted peeling of the internal limiting membrane, endodrainage, and silicone oil tamponade. Am J Ophthalmol. 2003; 136(5):879-887.
29. Schurmans A, Van Calster J, Stalmans P. Macular hole surgery with inner limiting membrane peeling, endodrainage, and heavy silicone oil tamponade. Am J Ophthalmol. 2009; 147(3):495-500.
30. Shimada H, Hattori T, Nakashizuka H, Mori R, Mizutani Y, Yuzawa M. Highly viscous fluid in macular holes. Int Ophthalmol. 2010;30(3):319-321.
31. Herbert EN, Sheth HG, Wickremasinghe S, Luthert PJ, Bainbridge J, Gregor ZJ. Nature of subretinal fluid in patients undergoing vitrectomy for macular hole: a cytopathological and optical coherence tomography study. Clin Exp Ophthalmol. 2008;36(9):812-816.
32. Gentile RC, Landa G, Pons ME, Eliott D, Rosen RB. Macular hole formation, progression, and surgical repair: case series of serial optical coherence tomography and time lapse morphing video study. BMC Ophthalmol. 2010;10:24.
33. Imai H, Azumi A. The Expansion of RPE Atrophy after the Inverted ILM Flap Technique for a Chronic Large Macular Hole. Case Rep Ophthalmol. 2014;5(1):83-86.