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Structural and Perfusional Study of Successfully Repaired Diabetic Tractional Retinal Detachment Involving the Macula

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Abstract: *Purpose*: Severe visual sequelae can be frequently observed in patients with diabetic tractional retinal detachment (TRD) involving the macula. We analyzed the postoperative structural spectral-domain (SD)-OCT and optical coherent tomography angiography (OCT angiography) findings in four selected eyes that were enrolled after successful anatomical diabetic macular detachment repair. These diabetic macular tractional detachments were evolved within 16 weeks. We also correlated the postoperative mean best-corrected visual acuity with the postoperative SD-OCT and OCT angiographic findings. *Methods*: This case series included 4 selected eyes of 4 patients with a mean diabetes evolution period of 18.4±4.8 years SD. Vitrectomy techniques were successfully used for TRD involving the macula. Postoperative SD-OCT, and final postoperative functional evaluations, including BCVA and OCT angiographic evaluation were performed at the final postoperative follow-up visit. *Results*: The mean difference between the preoperative (0.87±0.15) and final postoperative (0.35±0.21) BCVA was significant ($p<0.05$). The mean duration of vision loss before surgery was 11.6±2.3 weeks. The mean time for postoperative macular detachment resolution was 3.6±1.7 weeks SD. A mean follow-up evaluation of 13.1±2.7 SD months. Final postoperative imaging tests demonstrated multiple abnormalities of the foveal avascular zone and different areas of non-perfused macula on OCT angiography. The presence of disorganization of the retinal inner layers (DRIL) and chronic ischemic macular edema changes in 3 eyes (75.0%) as well as the OCT angiography abnormal findings in 3 (75.0%) were analized and correlated. *Conclusion*: In successfully reattached macula, postoperative microcirculatory abnormalities consistent with superficial and deep plexuses deficiencies and vessel densities alterations were detected as well as persistent DRIL, EZ and ELM line abnormalities.

Keywords: Disorganization of the Retinal Inner Layers, Ellipsoid Zone, External Limiting Membrane, Optical Coherent Tomography Angiography, Proliferative Diabetic Retinopathy, Tractional Retinal Detachment

1. Introduction

Diabetes Mellitus (DM) is a worldwide problem specially in developing countries due to poor medical care. Among the main causes of severe visual loss is diabetic macular edema (DME), chronic cystic macular edema (CME) and complications related to proliferative diabetic retinopathy (PDR). The complications such as recurrent vitreous hemorrhages (VH), tractional retinal detachment (TRD), refractory macular edema, combined traction and rhegmatogenous retinal detachment and epiretinal membranes (ERMs) proliferation, are the most common indications of surgical vitrectomy [1–3].

Anti-VEGF (anti-vascular endothelial growth factor) is a very useful method in the management of diabetic retinopathy (DR). In selected patients the applications of adjuvants as steroids in paraocular injections or by intravitreous extended-release devices have gained popularity for their practicality effectiveness in maintaining long-term vision. It has left the panretinal photocoagulation (PRP) as a second-line treatment in developed countries [4].

The results of the Diabetic Retinopathy Clinical Research Network Protocol and the CLARITY (clinical efficacy and mechanistic evaluation of aflibercept for proliferative diabetic retinopathy) trials has been used as guidelines for the surveillance and management of patients with macular edema and complications related to proliferative diabetic retinopathy, these results are found to be better over classical PRP treatment [4].

In case of delayed detection of diabetic retinopathy, it must be treated by advanced pars plana vitrectomy (PPV) techniques. The visual outcomes after diabetic vitrectomy, however, have not undergone a similar change [5, 6]. In spite of numerous studies, the predictive factor of visual outcomes remains to be elucidated [7].

Sun et al. [8] have used the horizontal B-scan of optical coherence tomography (OCT) images to characterize the disorganization of the retinal inner layers (DRIL) as the inability to distinguish any of the boundaries of the ganglion cell layer-inner plexiform layer (GCL-IPL) complex, inner nuclear layer (INL), and outer plexiform layer (OPL). Regarding DME, DRIL was reported to be associated with poor BCVA and changes in the DRIL affects the subsequent changes in final BCVA

OCT angiography is a noninvasive OCT platform to create in vivo 3-dimensional composites of separate layers of the retinal and choroidal vasculature without the use of a contrast agent [9]. Sensitivity can be increased through multiple algorithms for detailed imaging of each superficial and deep retinal capillary plexus as well as the choriocapillaris [10-12]. The OCT angiography images can be automatically segmented to provide an en face, depth-encoded region of the vasculature that is co-registered with the structural OCT B-scan.

OCT angiography eliminates the need for a dye [13, 14], and eliminates the “transit window” seen with both fluorescein angiography (FA) and indocyanine (ICG). OCT angiography also avoids the dark artifact of retinal and vascular features that may occur with dye leakage [15]. The capillary-level detail with high depth resolution provides information given only by histological studies [16–20].

In patients with DR, OCT angiography demonstrates retinal foveal avascular zone (FAZ) enlargement, and microaneurysms. The ability to separately examine the superficial and deep capillary plexuses with OCT angiography helps users delineate retinal involvement in various diabetic lesions. AngioVue imaging showing superficial and deep plexuses with vessel density (VD) quantification of proliferative DR shows areas of nonperfusion, microaneurysms, and clear enlargement of the FAZ [21].

Studies shows that FA cannot resolve the deep capillary plexus or peripapillary radial capillaries at all [15, 16, 22]. Most, if not all, of the clinically relevant macular findings are demonstrable and correlated with OCT angiography findings in DR [23, 24]. OCT angiography is a superior tool for quantitatively evaluating the severity of non-perfused retina.

OCT angiography can reliably detect both neovascularization of the disc (NVD) and elsewhere (NVE), assuming that the pathology is within the field of view [25-27]. These advancements are expected to improve the management of DR. It includes the monitoring in quantification of retinal capillary perfusion while treating patients with anti-VEGF and after surgical treatment of diabetic TRD involving the macula as we did in this study. Alterations in the retina perfusion during or after macula surgery, or due to microangiopathy natural progression may be prevented with sustained anti-VEGF therapy [19]. This study attempts to predict best-corrected visual acuity (BCVA) after successful macular surgery. Specific spectral-domain (SD)-OCT findings, such as DRIL and ellipsoid zone (EZ) have been used as reliable biomarkers for the BCVA prediction. DRIL has been used as it behaves longitudinally after anatomically and structurally successful surgery of the macula. The study also aimed to analyze some OCT angiography findings, such as superficial and deep capillary plexuses, VD and FAZ enlargement and correlate those findings with the final postoperative BCVA.

2. Patients and Methods

2.1. Study Design and Patient Selection

The present study adhered to the tenets of the Declaration of Helsinki. All the required approval were taken from the institution enrolled (no reference number was provided for the present study). Written informed consent in accordance with the institutional guidelines was obtained from all four patients.

The clinical charts of four symptomatic eyes of four patients were included with the following criteria:

1) 18 years or older,
2) being a controlled diabetic,
3) progressive loss of vision of less than 16 weeks due to macular tractional retinal detachment (TRD),
4) TRD involving the macula confirmed by SS-OCT or B-mode ultrasonography,
5) an axial length of <26.5 mm,
6) no evidence of vascular macular pathology other than PDR,
7) at least six months of folow-up after surgery,
8) had undergone successful vitrectomy techniques with clear media at the end of follow-up,
9) evidence of TRD resolution with the macula attached in the last follow-up visit,
10) have at least one postoperative OCT angiography, SS-OCT or SD-OCT assessment.

The exclusion criteria were as follow:

1) loss of follow-up,

2) TRD from other vascular etiology,
3) postoperative complications with opaque media at the last follow-up visit,
4) developing neovascular glaucoma with no light perception during follow-up.

Four selected eyes were found to meet the aforementioned criteria and their charts were reviewed and analyzed from January 2018 to October 2020.

2.2. Examination

All patients underwent a general ophthalmic evaluation and preoperative examinations. It includes a BCVA assessment, slit lamp biomicroscopy examination, fundus examination with panfundoscopic contact lenses, and indirect ophthalmoscopy. In clear media eyes, cross-sectional images of the macular region were acquired using SD-OCT (Retvue-3.4 OCT, Optovue Inc., Fremont, CA, USA). The axial lengths were measured using partial coherence laser interferometry (Zeiss IOL Master 700; Carl Zeiss Meditec, AG, Oberkochen, Germany). The presence of tractional macular detachment was confirmed by SD-OCT, B-scan ultrasonography (A and B Ultrasound Unit, Quantel Medical, Du Bois Loli, Auvergne, France) and indirect ophthalmoscopy. A postoperative microstructural evaluation was performed using SD-OCT (Spectralis OCT; Heidelberg Engineering, Heidelberg, Germany) and the swept-source DRI OCT Triton device (Topcon Medical Systems, Inc.). The macular VD evaluation comprising four postoperated eyes, was performed using the OCT angiography device (RTVue XR OCT Avanti with AngioVue Software by OptoVue, Inc., Fremont, CA, USA) at the superficial vascular macular plexus with a default 3x3 mm macular scan.

2.3. Surgical Procedures

Standard 25-gauge three-port pars plana vitrectomy was performed in the four eyes under local anesthesia plus sedation by one of the authors (MAQR). In addition to central vitrectomy, triamcinolone acetonide (Kenalog 40 mg/mL; Bristol-Myers, New York, NY)-assisted removal of the cortical vitreous from the surface of the retina was performed using a silicone-tipped cannula and active suction, paying special attention to detect macular preretinal fibrovascular proliferations. Removal of the hyaloid was done with a combination of delamination alternating with segmentation along with viscodissection techniques for adherent vitreous and epiretinal fibrovascular proliferative tissue. To maintain hemostasis throughout the procedure, attention was given to any foci of perfused retinal neovascularization. After removal of the anterior-posterior traction, we then focused on tangential or circumferential traction, and surgical macular evaluation was performed in the four cases by using trypan blue 0.15% ophthalmic solution (Membrane Blue; Dutch Ophthalmic, USA) to stain cortical vitreous remnants or epiretinal macular membranes. We used a mixture of 0.15 mL of 0.25 mg/mL (0.025%) diluted isomolar solution (pH 7.4) of Brilliant Blue G (BBG) dye to stain and remove the ILM to assure all epiretinal traction was removed. Once the tractional components were released scatter panretinal photocoagulation (PRP) with an argon laser was performed in all cases. In the four cases only long-acting non-expandable perfluoropropane (C_3F_8) gas mixture at 15% was used as a tamponade; phacoemulsification followed by intraocular lens implantation was performed in 2 phakic eyes.

2.4. Study Outcomes

The primary aim was to analize the structural and perfusional postoperative findings of the intentionally selected eyes with a fully resolved diabetic TRD that underwent timely sophisticated pars plana vitrectomy (PPV) techniques. The secondary aim was to correlate the long-term final postoperative BCVA with OCT and OCT angiographic findings.

The patients' general and demographic data are listed in Table 1.

Table 1. *Diabetic TRD patients´ general and demographic data in the sample (n= 4 eyes).*

Variable	Mean	Standard deviation
Age (years)	59.43	±8.96
Axial length (mm)	21.8 (21.2 to 23.3)	±1.67
Mean follow-up (months)	13.1	±2.7
Mean time preoperative TRD evolution (weeks)	11.6	±2.3
Mean time postoperative TRD resolution (weeks)	3.6	±1.7
Preoperative BCVA (logMAR)	0.87	±0.15
Final BCVA (logMAR)	0.35 (P <0.05)	±0.21

	n	%
Female gender	3	75.0
Right eye	2	50.0
Phakic	2	50.0
Additional retinal surgery	1	25.0
Complications:		
VH	1	25.0
Macular redetachment	1	25.0

TRD, tractional retinal detachment; BCVA, best corrected visual acuity. VH, vitreous hemorrhage

2.5. Clinical Case 1

46-year-old Female patient, carrier of type 2 diabetes of 18 years of evolution, has had irregular metabolic control, her last glycosylated hemoglobin was 7.2, she is a carrier of proliferative diabetic retinopathy and has had panretinal photocoagulation twice in each eye; she was accomplished a 15 weeks period with progressive loss of vision in her right eye; The ophthalmological examination shows a pseudophakic right eye, with cloudy media, the TOA is 14 mmHg without manifestations of anterior segment ischemia, signs of moderate vitreous hemorrhage and evidence of fibrovascular tissue that detaches the macula. Mode B ultrasound confirms the diagnosis of tractional retinal detachment with macular involvement. She underwent vitrectomy and endophotocoagulation, achieving successful reapplication of

the macula without trans- or postoperative complications. Postoperative evaluation at 8 postoperative months showed residual cystic macular edema (a and b image), the final postoperative segmented superficial vascular plexus evaluation showed areas of capillary closure (c image), the foveal avascular zone (FAZ) looked enlarged and irregular. There was an irregular deep vascular plexus with a smaller, preserved FAZ, depicting some remodeling of the FAZ (d image), a lower VD was detected on the 9-grid based measurements over each subfield (e image). Postoperative extrafoveal residual superficial traction without macular distortion (f image) with moderate residual macular edema were detected at the last follow-up visit evaluation (g image).

2.6. Clinical Case 2

49-year-old male patient with chronic complications of proliferative diabetic retinopathy with evidence of vitreous bleeding on several occasions, he has not been able to be photocoagulated satisfactorily and due to the presence of fibroglial tissue, he was not managed preoperatively with antiangiogenic therapy, he has 16 weeks with significant low vision and the ophthalmoscopic and ultrasound examination showed complex tractional detachment of the macula (a image). Seventeen months after vitrectomy he was evaluated with OCT angiography, an Angio montage of the papilla and macula shows restored perfusion quite close to normal, with an irregular and enlarged avascular foveal zone and interruptions of the capillary margin at the level of the superficial plexus (b image); horizontal OCT shows an irregular foveal contour and diffuse edema, evidence of DRIL and external markers preserved on OCT (c image), the superficial vascular plexus is altered and shows important capillary closures in the vicinity of the FAZ which is enlarged (d image). the macular topography shows discrete and irregular edema (e image), a qualitatively altered VD pattern considered lower than normal was detected (f image), and the deep vascular plexus showed very evident microvascular alterations and capillary vascular closures (g image)

2.7. Clinical Case 3

Female patient, 62-year-old diabetic from 22 years of evolution with significant drop in left eye vision of 14 weeks of evolution, with no history of photocoagulation or therapy with antiangiogenics. Ophthalmoscopic examination (a image) and B-mode ultrasound showed extensive tractional detachment of the posterior pole with involvement of the macula; she underwent uncomplicated vitrectomy and phacoemulsification with successful reattachment and no complications. At 14 months postoperative, perfusion evaluation was performed using OCT angiography detecting a diffuse thickening of the macula (b image), SD-OCT showed significant thickening with large intraretinal cysts and important alterations in the macular structure with the presence of subfoveal DRIL, other external retina layer biomarkers were hardly recognizable (c image); the superficial vascular plexus showed multiple irregularities (d image), the deep vascular plexus showed capillary closures and multiple microaneurysms (e image), the vertical OCT image of the macula showed severe cystic macular edema, ischemic structural DRIL alteration with loss of biomarkers (f image); the topography of the superficial retina is abnormal and irregular in thickness (g image), the qualitative evaluation of the VD pattern was considered lower (h image).

2.8. Clinical Case 4

59-year-old female patient with rapid and progressive loss of vision of 8 weeks of evolution, carrier of diabetes mellitus of 21 years of evolution with good glycemic control and glycosylated hemoglobin of 7.9, the diagnosis of tractional detachment of the retina was made. With the macula involved (a image), the preoperative SD-OCT allowed to appreciate the complexity of the vitreoretinal interface with the presence of abundant epi- and preretinal membranes and abundant amount of subretinal fluid (b image), she underwent vitrectomy surgery and endophotocoagulation, 4 weeks postoperatively, a significant postoperative vitreous bleeding was identified with re-detachment of the macula, for which a revision of vitrectomy and successful reapplication of the macula were performed. The final postoperative evaluation at 13 months follow-up showed irregular thickening of the superficial layers of the retina in the superficial topography of the macula (c image), the full-thickness topography evidenced moderate and uniform thickening of the macula (d image), the VD was deficient qualitatively with several areas of lower than normal VD (e image), the superficial vascular plexus showed great alterations of the microcirculation, capillary closures and the enlarged FAZ without precise limits to be measured (f image), the deep vascular plexus with significant alterations and important capillary closures (g image), horizontal OCT showing irregular foveal contour, thickening at the expense of persistent edema, EZ is identified with multiple irregularities and it is not possible to identify continuity in the ELM line biomarker (h image), vertical OCT showed irregularities in the superficial layers with subfoveal DRIL, irregular foveal contour, diffuse thickening and subfoveal EZ with very distinct disruptions (i image).

Table 2. *Summary of preoperative and postoperative TRD structural and perfusional findings (n=4 eyes).*

SD-OCT and OCT angiography Findings		
Mean time preoperative evolution TRD	6.2 weeks	±3.5 SD
Mean postoperative TRD resolution	3.6 weeks	±1.7weeks
Postoperative normal contour profile	1	25.0%
CSFT abnormalities	3	75.0%
Presence of DRIL	3	75.0%
EZ (IS/OS) abnormalities	3	75.0%
ELM line abnormalities	2	50.0%
Superficial and deep plexus abnormalities	3	75.0%
Vessel density abnormalities	3	75.0%

BCVA, best corrected visual acuity; EZ, ellipsoid zone; TRD, tractional retinal detachment; CSFT, central subfoveal thickness; DRIL, disorganization of retinal inner layers; IS/OS, internal segment/external segment; ELM, external limiting membrane; logMAR, logarithm minimum of the angle resolution

3. Discussion

Technology has improved over the past decade, allowing the development of effective small-gauge vitrectomy, wide-field viewing systems, advanced fluidics, and precise tissue control, which may be especially useful in complex cases of TRD involving the macula. Thus, the complications of PDR may be addressed both medically and surgically, as we described in this report. However, the outcomes of surgical treatments for diabetic patients have not undergone a similar change [28, 29].

The probability of DR improvement is more likely in eyes receiving anti-VEGF injections than in eyes receiving laser treatment [25]. Eyes with vitreous hemorrhage that precludes the use of adequate laser treatment have traditionally two treatment options: wait for the hemorrhage to clear, with the inherent risk of rebleeding, and attempt additional laser treatment, or perform vitrectomy. The DRCR.net protocol N study examined the utility and effectiveness of intravitreal ranibizumab in comparison with intravitreal saline for facilitating clearance of vitreous hemorrhage and permitting and adequate PRP laser treatment [5]. Recurrent vitreous hemorrhage was noted in 6% of the eyes treated with ranibizumab vs. 17% of those treated with saline ($P = 0.01$). The 1-year results demonstrated low rates of recurrent vitreous hemorrhage in both arms (38% overall; 35% in the ranibizumab arm vs. 41% in the saline arm, $P > 0.05$) with a modest improvement in the PRP completion rate. The recently published DRCR.net Protocol S study examined the outcomes comparing PRP treatment with intravitreal ranibizumab for eyes with PDR [30]. Primary outcomes were measured at 2 years. Eyes that received ranibizumab demonstrated visual acuity (VA) outcomes that were non-inferior to those of eyes treated with PRP, had reduced OCT thickness, and had less need for vitrectomy surgery [29].

Diabetic macular ischemia due to microangiopathy leads to decreased perifoveal capillary blood flow, which in turn causes chronic ischemia of the retinal tissue. By assessing the point-to-point correlation between SD-OCT and non-perfusion on OCT angiography, we observed that retinal capillary nonperfusion is associated with photoreceptor compromise on OCT which is reflected in an evident alteration of the EZ (IS/OS) continuity. This study highlights a new concept explaining the possible contribution of the retinal deep capillary plexus to photoreceptor compromise in the tractional manifestations of the diabetic macula. Macular ischemia at the deep capillary plexus may play an important role in these outer retinal changes and photoreceptor ischemic compromise. We speculate a significant amount of ischemia of the detached external layers of the retina which contributes to the deficiencies of the deep capillary plexus in these eyes worsening the functional and structurally recovering of this tissue as long as the macula remains detached from the RPE. This study included four successfully reattached macula in four selected eyes, mostly all eyes showed outer retinal disruption revealed by SD-OCT and SS-OCT that colocalized to areas of enlargement of the FAZ and macular capillary nonperfusion and VD lower than normal in the corresponding OCT angiography in the postoperative examination, so we inferred that photoreceptor damage with EZ disruption, and presence of macular ischemia with evidence of DRIL are the possible reasons for the poor visual improvement after the remission of macular edema [27, 30] or diabetic TRD surgical resolution according with our results.

Foveal DRIL with enlarged FAZ has been shown to correlate with poor BCVA in patients with resolved DME [31], but there is very limited literature discussing how to establish the correlation between OCT angiography features and clinical testing parameters to verify whether OCT angiography parameters can serve as objective factors to predict visual improvements after treatment with surgery for TRD involving the macula. In this study, four OCT angiography biomarkers, namely, superficial vascular plexus, deep vascular plexus, FAZ characteristics, and VD qualitative assessment, were comprehensively analyzed along with their correlation with clinical markers, that is, BCVA and structural markers such as central subfoveal thickness (CSFT), presence of DRIL, and EZ appearance to determine how these SD-OCT and OCT angiography biomarkers looked at the last postoperative follow-up evaluation and how they might correlate with final postoperative BCVA.

Through our clinical experience with retinal microcirculation and microangiopathy development, we have found that, unlike FA, OCT angiography allows in-depth study of perfusional changes in DR. Changes in the structure of the superficial network can be observed in patients with macular ischemia, and the evaluation of macular ischemia has potential as a biomarker for DR, since the demarcation of nonflow areas is obvious in the superficial plexus.

We found that poorer VD in both the superficial and deep capillary plexuses in the parafoveal area was correlated with presence of DRIL, EZ abnormalities, and abnormal CSFT with a poorer final postoperative BCVA. This finding is consistent with that of a previous study of others [26, 32-34]. The outer parafoveal VD in the superficial layer has been shown to predict visual improvement after ranibizumab treatment, but this finding was not demonstrated in eyes after macula reattachment surgery [32]. VD in the macula could also be used in clinical applications to evaluate the perfused status of the macula after surgery, as demonstrated in this report.

Previous studies have shown that increased FAZ abnormalities, an increased nonperfusion area, decreased superficial VD at the parafoveal macula sectors and perifoveal capillary network abnormalities in OCT angiography were associated with worsening of DR [33, 35]. Here, we report our experience of evaluating capillary network of the FAZ as well as VD evaluation as potential signs of macular ischemia in successfully operated eyes with TRD involving the macula. The analysis of our long-term postoperative results showed that practically all four eyes showed structural alterations that were correlated with perfusion deficiencies in the AngioVue, and functional ones

reflected in a lack of better recovery in the final postoperative BCVA. In this way, this study evaluated the feasibility of using OCT angiography to evaluate capillary nonperfusion as a potential sign of macular ischemia in eyes that undergo vitrectomy due to TRD involving the macula.

It is possible that macular ischemia, in addition to photoreceptor disruption, also contributes to poor vision in our patients. Moein et al. [28] showed that a larger FAZ was correlated with poor VA in patients with resolved DME. In our report, a large FAZ was poorly correlated with BCVA owing to reduced number of studied patients enrolled, besides, this is one of the limitations of this study.

Durvin et al. [36] showed that the VD in the superficial layer, not the deep layer, was correlated with the BCVA in DR, perhaps due to the projection artifact on the deep layer, with improvements in the technique for projection artifact removal, enabling better visualization of the two distinct main retinal capillary plexuses. In this study, the VD was only evaluated at the level of the superficial vascular plexus.

In the present study, we also evaluated postoperative foveal DRIL and other SD-OCT and SS-OCT parameters, such as EZ and ELM integrity, to assess how they may predict BCVA in eyes undergoing successful surgery for TRD involving the macula. Our results demonstrate that DRIL can resolve very slowly over time and that resolution of DRIL might be a good predictor of subsequent improvement in the final BCVA. The decreased DRIL abnormalities presumably represents anatomical improvement toward a more normal morphology. We hypothesized that macular ischemia and enlargement of the FAZ may contribute to outer retinal and photoreceptor disruption on SD-OCT in diabetic patients as a possible consequence of ischemia at the level of the deep capillary plexus. Whether reversibility potentially declines with increasing duration of DRIL or can be induced to occur is unknown, but these findings would have important implications in the timing of diabetic TRD surgery.

It is unknown exactly what DRIL, as demonstrated on SD-OCT images, may represent histologically. This strong and very distinct biomarker may indicate tissue damage or a lower probability of tissue recovery. We believe that the mechanisms by which DRIL affects BCVA have not yet been determined, and further histological correlation is needed. Thus, we are also trying to correlate the postoperative structural evaluation of foveal DRIL with OCT angiography findings in eyes with successful surgical reattachment of the macula. These findings may support our results showing that the presence of significant DRIL length correlated with a poor VD pattern evaluation, and thus, possibly less viable remaining tissue are associated with worse visual outcomes in successfully repaired TRD involving the macula.

DRIL affecting 50% or more of the central 1-mm-wide zone centered on the fovea (foveal DRIL) is associated with worse VA. This description holds true in eyes with reduced or not recovered vision despite TRD anatomic resolution. The strong association of foveal DRIL with the BCVA in a previous cross-sectional study [32] supported the investigation of foveal DRIL as a potential biomarker of future BCVA in eyes with current TRD involving the macula.

Reports on PDR after surgery and numerous studies of various non-vascular macular diseases have shown that disruption of the outer retina mainly the EZ and ELM biomarkers are significant predictors of visual prognosis [34, 35]. In the present study, the presence or length of the DRIL and the integrity of the ELM and EZ were considered as factors that may predict visual outcomes. However, a multilinear regression analysis with a greater number of patients is needed to show that the DRIL, and the EZ or the ELM line abnormalities are associated with visual outcomes and might be used as visual predictors consecuently.

The study failed to detect any association between SD-OCT variables and subsequent BCVA in eyes with resolved TRD involving the macula; this failure may have occurred because we did not include the statistically significant number of patients, the multiple preoperative abnormalities in this group, and not a separate analysis was performed for each underlying abnormality. The present study shows that certain biomarkers are very important once the macula has been successfully reattached. Another advantage it has given us the information that once the macula has been detached and depending on the qualities of perfusion of the eye, the issue of macula detachment has to be attended in a timely and careful way to reattach the macula and ensure that the perfusion mainly of its outer layers is resumed. It is indicated in postoperative evaluations where better results are shown when the eye underwent a timely successfully surgery with total diabetic TRD resolution.

4. Conclusion

In conclusion, to best of our knowledge, this is one of the first reports that correlated DRIL evaluation, OCT angiography vascular plexus findings evaluation and VD quality characterization made besides BCVA evaluation after the resolution of TRD involving the macula. We observed damage of structural biomarkers with poorer than normal VD evaluation patterns with persistent capillary abnormalities at the level of superficial and deep vascular plexuses of the macula. The foveal area remained irregular and enlarged without showing complete recovery data, all this was correlated with a bad but functional final visual acuity.

This preliminary study demonstrates that diabetic ischemia is largely responsible for poor visual outcomes and that the limiting factors appear to be at the vascular and cellular levels. Obviously, the visual prognosis of ischemic macula worsens substantially when a tractional detachment of the macula occurs, hence the poor visual recovery with great structural and perfusion alterations of the macula. The final postoperative BCVA appears to be associated with multiple factors such as the preoperative perfused status of the macula, the preoperative evolution TRD time period, the control and possible sudden changes in the transoperative perfused status of the macula, the postoperative TRD resolution time period, and the subsecuent postoperative control of the perfused variables.

This report expands the knowledge of the significance of DRIL and other biomarkers in OCT and some biomarkers in OCT angiography in successfully operated eyes due to TRD involving the macula by showing the effect of different resolution patterns on BCVA recovery.

Further research is needed, and it is already on its way in our institution to determine the best timing to perform surgical interventions in patients with TRDs involving the macula secondary to PDR to minimize irreversible damage to the retinal tissue and improve BCVA in these complex patients.

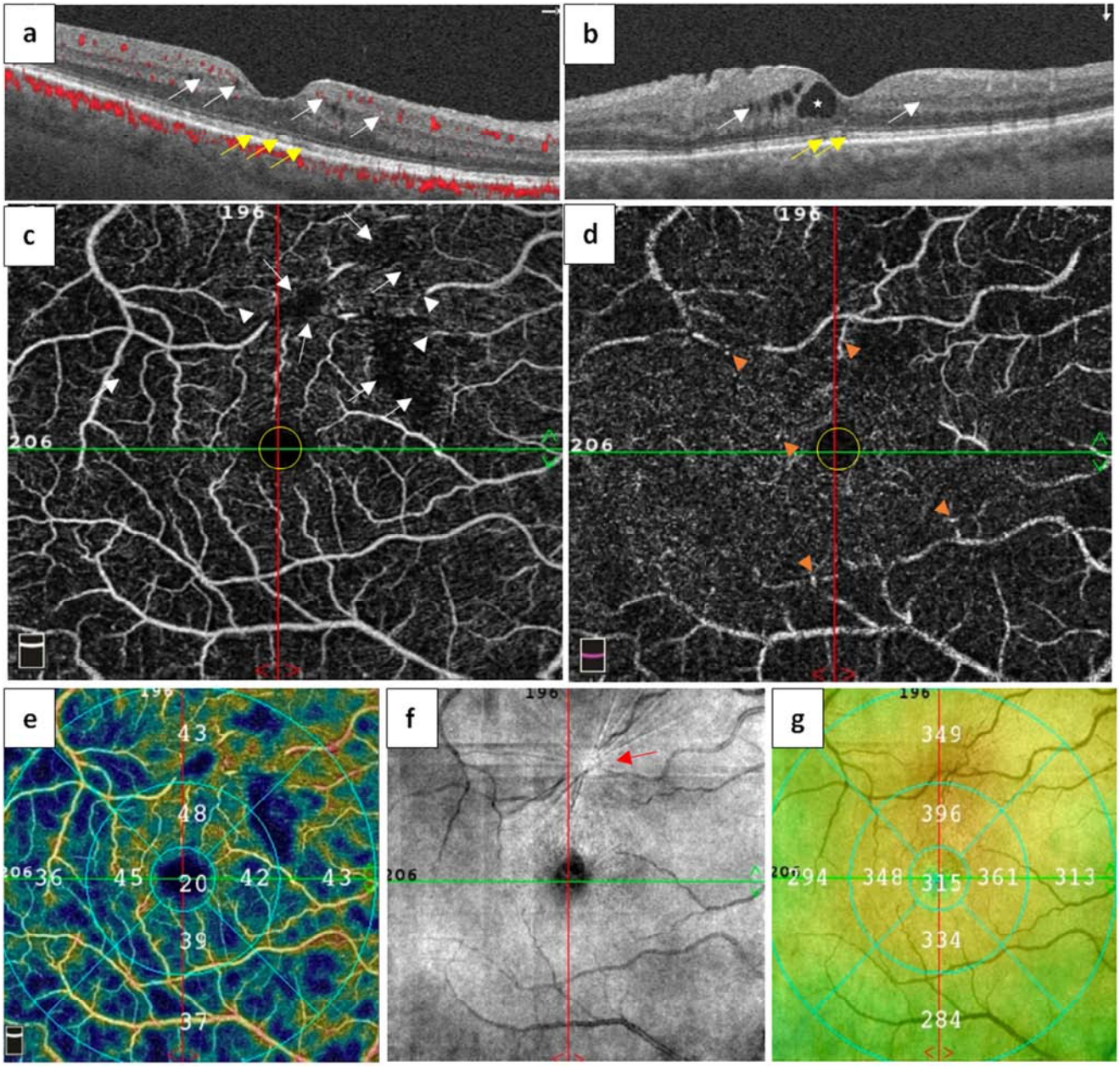

Figure 1. *Multipaneled figure corresponding to clinical case 1. a image postoperative horizontal scan depicting a recovered contour foveal profile, diffuse thickening of the macula, there is some disorganization of the retinal inner layers (DRIL) (white arrows) and some discontinuities (yellow arrows) of the ellipsoid zone (EZ). b image depicts a vertical B scan with retinal thickening owing to intraretinal retinal edema (white asterisk), DRIL (white arrows) and discontinuities over the EZ (yellow arrows) and external limiting membrane. c image depicts the final postoperative segmented superficial vascular plexus slab with areas of capillary closure (white arrows), the foveal avascular zone (FAZ) looks enlarged and irregular (yellow circle). d image depicts an irregular deep vascular plexus with a smaller, preserved and remodeling of the FAZ (yellow circle). e image depicts a lower vessel density slab showing the 9-grid based measurements with the value showed in white numbers over each subfield. f image depicts in the red free SLO segmentation a traction epicenter (red arrow). g image corresponds to full-thickness macular topography with diffuse thickening. g image corresponds to full-thickness macular topography with diffuse thickening.*

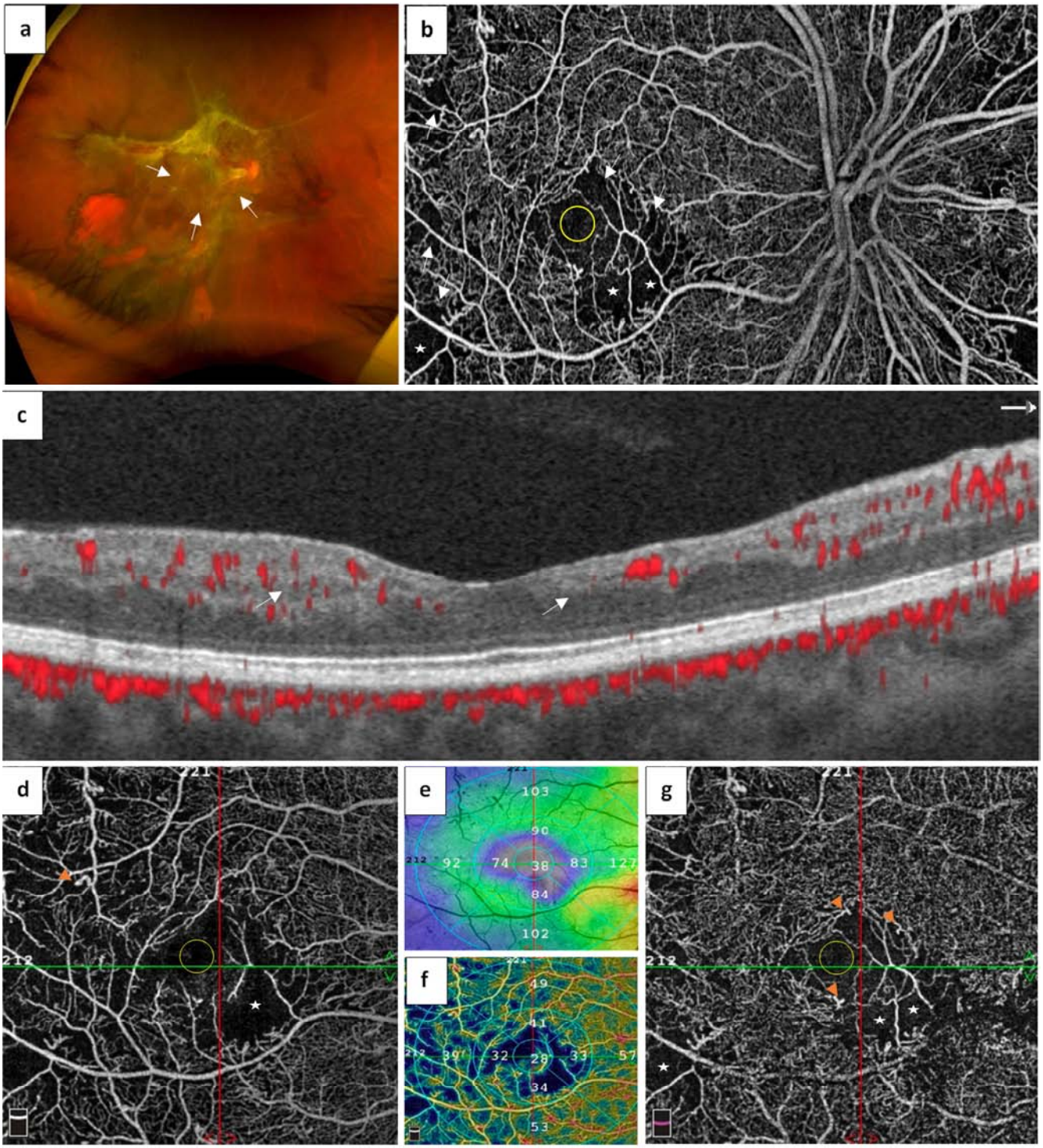

Figure 2. *Multipaneled figure corresponding to the clinical case 2. a image shows a wide-field color photo with fibrovascular tissue emerging from the optic nerve and running along the supertemporal vascular arcade that detached the macula (white arrows). b image is the corresponding final postoperative montage showing both capillaries' plexuses with some vascular irregularities mainly around the FAZ (yellow circle) which is enlarged and with some capillary dropout (white arrow heads).* ***c*** *image is the corresponding horizontal B scan SD-OCT with irregular retinal thickening mainly over the temporal side, there is evidence of DRIL (white arrows) and the ELM line and EZ look preserved, the red dots depict the tomographic retinal vessels and the choroidal capillaries. d image depicts the superficial vascular plexus with some areas of capillary non-perfusion (white asterisks), the FAZ is enlarged and the perifoveal capillary net is almost wipe-out. e image shows superficial partial-thickness retinal irregularities on the macula topography. f image is the corresponding abnormal vessel density slab of the different macular subfields with the vessel density in white numbers. g image depicts the abnormal deep vascular plexus with some capillary remodeling around the FAZ (yellow circle) and countless capillary micro aneurismatic dilations (orange heads).*

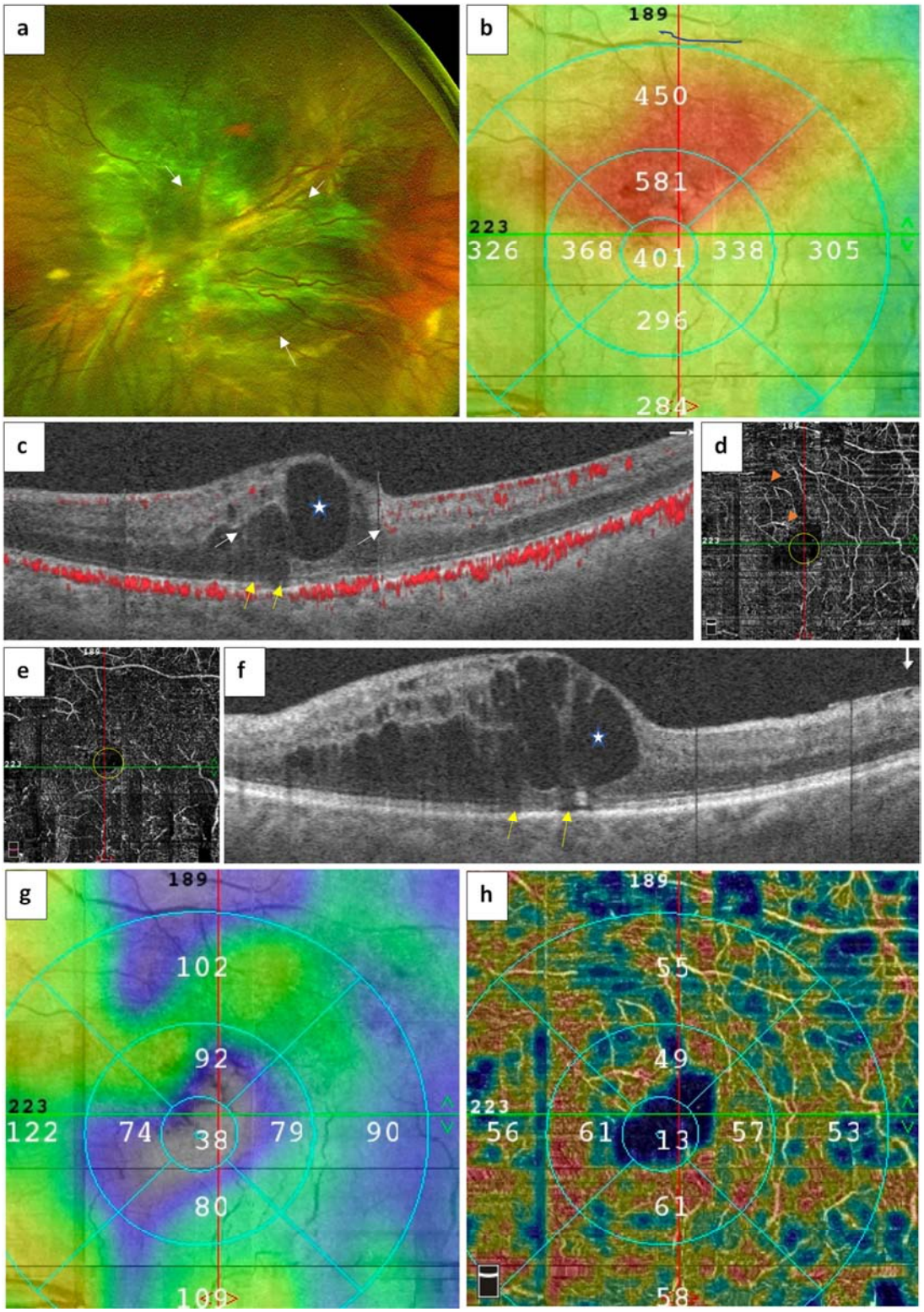

Figure 3. *Multipaneled figure corresponding to the clinical case 3. a image wide-field color photo image depicting an extensive tractional retinal detachment (white arrows). b image showing irregular and severe postoperative retinal thickening on the full-thickness macular topography. c image depicts horizontal B scan with severe macular thickening, and large cystic formation (white asterisk), severe postoperative DRIL (white arrows) and outer retina OCT biomarkers (EZ and ELM) severely disrupted (yellow arrows). d image depicts an abnormal irregular superficial vascular plexus with lots of abnormal capillary segments, micro aneurismatic vascular dilation and an enlarged FAZ (yellow circle), some mild saccadic eye movement artifacts are seen. e image depicts the abnormal vascular deficiencies of the deep vascular plexus. the FAZ looks smaller with some vessels remodeling (yellow circle)**. *f image depicts the corresponding vertical B scan with severe macular thickening owing to intraretinal multicystic presence of serous material (white asterisk). g image corresponds to the partial-tickness superficial irregular macular topography. h image corresponding to the abnormal vessel density segmentation image over the different macular subfields.*

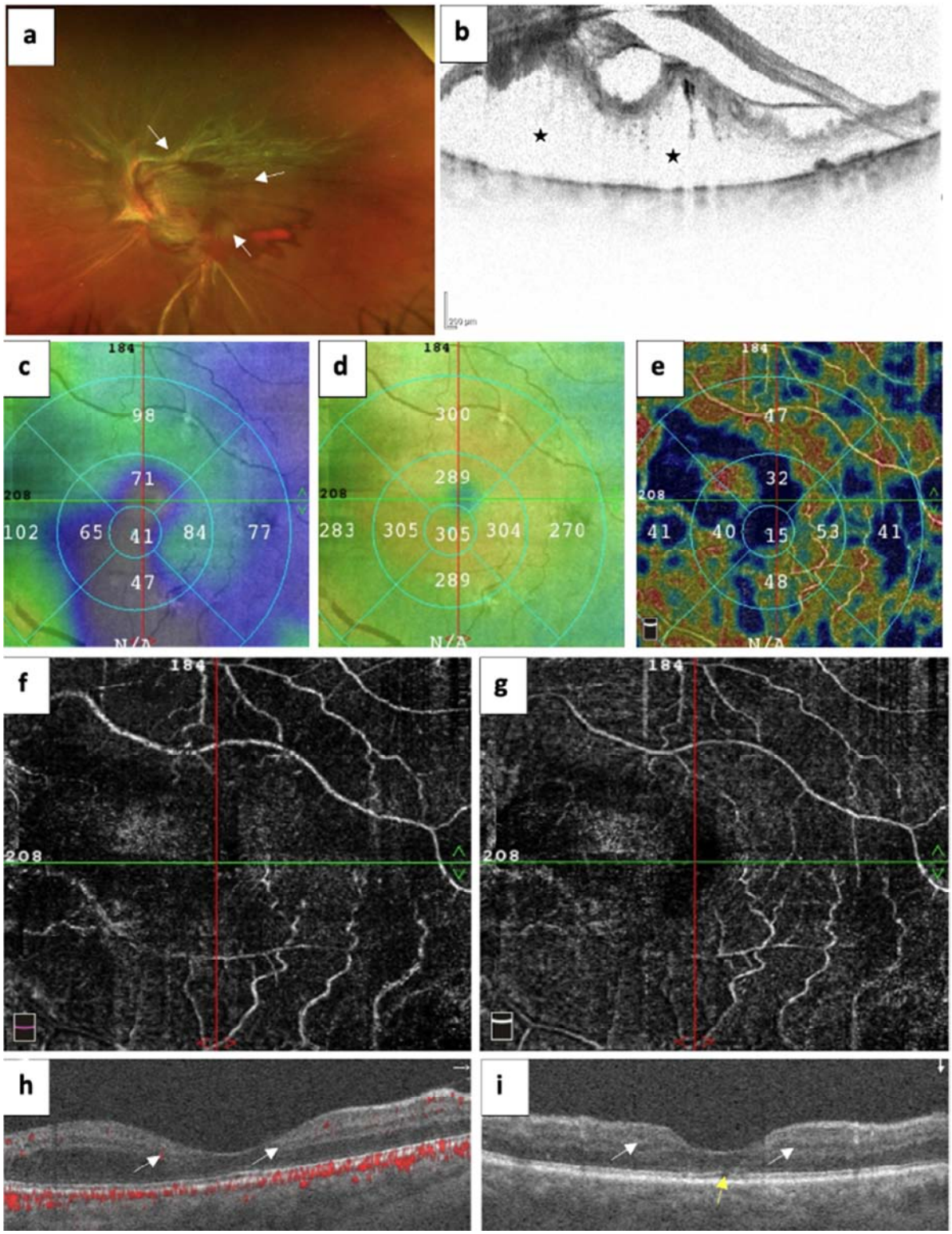

Figure 4. *Multipaneled figure corresponding to the clinical case 4. a image depicts a wide-field color photo of a left eye with 3 weeks evolution diabetic tractional retinal detachment involving the macula (white arrows). b image depicts a preoperative horizontal B scan OCT with a complex vitreoretinal interface and abundant presence of subretinal fluid (black asterisks). c image depicts a postoperative partial-thickness abnormal superficial macular topography. d image shows the corresponding postoperative full-thickness uniformly thick macular topography. e image depicts an abnormal qualitatively vessel density image at the different macular subfields. f image shows a very abnormal microcirculation at the level of superficial vascular plexus, it was not possible to determine de FAZ. g image depicts the deep vascular plexus with countless microvascular perfusional abnormalities. h and i images depict a crossline OCT B scan through the center of the fovea, there is an abnormal foveal contour and diffuse macular thickening, presence of DRIL can be observed (white arrows), the EZ and ELM line showed irregularities and discontinuities at subfoveal level (yellow arrow), the red dots indicate retinal vessels and the choroidal capillaries.*

Declarations

Ethics Approval and Consent to Participate

This study adhered to the tenets of the Declaration of Helsinki, received full ethical approval from the research ethics committee, and was approved by the institutional review committee and the teaching department of the institution enrolled (no reference numbers were provided for retrospective studies by this institution). Written informed consent was obtained from all patients in accordance with the institutional guidelines.

Consent for Publication

Written consent was obtained from all patients.

Availability of Data and Materials

The dataset supporting the conclusions of this article is available in the retina service of the Retina Specialists repository file at the Institute of Ophthalmology in http://www.oftalmologiainteralabc.com/retinaspecialists. The dataset supporting the conclusions of this article is included within the article.

Competing Interests

The authors declare that they have no competing interests.

Authors' Contributions

MAQR, Surgeon in Chief, study conception, writing the manuscript, dataset interpretation, final revision, conclusions; EAQG, figures artwork, tables; FEC, photographic material compilation; JHKL, photographic material compilation; ANJ, assistant surgeon, photographic material compilation; BMA, assistant surgeon, photographic material compilation; JGMN, material compilation; and FGW, final revision. All authors have approved the manuscript for submission.

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