Prognostic Factors of Fluid-gas Exchange Outcomes in Patients with Failed Primary Surgery for Idiopathic Macular Hole

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Abstract

This retrospective study aimed to evaluate prognostic factors associated with the success of fluid-gas exchange in patients with failed primary idiopathic macular hole (IMH) surgery. Outcomes of the fluid-gas exchange were categorised as unclosed, or U-type, V-type, or W-type closure. Patients were divided into the successful and unsuccessful groups according to the absence or presence of bare retinal pigment epithelium, respectively, following fluid-gas exchange. Demographics, baseline characteristics, and pre-procedure characteristics were assessed. A total of 19 eyes in 19 patients that had failed IMH surgery and then underwent fluid-gas exchange were included. Of those, 18 eyes had MH closure (successful, 15 eyes; unsuccessful, three eyes). One eye was unclosed after fluid-gas exchange; therefore, the patient underwent additional vitrectomy for MH closure (unsuccessful). The successful group showed significantly lower pre-procedure base diameters; higher baseline and pre-procedure macular hole index, hole form factor, and tractional hole index values; and lower baseline and pre-procedure minimum diameter and diameter hole index values. Moreover, a better visual prognosis was observed in the successful group. These results suggest that indices predicting favourable results of primary surgery for IMH are useful to predict the success of fluid-gas exchange in patients with failed primary MH surgery.

Introduction

A macular hole (MH) is a full-thickness defect in the fovea. Since Kelly and Wendel[1] reported the successful closure of an MH using pars plana vitrectomy with fluid-gas exchange, this surgical method combined with internal limiting membrane peeling has become the standard treatment for MH, showing an anatomical closure rate of more than 90%[2,3]. Various optical coherence tomography (OCT) parameters, such as the hole form factor (HFF), base diameter (BD), and macular hole volume (MHV), are prognostic factors that determine functional and anatomical success in primary MH surgery[4,5].

Unfortunately, about 10% of all MH surgeries fail and, therefore, may require additional procedures. Intravitreal gas injection or fluid-gas exchange using octafluoropropane (C_3F_8) or sulfur hexafluoride (SF_6) for MH closure has shown favourable results in such cases[6,7]. However, some of them with a failed primary MH surgery patients treated with additional procedure of injection or fluid-gas exchange have needed additional surgery to close the MH[8]. To the best of our knowledge, there have been no studies regarding the effectiveness of indices in predicting the outcomes of a fluid-gas exchange procedure following a failed primary MH surgery. Therefore, we aimed to evaluate the prognostic factors associated with the success of fluid-gas exchange after a failed primary idiopathic macular hole (IMH) surgery.

Results

Demographic characteristics

A total of 19 eyes in 19 patients were included in this study. The fluid-gas exchange procedure following the failed primary IMH surgery resulted in MH closure in 18 eyes (successful in 15 eyes and unsuccessful in three eyes, Fig. 1). The MH was unclosed in one eye after the fluid-gas exchange, and the patient underwent additional vitrectomy to close the MH (unsuccessful). All patients in the successful group showed a U-type closure, whereas all in the unsuccessful group presented a W-type closure[9]. The demographic data of all patients are shown in Table 1. The mean age was 67 ± 6 years in the successful group and 73 ± 7 years in the unsuccessful group; the difference was not statistically significant. Similarly, the affected eye and sex did not differ significantly between the two groups.

Table 1
Demographic and baseline clinical characteristics of the successful and unsuccessful groups of patients with unclosed macular hole treated with fluid-gas exchange.

Parameters	**Successful group** (n = 15)	**Unsuccessful group** (n = 4)	***p* value**
Age in years, mean (SD)	67 (6)	73 (7)	0.152
Sex, n (%) male	6 (40.0%)	1 (25.0%)	1.000
Laterality, n (%) right eye	10 (66.7%)	2 (50.0%)	0.603
Symptom duration, days, mean (SD)	57 (59)	87 (56)	0.262
Total follow-up period, months, mean (SD)	22 (6)	29 (6)	0.100
Baseline BCVA, logMAR, mean (SD)	0.85 (0.22)	0.70 (0.14)	0.185
Baseline IOP, mmHg, mean (SD)	14.5 (3.8)	14.0 (2.2)	1.000
Baseline spherical equivalent, mean (SD)	1.34 (1.59)	2.22 (1.42)	0.469
Baseline lens status, phakic, n (%)	10 (66.7%)	3 (75.0%)	1.000
Baseline central subfield retinal thickness, µm, mean (SD)	346.40 (48.62)	320.25 (132.51)	0.596
Baseline minimum diameter, µm, mean (SD)	450.20 (68.80)	825.25 (140.19)	0.001*
Baseline base diameter, µm, mean (SD)	1095.87 (475.92)	1248.50 (280.03)	0.357
Baseline height, µm, mean (SD)	562.53 (175.18)	489.50 (157.47)	0.469
Baseline axial length, mm, mean (SD)	22.76 (0.37)	22.73 (0.32)	0.736
Baseline macular hole index, mean (SD)	0.550 (0.153)	0.386 (0.040)	0.009*
Baseline hole form factor, mean (SD)	0.868 (0.146)	0.463 (0.204)	0.009*
Baseline diameter hole index, mean (SD)	0.476 (0.171)	0.669 (0.067)	0.014*
Baseline tractional hole index, mean (SD)	1.272 (0.437)	0.587 (0.128)	0.001*
Baseline macular hole volume, mm^3, mean (SD)	0.181 (0.016)	0.231 (0.013)	0.262
Type of primary surgery, vitrectomy alone, n (%)	12 (80.0%)	2 (50.0%)	0.272

*Statistically significant as calculated using the Mann-Whitney U test.

BCVA, best-corrected visual acuity, *IOP*, intraocular pressure, *SD*, standard deviation.

Parameters	Successful group (n = 15)	Unsuccessful group (n = 4)	*p* value
Type of primary gas tamponade, SF_6, n (%)	6 (40.0%)	3 (75.0%)	0.303
Percentage of primary gas tamponade, mean (SD)	18 (4)	19 (2)	0.411
*Statistically significant as calculated using the Mann-Whitney U test.			
BCVA, best-corrected visual acuity, *IOP*, intraocular pressure, *SD*, standard deviation.			

Baseline clinical characteristics of the successful and unsuccessful groups

A comparison of the baseline clinical characteristics between the two groups is shown in Table 1. A longer duration of decreased visual acuity was observed in the unsuccessful group (87 ± 56 days); however, this difference was not statistically significant, compared with that in the successful group (57 ± 59 days). The total follow-up period, baseline best-corrected visual acuity (BCVA), mean intraocular pressure (IOP), mean spherical equivalent, number of phakic patients at baseline, gas type of primary tamponade, percentage of primary gas tamponade, and mean central subfield retinal thickness (CSRT) at baseline were not significantly different between the two groups. The mean baseline minimum diameter (MD) was significantly lower in the successful group (363.87 ± 124.95 μm) than in the unsuccessful group (612.00 ± 11.43 μm); however, no difference was observed in the mean baseline BD between the two groups. The mean MH height also showed nonsignificant differences between the two groups. A significantly higher mean baseline macular hole index (MHI) was observed in the successful group (0.558 ± 0.159) than in the unsuccessful group (0.386 ± 0.041). The mean baseline HFF was significantly higher in the successful group than in the unsuccessful group (0.876 ± 0.154 versus 0.463 ± 0.204). The mean baseline diameter hole index (DHI) was significantly lower in the successful group (0.470 ± 0.182) than in the unsuccessful group (0.669 ± 0.067). The mean baseline tractional hole index (THI) was significantly higher in the successful group than in the unsuccessful group (1.404 ± 0.843 versus 0.587 ± 0.129). However, the mean baseline MHV was not different between the two groups.

Comparison of pre-procedure clinical characteristics between the successful and unsuccessful groups

A comparison of the pre-procedure clinical characteristics between the two groups is shown in Table 2. A longer interval between primary surgery and fluid-gas exchange was observed in the successful group (17 ± 8 days) than in the unsuccessful group (12 ± 3 days); however, this difference was not statistically significant. The mean pre-procedure CSRT also showed no difference between the successful group and unsuccessful group. Both mean pre-procedure MD and mean pre-procedure BD values were significantly lower in the successful group (276.13 ± 89.59 μm versus 633.00 ± 182.42 μm, and 638.20 ± 274.34 μm versus 831.00 ± 113.18 μm, respectively). In contrast, the mean pre-procedure MH height was not significantly different between the two groups. A significantly higher mean pre-procedure MHI was observed in the successful group (0.624 ± 0.193) than in the unsuccessful group (0.452 ± 0.054). The mean pre-procedure HFF was significantly higher in the successful group than in the unsuccessful group (0.881 ± 0.204 versus 0.511 ± 0.140). The mean baseline DHI was significantly lower in the successful group (0.474 ± 0.161) than in the unsuccessful group (0.751 ± 159), whereas the mean baseline THI was significantly higher in the successful group than in the unsuccessful group (1.419 ± 0.561 versus 0.640 ± 0.245). Moreover, the mean baseline MHV was significantly lower in the successful group than in the unsuccessful group (0.411 ± 0.334 versus 1.032 ± 0.426). The type of procedure gas (SF_6) did not differ between the two groups.

Table 2
Comparison of pre-procedure clinical characteristics between the successful and unsuccessful groups of patients with unclosed macular hole treated with fluid-gas exchange.

Parameters	**Successful group** **(n = 15)**	**Unsuccessful group** **(n = 4)**	***p* value**
Interval between primary surgery and fluid-gas exchange, days, mean (SD)	17 (8)	12 (3)	0.357
Pre-procedure central subfield retinal thickness, μm, mean (SD)	307.00 (31.90)	306.25 (18.84)	0.885
Pre-procedure minimum diameter, μm, mean (SD)	276.13 (89.59)	633.00 (182.42)	0.001*
Pre-procedure base diameter, μm, mean (SD)	638.20 (274.34)	831.00 (113.18)	0.049*
Pre-procedure height, μm, mean (SD)	364.00 (105.81)	371.75 (18.63)	0.810
Pre-procedure macular hole index, mean (SD)	0.624 (0.193)	0.452 (0.054)	0.037*
Pre-procedure hole form factor, mean (SD)	0.881 (0.204)	0.511 (0.140)	0.004*
Pre-procedure diameter hole index, mean (SD)	0.474 (0.161)	0.751 (0.159)	0.006*
Pre-procedure tractional hole index, mean (SD)	1.419 (0.561)	0.640 (0.245)	0.006*
Pre-procedure macular hole volume, mm^3, mean (SD)	0.411 (0.334)	1.032 (0.426)	0.014*
Type of procedure gas, SF_6, n (%)	4 (26.7%)	1 (25.0%)	1.000

*Statistically significant as calculated using the Mann-Whitney U test.

SD, standard deviation.

Visual prognosis of the successful and unsuccessful groups

The successful group presented significantly better final BCVA values (0.33 ± 0.18 logMAR) than the unsuccessful group (0.78 ± 0.15 logMAR, Table 3). Furthermore, the final BCVA in the successful group was significantly improved compared to baseline BCVA (0.85 ± 0.22 logMAR), whereas the unsuccessful group demonstrated a poorer final BCVA compared to baseline (0.70 ± 0.14 logMAR); however, this difference was not statistically significant (Table 3).

Table 3
Comparison of baseline and final best-corrected visual acuity between the successful and unsuccessful groups of patients with unclosed macular hole treated with fluid-gas exchange.

Parameters	Baseline	Final	*p* value
Best-corrected visual acuity in the successful group, logMAR, mean ± (SD)	0.85 (0.22)	0.33 (0.18)	0.001*
Best-corrected visual acuity in the unsuccessful group, logMAR, mean ± (SD)	0.70 (0.14)	0.78 (0.15)	0.083
p value	0.185	0.001*	

*Statistically significant as calculated using the Mann-Whitney U test or Wilcoxon signed-rank test.

SD, standard deviation.

Discussion

This study retrospectively analysed the baseline and pre-procedure characteristics of patients with primary unclosed MH treated with fluid-gas exchange and showed that several baseline and pre-procedure OCT parameters were associated with the success of the fluid-gas exchange procedure after a failed primary IMH surgery. Various studies have reported relationships between preoperative OCT parameters and the prognosis of MH patients. Shpak *et al.*[10] demonstrated that a higher preoperative CSRT is related to the anatomical success of surgical IMH treatment. Similarly, our study showed increased baseline and pre-procedure CSRT values in the successful group compared to those in the unsuccessful group, although this difference was not statistically significant. Wakely *et al.*[11] reported that the parameters BD, MH inner opening, and MD were related to the anatomical and functional success in MH surgery. In patients with primary unclosed IMH treated with fluid-gas exchange, a smaller baseline MD, pre-procedure MD, and pre-procedure BD were also related to success. Kusuhara *et al.*[12] showed that IMH patients with MHI values ≥ 0.5 had a better postoperative BCVA than those with MHI values < 0.5. In this study, baseline and pre-procedure MHI values ≥ 0.5 were observed in the successful group with a better final BCVA than those in the unsuccessful group (baseline and pre-procedure MHI < 0.5). Several studies have reported that a higher HFF increases the closure rate and improves the postoperative visual outcome in MH patients[4]. In agreement with this publication, significantly higher baseline and pre-procedure HFF values with better final BCVA were observed in the successful group of our study. Ruiz-Moreno *et al.*[13] and Dai *et al.*[14] demonstrated that a higher THI is correlated with good visual prognosis, whereas DHI is not. However, our study revealed that both higher THI and lower DHI were related to the success of the fluid-gas exchange in patients with primary unclosed MH. Unsal *et al.*[5] reported that a higher MHV is associated with a poorer postoperative BCVA, whereas Ozturk *et al.*[15] detected no significant correlation. In this study, no difference in baseline MHV was noted between the two groups, but a significantly higher pre-procedure MHV was observed in the unsuccessful group. These findings suggest that MH indicators that are related to the success of primary surgery tend to be also correlated with the success of fluid-gas exchange in patients with failed primary MH treatment. Zou *et al.*[16] reported that a shorter symptom duration is associated with an earlier reconstruction of the external limiting membrane, resulting in better visual outcomes. Shorter symptom duration was also observed in the successful group of our study; however, compared with the unsuccessful group, the difference was not statistically significant.

The current consensus recommends internal limiting membrane peeling during a MH surgery; however, the face-down position after primary vitrectomy remains controversial[17]. Nonetheless, a previous meta-analysis concluded that the face-down position is highly recommended when the MH size exceeds 400 μm[18]. In this study, the MH size in all patients at baseline was > 400 μm, and all patients were positioned face-down after the primary vitrectomy. Among them, 94.74% (18 of 19 patients) had MH closure after the fluid-gas exchange procedure, with ≥ 7 days of additional period in face-down position. These findings highlight that an inadequate period of gas tamponade with face-down position might be associated with the failure of primary surgery in IMH patients, and the fluid-gas exchange procedure with the additional period in face-down position is useful in these failed primary IMH patients. One previous study mentioned that SF_6 and C_3F_8 gas tamponades during surgery show similar MH closure rates[19]. In agreement with these findings, we observed that the type of gas used for the fluid-gas exchange was not different between the successful and unsuccessful groups.

This study has some limitations. First, the retrospective design may have resulted in a patient selection bias. Second, this study included only a small number of patients. Therefore, further studies with larger numbers of patients with failed primary IMH treatment will be needed. Despite these limitations, to the best of our knowledge, this is the first study to evaluate the factors associated with the success in patients with failed primary IMH surgery treated with fluid-gas exchange.

In conclusion, lower pre-procedure BD, lower baseline and pre-procedure DHI and MD, and higher baseline and pre-procedure MHI, HF, and THI values are associated with the success of fluid-gas exchange in patients with failed primary IMH treatment. These results suggest that indices predicting the success of primary IMH surgery may also be useful to predict the success of fluid-gas exchange in patients with failed primary surgery.

Methods

Study design and subjects

This study was designed as a retrospective, comparative case series conducted in a single hospital. The study adhered to the tenets of the Declaration of Helsinki and was approved by the institutional review board of Keimyung University Dongsan Hospital (IRB no. 2020-12-069). The patients signed informed consent for the use of their data. We retrospectively reviewed the electronic medical records of patients with a history of a failed primary IMH surgery who were treated with fluid-gas exchange between January 2013 and December 2019. The patients with at least 6 months of follow-up period after the procedure were enrolled in the study. The exclusion criteria were as follows: myopia > 6 dioptres, presence of rhegmatogenous retinal detachment, diabetic retinopathy, age-related macular degeneration, or a history of previous vitrectomy due to causes other than IMH.

All patients had a full-thickness IMH and underwent primary vitrectomy with internal limiting membrane peeling using the inverted flap technique. Cataract surgery was performed simultaneously when the cataract impaired posterior visualisation. The patients were instructed to remain in a face-down position for ≥ 7 days. The fluid-gas exchange procedure was performed on 19 eyes in which an unclosed MH was noted in the spectral-domain OCT (Spectralis OCT/SLO; Ophthalmic Technologies, Toronto, Ontario, Canada) or swept-source OCT (DRI OCT-1; Topcon, Tokyo, Japan) during the follow-up period. The procedure was based on a previous report by Jang *et al.*[20], and the patients were instructed to stay in the face-down position for 7 days. The type and percentage of gas used in the primary surgery were determined by the surgeon’s preference. During the fluid-gas exchange, 16% of SF_6 gas or 14% of C_3F_8 gas was used. All aforementioned surgical and other procedures were performed by a single clinician (Y.C.K.).

Based on the classification by Imai *et al.*[6], the outcomes of the fluid-gas exchange procedure were classified as U-type closure, V-type closure, W-type closure, or unclosed. The patients were divided into the successful and unsuccessful groups according to the absence or presence of bare retinal pigment epithelium after the fluid-gas exchange procedure, respectively (Fig. 1). Demographic and clinical characteristics were compared between the two groups to assess the prognostic factors.

Clinical data collection

The demographic characteristics including age, sex, and laterality were assessed in all patients. Furthermore, the duration of decreased visual acuity, baseline IOP measured by a non-contact tonometer (Canon TX-20, Canon Inc, Kanagawa, Japan), spherical equivalent, lens status (phakic or pseudophakic), axial length, type of primary surgery (vitrectomy alone or combined cataract surgery) with the type of gas and the percentage used for tamponade during primary surgery, interval period between the primary surgery and fluid-gas exchange, and the type and percentage of gas used in the fluid-gas exchange were recorded. The baseline and final logMAR BCVA values were also assessed. OCT images of all patients were recorded at baseline, pre-procedure, and post-procedure until the last follow-up. CSRT, BD, MD, MH height, MHV height, left arm length, and right arm length were measured using the OCT software measuring tool at baseline and pre-procedure. In addition, the MHI based on the publication by Kusuhara *et al.*[12], the THI and DHI by Ruiz-Moreno *et al.*[13], the HFF by Ullrich *et al.*[4], and the MHV by Ozturk *et al.*[15] were calculated.

Statistical methods

Data were calculated as the mean ± standard deviation (SD) or n (%; e.g., number of eyes). Statistical analyses were performed using Statistical Package for the Social Sciences version 12.0 (IBM, Chicago, IL, USA). Between-group differences in age, symptom duration, total follow-up period, baseline and final BCVA, baseline IOP, baseline spherical equivalent, percentages of gas tamponade used in primary surgery and fluid-gas exchange, baseline axial length, and baseline and pre-procedure values of BD, MD, MH height, MHI, HFF, DHI, THI, and MHV were compared using the Mann-Whitney U test. Categorical variables, such as sex, affected eye, lens status, type of surgery, and type of gas used in the primary surgery and fluid-gas exchange were compared using the chi-square test or Fisher's exact test. The comparison of baseline and post-procedure BCVA between the two groups was performed using the Wilcoxon signed-rank test. All the tests had two-tailored critical regions for a significance level of 0.05.

Declarations

Data availability

The datasets generated and/or analysed during the present study are available from the corresponding author on reasonable request.

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Author contributions

Y.H.L. conceived and designed the study and wrote the manuscript. S.J.L. was responsible for data curation. J.H.J. reviewed the manuscript. Y.C.K. initiated and supervised the project and reviewed the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare no competing interests.

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Figures

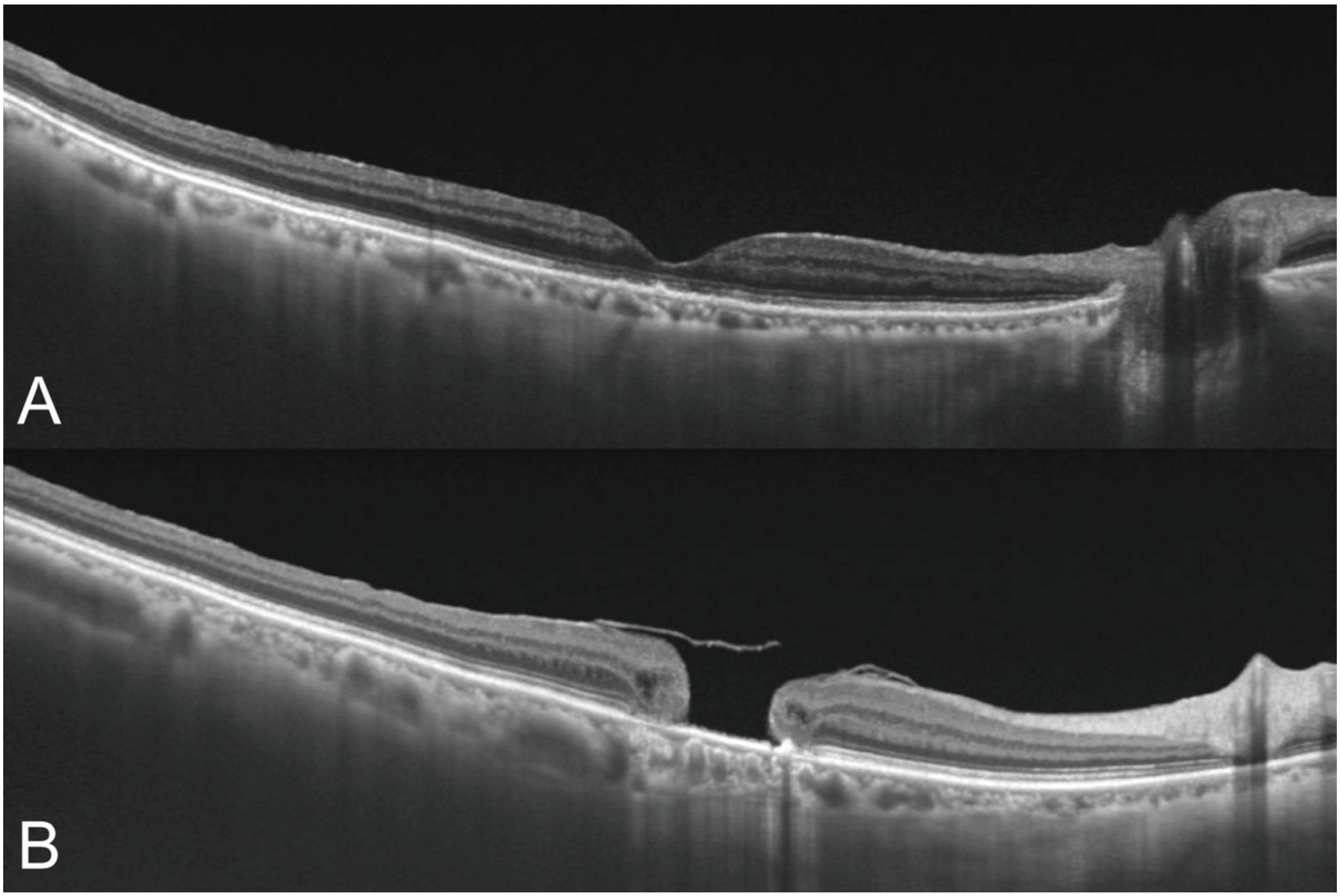

Figure 1

Optical coherence tomography images of successful and unsuccessful anatomical outcomes after fluid-gas exchange. (a) Example of a successful anatomical outcome showing the absence of bare retinal pigment epithelium. (b) An unsuccessful outcome showing the presence of bare retinal pigment epithelium.