

The anatomical and functional results of the aforementioned current standard of care are especially limited in large holes greater than 400 μm measured at the minimum aperture and persistent macular holes. Therefore, in order to improve surgical success in large and persistent macular holes, modifications of the standard surgical technique have been a subject of investigation. Very recently new surgical approaches have been published [14-16], including the positioning of autologous material such as retinal tissue, lens capsule or ILM inside or under the macular hole aperture or rim. Alternatively, subretinal BSS injection was recently published as an alternative method to mobilize retinal tissue at the posterior pole and allow for an attenuation of large macular holes [17]. However, while anatomical results appear promising, there is little knowledge on how tissue transplants inside or under the hole will integrate, whether there will be RPE alterations seen in the postoperative course, and how function will develop.

The endotamponade with silicone oil may offer an alternative, because there is not only no need for a postoperative face-down posture, but even more importantly the use of silicone oil avoids excessive manipulation in the macular hole area, except maybe for a careful aspiration using a soft tipped needle. A known drawback of silicone oil tamponade is the need for a secondary surgery for oil removal. In addition, its efficacy and safety are still being discussed [11,21-24].

Given this background, we conducted the present study to investigate the functional and anatomic results of macular hole surgery using silicone oil as a tamponade (5.000 centistokes [cst]) in 56 patients/57 eyes with a macular hole. Patients were mostly elderly (mean age of 71.5 ± 7.9 years) with a predominance of females (67%) similar to previous publications [25]. Higher age and comorbidities were reasons for the choice of an endotamponade with silicone oil, which is reflected by the fact that our patients with a primary silicone oil endotamponade were significantly older than patients in whom silicone oil was used in secondary surgeries (73.2 ± 7.0 years vs. 67.4 ± 8.4 years; $p=0.01$). Additionally, nine of 56 patients (16.1%) had refused to a gas endotamponade explicitly because they feared postoperative prone position. We included macular holes of all sizes from 94 μm up to 932 μm , which is reflected by the large range of function before surgery.

In 40 eyes of 39 patients the PPV with silicone oil was conducted as first intervention to close the macular hole and an anatomical closure was achieved in 36 eyes (90.0%). In a comparable study, Pertile and Claes reported on 35 eyes with macular holes stage 3-4, which were treated by means of PPV and peeling of ILM with silicone oil tamponade, and observed a higher closure rate of 97.1% [24]. Stalmans et al. compared 5.000 vs. 1.000 cst silicone oil ($n=36$ eyes each) as an endotamponade and even reported a closure rate of 100% [26]. In other studies, the closure rates covered a range from 65-100% [11,19,21-23]. Therefore, the closure rate of 90% as observed in our series is quite in line with the published literature and comparable to other studies [11,23,24].

The closure rate in our 17 patients who underwent a secondary surgery using silicone oil as a tamponade following failed gas

endotamponade was slightly lower (14 out of 17 eyes, 82.4%) compared to the aforementioned group. Previously reported results of anatomical closure following reoperation with gas tamponade varied in a similar range from 73%-91% [27].

In total, we could not achieve a closure of the macular hole in 7 eyes; there were no correlations to age, gender, primary/secondary SiO, or hole diameter/hole size. Our results indicate that the use of silicone oil in macular hole surgery is not disadvantageous for the patient compared to surgery using a gas endotamponade both for primary and secondary cases and appears beneficial for a great spectrum of macular hole sizes.

Successful closure of the macular hole is a prerequisite but not a guarantee for improved visual acuity [11,28,29]. In our series of macular hole surgery with silicone oil endotamponade, the visual acuity improved in 82.5%, remained unchanged in 10.0%, and worsened in 7.5% of primarily treated eyes. The mean value of best corrected visual acuity decreased from 1.01 ± 0.36 logMAR units preoperatively to 0.59 ± 0.31 logMAR units postoperatively ($p<0.001$), corresponding to a factor of improvement of 2.63 ± 2.57 .

The functional results of other studies on silicone oil endotamponade are variable and partially contradictory. Karia et al. observed any improvement in visual acuity only in 38% of their patients [30], while in the study of Goldbaum et al. the logMAR value of visual acuity improved by an average of 0.26 to 0.61 (20/81) [19]. Similar results were obtained by Ivanovska-Adjievaska et al. who found a mean BCVA improvement from 0.6 logMAR units to 0.8 logMAR units and a significant reduction of metamorphopsia in all patients [31]. Two-armed studies comparing gas versus silicone oil often favored gas endotamponade. Lai et al. reported that the final median visual acuity for the gas group was significantly better than for the oil group (20/50 vs. 20/70; $p=0.047$) [21]. Similar results were obtained by Tafuya et al. who saw improvements in visual acuity more frequently in eyes treated with gas endotamponade than following silicone oil endotamponade [23]. In another study visual acuity improved to 20/70 or better in only 17.3% eyes of the SiO group but in 73.0% eyes of the gas group [11]. In contrast, Pertile and Claes observed an excellent recovery of visual acuity up to 1.0 more frequently in the group treated with silicone oil tamponade. A visual acuity of 0.4 or better was seen in 74% of eyes in the SiO group, but only in 47% of eyes in the gas group ($p=0,0217$) [24].

In our series there were no significant differences in postoperative function comparing primary versus secondary surgery: The mean factor of BCVA improvement was 3.09 ± 2.52 in our primary and 1.82 ± 2.40 in our secondary treated eyes ($p=0.07$). A greater difference was observed by Kumar et al. who found a mean visual improvement of 0.41 logMAR units in primary and disappointing 0.03 logMAR units in secondary cases [22].

The partly very deviating results comparing studies on silicone oil assisted macular hole surgery are difficult to interpret. One reason may be different study designs with small or variable sample sizes as well as differences in age, comorbidities and ophthalmologic medical history of the patients. Results may

also be influenced by variable classifications, hole sizes and measurements as well as duration of symptoms. Surgeons' proclivity for a certain technique and corresponding surgical skill may also play a role. Furthermore, the surgical modalities may vary with regard to the silicone oil used (1.000, 2.000 and 5.000 cst) and the additional application of surgical adjuncts such as autologous serum [19,22].

However, we strongly believe that silicone oil tamponade to seal a macular hole is still a very useful technique for several reasons. One major advantage is the fact that, in contrast to "newer" surgical approaches [13-17], no manipulation of the macular hole and the neurosensory is required, nor is there a danger to negatively affect the subretinal space and the RPE. Furthermore, the installation of a silicone oil tamponade in macular hole surgery is quite easy to perform. More importantly, previous experimental studies evaluated the fluid under silicone ("sub-silicone oil fluid") and examined multiple inflammatory cytokine levels and osmotic pressures [32]. Lambrou et al. performed an animal experiment to examine the effect of silicone oil or sub-silicone oil fluid on RPE cells [33]. RPE is thought to be one of the major players in inducing PVR by biologically promoting epithelial-mesenchymal transition [33,34]. The authors suggested that silicone oil in the vitreous cavity had an increased mitogenic activity for RPE cells compared to gas-filled or fluid-filled-vitreous [33]. In 2004, Asaria and coworkers also demonstrated that the concentration of fibrogenic (bFGF) and inflammatory (IL-6) growth factors and protein is raised in retro-silicone oil fluid [35]. They suggested that this finding may contribute to the process of retro-oil perisilicone proliferation and subsequent fibrocellular membrane formation. Taken together, this data underline the fact that silicone oil fill of the vitreous cavity is associated with fibrocellular proliferation which may be very beneficial to assist the closure of macular holes, especially in cases with persistent holes and larger macular hole diameters.

Conclusion

In summary, we believe that silicone oil tamponade in selected macular hole cases should not be forgotten in the times of new and "sexier" surgical approaches for these cases, since it provides good anatomical and functional results without excessive manipulation at the central retina. We believe that there is an unmet need for larger, multicentric studies with a stringent study protocol comparing different surgical techniques especially for large and persistent macular holes including silicone oil assisted and recent techniques using autologous transplants in macular hole surgery.

Ethics Approval

Ethical approval was waived by the local Ethics Committee of Ludwig Maximilian University of Munich in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.

Conflicts of Interest

The authors declare that they have no conflict of interest.

Author Contributions Statement

All authors fulfill the ICMJE criteria for authorship.

References

1. Kelly NE, Wendel RT. Vitreous surgery for idiopathic macular holes. Results of a pilot study. *Arch Ophthalmol.* 1991;109:654-9.
2. Gupta D. Face-down posturing after macular hole surgery: A review. *Retina.* 2009;29:430-43.
3. Feng X, Li C, Zheng Q, et al. Risk of silicone oil as vitreous tamponade in pars plana vitrectomy: A systematic review and meta-analysis. *Retina.* 2017;37:1989-2000.
4. Vaziri K, Schwartz SG, Kishor KS, et al. Tamponade in the surgical management of retinal detachment. *Clin Ophthalmol.* 2016;10:471-6.
5. Briand S, Chalifoux E, Tourville E, et al. Prospective randomized trial: Outcomes of sf(6) versus c(3)f(8) in macular hole surgery. *Can J Ophthalmol.* 2015;50:95-100.
6. Hasegawa Y, Hata Y, Mochizuki Y, et al. Equivalent tamponade by room air as compared with sf(6) after macular hole surgery. *Graefes Arch Clin Exp Ophthalmol.* 2009;247:1455-9.
7. Rahman R, Madgula I, Khan K. Outcomes of sulfur hexafluoride (sf6) versus perfluoroethane (c2f6) gas tamponade for non-posturing macular-hole surgery. *The Br J Ophthalmol.* 2012;96:185-8.
8. Duker JS, Kaiser PK, Binder S, et al. The international vitreomacular traction study group classification of vitreomacular adhesion, traction, and macular hole. *Ophthalmology.* 2013;120:2611-9.
9. Pieczynski J, Kuklo P, Grzybowski A. Pars plana vitrectomy with silicone oil tamponade for primary and secondary macular hole closure: Is it still a useful procedure? *Eur J ophthalmol.* 2018;28:503-14.
10. Xia S, Zhao XY, Wang EQ, et al. Comparison of face-down posturing with nonsupine posturing after macular hole surgery: A meta-analysis. *BMC ophthalmology.* 2019;19:34.
11. Couvillion SS, Smiddy WE, Flynn HW Jr., et al. Outcomes of surgery for idiopathic macular hole: A case-control study comparing silicone oil with gas tamponade. *Ophthalmic Surg Lasers Imaging.* 2005;36:365-71.
12. Morimoto E, Shimada Y, Sugimoto M, et al. Adherence to face-down and non-supine positioning after macular hole surgery. *BMC ophthalmology.* 2018;18:322.
13. Michalewska Z, Michalewski J, Adelman RA, et al. Inverted internal limiting membrane flap technique for large macular holes. *Ophthalmology.* 2010;117:2018-25.
14. Grewal DS, Mahmoud TH. Autologous neurosensory retinal free flap for closure of refractory myopic macular holes. *JAMA ophthalmology.* 2016;134:229-30.

15. Rizzo S, Caporossi T, Tartaro R, et al. A human amniotic membrane plug to promote retinal breaks repair and recurrent macular hole closure. *Retina*. 2019;39:S95-S103.
16. Yopez JB, Murati FA, De Yopez J, et al. Anterior lens capsule in the management of chronic full-thickness macular hole. *Retin Cases Brief Rep*. 2018;12:286-90.
17. Fotis K, Alexander P, Sax J, et al. Macular detachment for the treatment of persistent full-thickness macular holes. *Retina*. 2019;39:S104-S107.
18. Fawcett IM, Williams RL, Wong D. Contact angles of substances used for internal tamponade in retinal detachment surgery. *Graefes Arch Clin Exp Ophthalmol*. 1994;32:438-44.
19. Goldbaum MH, McCuen BW, Hanneken AM, et al. Silicone oil tamponade to seal macular holes without position restrictions. *Ophthalmology*. 1998;105:2140-7.
20. Elliott DB. The good (logmar), the bad (snellen) and the ugly (bcva, number of letters read) of visual acuity measurement. *Ophthalmic Physiol Opt*. 2016;36:355-8.
21. Lai JC, Stinnett SS, McCuen BW. Comparison of silicone oil versus gas tamponade in the treatment of idiopathic full-thickness macular hole. *Ophthalmology*. 2003;110:1170-4.
22. Kumar V, Banerjee S, Loo AV, et al. Macular hole surgery with silicone oil. *Eye (Lond)*. 2002;16:121-5.
23. Tafoya ME, Lambert HM, Vu L, et al. Visual outcomes of silicone oil versus gas tamponade for macular hole surgery. *Seminars in ophthalmology*. 2003;18:127-131.
24. Pertile G, Claes C. Silicone oil vs. Gas for the treatment of full-thickness macular hole. *Bull Soc Belge Ophthalmol*. 1999;274:31-6.
25. Singh SR, Hariprasad SM, Narayanan R. Current management of macular hole. *Ophthalmic Surg Lasers Imaging Retina*. 2019;50:61-8.
26. Stalmans P, Pinxten AM, Wong DS. Cohort safety and efficacy study of siluron2000 emulsification-resistant silicone oil and f4h5 in the treatment of full-thickness macular hole. *Retina*. 2015;35:2558-66.
27. Christmas NJ, Smiddy WE, Flynn HW Jr. Reopening of macular holes after initially successful repair. *Ophthalmology*. 1998;105:1835-8.
28. Brooks HL Jr. Macular hole surgery with and without internal limiting membrane peeling. *Ophthalmology*. 2000;107:1939-48.
29. Freeman WR, Azen SP, Kim JW, et al. Vitrectomy for the treatment of full-thickness stage 3 or 4 macular holes. Results of a multicentered randomized clinical trial. The vitrectomy for treatment of macular hole study group. *Arch Ophthalmol*. 1997;115:11-21.
30. Karia N, Laidlaw A, West J, et al. Macular hole surgery using silicone oil tamponade. *Br J Ophthalmol*. 2001;85:1320-3.
31. Ivanovska-Adjievska B, Boskurt S, Semiz F, et al. Treatment of idiopathic macular hole with silicone oil tamponade. *Clin Ophthalmol*. 2012;6:1449-54.
32. Kaneko H, Takayama K, Asami T, et al. Cytokine profiling in the sub-silicone oil fluid after vitrectomy surgeries for refractory retinal diseases. *Sci Rep*. 2017;7:2640.
33. Lambrou FH, Burke JM, Aaberg TM. Effect of silicone oil on experimental traction retinal detachment. *Arch Ophthalmol*. 1987;105:1269-72.
34. Takayama K, Kaneko H, Hwang SJ, et al. Increased ocular levels of microrna-148a in cases of retinal detachment promote epithelial-mesenchymal transition. *Invest Ophthalmol Vis Sci*. 2016;57:2699-705.
35. Asaria RH, Kon CH, Bunce C, et al. Silicone oil concentrates fibrogenic growth factors in the retro-oil fluid. *Br J ophthalmol*. 2004;88:1439-42.

***Correspondence to**

Prof. Dr. Carl-Ludwig Schönfeld
Department of Ophthalmology,
Eyeclinic Herzog Carl-Theodor
München,
Germany
E-mail: cb.schoenfeld@gmx.net