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RETINAL DISORDERS

Deferred laser photocoagulation of relaxing retinotomies under silicone oil tamponade to reduce recurrent macular detachment in severe proliferative vitreoretinopathy

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Abstract
Purpose This study sought to investigate whether, in patients with retinal detachment complicated by proliferative vitreoretinopathy, we can re-attach the retina with a posterior relaxing retinotomy and silicone oil tamponade while postponing laser retinopexy for several months.
Methods In 13 consecutive patients we applied laser coagulation of the retinotomy edge 15±12 weeks after surgery. Silicone oil was removed 9±6 weeks after laser application.
Results After the retinotomy without laser, some degree of central shifting was seen in all patients, followed by obvious curling in 10 patients. The total follow-up was 24±7 months after retinotomy and 13±9 months after oil removal. The retina was attached in 12 patients at the last visit, with the oil still in situ in three patients. Seven patients, however, required additional surgery. Function remained stable with a mean preoperative and postoperative Snellen visual acuity of 0.09.
Conclusions Not anchoring retinotomy edges with a laser at the time of surgery allows inward curling and central slippage of retinal edges under silicone oil. This appears to compensate for the retinal fibrosis occurring in the weeks following surgery and may result in less macula-off re-detachments under oil, and potentially, in better visual outcome.

Keywords Inferior retinotomy · Laser photocoagulation · Retinal detachment · Vitreoretinopathy

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Introduction

Proliferative vitreoretinopathy (PVR) can be defined as vitreoretinal wound healing in response to a retinal break and consists of inflammation, cellular proliferation, and extracellular matrix remodeling. Following breakdown of the blood-retina barrier, a proinflammatory and fibrotic milieu (cells, cytokines, and growth factors) develops in the vitreous cavity and the subretinal fluid that ultimately may lead to epiretinal, intra-retinal, and subretinal fibrosis, causing (recurrent) retinal detachment (RD) [1]. Therapeutic strategies to prevent PVR or to temper its severity include pharmacological agents and endotamponades [2–8]. Endotamponades, apart from closing retinal breaks, can compartmentalize the hydrophilic PVR milieu away from the wound healing site [9].

In established PVR, surgery remains the mainstay of treatment, with meticulous surgical removal of epiretinal (and sometimes subretinal) tissue, relaxing retinotomies with or without a broad buckle in the case of retinal shortening due to peri- and intra-retinal fibrosis, and the closure of retinal breaks by an endotamponade. Endolaser photocoagulation would be applied around retinal tears and retinotomy edges. A recurrent retinal detachment, however, may develop in some patients after relaxing retinotomies under silicone oil, necessitating a series of repeat surgeries.

The application of a laser or cryocoagulation to the edges of retinal breaks is an important ingredient of successful treatment of uncomplicated rhegmatogenous retinal detachment (RRD) surgery. The scars seal the retinal breaks effectively, closing off the subretinal space and thereby preventing re-detachment. In cases of RRD complicated by PVR, however, the effect of immediate retinopexy may not be unequivocally beneficial. In inferior re-detachments that necessitate relaxing retinotomies, the retina is usually diffusely thickened and tense, even after meticulous membrane peeling. This is demonstrated by the often quite marked central displacement

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of the retina that can be observed immediately after performing the retinotomy. Inspection of the edge of the retinotomy usually shows a tense and shortened inner retinal surface, while the outer surface appears corrugated and redundant, resulting in a poor apposition between the outer retina and the retinal pigment epithelium (RPE), even under heavy (perfluoro carbon) liquids. Consequently, inducing laser burns at the retinotomy edge usually requires high energy. Extensive use of a laser can cause increased breakdown of the blood-retinal barrier and activate cell proliferation [10, 11]. The resulting scars could, rather than seal the retinotomy, increase epi- and/or intra-retinal fibrosis, promoting secondary shortening and traction. Traditional intraoperative laser application performed simultaneously with the retinotomies may then be a factor in the subsequent recurrent RD under silicone oil. We hypothesized that postponing laser photocoagulation along the retinotomy edges could allow central slippage of the remaining retina as well as inward curling of its edges, avoiding traction over the laser scars and limiting consequent recurrent retinal detachment. Once PVR fibrosis would have run its course and the retina is relocated to an unchallenged position, the postoperative laser would create retinochoroidal adhesion in that position and allow a relatively safe silicone oil removal.

We report here the results on the first case series of patients treated in this manner.

Patient and methods

A retrospective analysis of a series of 13 patients (13 eyes) was performed at the Rotterdam Eye Hospital, in whom we did not apply intra-operative laser retinopexy along the retinotomy edge ("the retinotomy procedure"). The first patient was operated on in January 2011, and the censoring date was January 2014. Patients were eligible if they previously underwent one or more vitreoretinal surgeries for retinal detachment repair, after which they developed a re-detachment of the inferior retina that was related to obvious PVR. The nature of the procedure and the need for additional laser application later was discussed with the patient by the surgeon and all patients consented to this treatment. Patients in whom we removed the silicone oil and performed laser surgery of the retinotomy edges in combination with a gas tamponade were excluded.

Preoperative data collected for each patient included age, gender, visual acuity (VA), intraocular pressure (IOP), lens status, and number and indication of previous vitreoretinal surgeries. Variables noted during surgery were the position and clock-hours of the retinotomy. Postoperatively, we analyzed the interval between the retinotomy procedure and slit lamp laser retinopexy, and between the slit lamp laser and silicone oil removal. In addition, postoperative VA, IOP, retinal status, number and indication of re-operations and presence of oil at the last visit were recorded.

Surgery

We used a 23-gauge standard three-port pars plana Baush & Lomb Stellaris vitrectomy system (Bausch & Lomb, Rochester, NY, US), a chandelier illumination, as well as a hand-held light pipe and intraocular forceps (Dutch Ophthalmic Research Center (DORC), Zuidland, the Netherlands). After the removal of the silicone oil, surgery entailed the removal of the inner limiting membrane (ILM) (if not previously removed) and all visible and/or graspable epiretinal tissue, identification of which was facilitated by Membrane Blue-Dual® vital staining (DORC). A relaxing retinotomy without intra-operative laser retinopexy followed by a silicone oil tamponade was performed in all patients. The vitreous cutter was used to create the retinotomy and to remove the retina peripheral to the retinotomy site (retinectomy). Injection of oil was preceded by a fluid-air exchange in all cases. Lensectomy and insertion of an intraocular lens was performed at time of the silicone oil removal in phakic patients. All surgeries were performed by one surgeon (JvM).

Laser coagulation along the retinotomy edge was applied postoperatively with a slit-lamp laser before eventual silicone oil removal.

Results

Baseline characteristics

The age of the patients (four females and nine males) was 63± 17 (mean±SD) years (range 19–84) (Table 1). The number of previous vitreoretinal surgeries ranged from one to four (mean 2). All patients had one or more vitrectomies before the retinotomy procedure. Three patients also underwent one scleral buckle procedure.

The original diagnosis was a rhegmatogenous retinal detachment in 12 patients (two of them after a blunt trauma and another patient also had a history of a central retina vein occlusion). One patient had an RPE-tear after intravitreal anti-VEGF injections for exudative age-related macular degeneration. This patient was treated with an autologous RPE-choroid graft translocation that was subsequently complicated by an inferior retinal detachment due to PVR. In seven patients the macula was attached before the retinotomy procedure, but in all but one (the patient with a preoperative VA of 0.6) had been detached at least once before. In the other six patients the macula was detached. Eight patients were pseudophakic and two aphakic at time of the retinotomy procedure.

Table 1 Patient demographics

Patient	Age (years)	Previous surgery (number)	Preoperative macula on/off	Preoperative VA	Last VA	Follow-up (months)	Postoperative re-detachment surgery (number)
1	66	2 ppv	off	2/300	0.5	11	–
2	51	2 ppv	off	1/60	2/60	28	2
3	19	2 ppv/ 1 sb	on	0.05	0.05	34	3
4	61	3 ppv	on	0.1	0.05	36	–
5	67	1 ppv/ 1 sb	on	0.2	0.05	13	2
6	81	3 ppv	off	0.05	0.05	24	–
7	69	1 ppv/ 1 sb	off	1/300	0.5/60	25	–
8	65	1 ppv	off	1/300	1/60	25	–
9	77	1 ppv	off	1/300	0.1	23	1
10	73	4 ppv	on	0.6	0.3	27	–
11	84	1 ppv	on	0.05	1/60	27	1
12	49	2 ppv	on	0.05	1/60	16	1
13	51	1 ppv	on	1/300	0.05	19	2

Sb scleral buckling, ppv pars plana vitrectomy, VA visual acuity, preoperative means before the retinotomy procedure without peroperative laser retinopexy

At the time of analysis, the patients had a total follow-up of 24±7 months (range 11–36) after the retinotomy procedure. The follow-up after oil removal was 13±9 months (range 2.5-31 months).

Surgery and postoperative laser slit-lamp retinopexy

The ILM was still present and peeled in three patients. We performed epiretinal membranectomy in 12 patients and the removal of subretinal membranes in two. Perfluoro carbon liquid to flatten the retina was additionally used in two patients. The total retinotomy size was 5.2±1.4 clock hours (range 3–8) and always located in the inferior quadrants. In all patients, a fluid-air exchange preceded the insertion of the silicone oil tamponade. There were no significant complications encountered during surgery.

The interval between the retinotomy procedure and slit-lamp laser retinopexy was 15±12 weeks (range 4–46). Subsequently, we removed the oil 9±6 weeks (range 3–24) after the laser in all patients. Curling of the retinotomy edge was left intact during silicone oil removal.

Anatomical and functional results

Mean VA was 0.09 (range 1/300 to 0.6) before the retinotomy procedure and remained unchanged upon the last examination (mean 0.09 with a range of 1/300 to 0.5). Five patients showed an increased intraocular pressure (≥ 25 mmHg). Four of them could be medically controlled and one patient needed trans-scleral cyclophotocoagulation to normalize the intraocular pressure. No cases of hypotony (< 7 mmHg) were recorded.

Initial retinal re-attachment after the retinotomy procedure was achieved in all patients (Table 1).

In most patients, a central shifting of the retina adjacent to the retinotomy site could already be observed at 1 day after surgery (Fig. 1). Curling of the retinotomy edge took more time to develop (Fig. 2).

In 11 patients, a postoperative slit-lamp laser could be applied to the attached retina just central to the curled retinotomy edge (Fig. 3). In one patient, the slit-lamp laser was incomplete due to poor visualization of the anterior retina and the laser surgery was completed at the time of oil removal using scleral depression. In two patients, the retina detached in the inferior quadrants under oil before the slit-lamp laser procedure could be performed, while their macula remained attached (Fig. 4). Re-detachment occurred in five more patients after the oil had been removed, with the macula off in three. Re-detachment occurred in total in 54 % of eyes (n=7).

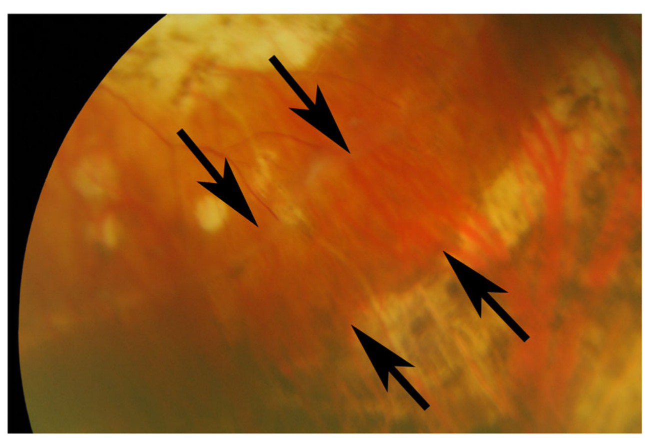

Fig. 1 Central shift of the retinotomy edge without curling (arrows) observed at 1 day after surgery (patient 5)

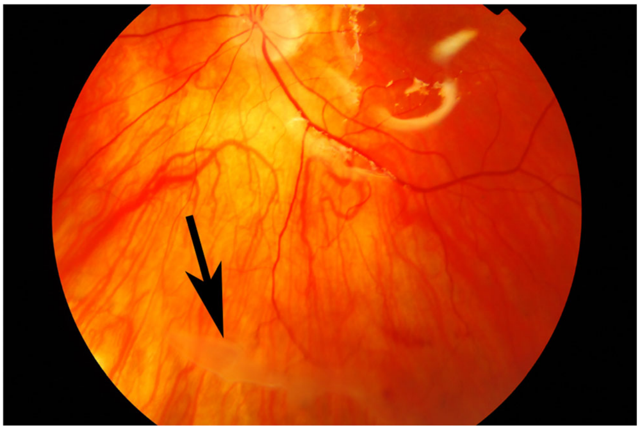

Fig. 2 Inward curling of the retinotomy edge (arrow) at 6 weeks after surgery (patient 1)

Fig. 4 Curling with significant re-detachment under oil, making laser surgery impossible. Therefore, a reoperation was needed in this patient before the oil was removed (patient 11)

Four patients of the re-detachment group needed 2–3 additional surgeries. The retina was attached in 12 patients at the last visit with the oil still in situ in three patients. Figure 5 shows a case of a curled retinotomy edge intact 8 months after silicone oil removal.

Discussion

In PVR surgery, epiretinal tissue is recognized as an important cause of re-detachment, much more often than subretinal membranes. Stiffness of the retina itself, persisting after membrane peeling, is clinically recognized and retinectomy was introduced as a means of treating this. This approach to established PVR has remained largely unchanged since it was popularized in the early 1980s by Zivojnovic [12]. Although this surgical technique meant a major breakthrough for previously intractable cases, the overall anatomical and functional outcome of RRD complicated by PVR remains disappointing, particularly when disease severity necessitates a relaxing retinotomy. A review of the literature by de Silva et al. revealed an ultimate anatomical success rate ranging between 52 and 93 %, whereas mean functional outcome was worse than 20/400 in 26 % of eyes [13].

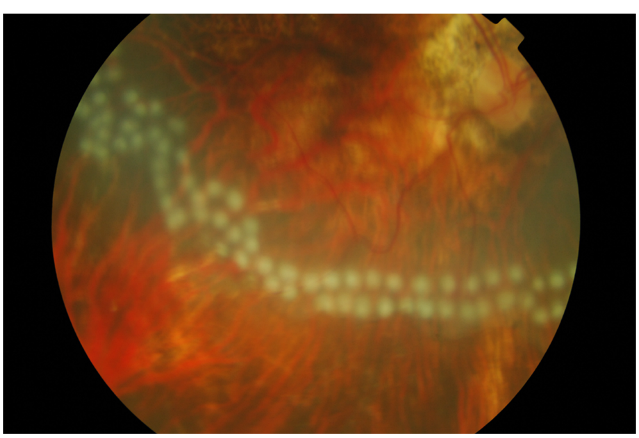

Fig. 3 Fresh postoperative laser applied at the slit lamp through oil to the flat retina near the retinotomy edge, 8 weeks after retinotomy (patient 8)

Recent insights through imaging and histology have prompted us to modify our surgical approach of cases with a particularly high risk of re-detachment.

Histopathological confirmation of intra-retinal fibrosis was obtained from excised retinectomy tissue, showing a predominantly glial cell activation and proliferation replacing the neuronal elements [14]. Retinal curling in the absence of obvious PVR, as can be seen at the edge of a horseshoe tear or along a giant retinal tear, is probably caused by a combination of the inherent stiffness of the inner retinal surface on one hand, and by some degree of swelling of the outer retina that occurs after detachment as seen on OCT [15, 16]. Contraction of epiretinal membranes in PVR can add to this phenomenon, causing extreme folding of the inferior retina after retinotomy [17]. Consequently, the position where the posterior retina settles immediately after the retinotomy, under perfluoro carbon liquid, should not be

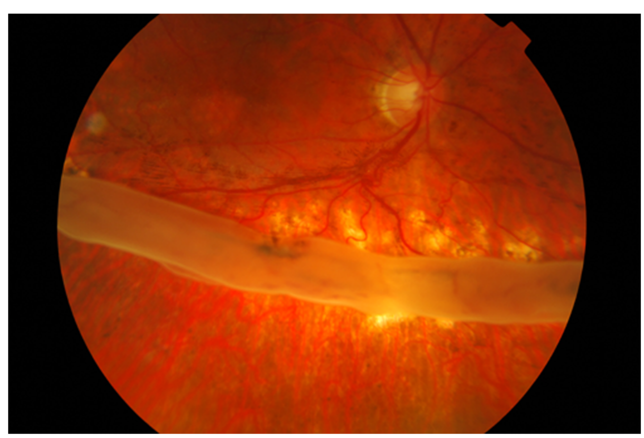

Fig. 5 Eighteen months after retinotomy under oil, 10 months after laser use at the slit lamp and 8 months after oil removal: pronounced curling of the retinotomy edge is seen, but with a completely flat central retina (patient 4)

considered unchallenged and thus, intra-operative anchoring of the retina in this position may not be optimal. Several issues may have bearing on this.

1. The time course of PVR remains unpredictable and identification of the phase of the disease based on clinical signs is almost impossible. The timing of surgery is usually based on (impending) macular detachment. A retinotomy may thus be performed when the PVR response is not in a quiescent phase [18].
2. The trauma of cutting the retina, although immediately releasing traction, may (re-)activate the scarring process.
3. Re-attaching the retina, while essential for functional recovery and ultimately inhibiting the PVR response may, according to the feline model, initially activates Muller cell outgrowth [19].
4. Intra-operative (often heavy) laser burns increase the blood-ocular breakdown and cellular proliferation [10, 11].

We hypothesized that intra-operative anchoring of retinotomy edges would not only prevent settling of the shortening retina into an unchallenged position, but would also promote further traction and detachment through reactive fibrosis. The end result would be either an anterior relocation of the retina central to the retinectomy when sufficiently elastic, or in retinal re-detachment in the case that it was not elastic.

It is unknown for how long a period PVR changes occur, but clinically, 2–16 (median 8) weeks are thought to be a reasonable estimate [18]. Typically, recurrent retinal detachment after retinectomies are slow to develop, suggesting that retinal fibrosis becomes manifest after the laser scars have healed and have reconstituted chorioretinal adhesion at the laser site, a much faster process than the spontaneously occurring slow recovery of adhesion elsewhere [20].

Patients included in this series were judged to be at high risk of recurrent retinal shortening and re-detachment. In comparison, in patients where this risk is estimated to be low, we usually choose a gas tamponade even when a retinotomy is performed and rely in these cases on laser scar adhesion to form while the breaks are temporarily closed by the gas bubble. The 13 patients in this series were given lighter-than-water silicone oil, rather than a gas tamponade. Avoiding retinopexy could theoretically increase the likelihood of re-detachment, as fluid could gain access to the subretinal space that is not occluded by laser scars. We have previously demonstrated that a buckle without intra-operative retinopexy can sufficiently occlude the retinal breaks, leading to successful re-attachment in conventional buckling surgery [21]. Similarly, an intra-ocular tamponade can displace fluid away from a retinal break, allowing the retina to re-attach as can be observed in pneumatic retinopexy. Postponing laser surgery under silicone oil has been described before the era of routine availability of endolaser procedures. It has also been suggested as a strategy to reduce reproliferation in inflamed eyes [22]. In this series, the silicone oil bubble in itself seemed to sufficiently tamponade the retinotomy and prevented residual vitreous fluid from gaining access to the subretinal space. Lighter-than-water silicone oil does not provide an actual closure of inferior retinotomies but would decrease the risk of recurrent retinal detachment by decreasing fluid currents around the retinotomy edge [23]. Recurrent RD is thought to be more common in the inferior quadrants because cells gravitate there in a watery milieu, which also contains the hydrophilic growth factors and cytokines. The use of heavy silicone oil was thought to result in a lower tendency for PVR by shifting this PVR milieu away from the inferior retina. This hypothesis, however, was not fully realized in practice in two clinical studies. In an observational study, 39 patients with a lighter-than-water silicone oil tamponade with an inferior chorioretinal wound in contact with the watery milieu did not develop PVR more frequently than 170 patients with a similar wound in the superior quadrants tamponaded by the same silicone oil [24].

In the HSO (heavy silicone oil) study, heavier-than-water silicone oil was compared to lighter-than-water silicone oil, but no difference in the rate of recurrent retinal detachment was found. However, recurrent retinal detachment did develop in the quadrants where an aqueous compartment was left [8]. A large inferior retinotomy without retinopexy may therefore be an interesting indication for HSO tamponade, as it may prevent the excessive curling we have seen in some of our patients (Fig. 5) and may reduce the re-detachment rate under oil. We intend to investigate whether HSO tamponade could indeed reduce the recurrence rate under such circumstances.

Scleral buckling in addition to vitrectomy is another well-accepted technique for dealing inferior retinal shortening and possibly reducing the need for relaxing retinotomies. Initial experience with combined vitrectomy and external scleral buckle for proliferative vitreoretinopathy often had modest anatomical outcomes, but no comparative trials of the two techniques have been undertaken, however, and the choice of technique remains governed by surgeon personal preference [25–27]. The added value of a buckle was not investigated in this study.

To allow central relocation of the shortening retina, we delayed laser surgery until several weeks after the procedure. We performed slit-lamp laser photocoagulation of the retinotomy edges, central to the curled areas, and assumed that the retina would by then be in a position no longer under contraction. In addition, some recovery of the physiological adhesion between the retina and RPE would have occurred and the retinal swelling subsided, reducing the need for extensive and heavy laser use. This modified surgical approach to PVR could theoretically improve functional outcomes by a reduced incidence of macula-off re-detachments under oil.

In 10 patients we have observed signs of curling or central slippage, confirming our assessment of residual fibrosis. In two patients, with their macula still on, we did not apply deferred laser use, as the recurrent detachment was too extensive, but proceeded to surgery, again with deferred lasering. Eventually, postponed lasering allowed oil removal in all 13 patients. Recurrent detachment, however, developed in five (three with their macula off) after some weeks.

Hence, the overall anatomical outcome is not significantly superior to previous reports. Nevertheless, as we only included challenging cases with poor prognosis in this series, the hypothesized mechanism of recurrent RD after relaxing retinotomy in relation to intra-operative laser photocoagulation may be realistic, and postponing laser use may merit consideration in selected patients suspected of future inferior recurrent RD under silicone oil.

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