

Use of Heavy Silicon Oil as Intraocular Tamponade for Inferior Retinal Detachment Complicated by Proliferative Vitreoretinopathy: A Multicentric Experience

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Keywords

Heavy silicon oil · Retinal detachment · Proliferative vitreoretinopathy · Vitrectomy · Tamponade

Abstract

Introduction: This is a multicentric study on the use of heavy silicon oil (HSO) as an intraocular tamponade for inferior retinal detachment (RD) complicated by proliferative vitreoretinopathy (PVR). **Methods:** 139 eyes treated for RD with PVR were included in the study. 10 (7.2%) were affected by primary RD with inferior PVR, while 129 (92.8%) were affected by recurrent RD with inferior PVR. 102 eyes (73.9%) had received a silicon oil (SO) tamponade in a previous intervention prior to receiving HSO. Mean follow-up was 36.5 (standard deviation = 32.3) months. **Results:** The median interval between HSO injection and removal was 4 months (interquartile range: 3). At the time of HSO removal, the retina was attached in 120 eyes (87.6%), whereas in 17 eyes (12.4%), it had re-detached while the HSO was in situ. 32 eyes (23.2%) showed recurrent RD. A subsequent RD relapse was

observed in 14.2% of cases with no RD at the time of HSO removal, and in 88.2% if an RD was present at the time of HSO removal. Advancing age showed a positive association with retinal attachment at the end of follow-up, while the risk of RD relapse at the end of the follow-up showed a significant negative association with HSO tamponade duration and with the use of SO rather than air or gas as post-HSO tamponade materials. Mean best corrected visual acuity was 1.1 logarithm of minimum angle of resolution at all follow-up time points. 56 cases (40.3%) needed treatment for elevated intraocular pressure (IOP), with which no clinically relevant variables were associated during follow-up. **Conclusion:** HSO represents a safe and effective tamponade in cases of inferior RD with PVR. The presence of RD at the time of HSO removal is a negative prognostic factor for the development of a subsequent RD relapse. According to our findings, in cases of RD at the time of HSO removal, a short-term tamponade should definitely be avoided, in favor of SO. Special attention must be paid to the risk of IOP elevation, and patients should be closely monitored.

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Introduction

Inferior retinal detachment (RD) complicated by proliferative vitreoretinopathy (PVR) represents a significant surgical challenge, especially given its high recurrence rate. PVR is estimated to occur in 5–10% of all RD cases and represents the main cause of poor anatomical and functional outcomes after surgery [1–4]. While it may manifest prior to surgical intervention for RD, it more commonly occurs thereafter [5, 6]. It is characterized by the growth of membranes on both surfaces of the detached retina and on the posterior hyaloid. Posterior contraction of these membranes causes distortion of the retina and keeps it detached [7]. The pathogenesis of this complication progresses through several steps: (1) migration of cells, mainly retinal pigment epithelial and glial cells; (2) proliferation of the migrating cells; (3) membrane development; (4) contraction of the cellular membrane; (5) extracellular collagen production; and (6) creation of fixed folds in the retina. Despite these pathophysiological sequelae, no relevant advances in clinical management have yet been made [5, 8]. Pars plana vitrectomy (PPV) and silicone oil (SO) tamponade are the most widely adopted surgical approaches to treat advanced PVR. Due to its high surface tension and viscosity, SO covers retinal defects and prevents the passage of vitreous fluid into the subretinal space. In addition, SO mechanically inhibits the contraction of epiretinal membranes and acts as a space filler that compartmentalizes proliferative cells and biochemical mediators in the vitreous cavity. SO has a specific gravity of 0.97 g/cm^3 which is lower than that of water, and although it is an excellent tool in PVR RD of the upper parts, inferior sectors are left poorly supported and vulnerable to PVR pathogenesis [9–12]. Perfluorohexyloctane (F6H8) was the first heavy tamponade to be utilized in such cases; however, due to significant side effects, its use has since ceased [10, 13]. Densiron® 68 (Fluoron GmbH, Neu-Ulm, Germany) is a new-generation heavy SO (HSO) with high specific gravity [8]. It is a mixture of 70% 5,000 cSt silicone oil and 30% F6H8. It has a specific gravity of 1.06 g/cm^3 and a viscosity of 1,387 cSt. HSO is a combination of SO with heavy liquid and represents a tamponade agent that is potentially ideal for inferior proliferations; however, the use of HSO in inferior PVR is controversial with some studies reporting an increased incidence of secondary glaucoma and uveitis [14–20].

The aim of our study was to investigate the effectiveness and safety of HSO in the treatment of inferior RD complicated by PVR. In particular, the primary aim was

to study the HSO effectiveness in achieving retinal attachment, preventing RD relapse. The secondary outcome is to evaluate HSO limits and complications arising from its use.

Methods

This was a consecutive, retrospective, nonrandomized, multicentric case review. The study was performed in accordance with the current version of the Declaration of Helsinki (52nd WMA General Assembly, Edinburgh, Scotland, October 2000), and written informed consent to participate in the study was obtained from participants prior to participation. Institutional review board/ethics committee approval was also obtained (Verona and Rovigo Ethical Committee, approval number Prog. 2612CESC). This research did not receive grants from any funding agency in the public, commercial, or not-for-profit sectors. The authors have no conflicts of interest to declare. Raw data are stored in IRCCS Sacro Cuore Don Calabria Hospital and are available on request.

We reviewed the records of 145 eyes of 145 patients affected by rhegmatogenous RD complicated by PVR involving the inferior quadrants who had consecutively undergone PPV with HSO tamponade at IRCCS Sacro Cuore Don Calabria Hospital in Verona and Sant'Anna Hospital in Brescia between 2006 and 2017. Patients treated for both primary and recurrent RD with inferior PVR were included. Exclusion criteria were a postoperative follow-up of less than 4 months, preoperative myopia higher or equal to 6.0 D, previous history of uveitis, and ocular surgery for something other than primary or recurrent RD, inadequate follow-up such as not to allow a reliable reconstruction of the eye clinical course. In case of pre-phaco unknown refractive data, patients were not included.

All surgical procedures were carried out by experienced surgeons who performed either 20-gauge or 23-gauge PPV. In cases of previous SO tamponade, the oil was removed at the beginning of the procedure. Phakic patients underwent cataract extraction at the time of HSO injection. Cataract removal was conducted as the first step of surgery, through phacoemulsification, and an intraocular lens was then implanted in the bag.

In cases of recurrent RD, possible vitreous remnants were stained with triamcinolone and removed up to the vitreous base, which was carefully shaved. PVR membranes were mostly peeled using a bimanual technique with a chandelier light. The retina was stabilized with PFCL. In cases of residual contraction that was not resolvable with peeling, a retinectomy was performed. In case of a previous retinectomy, our surgical steps were almost the same. Membranes were peeled as completely as possible and, in case of residual contraction affecting retinal attachment, retinotomy was extended. A 360° endolaser was used, and HSO tamponades were achieved through HSO/air/PFCL exchanges or direct HSO/PFCL exchange. After a variable interval, HSO was removed using a 20-gauge or 23-gauge vitrectomy system. In cases of RD recurrence, epiretinal or subretinal membranes were peeled and an appropriate endotamponade (air, SF₆, SO, or HSO) was selected according to the retinal status. In case of RD with PVR, either SO or HSO was used according to the site (superior or inferior) of the prevalent PVR membranes. In case of RD with no PVR, air was generally chosen. SF₆ was then chosen in case of very mild PVR with flat retina or limited RD.

Table 1. Baseline characteristics

	<i>n</i> (%)	Mean (SD)	Range
Hospital			
Center 1 - Verona	98 (70.5)		
Center 2 - Brescia	41 (29.5)		
Gender			
Male/female	75/64		
Age			
Years		60.4 (14.4)	18–85
Refraction			
MSE <6 D	93 (73.8)		
MSE >6 D	33 (26.2)		
Lens status			
Phakic	24 (17.8)		
Pseudophakic	107 (79.2)		
Aphakic	4 (3)		
Previous surgery			
Yes	129 (92.8)		
No	10 (7.2)		
Number of previous surgeries		1.67 (1.15)	0–6
Previous SO tamponade	102 (73.9)		
Macula involvement (on/off/not specified)	35/88/16		
BCVA (logMAR)		1.44 (0.88)	0–4
IOP, mm Hg		14.18 (5.11)	2–40
Previously raised IOP	8 (5.98)		

SD, standard deviation; MSE, mean spherical equivalent; SO, silicon oil; BCVA, best corrected visual acuity; IOP, intraocular pressure.

The follow-up visit prior to HSO administration was considered to be baseline. At baseline and at each follow-up visit thereafter, a complete ophthalmic examination was performed, including best corrected visual acuity (BCVA) measurement, slit-lamp biomicroscopy, intraocular pressure (IOP) evaluation, and dilated fundus examination with a 90-diopter indirect lens. A Snellen chart was used for the assessment of BCVA and converted into the logarithm of minimum angle of resolution (logMAR) for statistical analysis. The semi-quantitative scale “counting fingers” was transposed into logMAR 2 and “hand motion” into logMAR 3. 20 mm Hg was arbitrarily chosen as a cut-off value for raised IOP. With the exception of visits at 1 week and 1 month after HSO injection, the time was not always the same. On average, the patients were visited monthly till HSO removal and subsequently according to the clinical needs and additional surgeries.

Statistical Analysis

Descriptive statistics, measures of variability, and precision summarized demographic and clinical data, depending on the type of variable (categorical or continuous) performed. A skewness or kurtosis test was carried out to test the normality in distribution of continuous variables. A two-sample *t* test for paired normally distributed data or its correspondent nonparametric Wilcoxon matched-pairs signed-ranks test was performed to compare the means of BCVA and IOP, as measured at baseline and each follow-up. Retinal reattachment at the end of the follow-up period, RD recurrence during follow-up, and risk of raised IOP during follow-

up were considered to be dependent variables that were modeled by multivariate logistic regression as adjusted for confounders (eye, sex, age, previous surgeries, number of previous surgeries, previous SO tamponade, HSO removal timing, tamponade after HSO removal, number of reinterventions).

Stata software was used to perform statistical analysis (StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC.). A *p* value <0.05 was considered to be statistically significant.

Results

139 patients met the inclusion criteria. 6 subjects were excluded for an inadequate follow-up. The demographic and baseline characteristics of which are summarized in Table 1. 10 subjects (7.2%) were affected by primary RD with inferior PVR, while 129 (92.8%) were affected by recurrent RD with inferior PVR and had undergone a mean of 1.7 previous surgeries (standard deviation = 1.2). 102 eyes (73.9%) had undergone SO tamponade before HSO administration. At baseline, 8 cases (6.0%) had already been treated with topical therapy for ocular hypertension. Mean follow-up was 36.5 (standard deviation = 32.3) months (range 4–152 months). The median

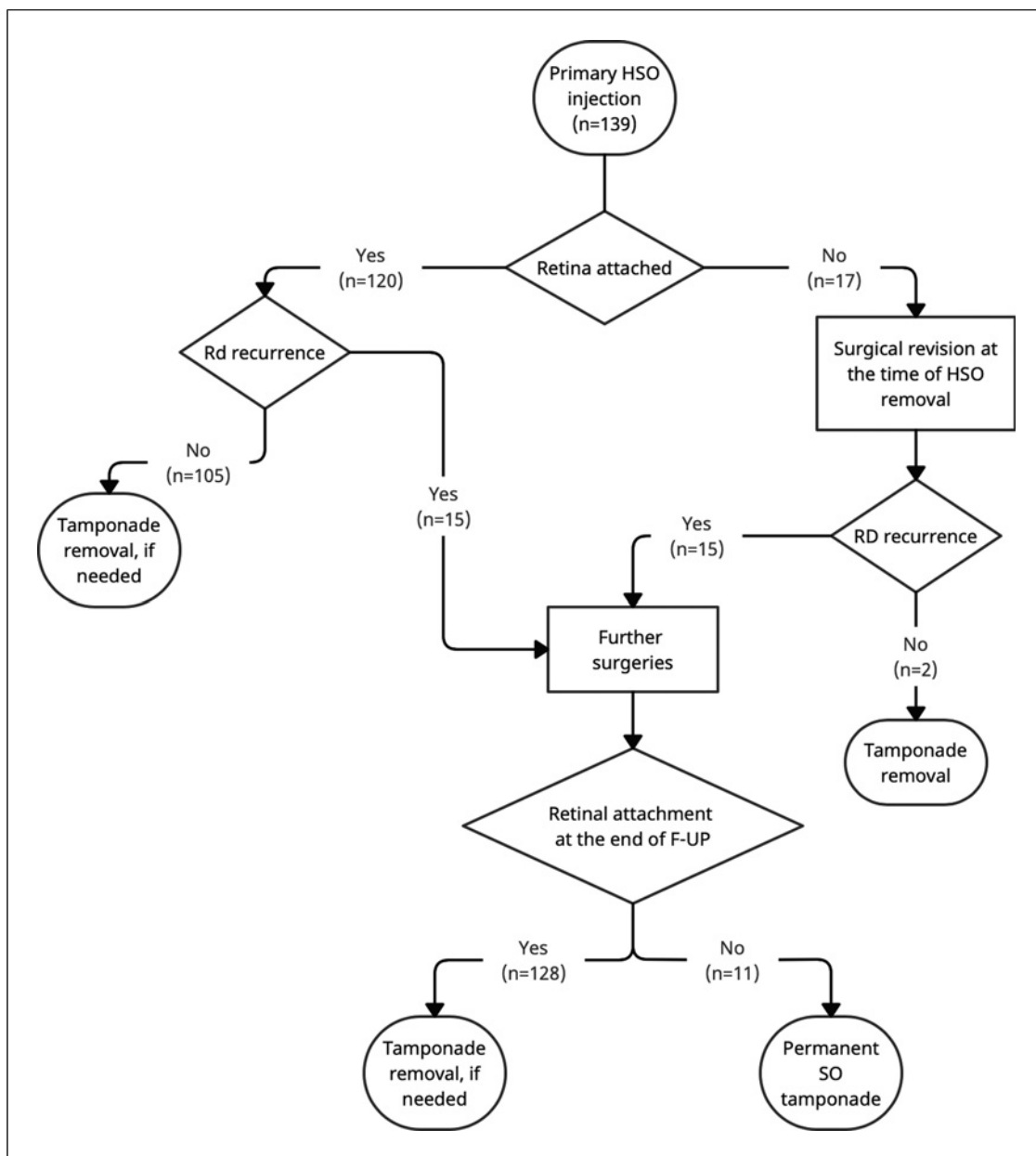


Fig. 1. Flow diagram showing the patients' postoperative follow-up in term of retinal attachment.

interval between HSO injection and removal was 4 months (interquartile range: 3. Range 1–24 months).

Figure 1 shows the postoperative follow-up of the included eyes in term of retinal attachment. Retinal reattachment achieved with one HSO operation (and subsequent removal) without remaining tamponade was achieved in 120 eyes (87.6%). In these cases, eyes were filled with balanced salt solution ($n = 2$) or air ($n = 118$) after HSO removal. Conversely, 17 eyes (12.4%) had re-detached retinas with HSO in situ. These cases underwent surgical

revision, and gas ($n = 1$), SO ($n = 14$), or HSO ($n = 2$) was chosen for intraocular tamponade. In all cases, the retina was reattached at the end of the surgical procedure.

Thirty two eyes (23.2%) showed recurrent RD, including those that received both SO and gas tamponade at the time of HSO removal. The RD recurrence dropped to 14.2% (15 cases) in the subgroup of eyes with an attached retina at the time of HSO removal. 15 out of 17 cases (88.2%) with RD at time of HSO removal developed a subsequent RD recurrence.

Table 2. Multivariate logistic regression models for retinal reattachment at the end of the follow-up

	Odds ratio [95% CI]	<i>p</i> value
Sex	0.49 [0.17–1.39]	0.177
Advancing age	1.03 [1.01–1.05]	0.014*
Refraction	0.89 [0.28–2.87]	0.846
Previous surgeries	1.58 [0.22–11.41]	0.648
Number of previous surgeries	1.29 [0.73–2.29]	0.379
Previous SO tamponade	0.83 [0.20–3.47]	0.800
HSO removal timing	1.31 [0.15–11.84]	0.809
SO tamponade after HSO removal	0.75 [0.06–9.87]	0.826
Number of reinterventions	0.10 [0.005–1.82]	0.120

SO, silicon oil; HSO, heavy SO; CI, confidence interval. *Statistically significant association.

Following SO or HSO removal, 95 eyes (68.4%) required no further surgery, whereas 32 eyes (23.0%) required 1 further surgery, and 12 eyes (8.6%) required more than 1. Final surgical success rate was 92.8% (128 eyes). In these cases, a flat retina without tamponade at the end was achieved. Eleven cases (7.2%) showed persistent RD and required permanent SO tamponade. Retinal attachment was achieved in 128 eyes (92.8%) at the end of the follow-up, while only 11 cases (7.2%) showed persistent RD and required long-term SO tamponade.

According to multivariate logistic regression models, no significant associations were found with retinal attachment at the time of HSO removal. The risk of RD relapse after HSO removal showed a marginally significant positive association with advancing age (OR = 1.06, *p* = 0.07) and a stronger positive association with the use of SO over air or gas as tamponade after HSO removal (OR = 7.01, *p* = 0.03) and with a number of further reinterventions higher than 2 (OR = 44, *p* = 0.001).

Advancing age showed a marginally significant positive association with retinal attachment at the time of HSO removal (OR = 1.06, *p* = 0.07). No other baseline variables, including previous surgeries or previous SO tamponade, showed a significant association (Table 2). Conversely, the risk of RD relapse after HSO removal showed a significant negative association with HSO tamponade duration (OR = 0.82, *p* = 0.02) and with the use of SO over air or gas as tamponade after HSO removal (OR = 14.0, *p* < 0.0001). In such cases, neither previous surgery nor previous SO tamponade showed any significant association (Table 3).

The mean BCVA after HSO injection was 1.1 logMAR (0.6) at each time point (1 week and 1 month after HSO injection and at the end of follow-up). BCVA variations

in comparison to those of baseline were also recorded at each time point. One month after HSO administration, an improvement was noted in about 52.1% of cases, while 29.6% worsened, and 18.3% remained unchanged. Immediately before HSO removal, 50% of eyes showed improvement, 27.5% worsened, and 22.5% remained unchanged. At the end of the follow-up, 64.1% had improved, 23.1% worsened, and 12.8% were the same; however, the variations observed were not statistically significant.

During follow-up, 77 eyes (55.8%) developed no complications. Anterior chamber inflammatory reactions were observed in 5 cases (3.6%) during the initial postoperative period, but these were quickly resolved under intensified topical steroid treatment. The mean IOP was 17.0 mm Hg (5.8) 1 week after HSO injection, 15.4 mm Hg (5.8) 1 month after HSO injection, and 15.4 mm Hg (4.6) immediately before HSO removal. At the end of follow-up, the mean IOP was 14.4 mm Hg (5.1). One week after HSO administration, IOP was significantly higher than at baseline (*p* = 0.0001). No other significant differences were found at any other time points. Raised IOP was found in 39 cases (33.1%) 1 week after HSO administration and in 19 cases (14.8%) 1 month after HSO administration. Immediately before HSO removal, elevated IOP was found in 13 cases (9.8%), and in 11 cases (8.2%) at the end of follow-up. 56 eyes (40.3%) needed treatment for raised IOP during the follow-up period; in 51 cases (36.7%), it was resolved by chronic topical therapy, while in 5 cases (3.6%), glaucoma valve implantation was required after HSO removal. A multivariate logistic regression model showed that no variables predicted the risk of raised IOP during follow-up, other than male sex (OR = 2.55, *p* = 0.021).

Table 3. Multivariate logistic regression models for RD recurrence development during the follow-up

	Odds ratio [95% CI]	<i>p</i> value
Eye	0.50 [0.17–1.44]	0.200
Sex	1.1 [0.37–2.76]	0.985
Age	1.00 [0.97–1.02]	0.675
Refraction	2.15 [0.66–6.94]	0.202
Previous surgeries	0.37 [0.04–3.36]	0.376
Number of previous surgeries	0.96 [0.58–1.59]	0.878
Previous SO tamponade	1.12 [0.27–4.59]	0.878
HSO tamponade duration	0.82 [0.69–0.97]	0.022*
Post-HSO removal tamponade (air/gas or SO/HSO)	13.97 [4.75–41.05]	<0.0001*

SO, silicon oil; HSO, heavy SO; CI, confidence interval. *Statistically significant association.

Discussion

When air or gas tamponade are not viable options, complicated RD can be treated with conventional SO [21, 22]. In cases of PVR, retinal attachment rate of superior and inferior detachments is reported to be between 30 and 95% [23, 24]. As SO and gas are lighter than water, inferior RD is more difficult to tamponade, resulting in higher reproliferation rates in the inferior free space. In the last 20 years, great efforts have been made to develop an effective and well-tolerated tamponade with a heavier-than-water density [25–27]. Perfluorocarbons liquids (such as perfluorooctane) are very effective intraoperatively but have unacceptable safety profiles for long-term intraocular tamponade. HSO represents a more suitable inferior tamponade agent in model eye experiments and in recent clinical studies as compared to other available agents [13, 25, 26, 28, 29]. Nevertheless, its use is limited due to the risks of developing inflammation, emulsification, IOP elevation, and cataract formation [30–32]. HSO is heavier than water and sufficiently viscous to have a much lower propensity for dispersion (compared to F6H8 on its own). Long-term heavy tamponades with a specific gravity greater than that of water function most effectively as postoperative tamponades of the inferior quadrants in particular.

Several studies have described a high retinal attachment rate after HSO use. Li et al. [33] reported the outcome in 21 eyes affected by RD complicated by PVR. They showed retinal attachment following 1 surgery in 85.7% of eyes and in an additional 5% of eyes with further surgery. They also described a significant increase in BCVA. Notably, in their cohort, the large majority of patients were affected by primary RD, which will likely have had a significant impact on visual acuity. Similarly, Hussain et al. [14] showed a 91% retina attachment rate in

12 eyes having undergone HSO tamponade for inferior RD with or without PVR either as a primary or secondary intervention. A slightly lower success rate was described by Levasseur (85% with one procedure and 95% with additional surgeries) [20]. Further to this, Auriol et al. [17] have reported anatomical success in 92.5% of cases among 27 eyes with severe anterior PVR involving the inferior quadrant and requiring a large inferior retinectomy. HSO was removed in 19 patients between 5 and 42 weeks (mean 14 weeks) after initial surgery with anatomical success being achieved in 18 patients after HSO removal. HSO was maintained in 7 patients. The authors did not report the number of reinterventions required before achieving retinal reattachment. Furthermore, Sandner et al. [34] have reported a primary anatomical success rate of 33.3%. However, the surgical success increased to 75% after reintervention, even without the use of an additional encircling band. Mean BCVA improved from 2.95 (1.21) to 1.87 (1.32). This change was statistically significant, even if clinically not relevant. Previously, the same authors reported a reattachment rate of 45.8% in 48 eyes affected by complex inferior RD with the mean BCVA improving from logMAR 1.66 (1.03) to 1.47 (0.97), although this was not statistically significant [35]. Recently, Davidson presented the results of a retrospective multicenter study on 134 cases undergone HSO administration. The series is potentially heterogeneous, since no restrictive inclusion criteria had been reported. However, they reported a primary success rate in term of retinal attachment of 48–5% and a final rate of 73.4%.

The largest series in the literature describes 122 eyes including cases of PVR, RD relapse, RD arising from posterior or inferior retinal breaks, and inability of the patient to posture. 71.3% patients achieved retinal reattachment with one surgery and ultimately no tamponade,

and 83.6% with more than one surgery. 12 of 122 eyes had permanent SO tamponade, and the retina was attached in all but 2 eyes. Mean BCVA rose from 1.38 logMar (0.87) to 1.06 (0.83) [18]. In our series, high-myopic patients were excluded to reduce the sample variability. In fact, high myopia complications are characterized by different pathophysiological and clinical features. Although the large majority of included cases were recurrent RD, we also included a few of primary RD with inferior PVR. We believe that should not affect the results, since the totality of cases share the peculiarity of an inferior PVR that guided the choice of HSO as endotamponade.

In our series, retinal attachment at the first HSO administration was achieved in 86.7% of cases. These data substantially aligned with the literature. We report an improvement in BCVA in 64.5% of cases, although a statistically significant increase in mean BCVA was not observed. Such variability in functional outcomes might be attributable to differences in case selection. Sander et al. [35], for example, applied HSO exclusively to cases that had failed previous retinal surgery. It is important to note that the two centers involved in our study are tertiary referral hospitals that include advanced cases, often sent after failure of several previous interventions. As far as we know, our series is characterized by the longest follow-up reported to date.

In our series, encircling scleral buckling (ESB) was not used as an adjuvant of PPV. ESB is not routinely used in the management of RD in our center given the lack of robust evidence supporting its systematic use. Comparing 23-gauge PPV with HSO tamponade and 360° endolaser versus 20-gauge PPV with ESB and an SF6 gas tamponade for the repair of primary pseudophakic RRD with inferior retinal breaks, Romano et al. [36] found that the two techniques had similar efficacy. Thus, supplementary scleral buckling may not be necessary in the context of HSO tamponade. Moreover, Ghoraba et al. [37] have demonstrated that the use of ESB in combination with PPV and SO offered no additional effect on either the anatomical success or the rate of macular hole closure in the management of myopic macular hole RD. Eleinen et al. [38] described similar anatomical and functional outcomes by combining PPV with ESB or inferior retinectomy for the treatment of primary RRD with PVR and inferior breaks. A recent study by Rossi et al. [39] using an elegant *in vivo* model has demonstrated that 360° scleral indentation did not improve SO-retinal contact and that it promotes a significant shear stress increase at the indentation site. Even when a 90% SiO fill was considered, none of the retinal sectors maintained a satisfying tamponade contact, regardless of the positioning. Conversely,

Storey et al. [40] found that PPV with ESB was associated with significantly higher rates of anatomical success compared with PPV alone in patients with RRD at high risk of postoperative PVR. However, taken together, these data do not demonstrate the superiority of PPV with ESB in preventing RRD relapse secondary to PVR.

The mean HSO tamponade duration reported in the literature varies from 5 to 35 weeks [14, 17, 18, 33]. In our study, HSO was left *in situ* for a median time of 4 months, with the multivariate models suggesting that HSO tamponade duration was associated with a lower RD relapse risk. This might support the idea of deferring HSO removal, especially when it has been administered following the removal of severe PVR. This could present an original and interesting finding; however, it is important to note that, in cases of RD relapse, further surgery with HSO removal is generally performed promptly thereafter. Recently, Dubroux et al. [41] investigated the effect of tamponade duration on retinal changes induced by SO in patients who had undergone successful RRD surgery. SO tamponade was found to cause a thinning of all retinal layers, mainly affecting the inner retinal layer. However, these changes resolved following SO extraction and were not affected by longer tamponade duration. A possible pathophysiological explanation may include mechanical pressure on the retina induced by the SO bubble, retinal ionic environmental changes, and inflammatory reactions involving microglial cells and various cytokines [42]. However, SO specific gravity is 0.97; thus, the mechanical effect exerted on the retina is essentially negligible.

Previous studies have failed to demonstrate an association between tamponade duration and RD relapse risk. This may be due to a tamponade period of 3–6 months being insufficient to reveal any such effects [42–44]. However, as far as we know, such an association has not been investigated before.

The presence of RD at the time of HSO removal was significantly associated with RD relapse risk. Caution must therefore be exercised in the choice of tamponade after HSO removal if RD is present. In fact, when a gas tamponade was used to treat an RD relapse occurred with HSO still *in situ*, a further RD occurred in 88% of cases. In such cases, it might be safer to use SO until the retina is firmly attached or to consider long-lasting gas tamponade instead of SF6.

We have observed that advancing age plays a protective role in terms of retinal reattachment. It is well known that younger patients have a higher predisposition to aggressive PVR, which could offer a possible explanation for this result.

The serious adverse events associated with heavy tamponades have deterred many retinal surgeons from their use [45]. The main adverse events reported in the literature after HSO include cataract formation, IOP elevation, intraocular inflammation, and oil emulsification.

Several studies have confirmed the regression of anterior chamber inflammation under topical steroid therapy, with the need for oil removal rarely being called for [33]. Our experience confirms this result, in contrast to the findings of Theelen et al. [46], who observed chronic intraocular inflammation in 7 of 19 patients treated with Oxane HD. They reported inflammation with keratic precipitates, pigmented clumps, and cellular reactions in the anterior chamber that did not respond to topical steroids. Interestingly, Oxane HD removal resulted in the complete resolution of inflammation, with the authors suggesting that an aberrant immune response may have been involved [46].

Reports of IOP elevation following HSO are variable. Li et al. [33] reported raised IOP in 19% of patients during follow-up, which was successfully treated. Hussain et al. [14] found raised IOP following HSO administration in 6 patients (50%), which resolved in the majority of cases following removal of the oil; 2 patients had long-term raised IOP requiring topical therapy, and one required a Baerveldt tube insertion. Romano et al. [16] observed elevated IOP in 5 cases (12%) at 1-week follow-up and in 8 cases (19%) at 1-month follow-up. In one case, elevated IOP persisted through to 3-month follow-up after HSO removal. In all cases, increased IOP could be controlled with topical and/or temporary oral administration of anti-glaucomatous medication. In our study, we have observed an increase in IOP in 56 cases (40.5%), with a glaucoma valve implantation being required in 5 cases. A comparatively higher rate of IOP increase seems to be apparent in our study, which is perhaps due to our sample composition containing patients having undergone previous surgeries and who were very complex cases. About 74% of our patients had a previous SO tamponade, and about 6% of cases had raised IOP before HSO administration. In a systematic review, Miele et al. [47] found evidence from comparative nonrandomized studies, suggesting a greater risk of developing open-angle glaucoma and ocular hypertension after PPV, compared with the fellow eye. However, the risk of raised IOP, in the large majority of cases, did not seem to be directly correlated with HSO tamponade duration. A possible explanation for IOP increase after HSO administration could be given by macrophage responses to the tamponade emulsion, as has been reported by Hiscott et al. [13] for F6H8. In another report, a comparison between SO and HSO suggests a trend for somewhat higher IOP values in the HSO group, both in the

early postoperative period and at longer follow-up time points, with chronically elevated IOP being observed in 8% of patients with SO [48]. Other studies have indicated an incidence ranging from 3% to 40% [49–52]. There is also evidence that the rate of raised IOP is higher with HSO in the initial few days postoperatively but that it equalizes to that of SO in the subsequent weeks [22]. Taken together, these findings could be explained by the lower tendency for emulsification of HSO in comparison to SO [53]. We also found a statistically significant association between IOP elevation and sex in that being female seemed to be protective; however, we believe that these data are not clinically relevant.

The HSO study was the first multicenter, randomized, prospective controlled clinical trial aimed to compare SO and HSO in inferior PVR cases. 350 consecutive patients are recruited per group. The main endpoint criteria are complete retinal attachment at 12 months, and change of BCVA 12 months postoperatively compared with the preoperative BCVA. Secondary endpoints include complete retinal attachment before endotamponade removal, quality of life analysis, and the number of retina affecting re-operation within 1 year of follow-up [54]. Although the HSO study still represents the only prospective study, an interim analysis failed to demonstrate superiority of HSO in managing inferior PVR with respect of SO [55].

In summary, our retrospective study confirms a high anatomical success rate whether the use of HSO as an intraocular tamponade is as a primary agent or as a subsequent procedure following single or multiple failed surgical interventions. The presence of RD at the time of HSO is a negative prognostic factor. According to our findings, in cases of RD at the time of HSO removal, a short-term tamponade should be avoided, in favor of SO which appears to play a role in preventing RD recurrence. Furthermore, there is no clear evidence for an ideal HSO tamponade duration, and our data seem to recommend close monitoring of young patients in particular, with adjustments being made to tamponade duration depending on RD evaluation. However, our data suggest that a longer HSO permanence seems to be related with a higher anatomical success rate, except for RD relapses under HSO. Special attention must be paid to the risk of IOP elevation, although it can be managed with topical therapy in the large majority of cases.

To our knowledge, this study has included the largest cohort reported thus far in the literature. Although it is a multicentric study, its retrospective nature represents a potential weakness. In conclusion, despite its effectiveness in the management of inferior RD complicated by PVR, the role of HSO is not yet clinically fully defined.

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Statement of Ethics

The study was performed in accordance with the current version of the Declaration of Helsinki (52nd WMA General Assembly, Edinburgh, Scotland, October 2000), and written informed consent was obtained from the patients (or their parent/legal guardian where appropriate) to participate in the study. This study protocol was reviewed and approved by Verona and Rovigo, approval number Prog. 2612CESC.

Conflict of Interest Statement

The authors have no financial/conflicting interests to disclose.

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Author Contributions

Maurizio Mete (author): the four ICMJE criteria are met; Barbara Parolini: substantial contributions to the conception or design of the work; Emilia Maggio (co-author): final revision; Giulia Airaghi (co-author): data collection; Nicoletta de Santis (co-author): data analysis; Massimo Guerriero (co-author): data analysis and study design; and Grazia Pertile (co-author): final revision and study design.

Data Availability Statement

Raw data are stored in IRRCS Sacro Cuore Don Calabria Hospital and are not publicly available due to ethical reasons. Further inquiries can be directed to the corresponding author.

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