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RETINAL DISORDERS

Application of subretinal fluid to close refractory full thickness macular holes: treatment strategies and primary outcome: APOSTEL study

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Abstract

Introduction Persisting macular holes (PMH) after surgical release of any epiretinal traction of the vitreous and adjacent membrane may rely on secondary firm adhesions between the retracted retina and adjacent retinal pigment epithelium. Secondary application of subretinal (SR)-fluid may release these adhesions followed by an anatomical closure.

Methods Twelve surgeons applied in a consecutive case series SR-fluid in 41 eyes with PMH and reported retrospectively their initial surgical, anatomical and functional experience with this approach.

Results The mean duration of the MH prior to SR-fluid application was 17 months (6–96 months). The mean age of the patients at the time of surgery was 72 years (54–88). The mean preoperative aperture diameter of the opening was 1212 μm (239–4344 μm), base diameter 649 μm (SD 320 μm). The mean preoperative BCVA prior to surgery was 0.1 (0.01–0.3). All patients (41/41) complained about reduced BCVA and a significant central scotoma (negative scotoma) in their central field of vision. The secondary closure rate for our PMH was 85.36% (35 out of 41 eyes) at 6 weeks after surgery. The postoperative BCVA improved to 0.22 (0.02–0.5). The application of SR-fluid was not associated with major intraoperative adverse effects.

Conclusion Remaining SR-adhesions may inhibit PMH closure. Their release by application of SR-fluid will lead to a fast and immediate anatomical closure in many cases without serious adverse events.

Keywords Vitreoretinal surgery · Vitrectomy · Macular hole · Subretinal fluid · Retreatment · Large aperture

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Introduction

Full thickness macular holes (FTMH) are defects of the entire neuroretina at the inner fovea. Its treatment by pars plana vitrectomy (PPV) and consecutive gas tamponade was first described by Kelly and Wendel and has been modified since then to improve functional and anatomical outcomes [1]. The current standard approach treats the underlying epiretinal pathology by removing vitreous adhesions, including the internal limiting membrane (ILM) and adherent epiretinal membranes (ERM), to release any tangential traction from the epiretinal surface. This eliminates all centrifugal forces, so that the retracted elastic retina may relocate to its original position, closing the FTMH within days. Using this approach, most authors report an anatomical closure rate greater than 95% [2]. Secondary attempts to close refractory FTMH include additional installation of silicone oil [3], application of autologous platelet concentrates [4, 5] and more recently inverted internal limiting membrane flap application [6] or autologous neurosensory retinal free flap transplantation [7]. All these procedures have scaffold the MH, inducing centripetal force to readapt refractory macular holes. However, if a refractory FTMH fails to close after eliminating its origin centrifugal force, additional subretinal (SR) adhesions may play an important role in preventing the closure of a persisting macular hole (PMH). Known risk factors for PMH include large-sized FTMH [8], long duration of macular holes [9], traumatic macular holes [10] and FTMH in eyes with uveitis or drusen [11]. In all these circumstances, we find after the initial centrifugal driving force for the development of the macular hole, secondary alterations occur between the photoreceptors and retinal pigment epithelium (RPE), which may induce firm adhesions between the neuroretina and adjacent the RPE-choriocapillaris complex, thus preventing the natural relocation of the retracted elastic neuroretina. The goal of this case series is to present the concept of closing large PMH by the release of SR fluid applications. The closure of FTMH by SR fluid application has been described in the past by several groups. Gonvers et al. [12] presented a case series of SR fluid application in FTMH during the XXIII Meeting of the Club Jules Gonin in September 2002 in Montreux. Independently, Oliver and Wojcik [13] published their technique in 2011 in a case report. Wong et al. described his technique in greater detail and published a case series [14]. He reported a closure rate 80% and recommended his technique for experienced vitreoretinal (VR) surgeons as a secondary novel subretinal option to close PMH. Here, we present the early experience of 12 VR surgeons performing this novel technique for the first time in FTMH. The primary outcome of this survey was to evaluate and determine the pitfalls and most challenging steps for the surgeon and the assisting team. The secondary outcome measure was to report patient preoperative retinal characteristics, anatomical closure rate and initial functional outcome.

Patients and methods

We reviewed retrospectively the records of 41 consecutive patients who were treated by SR fluid application and endotamponade between March 2018 and July 2019. Twelve experienced VR surgeons from 10 participating centres reported their application of subretinal fluid in refractory macular holes for the **APOSTEL** study. All critical aspects of SR fluid application were discussed with participating physicians and summarised in greater detail [15]. In a 17-question survey, we asked the participating surgeons how feasible these recommendations are and if they followed these guidelines based on their own discretion. The survey was performed in accordance with the ethical standards laid downs in the Declaration of Helsinki. Approval from the ethics committee was obtained for this retrospective survey by the ethics committee of the Bayrischer Landesärztekammer.

Inclusion criteria

(A) Each participating surgeon was allowed to submit their 1–8 initial consecutive cases in this retrospective survey. (B) FTMH with high risk characteristics for large PMH with an inner diameter of greater 550 μm on optical coherence tomography (OCT) [16] or presence of drusen in age-related macular degeneration (AMD) [11]. (C) Previous unsuccessful standard three-port pars plana chromovitrectomy including a full PPV, induction of a posterior vitreous detachment, staining of the epiretinal surface with vital dyes, arcade-to-arcade ILM peel and gas endotamponade. (D) Additional previous unsuccessful procedures including restaining of the retinal surface with secondary peeling attempts, applications of thrombocyte concentrate, additional long-acting gas or silicone tamponades as well as failed ILM flap applications were allowed.

Technical approach and surgical considerations

Our modified technique was initially presented at the previous Vail Vitrectomy meeting in 2019 and has been described elsewhere [15]. A corresponding instructional video may be seen on the AAO website (https://www.aao.org/clinical-video/how-to-close-macular-hole-using-subretinal-fluid). Most eyes with failed MH surgery are already completely vitrectomized;

therefore, retreatment is a straightforward approach. Prior to surgery, the last postoperative OCT should be meticulously examined scan by scan, searching for persisting epiretinal structures on the retinal surface. In the absence of epiretinal structures, the SR approach may be considered:

A. Confirm that the initial ILM peeling was complete. Staining the epiretinal surface with vital dyes (chromovitrectomy) [17] may confirm the presence or absence of vitreous, ILM or epiretinal membrane.
B. Installation of a small heavy liquid perfluoroctane (PFO) bleb (2–3-disc diameter (DD)) over the FTMH to cover the edges of the cuff (Fig. 1a). The purpose of this PFO bleb is to seal the MH, thus preventing an early antegrade draining of SR fluid from the SR space through the FTMH. We recommend performing this step during your first surgery with SR fluid application in MH. Once you are familiar with that, you may skip this step.
C. Application of three small SR blebs of 2–3 DD in the superior, temporal and inferior quadrant using a 41-gauge subretinal cannula connected to a 1 cc syringe filled with balanced salt solution (BSS) (Fig. 1b). Lower the infusion bottle to < 20 mmHg, so the intraocular pressure is low, and the resistance to detach the retina is not artificially elevated [18].
D. For SR fluid application, you may follow two strategies: many surgeons prefer to start with gentle injection prior to penetrating the retina. This approach comes from pioneering work in macular translocation [19] and cell-based and/or gene-based therapy [20].
E. Place the retinotomy in the mid distance between the edge of the macular hole and the arcade of the upper or perpendicular lower arcade of the retinal vessels.
F. Once 2–3 SR blebs have created the intended SR detachment and stretching of the retina, the sealing PFO bleb may be withdrawn (Fig. 1c).
G. Now, while the epiretinal tamponade is gone, SR detachment is completed by gently injecting more fluid through one retinotomy site into the SR space (Fig. 1d, e). SR detachment will now expand towards the centre and the PMH (Fig. 1f). The application of intraoperative OCT may be used [21, 22].
H. Controversy remains about the need to massage the released elastic retina centripetally towards the centre of the foveola. While Carl Claes recommends closing the hole in the operating room on the table [23], most surgeons think that this manoeuvre is an additional trauma. Some additional groups have reported aspirating with a Steve Charles cannula at the inner aspects of the FTMH [24].
I. Finally, the PMH needs to be closed by a temporary endotamponade. Early reports for his surgery recommended a long-term endotamponade; however, most PMH close within 4–5 days, so conventional gas application and posturing for 2–3 days is currently recommended.

Pre- and postoperative evaluation

Patient demographics, gender, age as well as the duration of the PMH and the best corrected visual acuity (BCVA) prior to surgery were evaluated.

The greatest complain of patients with macular holes is the reduced BCVA and induced central scotoma. We evaluated and questioned the patients 6 to 9 weeks after surgery for possible presence and disappearance of central negative scotoma. An accurate selection of a horizontal B-scan OCT image with the central largest extent of the hole's aperture is recommended. The hole size measure 'aperture diameter' is the maximum diameter of the opening width of the MH measured in microns. The 'base diameter' is the floor size measured with a calliper at the largest distance between the tips of the external limiting membrane (ELM).

Results

All 12 participating VR surgeons with an experience of 5–15 years of VR surgery reported here their initial experience with SR fluid application in FTMH during their initial 1–8 cases and submitted our survey for further evaluations. The survey showed that, most importantly, all surgeons came along very well with our technique and felt comfortable with the surgery (12/12). Eleven out of 12 physicians inspected the most recent OCT for persisting epiretinal ERM or additional ERM (11/12). The configuration of the MH appeared to have no influence on the surgical outcome (12/12). Nine out of 12 surgeons confirmed complete ILM peeling by the application of vital dyes prior to SR fluid application (9/12). The initial installation of an epiretinal PFO bleb was done by all surgeons (12/12) to secure this step during the first manoeuvres (Fig. 2a). All but two surgeons installed three SR blebs, namely in the superior, interior and temporal quadrants (10/12); two additional surgeons preferred only two retinotomies (Fig. 2b–d). All participating surgeons selected BSS as the preferred fluid in the SR space (12/12). A meticulous inspection of the tubing system for remnants of air bubbles was done by all (12/12). Fluid application was predominantly done manually by the assisting physician (7/12). Additionally, five surgeons preferred using a food pedal to inject the fluid (5/12). Prior to SR fluid application, most surgeons (11/12) lowered the IOP significantly to 5–15 mmHg. Most surgeons located their retinotomy sights in the mid distance between the edge of the FTMH and the arcade (11/12) (Fig. 2b). One physician reported placing the retinotomy sites outside of the arcade. All

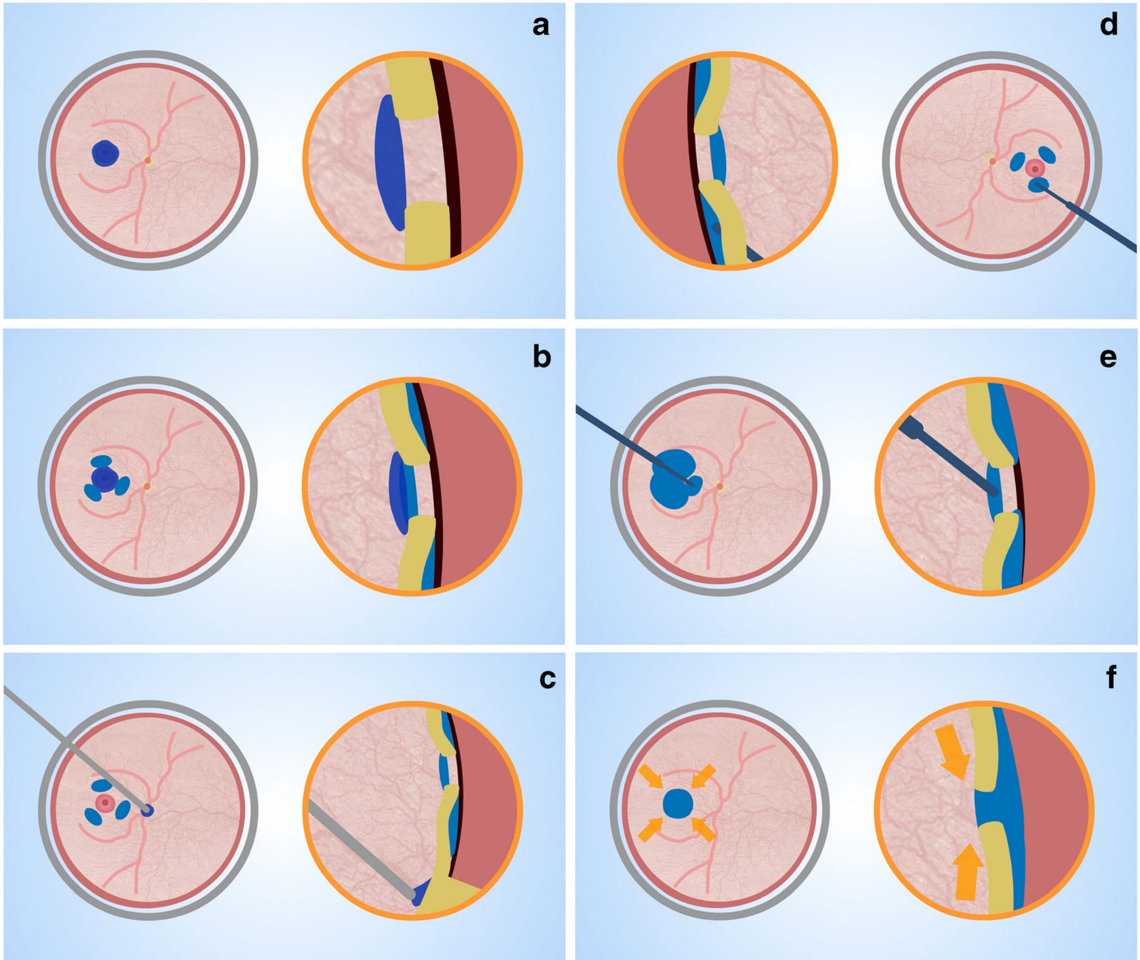

Fig. 1 **a** Application of a 2-disc diameter PFO bubble over the macular hole to seal the edges of the cuff. **b** Apply 2–3 small subretinal retinal detachments. **c** Drainage of PFO from the disc. **d** Application of additional subretinal fluid to confluent the serous detachments. **e** application of additional subretinal fluid until the retina adjacent to the aperture of the cuff is detached. **f** The retracted elastic retina has no more adhesions to subretinal structures and can shift centripetally to original location sealing the macular hole

physicians agreed that a successful manoeuvre is completed with the full detachment of the edge of the FTMH (12/12). The use of a Tano scraper was recommended by only two surgeons, to occasionally massage the retinal surface centrally (2/12). Although some surgeons injected silicone oil during their initial cases, all surgeons referred to a gas endotamponade during subsequent cases (12/12). A fast closure of the treated PMH within 5–7 days of observation may have driven this modification (12/12) (Fig. 3a–c). The complete release of the retina from the adjacent RPE was confirmed by an intraoperative OCT in two centres (2/12), although this imaging appears not necessary for all cases.

Clinical findings prior to and after surgery

Preoperative parameters

The mean duration of the FTMH prior to SR fluid application was 17 months (6–96 months). The mean age of the patients at the time of surgery was 72 years (54–88). The mean preoperative '**aperture diameter**' or maximum diameter of the opening was 1212 μm (239–4344 μm). The '**base diameter**', measured as the largest distance between the tips of the ELM, was the maximum width at the base diameter of the MH 649 μm (116 μm-1789 μm) in mm. The mean preoperative BCVA prior to surgery was 0.1 (0.01–0.3). All patients (41/41) complained about reduced BCVA and a significant central scotoma (negative scotoma) in their central field of vision. Previous surgery of the FTMH included PPV with ILM peeling, silicone oil or thrombocyte concentrate application (Table 1).

Intraoperative parameters

The ad hoc survey showed that the application of SR fluid was not associated with major intraoperative adverse effects (0/41). Small limited SR bleedings occurred at two retinotomy sites and resolved without affecting the functional or

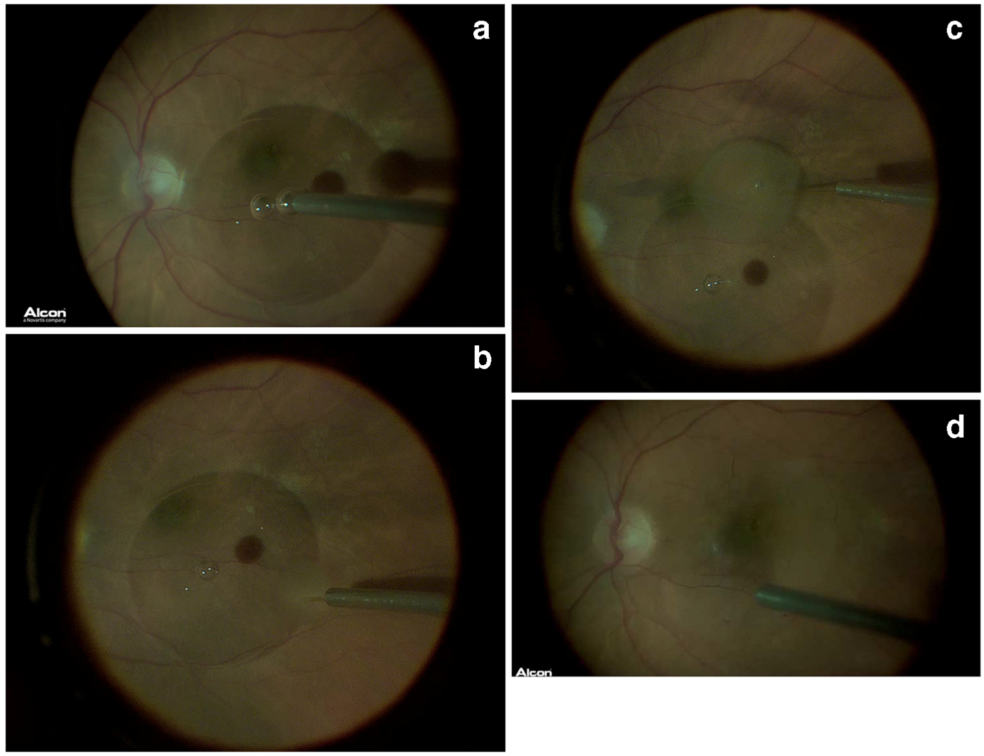

Fig. 2 **a–d** Intraoperative fundus images: **a** application of PFO over the macular hole, **b**, **c** subretinal fluid application in the temporal superior quadrant. A bullous retinal detachment with release of subretinal adhesions and gentle stretching of the neuroretina, **d** release of the perifoveal retina with a shallow subretinal detachment prior to fluid air exchange

anatomical prognosis within 3 weeks (2/41). Accidental application of a small air bubble occurred in two cases, which resolved spontaneously through the cuff of the MH (2/41). Additional ILM peeling after staining the retinal surface with vital dyes was not required (0/41). Endotamponade with gas was applied in 32 cases (21x C2F6, 9x SF6, 2x C3F8) and 9x silicone oil endotamponades were applied in early cases. A gentle centripetal massage of the released elastic retina towards the foveola was applied in two eyes (2/41) (Table 2).

Postoperative parameters

The secondary closure rate for our PMH cases was 85.36% (35 out of 41 eyes) at 6 weeks after SR fluid application. The postoperative BCVA improved to 0.22 (0.02–0.5) at 4 weeks after surgery. All eyes with a closed MH experienced a gain in their VA and loss of their central negative scotoma. The negative scotoma disappeared in all 41 included eyes. The duration to close the PMH was similar and to that of normal, primary FTMH. Complete closure was apparently visible by OCT 4–7 days after surgery (Table 3). In six eyes (14.64%), the PMH remained open. In three eyes, the edges of the rim attached, and the cuff of the open aperture was reduced. Risk factor analysis for a reduced closure rate was determined that two of these eyes had a significant greater duration of 48 and 96 months prior to surgery; one eye was associated with previous SR haemorrhage due to an adjacent retinal aneurysm. The PMH in one additional eye presented with a markedly rigid retina intraoperatively. The increased retinal stiffness was associated with Alport syndrome [25].

Discussion

Idiopathic FTMH develops through epiretinal traction of the vitreous and adjacent membrane; its complete release is therefore primarily mandatory for the successful closure of any FTMH [26, 27]. With enhanced intraoperative visualisation of epiretinal structures today, we can expect a primary closure rate of more than 90%. Thus, PMH are the exceptions and occur more frequently in large, old or traumatic FTMH, as well as in the consecutive presence of drusen or uveitis. All these circumstances may be associated with secondary firm adhesions between the photoreceptors of the retracted retina with the adjacent underlying RPE. While conventional secondary treatment options are to apply additional epiretinal treatment approaches with silicon oil or ILM patches, we here evaluate a new concept of simple SR fluid application to release secondary firm adhesions that were possibly preventing the initial closure of the FTMH.

Although all participating surgeons agreed on the principle of SR fluid application, several steps gained further importance or remained under discussion. We clearly underline that this novel procedure is not intended to replace or even question the success of vitrectomy and ILM peeling as a first step procedure. However, once the epiretinal traction is released from traction, we may consider SR fluid injection to rerelease

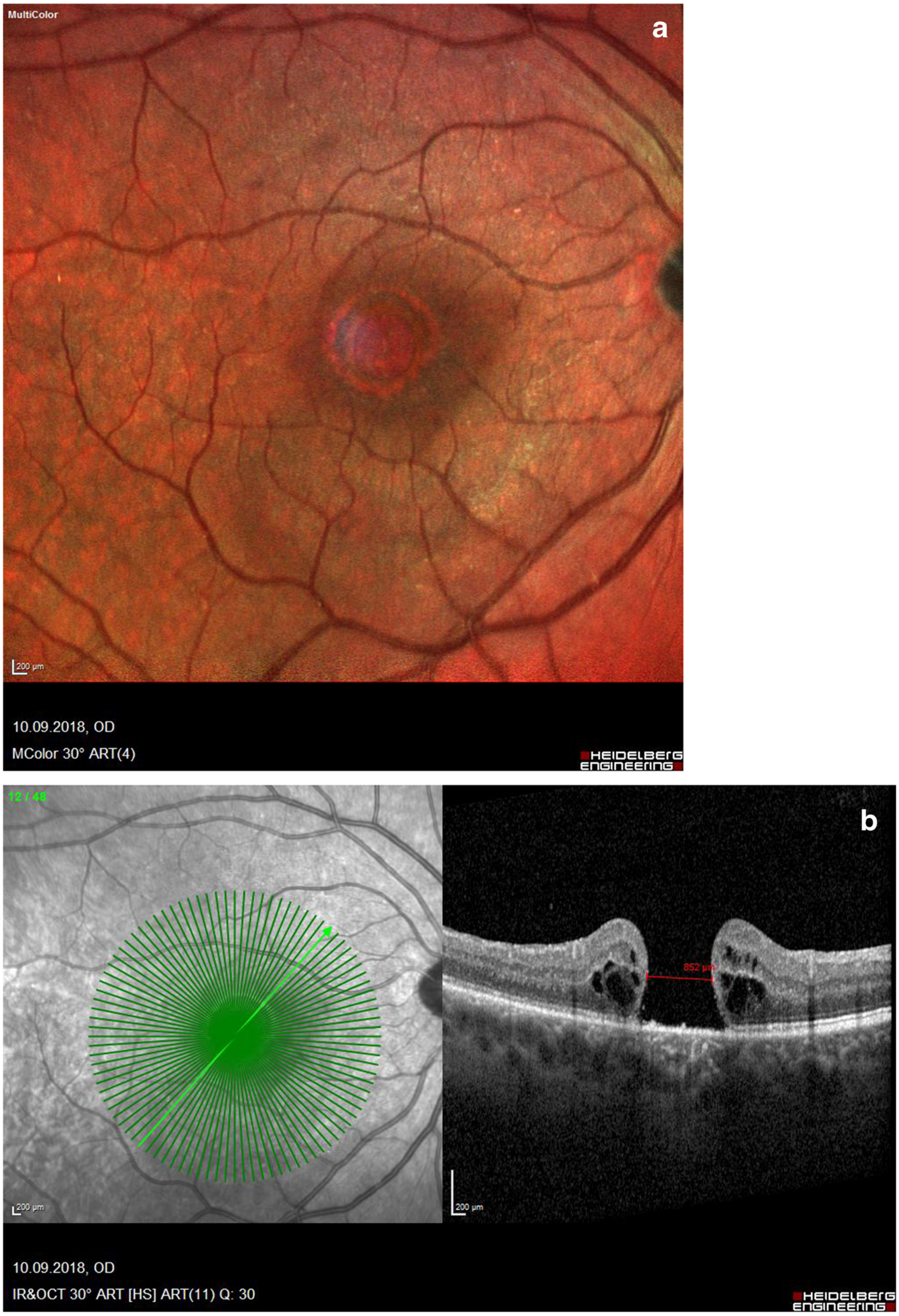

Fig. 3 Preoperative fundus and OCT image of a PMH prior to subretinal fluid application (**a**, **b**). Postoperative OCT confirming the anatomical closure of the macular hole 6 days (**c**) and 6 months (**d**) after surgery

adhesions as a secondary effect causing PMH [28]. In these cases, we may prefer the novel concept of SR fluid application as the treatment of choice, with a similar high anatomical closure rate. Unexpectedly, we determined a high closure rate, even in large holes. Previous pioneering work on limited translocation confirmed that an iatrogenic retinal detachment one quadrant above the fovea is capable of moving the retina up by 1700 μm [19]. Thus, bilateral detachment of the perifoveal retina may release enough tissue for a centrifugal pedal movement to close even large MH. The release of the edges of the FTMH appears to be an essential step, as we experienced the firmest unexpected SR adhesions in this area, presumably limiting the secure closure of the MH. However, the technique may have its limitations with a less elastic retina.

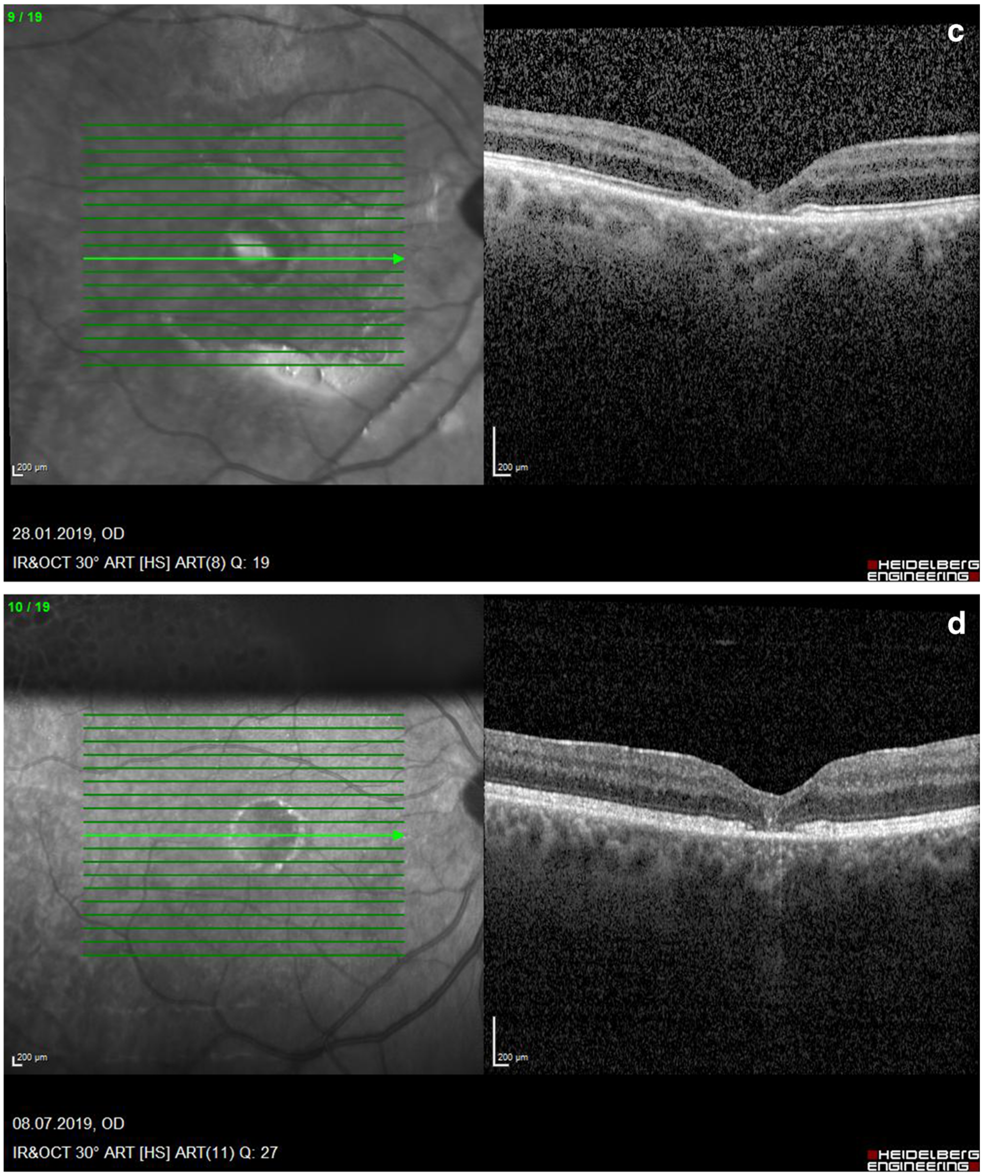

Fig. 3 (continued)

We noticed unsuccessful attempts in two long-lasting PMH of 24 to 48 months. One additional PMH remained unchanged in an eye with Alport syndrome [25]. We speculate that an even stiffer retina may have prevented the closure of these MH. It remains open was to whether additional epiretinal massage may have released firmer intraretinal fibroses, thus, mobilising enough tissue to close the anatomical hole.

Although Gonvers et al. initially described SR fluid application to treat MH in 2002 [12], it took another decade until several surgeons supported this concept for PMH and reported their individual techniques and results. Charles et al. detached the retina and performed a full thickness arcuate retinotomy temporal to the MH to release retinal tissue and shift it centrally to close a large MH. They reported anatomical repair in five out of six MH (83%) exhibiting visual improvement [29]. Carl Claes used SR fluid application to induce full 360° detachment around the MH, followed by a meticulous fluid-air exchange. He performed complete drainage of the perimacular fluid with a specially designed 30-gauge flute needle with a tapered shaft to induce an approximation of the edges of the MH. A lot of care was taken not to engage the edges of the MH, nor to damage the RPE with the tip of the needle. The MH was finally sealed by a silicon oil tamponade [23]. Conversely, Rubin et al. recommended in large traumatic MH with presumably stiffer retinal tissue to perform after SR fluid application a gentle centripetal massage with a backflush cannula to achieve sufficient intraoperative foveal displacement. He reported successful closure in six out of seven large traumatic MH with an average diameter of 825 µm [30]. Roger Wong used a Tano silicone-tipped

Table 1 Preference, performance and advice of the 12 VR-surgeons

Preference, performance and advice of the 12 VR-surgeons	Number of surgeons
Felt overall comfortable with the SR-surgery	(12/12)
Preoperative inspection of the most recent OTC^^CT is essential	(11/12)
Preoperative MH configuration had no influence on surgical outcome	(12/12)
Intraoperative staining of ILM essential prior to SR fluid application	(9/12)
Initial installation of epiretinal PFO bleb helpful	(12/12)
Installation of 3 SR blebs (superior, interior, temporal quadrant)	(10/12)
Installation of 2 SR blebs	(2/12)
Manually used BSS for SR fluid application	(12/12)
Inspect tubing system for remaining air bubbles	(12/12)
By fluid application manually by the assisting physician	(7/12)
Fluid application by food pedal of machine	(5/12)
Lower the IOP to (5–15 mmHg) during SR fluid application	(11/12)
Retinotomy sights mid distance between the edge of FTMH and the arcade	(11/12)
Retinotomy sites outside the arcade	(1/12)
All edge of the FTMH must be detached	(12/12)
Additional massage of the retinal surface essential	(2/12)
Recommend a gas endotamponade	(12/12)
Observed closure within 5–7 days postoperatively	(12/12)
Application of intraoperative OCT	(2/12)

scraper to manoeuvre the retina radially, approximating the edge 'retinal apposition', and reported a closure of three MH with a diameter of 690 to 736 μm [14]. Wong et al. confirmed additional safety and efficacy results after SR injection of saline in an additional 16 patients in with a mean PMD diameter of 739 μm (SD: 62 μm). PMH closed in 14 of 16 eyes (83%) with consecutive visual improvement. No patient lost their vision due to the procedure [31]. Felfeli and Mandelcorn named their surgical approach 'retinal hydrodissection' and treated 39 eyes with persistent (failed previous vitrectomy surgery), chronic (diagnosis for ≥ 1 year) and/or large MH (aperture diameter of ≥ 400 μm) by one surgeon. They reported closure in 87.2% (34/39) of MH with a mean visual improvement of ≥ 2 lines. Intra- or postoperative complications related to the proposed technique were not noted [32]. More recently, Frisina et al. followed 10 eyes with PMH after treatment by SR fluid application by fundus autofluorescence (FAF) and OCT for 6 months after surgery. They obtained closure in nine out of ten MH associated with improved BCVA from 1.06 ± 0.1 at baseline to 0.56 ± 0.2 (final) logMAR and visible outer retinal layer (ORL) restoration. The retinotomy site showed small, permanent RPE damage by FAF and OCT; thus, they recommend localising the retinotomy site with a safety margin to the central foveola [33]. Although all these reports generated important information regarding the safety, reliability and efficacy of this surgical approach, their results remained limited to a specialised single centre, a single surgeon's approach and personal digression.

Table 2 Intraoperative observations and preferences of the 12 VR-surgeons

Intraoperative parameters	
Major intraoperative adverse effects	(0/41)
small SR bleedings at 2 retinotomy sites	(2/41)
Accidental SR application of air bubble	(2/41)
Additional ILM peeling after staining	(0/41)
Endotamponade gas (21x C2F6, 9x SF6, 2xC3F8)	(32/41)
Silicone oil	(9/41)
Applied massage the retinal surface with a scraper	(2/41)

Large MH can be challenging, so several national initiatives [34–36] have investigated its incidence and the best treatment strategies. The Manchester large macular hole study evaluated in a retrospective case series 258 eyes with FTMH larger than 400 μm following vitrectomy, ILM peeling and gas tamponade. The determined closure rate was 98% in small (400–477 μm), 91% in medium (478–558 μm) and 94% in large sized (559–649 μm) MH, while giant MH (650–1416 μm) closed only in 76% of cases. The authors determined a high success rate in eyes with a FTMH up to a diameter of 650 μm and concluded that new surgical techniques such as internal limiting membrane flaps should be reserved for macular holes larger than 650 μm [34]. The Japan-Clinical Retina Research Team (J-CREST) compared the surgical outcomes of vitrectomy with solely conventional internal

Table 3 Intraoperative observations

Macular parameters		
		Mean (min–max)
Duration	Duration of FTMH prior to SR fluid surgery	17 months (6–96)
	Patient`s age at SR fluid surgery	72 years (54–88)
Structure	Preoperative aperture of FTMH	1212 μm (239–4344)
	Preoperative base diameter of FTMH	649 μm (116-1789)
	Closure rate of FTMH	85.36% (35/41)
Function	Preoperative BCVA	0.1 (0.01–0.3)
	Postoperative BCVA	0.22 (0.02–0.5)

limiting membrane (C-ILM) peeling with the inverted ILM (I-ILM) flap technique. The authors compared medium MH with a diameter of 400–550 μm and large MH (> 550 μm). The closure rate in medium MH was 95.2% (59/62) by C-ILM peeling and 100% (19/19) by the I-ILM technique. In large MH, the closure rate was 88.4% (38/43) by C-ILM peeling and 100% (41/41) by the I-ILM technique. They concluded that although the difference between the two methods was statistically not significant, the I-ILM technique was more effective for closure in eyes with extra-large MH [35]. Finally, the New Zealand Society of Retinal Specialists Macular Hole Study Group evaluated 103 patients after failed macular hole surgery. The mean MH size was 562 μm prior to retreatment and resulted a final MH closure rate of 85%. All these case series demonstrated that most MH up to a diameter of 550-μm close during the first surgery [36]. In agreement with these trials, we confirmed that persisting PMH tend to have larger diameter and benefit from retreatment. These national retreatment surveys identified large and persisting MH as the most challenging cases to treat. Our novel SR approach demonstrated noninferior results compared with the established ILM flap technique.

The current literature on SR fluid application in PMH depends predominantly on the experience of a single surgeons and a selected number of eyes, thus limiting the relevance of their findings. The goal of this case series was to present early results from 12 participating experienced VR surgeons during their first cases with this novel treatment option. The APOSTEL study evaluated the largest available multicentre consecutive case series, their personal intraoperative observations and initial anatomical experience with SR fluid application in PMH. The participating VR surgeons reported inspiring effects and the absence of serious adverse events, combined with a high success rate. The observed short duration for anatomical closure, as well as the unexpectedly high number of successfully closed PMH provides further evidence that the dissection and liberation of the presumed causative pathogenic SR adhesions between the photoreceptors and the RPE may play a previously underestimated critical role in eyes with PMH.

A comparison of national trials also demonstrated a similar closure rate after the well-established ILM flap technique and the novel SR fluid application method presented here. Retreatment of PMH with the ILM flap technique or SR fluid application reported a final closure greater 80%; thus, retreatment (regardless of the applied technique) should be recommended to all patients with PMH. An additional comparison of SR fluid application in our early multicentre study and the abovementioned single centre studies showed a similar closure rate above 80%, indicating that the procedure is feasible and can be performed by most surgeons without a significant learning curve, as most surgeons reported some previous experience in subretinal rtPA application in giant SR haemorrhages. Specialized single centre trials with larger group sizes and more experience with SR fluid application showed nonsuperior results as compared with our trial including less experienced VR surgeons in this indication and procedure.

Our study has some limitations. Firstly, due to the initially high success rate of treated MH, we were not able to perform a prospective study with a reasonable number of eyes at this stage. To assess the primary goal of the study, we had to include in this retrospective study design a limited number of eyes. The incidence of large, old or persistent MH remains limited, so we included all available cases in this study to evaluate the surgical procedure. Secondly, the number of previous treatments and disease duration until SR fluid application vary between cases. Thirdly, the postoperative follow-up was limited to 6 weeks. However, our main intention of this interventional case series was to evaluate the feasibility of this novel surgical approach by several VR surgeons.

Our trial provides important new information to interested surgeons globally. The eyes treated here showed functional recovery, even after years of PMH, although the main goal of this trial was not to select the best patients for a maximal visual improvement. The greatest preoperative complaint and the postoperative relief for most participating patients was the immediate disappearance of the very irritating negative scotoma in their central field of vision. Our presented case series provides evidence for the safety and efficacy of SR fluid in PMH, and further trials are warranted with long-term results. We have initiated an international registrar with 32 participating surgeons globally. The goal is to study pre- and postoperative OCT scans, to determine preoperative anatomical risk factors and to evaluate the anatomical closure pattern of PMH after SR fluid application over a long follow-up period.

Conclusion

In summary, the APOSTEL study is the first multicentre study of PMH treated with SR fluid. Our surgical results confirmed easy and fast application, with minimal adverse events and a high surgical success rate In agreement with previous case series, we observed within days a complete anatomical closure in more than 80% of cases, supporting our hypothesis that pathologic SR adhesions may be causative of PMH in selected cases. The physiologic elasticity of the retracted liberated retina was capable of closing even large holes with an aperture diameter greater 3000 μm. The disappearance of an irritating central negative scotoma was the greatest relief for affected patients associated with an improvement in their central vision.

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The APOSTEL study received the distinguished Leonhard-Klein Award for ocular surgery 2020 at the Deutsche Ophthalmologische Gesellschaft (DOG).

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the (place name of institution and/or national research committee) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study treatment.

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