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Effect of silicone oil on retinal microcirculation after vitrectomy for rhegmatogenous retinal detachment evaluated by OCT angiography: a literature review

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***Abstract*:** Silicone oil (SO) has been widely used as intravitreal tamponade agent for rhegmatogenous retinal detachment (RRD) and has been occasionally associated with incomplete retinal structural and functional recovery. The use of Optical Coherence Tomography Angiography (OCT-A) has recently attracted significant attention for detailed analysis of retinal capillary plexus and blood flow changes as predicting factors for postoperative outcomes. A detailed literature search was performed in PubMed database until October 2022. The following keywords were used: rhegmatogenous retinal detachment, silicone oil, optical coherence tomography angiography, macular microvasculature, peripapillary capillary plexus, vessel density, and foveal avascular zone. We identified and reviewed 19 studies referring to microcirculation alterations of the retinal capillary plexus as seen on OCT-A in eyes treated by vitrectomy with intravitreal SO for RRD. A comprehensive update revealed variability of microcirculation characteristics of the retinal capillary plexus including the macular and the peripapillary capillaries. Further studies are warranted to clarify the OCT-A values in an attempt to identify the potential effect of SO on retinal tissue in clinical practice. A review of the existing literature sheds light on the effect of SO on retinal capillary plexus and the potential impact on functional outcomes after vitrectomy for RRD. This article discusses important aspects of key publications on the topic, highlights the importance to identify distinct alterations of the microvasculature status, and proposes the need for further future research in this field.

Keywords: macular microvasculature, optical coherence tomography angiography, peripapillary capillary plexus, rhegmatogenous retinal detachment, silicone oil

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Introduction

Silicone oil (SO) has been widely used as a retinal tamponade, especially in complex vitreoretinal disorders.[1–3] Although efficacious in the management of retinal detachment, intravitreal SO has been associated with incomplete retinal restoration and deficient functional recovery. Indeed, unexplained visual impairment, structural, and microcirculation alterations have been reported after uncomplicated rhegmatogenous retinal detachment (RRD) repair with SO tamponade.[4–6] Possible explanations for these phenomena include reduced transfer of oxygen and electrolyte homeostasis dysregulation due to the presence of SO, mechanical pressure leading to metabolic retinal derangement, the surgical intervention *per* *se*, or the potential of retinal degeneration due to intrinsic SO properties. Emerging evidence has suggested a coexistence of neuronal and microvasculature damage both in SO-filled eyes and after silicone-oil removal (SOR).[4–6]

The novel imaging technology of Optical Coherence Tomography Angiography (OCT-A) allows direct visualization of retinal microcirculation, thus giving new insights in understanding the pathobiology of various conditions.[7–10] Varying regions of the posterior segment vasculature of the eye, including the macula and the optic nerve have demonstrated alterations in RRD eyes undergoing vitrectomy with SO tamponade.[11–32] These emerging findings provide abundant evidence for the potential impact of SO on retinal microcirculation.

A literature search revealed numerous studies that focus on OCT-A characteristics of the retinal capillary network in RRD eyes after vitrectomy with intravitreal SO in an attempt to indicate the potential of a SO-related deleterious effect on retinal tissue.[11–29] To our best knowledge, this is the first review article that presents selected pertinent evidence of OCT-A characteristics after successful RRD surgery with intravitreal SO, perceives possible explanations for the microcirculation status, and proposes the need for further future research.

Methodology

Articles published in PubMed without restriction on year of publication and until October 2022 were considered. Keywords with appropriate Boolean operators were used, using the search terms 'rhegmatogenous retinal detachment', 'silicone oil', 'optical coherence tomography angiography', 'macular microvasculature', 'peripapillary capillary plexus', 'vessel density', and 'foveal avascular zone'. Furthermore, the relevant reference list of the retrieved articles was carefully reviewed. We identified 19 studies focusing on this topic.[11–29] All included papers have considered the use of OCT-A for evaluating retinal microvasculature at the macula and the optic nerve and for identifying potential alterations in RRD eyes following vitrectomy with SO tamponade. This article is based on previously published studies and does not include any studies performed by the authors.

OCT-A technical principles

The advent of OCT-A in recent years has given new insights in noninvasive, angiographic visualization with unprecedented resolution of the retinal and choroidal capillaries.[7,8] OCT-A images provide quantification of vascular characteristics and blood flow at the posterior segment of the eye, especially the macula and the peripapillary area. The mechanism of action of OCT-A is based on erythrocytes movement to distinguish blood cells from static tissue and accurately depict vessels on high-resolution, three-dimensional maps with depth-resolved capability.[7,8]

Numerous studies have employed OCT-A to investigate retinal microcirculation with high accuracy and repeatability in normal subjects and in retinal disorders.[7,8] OCT-A is a useful tool for acquisition of volumetric data and segmentation of retinal and choroidal layers in en face images; retinal layers, namely, superficial capillary plexus (SCP), intermediate capillary plexus (ICP), deep capillary plexus (DCP), and the innermost part of the choroid, the choriocapillaris are adequately visualized. The macular scan area is automatically divided into three subfields that are topographically described as follows: the foveal area, a central circle with a diameter of 1 mm; the parafoveal area, an inner ring between the 1-mm and 3-mm circles; and the perifoveal area, an outer ring between the 3-mm and 6-mm circles. The peripapillary scans refer to a wide annulus region centered on the optic nerve head. By enabling automated algorithms, this technology widely contributes to the thorough analysis of retinal microvasculature; vessel density (VD), defined as total length of perfused vasculature per unit area in a region of measurement; perfusion, defined as percentage of area of perfused vasculature per unit area in a region of measurement; foveal avascular zone (FAZ) characteristics, including total area, perimeter, and circularity index; radial peripapillary capillary parameters, including perfusion and flux index.[7,8]

Notwithstanding the aforementioned facilities of OCT-A, we should definitely consider some weaknesses that arise from the use of this technique: projection artifacts, media opacities limiting signal intensity, limited field of view in the posterior pole precluding evaluation of vasculature in the retinal periphery, and inadequate visualization of deep choroid. Other critical limitations include the absolute cooperation from the patient and the susceptibility to axial and transverse eye motion. Especially in patients with low fixation due to eye disorders such as macula-off RRD, OCT-A imaging can be challenging; decorrelation tails and magnification errors in SO-filled eyes may interfere with the interpretation of angiographic results.[7,8]

Pathophysiology of chorioretinal capillary plexus

The microvasculature of the posterior segment provides blood flow information for the macular and the peripapillary area.[33–35] Morphological studies in human and animal models have demonstrated distinct retinal and choroidal capillary networks.[33] The retinal vessels at the macula are located in three capillary layers: superficial, intermediate, and deep vessel plexus. The superficial and DCP are predominantly located within the ganglion cell layer and the inner nuclear layer, respectively; they provide nourishment and remove metabolic products from the inner retinal layers. The ICP is supplied by vertical anastomoses from the superficial network. The three capillary plexuses merge into one at the edge of the FAZ, while intermediate and deep merge into a single layer temporal to the fovea. The outer retinal layers are avascular and supplied with nutrients and oxygen by diffusion from the choriocapillaris. Microcirculation changes in each capillary network seem to occur in a distinct way dependent on their location and tolerance to hyp oxia.[33–39]

The origins of the radial peripapillary capillary network differ from that of the macular vasculature; capillaries located around the optic disk are supplied by the choroidal ciliary vessels.[40,41] In addition, peripapillary plexus is composed of long straight capillaries and rare anastomotic connections, which is different from the macular vascular plexus. These anatomical discrepancies could explain potential inconsistency between microcirculation changes in various retinal regions that might be mainly attributed to the different state of the vasculature.[40,41]

In the process of RRD, retinal homeostasis and metabolism may be disrupted with resultant modifications in retinal and choroidal tissue.[42] Numerous hypotheses could be made regarding the mechanisms causing retinal vascular insufficiency in patients with RRD. Macular vasculature impairment has been shown even in eyes without macular involvement suggesting that variable factors (molecular biologic milieu during RRD, surgical intervention, tamponading agent) may be accountable for deterioration of microvessels. In cases that RRD extends beyond the fovea, the subretinal fluid (SRF) (with composition of inflammatory, immunological and vascular mediators, such as prostaglandins and cytokines) may limit free diffusion of oxygen to the detached macula leading to nonperfusion areas, tissue hypoxia, nutrient deprivation, and retinal degeneration. In addition, the mechanically induced neuronal damage may lead to retinal ischemia. Another potential pathophysiologic mechanism for localized flow reduction leading to hypoperfusion may be a reversible vasoconstriction. Indeed, an autoregulation phenomenon secondary to hypoxia may protect the retinal tissue against the damaging effect of irregular blood flow.[36,43,44]

Retinal microvasculature blood flow changes

Macular microvasculature

The first analysis of OCT-A characteristics in macular capillary plexus after RRD surgery with SO tamponade emerged in 2018. Clinical results of the effect of SO on macular microcirculation as seen on OCT-A were initially reported by Suren *et al.*[11] at the European Vitreoretinal Society Congress. The investigators aimed to evaluate FAZ and foveal VD in patients with RRD at 1 month after surgery. They conducted a retrospective, case–control study that included 37 eyes (37 patients) with recent onset RRD that were successfully treated with a single, uncomplicated pars plana vitrectomy (PPV) with gas or SO tamponade. Their study notably indicated a reduction of VD at both SCP and DCP accompanied by an enlargement of FAZ at the deep vascular plexus in treated eyes postoperatively as compared with fellow. Overall, this report showed that microvasculature alterations may indicate ischemic damage to foveal capillary plexus.

Angelova[12] assessed OCT-A characteristics in a 12-month prospective study with 24 patients (48 eyes) with monocular RRD who underwent PPV with intravitreal SO. The aim of the study was to evaluate vascular alterations at the macular area and investigate potential links between visual outcomes and microcirculation parameters. The authors included RRD cases with or without macular involvement, 18 and 6 eyes, respectively, and the unaffected fellow eyes were served as controls for comparison. OCT-A imaging was performed pre- and post-operatively by acquiring a $3\times3\,mm^2$ macular scan using spectral domain (SD) OCT-A. This study aimed to identify microcirculation alterations in RRD eyes treated with intravitreal SO in the following cases: (1) preoperatively, as well as following vitrectomy and SOR and (2) in comparison to the values of fellow unaffected eyes. All patients were followed up on the first week and first month following vitrectomy, as well as on the first and second month after SOR. Concerning macula-off eyes, the authors found decreased macular vascular density of both the SCP and DCP. In particular, they noted significant reduction of the superficial vascular density at the whole macular area from 45% prior to vitrectomy to 43% at the second month after SOR ($p=0.049$). Moreover, they observed a significant difference of the deep vascular density between the operated eyes at the second month after SOR compared with the healthy fellow eyes, with median values at 48% and 54% ($p=0.028$), respectively. Conversely, the values of superficial and deep VD in macula-on RRD eyes remained unchanged. Of note, notwithstanding the variable alterations in VD, the investigators did not identify vascular flow instability. This observation may be attributed to the vascular flow index being more sensitive when detecting metabolic and physiological changes in the retina rather than vascular pathology, which mainly affects VD. Angelova[12] interpreted their results based on RRD pathophysiology; inflammatory and vascular mediators in the SRF may inhibit oxygen diffusion from the choriocapillaris to the detached retina leading to ischemia and in turn, macular vascular changes and degeneration of photoreceptors. In addition, accumulation of proinflammatory cytokines in the retro-SO fluid and activation of the retinal micorglia inflammatory process may further contribute to microcirculation alterations.[2,45] Overall, macular microvasculature alterations may provide a quantitative explanation for the suboptimal visual recovery after macula-off RRD with intravitreal SO, even after anatomical retinal reattachment and removal of SO.

In an attempt to assess the effect of SO on macular microcirculation, Xiang *et al.*[13] retrospectively investigated 23 patients (23 eyes) who underwent PPV with intravitreal SO for macula-off RRD (almost all cases) and 20 patients (20 eyes) who were previously treated and required SOR. The aim of the study was to analyze foveal and parafoveal capillary plexus VD of the superficial and DCP along with FAZ area within a 6-month period. In particular, cases with intravitreal SO were examined at the first and third month of follow-up, while those that required SOR were imaged at 1 week prior to as well as at 3 months after SO extraction. OCT-A was performed using a split-spectrum amplitude decorrelation angiography (SSADA) algorithm by acquiring $3\times3\,mm^2$ macular scans. The results demonstrated that vascular density of the superficial and deep macular capillaries along with FAZ area were retained at a stable level following both SO tamponade and removal, thus indicating that SO may not adversely affect microvessels when used less than 6 months. This finding was consistent with previous evidence supporting that intravitreal SO in rabbit eyes may not cause pathological changes in retinal vasculature or hypoxia during 6 months period.[46] Consequently, the authors noted that despite SO may not have direct impact on retinal vasculature, it may be detrimental in prolonged use; therefore, SO is advisable to be removed from the vitreous cavity once the retinal disorder has been stable.

Lee *et al.*[14] performed a retrospective, single-center study that investigated foveal microvasculature changes in RRD eyes. They analyzed 38 eyes with primary RRD (27 macula-off, 11 macula-on) that were successfully treated with 25-gauge PPV with SO tamponade. En face OCT images were obtained in scanning area of $3\times3\,mm^2$ centered at the fovea using swept source (SS) OCT-A. The purpose of the study was to compare the structural changes of the foveal microvasculature between the operated and unaffected contralateral eyes at 3 months after SOR and to evaluate their influence on the final visual outcomes. The FAZ area along with the parafoveal VD in the SCP and DCP was analyzed. The authors markedly noted no significant differences in FAZ area and VD in the SCP between RRD and fellow eyes. Contrary to these findings, they indicated prominent alterations in the DCP; in particular, an enlargement of FAZ ($p<0.001$) accompanied by diminished VD ($p=0.022$) was observed in SO treated eyes as compared with fellow. A potential explanation may be related to the fact that DCP is located in the watershed zone in which oxygen saturation is significantly lower than in the inner and outer retina, and therefore, it might be more susceptible to hypoxia. In addition, the duration of SO tamponade was strongly correlated with enlargement of FAZ and reduction of VD in the DCP, which suggests that removal of SO should be performed timely in order to avoid mechanical stress to the fovea and vascular insufficiency of the DCP. Interestingly, the authors noted that FAZ area and VD were not associated with visual outcomes. Indeed, visual acuity (VA) RRD eyes might be affected by various factors, such as macular detachment, duration of retinal detachment, or foveal photoreceptor integrity.[47,48] Conclusively, the authors suggested that RRD eyes with SO tamponade demonstrated pivotal changes of the foveal microvasculature which may be attributed to the properties of SO *per se*, the detached macula or a combination of both.

To further assess macular blood flow of patients with RRD treated with PPV and intravitreal SO, Xu *et al.*[15] carried out a retrospective, cohort-controlled study. They included 35 eyes that were diagnosed with RRD associated with choroidal detachment, 36 eyes with primary RRD, and 40 eyes with normal controls. Macular involvement was similar among RRD eyes. Visual outcomes and OCT-A parameters were examined regularly at 1 day, 1 week, 1 month and 3 months postoperatively. Imaging was performed by acquiring a macular scan using SD-OCT-A. The aim of the study was to characterize changes in the macular FAZ area of both superficial and DCP in SO-filled eyes after RRD and explore the correlation between FAZ and visual outcomes. Notably, the authors did not mention any SO-related changes on the superficial FAZ, which remained stable in SO-filled eyes. The deep FAZ of both RRD groups, however, was larger than that of control eyes postoperatively, while deep FAZ continued to further increase in cases of RRD associated with choroidal detachment within the first month. A potential explanation of the latter is that oxygen transfer from choroidal capillaries to the deep vessel plexus may be affected by the SRF leading to irreversible tissue ischemia and atrophy even after retinal reattachment. Furthermore, the correlation between the deep FAZ at 1–day and visual outcomes at 3–months postoperatively implies that deep FAZ may consist an indicator of postoperative VA. Overall, Xu and co-authors identified expansion of the deep but lack of any obvious changes in the superficial FAZ in patients with RRD associated with choroidal detachment and sought to clarify the degree to which deep FAZ enlargement may be correlated with the severity of ischemia and vision prognosis.

A prospective cohort study was conducted by Roohipoor *et al.*[16] who analyzed 45 eyes in order to evaluate changes in the microcirculation of macular capillary plexus following successful repair of macula-off RRD. The purpose of the study was to perform quantitative analysis on retinal vascular density, FAZ, retinal thickness, and choroidal flow of eyes after PPV and SO tamponade. Similar to the study by Angelova *et al.*,[12] the authors suggested that RRD eyes demonstrated remarkable decrease in macular VD postvitrectomy. In particular, vascular density of parafoveal SCP and total retina were markedly lower in SO-filled eyes as compared with fellow ($p < 0.0001$). Notwithstanding that separate measurements of parafoveal SCP and DCP density did not show significant changes, the values of total vascular density presented amelioration of follow-ups at first and third month postoperatively ($p < 0.0001$ and $p = 0.01$, respectively), approximating but not reaching values of normal eyes. Concerning foveal VD, the values were diminished at first and third month following surgery, especially those of DCP ($p = 0.002$ and $p = 0.005$, respectively). Previously, macular blood flow alterations in RRD eyes with intravitreal SO have been reported using Doppler laser scanning at 1–3 days after surgery that persist until 1 month.[49] Interestingly, FAZ measurements did not present significant changes after PPV with SO tamponade in this study. Overall, impairment of retinal vascular density at 3 months postoperatively could be attributed to mechanical pressure from SO and limited diffusion of oxygen to the retina resulting in metabolic derangement and ischemic damage.

Maqsood *et al.*[17] further analyzed OCT-A measurements in a prospective, comparative, observational study that included 14 patients (14 eyes) with unilateral macula-off RRD successfully treated with a single PPV with intravitreal SO. Macular microcirculation changes were evaluated at 1, 6, and 12 weeks postoperatively. OCT-A was performed in $3 \times 3\,mm^2$ macular area. The results of this study revealed larger superficial FAZ area compared with DCP in SO-filled eyes, possibly attributable to the longer preoperative duration of macular detachment than that of former studies (20.5 and 10 days in Maqsood *et al.*'s[17] and Roohipoor *et al.*'s[16] study, respectively). Despite this observation, the authors did not notice any correlation between duration of retinal detachment and percentage of both superficial and deep FAZ changes. An interesting point to consider is that FAZ DCP was markedly larger at 12 weeks as compared with the first week following surgery ($p = 0.009$). This is in line with the study by Lee *et al.*[14] who demonstrated that the use of intravitreal SO may affect the vascular integrity especially of the DCP and that progressive enlargement of deep FAZ was associated with the duration of SO tamponade. Regarding visual outcomes, the authors did not mention any correlation with FAZ area in this study. Maqsood *et al.*[17] suggested that the use of OCT-A could be promising for designating the effect of SO on retinal microcirculation and providing explanations for visual impairment.

Zhou *et al.*[18] performed a retrospective, single-center study that investigated macular blood flow density changes in eyes with macula-on RRD. They evaluated 21 eyes that were operated with a single uncomplicated PPV, 7 eyes were treated with intravitreal SO, and 14 eyes were treated with gas tamponade. OCT-angiograms were acquired in $6 \times 6\,mm^2$ scan using SSADA. The vasculature was automatically segmented into three layers: superficial, deep, and choriocapillaris plexus, while for each layer, blood flow density was calculated separately in three regions: fovea, parafovea, and perifovea according to EDTRS grids. This study sought to characterize macular perfusion changes throughout an observation period of 12 weeks following vitrectomy. The authors remarkably chose to assess cases that the macular area was not involved in the detachment so that macular status and vasculature could remain intact preoperatively. Inevitably, detachment of the macula could possibly influence macular perfusion even after retinal reattachment. Thus, potential differences in retinal blood flow among macula-on RRD eyes could be more likely to present vasculature changes solely due to distinct intravitreal tamponade agents. Interestingly, Zhou *et al.*[18] found deterioration in blood flow of both SCP and DCP in eyes with SO tamponade. Conversely, parafoveal choriocapillaris flow density presented amelioration in SO-filled eyes possibly resultant of postoperative choroidal inflammation due to SO. Overall, the authors presented conclusive evidence that SO may adversely affect macular microcirculation.

A retrospective observational cross-sectional study was conducted by Lee and Park[19] to explore macular microcirculation changes after RRD with SO tamponade. The analysis included 48 patients (25 macula-off and 23 macula-on) that were successfully treated by PPV with intravitreal SO and their condition remained stable after SOR. Imaging was performed using SS-OCT-A at $4.5 \times 4.5\,mm^2$ scan at 3 months after primary vitrectomy and at 3 months following SOR. VD of the superficial and deep vascular capillary plexus as well as FAZ area was examined. This study revealed that FAZ of the superficial and deep vessel plexus was markedly increased in RRD as compared with fellow eyes ($p = 0.002$ and $p = 0.043$, respectively). Furthermore, the values of the average VD in the DCP and VD of the nasal parafoveal area in both SCP and DCP were significantly diminished in operated eyes ($p = 0.026$, $p = 0.028$, and $p = 0.031$, respectively). Indeed, given that deep retinal layers may be more susceptible to ischemia, microvasculature changes are more obvious in this plexus. An interesting point to consider is that the profound changes of OCT-A parameters in the nasal region of the macula may reflect the microvasculature alterations in the papillomacular bundle which is particularly vulnerable to ischemic changes.[50] In addition, the macula-off cases demonstrated markedly lower VD along with enlargement of deep FAZ than the macula-on ($p = 0.048$ and $p = 0.009$, respectively). The authors concluded that SO may have an adverse effect on retinal microvessels; macula-off cases may experience further vascular impairment due to inflammatory and vascular mediators in the SRF leading to reduced oxygen supply and ischemic changes at the detached macula.

Fang *et al.*[20] analyzed macular perfusion changes after vitrectomy for macula-off RRD in a prospective, observational, case–control study; 20 eyes treated with intravitreal SO and 9 eyes treated with gas tamponade were analyzed. In this way, the authors directly compared macular perfusion status between eyes with SO and gas in an attempt to precisely assess the tamponading agent impact on microvessels by excluding potential bias such as retinal detachment or vitrectomy procedure. Imaging acquisition was performed in a 3×3-mm^2 scanning area. OCT-A parameters were investigated at the first and third month postoperatively. The authors noted that, while macular superficial VD decreased in eyes with SO tamponade, macular perfusion showed improvement in those with gas. The deterioration of the superficial macular VD potentially attributable to compression of inner retinal layers by SO has been previously reported by Ma *et al.*[32]; macular perfusion was diminished in a case series of seven patients with unexplained visual loss following SO tamponade.

Jiang *et al.*[21] retrospectively explored macular VD changes in 19 patients (19 eyes) with macula-off RRD who underwent 25-gauge PPV with intraocular SO tamponade. OCT-A images were obtained in $6 \times 6\,\text{mm}^2$ scanning area. The purpose of the study was to assess vascular density during a 16-week follow-up period; the parafoveal VD per layer in the retinal and choroidal circulation including SCP, DCP, and choriocapillaris layer was analyzed and then compared with that of the fellow unaffected eye. The authors noted that the parafoveal flow density at retinal (SCP and DCP) and choriocapillaris plexus was decreased at 2 weeks postoperatively, with a gradual recovery over time from 2 to 12 weeks, approximating but not reaching the values of the normal eyes. This is in line with the study by Wang *et al.*[51] who reported constant improvement in macular perfusion during a 12-week period postoperatively in gas-filled eyes after RRD, although being lower than healthy eyes. Nonetheless, despite Jiang *et al.*[21] showed macular VD rehabilitation after PPV in SO-filled eyes, the values decreased unexpectedly at 16 weeks after surgery. A speculation concerning this outcome is that SO may have an adverse effect on retinal tissue beyond 3 months of tamponade and is advisable to be removed earlier. Besides, the duration of SO tamponade has been previously found to correlate with macular microvasculature alterations.

In the study by Liu *et al.*,[22] macular VD changes were evaluated in macula-on RRD eyes successfully treated with PPV. This was a single-centered, retrospective, cohort study that included 17 eyes with intravitreal SO and 16 eyes with gas tamponade. OCT-A scans were acquired at $3 \times 3\,\text{mm}^2$ and $6 \times 6\,\text{mm}^2$ areas of the macula. This study reported the long-term results (minimum 30-month follow-up) on the differences of macular vascular density after PPV in order to identify potential reestablishment of macular microcirculation during a prolonged observation period. Notably, eyes with SO tamponade had deterioration in visual outcomes and lower parafoveal vascular density in SCP as compared with those with gas tamponade. The authors postulated that the prone positioning during SO tamponade may cause mechanical compression to the SCP, leading to ischemia, and therefore microvessels alterations at the macula.

Macular microvasculature was further examined prior to and following SOR in a retrospective study with 30 eyes (30 patients) who underwent PPV for RRD by Lee *et al.*[23] The authors of this study assessed OCT-A parameters using SS-OCT-A in $4.5 \times 4.5\,\text{mm}^2$ macular scans. Interestingly, these data showed that FAZ area and VD at SCP and DCP were not significantly different between RRD and unaffected fellow eyes at 6 months after SOR suggesting that SO may have not affected macular blood flow. The authors speculated that even if microvasculature has been compressed during the tamponade period, the blood flow might have recovered within a 6-month period after SOR.

In a recent study, evaluation of the macular microcirculation was performed in RRD eyes that underwent 23-gauge PPV with intravitreal SO and following its removal. Specifically, Bayraktar *et al.*[24] prospectively analyzed a cohort of 24 eyes – 17 with macula-off and 7 with macula-on – and compared them with healthy fellow eyes during a period of 3.4 months after SOR. All patients underwent imaging with OCT-A by acquiring $3 \times 3\,\text{mm}^2$ scans. Similar to a number of previous studies, the authors concluded that all VD measurements in the group of eyes with macula-off were statistically lower than the fellow eyes. In particular, at the level of SCP, significant differences were documented at each retinal zone (foveal, parafoveal, and whole macular area, $p = 0.023$, $p = 0.026$, and $p = 0.026$, respectively); however, only the reductions of foveal VD were significant at the level of DCP ($p = 0.002$). In addition, foveal VD (both at the level of SCP and DCP) of the macula-off eyes showed a progressive decline during the entire follow-up ($p = 0.01$ and $p < 0.0001$, respectively) and did not improve following SOR. Contrary to these findings, in the macula-on eyes, VD measurements were relatively stable during the entire follow-up at all macular regions and did not differ from their fellow eyes. Another point to be mentioned is that eyes with preoperative macular detachment experienced an enlargement of FAZ after SOR, which was notably not observed in cases that macula was attached. The results of former studies concerning macular condition after SOR have stirred controversy; Lee and Park[19] demonstrated decreased values of VD at DCP accompanied by enlargement of FAZ, whereas Xiang *et al.*[13] found no significant changes in VD or FAZ. Overall, as previously described, preoperative macula status comprises as a major risk factor for macular microvasculature alterations. In this study, treatment of macula-off RD with SO tamponade has been associated with vascular retinal alterations which did not improve following SOR, while several transient changes in macula-on SO-filled eyes displayed improvement and almost reached normal following SOR.

Currently, Prasuhn *et al.*[25] were the first to provide evidence of the impact of SO tamponade following RRD repair on choroidal circulation. They retrospectively investigated 19 eyes that were successfully treated with 23-gauge PPV. OCT-angiograms were acquired in $6 \times 6\,mm^2$ scans. The authors investigated macular perfusion within choroidal sublayers (choriocapillaris, Sattler's and Haller's layer) in SO-filled eyes and at 4 weeks following SOR. Notably, they demonstrated that perfusion of choriocapillaris markedly increased after SOR ($p = 0.0013$), while perfusion of Sattler's and Haller's layer decreased ($p = 0.034$ and $p = 0.0402$, respectively). Indeed, underlying pathophysiological mechanisms for this perfusion shift remain elusive. One could hypothesize that intravitreal SO could mechanically compress the adjacent choriocapillaris, with this physical pressure on choriocapillaris being eliminated after SOR; this could subsequently lead to amelioration of choriocapillaris flow and consecutive diminishment of the outer choroidal layers' flow.

Finally, macular microcirculation changes after RRD with SO tamponade was analyzed by our team[26] in a prospective study with 14 patients. OCT-angiograms were captured in $6 \times 6\,mm^2$ scans. This study focused entirely on topographic changes of vascular flow density concerning each separate macular region (foveal, parafoveal, and perifoveal area) in an effort to understand the potential role of SO on inner retinal layers microcirculation during the early post-treatment period (at first month). Our results demonstrated enlargement of FAZ and decrease in VD and perfusion at SCP, possibly attributable to ischemic changes of the macular detachment *per se* or the potential effect of SO tamponade on macular microcirculation.

Peripapillary microvasculature

Concerning peripapillary microvasculature, there is limited evidence of the impact of SO tamponade after vitrectomy for RRD. Despite the extensive and meaningful research on the effect of SO on macular microcirculation, outcomes concerning the optic nerve remain largely unexplored. Detailed information regarding the microvasculature pattern as depicted by OCT-A has been investigated in only three studies.[27–29] Wang *et al.*[27] aimed to determine the effect of SO on peripapillary blood flow; radial peripapillary capillaries VD was analyzed prior to and until 3 months following SOR at 22 eyes (19 macula-off, 3 macula-on). Measurements were performed with SD OCT-A in an area between 2- and 4-mm diameter annular zone around disk margin. The authors noted that after SOR, total radial peripapillary capillary VD significantly increased by 1.3% in RRD eyes as compared with contralateral ($p = 0.007$), with a more prominent improvement occurring in the superior rather than the inferior hemifield (1.6% and 1%, respectively). One might support that the recovery of peripapillary vessel density could reflect an amelioration of optic nerve microcirculation subsequent to retinal reattachment. Given that peripapillary vessel density increase was not observed from 1 to 3 months after primary vitrectomy, however, this outcome might not be part of a prolonged recovery process. In addition, the buoyancy of SO may have exerted greater compression on superior peripapillary capillaries, thus explaining vascular recuperation after its removal. Overall, this study showed that intravitreal SO could adversely affect peripapillary blood flow, possibly by capillary compression, although being reversible after extraction from the vitreous cavity.

Lu *et al.*[28] further evaluated peripapillary VD in eyes with RRD and SO tamponade and explored the potential association of microvasculature changes with visual outcomes. This observational study included 31 eyes with macula-off RRD who were treated with PPV and SO (8 eyes) or gas tamponade (23 eyes). OCT-A was performed at $4.5 \times 4.5\,mm^2$ to measure VD of the optic nerve head and peripapillary region. The authors concluded that compared with the fellow, eyes after RRD operation had lower peripapillary VD ($p < 0.01$), although there were no differences in superficial and deep microcirculation of the macula. These findings were in line with other studies indicating decreased blood flow of the optic nerve head by laser speckle flowgraphy.[52] Furthermore, eyes with higher peripapillary VD had a better prognosis of visual outcomes; indeed, eyes with RRD may develop rarefaction of retinal vessels and tissue hypoxia in both the macula and the optic nerve head, leading to persistent postoperative hypoperfusion, and thus compromising functional outcomes. It is noteworthy that SO-filled eyes experienced lessened visual disturbances than those with gas tamponade, possibly attributable to retinal displacement in cases treated with gas. Ultimately, milder decrease in peripapillary VD, better VA at baseline, and choice of SO tamponade were more likely to achieve better functional outcomes at 3 months after vitrectomy.

Quantitative assessment of peripapillary microcirculation after PPV with SO tamponade was recently performed in the study by Jiang *et al.*[29] The authors reviewed retrospectively 22 SO-filled eyes, while fellow unaffected eyes were served as controls. OCT-A images were obtained in $4.5 \times 4.5\,mm^2$ optic disk scan. Interestingly, when compared with fellow eyes, SO-filled eyes demonstrated significantly lower radial peripapillary capillary VD at 2 weeks ($p < 0.001$) with a gradual improvement approximating normal limits until 4 weeks, which was, thereafter, followed by VD deterioration over time. In fact, reduced preoperative retinal blood flow has been previously found to recover after vitrectomy using the laser speckle flow graph. Besides, the initial increase along with a subsequent reduction in radial peripapillary capillary VD was consistent with macular VD changes in the early postoperative period, as formerly reported. Surprisingly, the timepoint for the decline in radial peripapillary capillary VD was earlier than that of the macular VD; this may happen because the peripapillary plexus is composed of long straight capillaries with rare anastomotic connections, which makes the optic nerve head vulnerable to mechanical stress of SO, especially in the superior hemifield due to SO buoyancy. Table 1 summarizes study characteristics and their results.

Conclusion

An emerging body of literature has evaluated the retinal microcirculation characteristics as portrayed by OCT-A in patients with RRD treated by vitrectomy with intravitreal SO.[11–29,53] The current evidence demonstrates quantitative vascular alterations at the macula and the peripapillary capillary plexus. Admittedly, we could anticipate an inconsistency between microcirculation changes in various retinal regions that might be related to the different origins of microvessels. Furthermore, it is pivotal to distinguish changes attributable to RRD *per se* (especially in macula-off cases) and those potentially related to intrinsic properties of SO. We consider this information highly relevant for clinical practice, as blood flow changes could serve as a predicting factor for postoperative functional outcomes.

Retinal microcirculation alterations may provide insight into the underlying pathophysiology of structural and functional changes in SO treated eyes, including unexplained visual loss. Examination of OCT-A characteristics has contributed to the pursuit of identifying useful biomarkers that contribute to an overall postoperative approach with important implications for improving the ability to counsel patients regarding prognosis. It is strength of our survey that we included all studies assessing RRD cases successfully repaired with uncomplicated vitrectomy with SO tamponade. Furthermore, the studies analyzed in this review article excluded patients with other concomitant ocular disorders, macular or vitreoretinal interface pathology, and postoperative complications. Notwithstanding the fact that the conclusions of the researchers were not constantly consistent, potential explanations could be provided for these discrepancies; the baseline characteristics of the subjects, the ocular axial length and refractive errors, the duration of SO tamponade and the follow-up period, the region of the macula that is analyzed, the number of examined patients, and the intrinsic differences of the OCT-A technology varied among studies and should be inevitably considered. Besides, physiological differences among individuals might have been source of bias and should be accounted for.

This review article offers evidence that OCT-A characteristics may comprise useful indicators of the effect of intravitreal SO on retinal microcirculation after RRD repair. Additional longitudinal studies are warranted to clarify the role of OCT-A values, provide data referring to changes in vascular parameters and their potential association with functional and morphological outcomes, and characterize their long-term effectiveness in clinical practice. Conceivably, whether potential vascular insufficiency in SO-filled eyes is attributable to tissue hypoxic changes due to retinal detachment *per se* or the effect of SO on retinal tissue should be unequivocally determined.

Table 1. Summary of study characteristics and results.

Study	Design	Number of RRD eyes	Macular condition	Scan area (mm²)		Study of OCT-A characteristics						Postoperative follow-up
				Macula	Optic nerve	FAZ		VD macula			VD optic nerve	
						SCP	DCP	SCP	DCP	CC		
Suren *et al.*[11]	Retrospective, case–control	37	N/A	N/A	–	+	+	+	+	–	–	1 month
Angelova *et al.*[12]	Prospective	48	On/off	3 × 3	–	–	–	+	+	–	–	1 month post PPV – 2 months post SO removal
Xiang *et al.*[13]	Retrospective	23	Off	3 × 3	–	+	+	+	+	–	–	6 months
Lee *et al.*[14]	Retrospective, single-center	38	On/off	3 × 3	–	+	+	+	+	–	–	3 months post SO removal
Xu *et al.*[15]	Retrospective	36	On/off	N/A	–	+	+	–	–	–	–	3 months
Roohipoor *et al.*[16]	Prospective	45	Off	N/A	–	+	+	+	+	–	–	3 month
Maqsood *et al.*[17]	Prospective, comparative, observational	14	Off	3 × 3	–	+	+	+	+	–	–	12 weeks
Zhou *et al.*[18]	Retrospective, single-center	7	On	6 × 6	–	–	–	+	+	+	–	12 weeks
Lee and Park[19]	Retrospective, observational, cross-sectional	48	On/off	4.5 × 4.5	–	+	+	+	+	–	–	3 months post PPV – 3 months post SO removal
Fang *et al.*[20]	Prospective, observational, case–control	20	Off	3 × 3	–	–	–	+	+	–	–	3 months
Jiang *et al.*[21]	Retrospective	19	Off	6 × 6	–	–	–	+	+	+	–	16 weeks
Liu *et al.*[22]	Retrospective, single-center	17	On	3 × 3, 6 × 6	–	–	–	+	+	–	–	30 months
Lee *et al.*[23]	Retrospective	30	On/off	4.5 × 4.5	–	+	+	+	+	–	–	6 months post SO removal
Bayraktar *et al.*[24]	Prospective	24	On/off	3 × 3	–	+	+	+	+	–	–	3.4 months post SO removal
Prasuhn *et al.*[25]	Prospective	19	On/off	6 × 6	–	–	–	–	–	+	–	4 weeks post SO removal
Christou *et al.*[26]	Prospective	14	Off	6 × 6	–	+	–	+	–	–	–	1 month
Wang *et al.*[27]	Prospective	22	On/off	–	4.5 × 4.5	–	–	–	–	–	+	3 months post SO removal
Lu *et al.*[28]	Observational	8	Off	6 × 6	4.5 × 4.5	+	+	+	+	–	+	3 months
Jiang *et al.*[29]	Retrospective	22	N/A	–	4.5 × 4.5	–	–	–	–	–	+	3 months

CC, choriocapillaris; DCP, deep capillary plexus; FAZ, foveal avascular zone; N/A, not applicable; OCT-A, optical coherence tomography angiography; PPV, pars plana vitrectomy; RRD, rhegmatogenous retinal detachment; SCP, superficial capillary plexus; SO, silicone oil; VD, vessel density.

Declarations

Ethics approval and consent to participate
This article is based on previously conducted studies and does not contain any studies with human participants or animals conducted by any of the authors.

Consent for publication
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