

Changes in the retinal thickness after microinvasive vitrectomy with inner limiting membrane removal in patients with diabetic retinopathy

M.I.Kerimov

National Centre of Ophthalmology
named after acad. Zarifa Aliyeva

Baku (Azerbaijan)

E-mail: mushfikk@mail.ru

The purpose. To study changes in the macular retinal thickness in patients with diabetic retinopathy after microinvasive vitrectomy with inner limiting membrane (ILM) removal.

Material and Methods. This was a retrospective analysis of spectral OCT data of the macula of eighty-eight eyes (77 patients) after 23 gauge vitrectomy for proliferative diabetic retinopathy. The surgeries were performed at National Centre of Ophthalmology named after acad. Zarifa Aliyeva, Baku, Azerbaijan, in the period between 2010 and 2015. Study group comprised fifty-nine eyes in which vitrectomy was performed with ILM removal; Control group comprised thirty eyes in which ILM was not removed during the surgery. ILM was peeled using ILM forceps (Alcon, the USA) after brilliant blue G (BBG) staining. For statistical analysis, we used three Cirrus-HD OCT measurements: central (1 mm), inner temporal (1-3 mm), and inner nasal (1-3 mm) retinal thickness.

Results. At 12 months after surgery, the mean macular thickness in the inner temporal subfield was much thinner in the eyes with ILM removal than in those without ILM removal, $279 \pm 51.9 \mu\text{m}$ vs. $332 \pm 93.8 \mu\text{m}$, ($p=0.002$), respectively. The macular thickness in the central, foveolar subfield almost did not differ in different groups as well as the thickness in the inner nasal subfield ($p>0.05$ in both cases). Since there was not a healthy paired eye, we compared our data with the normative data obtained from the paper by Liu et al [2011], in which Cirrus HD OCT showed the macular thickness in the inner temporal subfield equal to $313.4 \pm 18.5 \mu\text{m}$ in diabetic patients without retinopathy signs, which was significantly higher than in our patients after vitrectomy with ILM removal ($295 \pm 43.1 \mu\text{m}$, $p=0.002$). And the macular thickness in the nasal and central foveal subfields did not differ significantly from our data.

Conclusions. We revealed thinning of the macular temporal subfield after vitrectomy with ILM removal not only in patients with diabetic macular edema but also with tractional retinal detachment and vitreous hemorrhage. Our data confirm, once again, a universal character of the asymmetric changes in the macular thickness in the temporal and nasal subfields after vitrectomy with ILM removal for various pathological changes in the retina. However, to clarify the practical meaning of this phenomenon, the further functional investigations are required.

Key-words:

retinal thickness, vitrectomy with inner limiting membrane removal, diabetic retinopathy

Background

Diabetic retinopathy (DR) is one of the leading causes of low vision among working-age adults in the developed countries [1, 2]. Vitrectomy is an effective treatment method for such DR complications as nonclearing vitreous hemorrhage, tractional retinal detachment, vitreomacular traction and others. Introducing a microinvasive 23-27 gauge technique into the clinical practice over the last decades, improving technical characteristics of surgical systems for vitrectomy, and using various supporting

tools, in particular, vital dyes in the vitreoretinal surgery (chromovitrectomy), make it possible to improve outcomes of the surgical treatment [3-6].

Originally, vitrectomy with the removal of the inner limiting membrane (ILM) has been performed for surgical treatment of idiopathic macular holes [7]. Later on, ILM peeling has come into use for treatment of epiretinal

membrane (ERM), tractional diabetic macular edema (DME) etc. [8, 9]. In literature, there has been reported that ILM peeling can help in preventing epiretinal membrane development (re-proliferation) after vitrectomy for rhegmatogenous retinal detachment and diabetic tractional detachment [10-13].

At the same time, only since spectral coherent tomography (OCT) was introduced into the clinical practice, in-life observation over morphological changes in the retinal macula after vitrectomy, including those after ILM peeling, has become possible. Following up patients operated on for macular holes has made it possible to reveal such specific changes after ILM peeling as dissociated optic nerve fiber layer (DONFL) and temporal macula thinning [14]. Recently, there have been papers pointing similar changes in the retina after ILM removal in patients with epiretinal membranes (ERM) [15, 16]. To our best knowledge, there is only one paper on the changes in the retina with diabetic macular edema after vitrectomy with ILM removal [17].

The purpose of the present paper was to study changes in the macular retinal thickness in patients with diabetic retinopathy after microinvasive vitrectomy with inner limiting membrane removal.

Material and Methods

The present paper is a retrospective analysis of spectral OCT data of the macula of eighty-eight eyes (77 patients) after 23 gauge vitrectomy for proliferative diabetic retinopathy. The surgeries were performed at National Centre of Ophthalmology named after acad. Zarifa Aliyeva, Baku, Azerbaijan, in the period between 2010 and 2015. The study included only cases, in which anatomical success was achieved; the cases were followed up for twelve months and OCT study was performed. Study group comprised fifty-nine eyes in which vitrectomy was performed with ILM removal; Control group comprised thirty eyes in which ILM was not removed during the surgery. The study excluded the eyes in which silicone oil remained for more than six months.

The main characteristics of the patients observed and the eyes operated on are given in the table 1.

A surgery technique. Microinvasive 23 gauge pars plana vitrectomy was performed using Accurus 800CS and Constellation surgical systems (Alcon, the USA) under Lumera 700 and Lumera T surgical microscopes (Zeiss, Germany) and a viewing system BIOM 4m (Oculus, Germany) to visualize the anterior segment. When performing a combined surgery, cataract phacoemulsification and IOL implantation in the capsular bag was performed in the beginning of the surgery. In most cases, epiretinal membranes were removed with a vitreous cutter; scissors were rarely used. ILM was peeled using ILM forceps (Alcon, the USA) after brilliant blue G (BBG) staining; a micropick and a Tano scraper were not used.

Optical Coherent Tomography (OCT) was performed using spectral OCT Cirrus-HD (Carl Zeiss Meditec, the USA). Two protocols, Macular cube 512 × 128 with

measurements of the retinal thickness in nine zones and 5-line HD raster, were used. For statistical analysis, we used measurements in three subfields: central (the diameter of the ring was 1 mm); inner temporal (the diameter of the ring was 1-3 mm); and inner nasal (the diameter of the ring was 1-3 mm). In doubtful cases, the retinal thickness was measured manually.

Statistical Analysis. The data obtained were processed using SPSS statistic software (IBM SPSS Statistics, 20.0). The quantitative values were presented as mean±standard deviation. Student t-criterion was used to compare the mean values in different groups for independent samples and t-criterion was used to assess the dynamics of changes for paired samples. A level of significance was accepted as $p=0.05$, which corresponds to criteria accepted for medical investigations. If the p -value was lower than 0.001, it was pointed as $p<0.001$.

The study was approved by Academic Council of National Centre of Ophthalmology named after acad. Zarifa Aliyeva. The informed consent was obtained from each patient.

Results

To determine the effect of ILM removal on the post-operative retinal thickness, we compared the retinal thickness in the inner temporal, central, and inner nasal subfields using data of spectral OCT at 12 months after microinvasive vitrectomy with and without ILM removal during the surgery for DR complications.

As it can be seen in Table 2, at 12 months after surgery, the mean retinal thickness differed significantly in different groups only in the inner temporal subfield of the macula. Thus, temporal macula was much thinner ($279\pm51.9\ \mu\text{m}$) in the eyes where ILM was removed than in those without ILM removal, ($332\pm93.8\ \mu\text{m}$, $p=0.002$). The thickness in the central, foveolar subfield almost did not differ in different groups as well as the thickness in the inner nasal subfield ($p>0.05$ in both cases).

Besides, at 12 month after surgery, we compared the retinal thickness in groups depending on the vitrectomy indications: vitreous hemorrhage, tractional retinal detachment, and vitreomacular traction. The results are given in Table 3.

As it can be seen in Table 3, the retinal thickness at 12 months after surgery differed significantly between cases with and without ILM removal in all groups. In a group with vitreous hemorrhage, the mean retinal thickness in the temporal subfield of the inner ring was $258\pm54.2\ \mu\text{m}$ in the eyes with ILM removal vs. $345\pm47.9\ \mu\text{m}$ in the eyes where ILM was not removed ($p=0.008$). Of a lower rate were the values of the mean thickness in the central and nasal subfields in the group with the removed ILM; however the difference was not significant.

The mean thickness in the temporal subfield was also significantly thinner after vitrectomy for tractional retinal detachment in the eyes with ILM removal as compared with eyes where ILM was not removed, $266\pm59.5\ \mu\text{m}$ and $331\pm120.9\ \mu\text{m}$, respectively, ($p=0.030$). The thickness

in the foveolar zone and in the inner nasal subfield little differed after vitrectomy with and without ILM removal in patients with tractional retinal detachment.

In a group with tractional macular edema (vitreomacular traction), there were similar tendencies; however, the difference between groups was not statistically significant because of the lack of observational cases.

OCT measurements of the macular area before surgery were possible to perform only in the eyes with vitreomacular traction (VMT). As it can be seen in Table 4, in a group with the removed ILM, all OCT values in the inner ring decreased at one year after surgery. So, the mean thickness in the inner temporal subfield of the macula before surgery was $464 \pm 97.7 \mu\text{m}$ vs. $295 \pm 43.1 \mu\text{m}$ at 12 months after surgery ($p < 0.001$). The mean thickness decreased significantly, from 520 ± 167.9 to $292 \pm 78.7 \mu\text{m}$ in the foveolar subfield ($p = 0.001$) and from 495 ± 191.8 to $377 \pm 102.5 \mu\text{m}$ in the inner nasal subfield of the macula ($p = 0.007$). In seven eyes with VMT, where ILM was not removed, a decrease was significant only in the foveolar thickness, from 498 ± 87.3 to $296 \pm 90.8 \mu\text{m}$ ($p = 0.014$); although other values were decreased, they, especially the temporal thickness, were not as significant as in the group with the removed ILM.

Besides, because of the absence of a healthy paired eye, we also compared data on the macular thickness after vitrectomy with ILM removal with the normative data from the literature. Liu et al. [18] has reported on Cirrus HD OCT data that, in diabetic persons without retinopathy signs, the mean macular thickness in the inner temporal subfield is $313.4 \pm 18.5 \mu\text{m}$, which is significantly higher than in our patients after vitrectomy with ILM removal, which was $295 \pm 43.1 \mu\text{m}$ ($p = 0.002$). And the macular thickness in the nasal and central foveolar subfields do not differ significantly from our data, $315.9 \pm 18.8 \mu\text{m}$ vs. $341 \pm 99.4 \mu\text{m}$ ($p = 0.180$) and $258.5 \pm 21.6 \mu\text{m}$ vs. $285 \pm 96.6 \mu\text{m}$ ($p = 0.251$), respectively.

Figure 1 demonstrates an eye of a patient with vitreomacular traction and extramacular tractional detachment before and after 23 gauge vitrectomy with ILM removal; and Figure 2 demonstrate an eye of a patient with tractional retinal detachment before and after vitrectomy without ILM removal.

Discussion

Vitrectomy with ILM removal was originally proposed for macular holes [7], and, later on, for other pathologic changes of the vitreomacular interface including idiopathic epiretinal membranes, tractional diabetic macular edema and others [8, 9, 19]. Improvements and innovations in the diagnostic equipment, in particular, the advent of OCT, have made it possible to reveal specific changes in the inner retinal layers occurring after ILM removal in patients with macular pathology. First, Tadayoni has noted changes in the nerve fiber layer, which he called dissociated optic nerve fiber layer (DONFL), in the eyes with macular holes after removing the ILM [14]. These changes, according to authors, were noted at 1-3 months after surgery and were not

associated with functional changes according to findings of visual acuity test, visual field test, and microperimetry [20, 21]. Other changes having been detected after ILM removal in the eyes with macular holes are thinning of the temporal part and thickening of nasal part of the macula, numerous dimples on the retina surface, displacement of the fovea to the optic disc, paracentral macular holes [22-25]. Later on, similar changes have been described for patients with ERM, whereby the authors have concluded that the pointed changes in the retina after ILM removal can be of a universal character [15, 26, 27].

Although the experience of ILM removal in surgery for diabetic macular edema is sufficient, there are a few reports on postoperative changes in the retina according to OCT findings. To the best of our knowledge, there is a single paper by Yoshikawa et al. [17], in which the authors have paid more attention to displacement of the fovea toward the optic disc than to changes in the retinal thickness in eyes with ILM peeling for DME. We revealed thinning of the temporal subfield and thickening of the macula in patients with ILM peeled for various DR complications. Contrary to the previous papers on macular holes and ERM, in which authors could use a healthy paired eye for comparison, we could not do it because of severe PRD-associated structural changes in the paired eyes. That's why we compared our findings on the retinal thickness with those for the diabetic eyes without diabetic retinopathy signs, obtained from the literature [18]; herewith, the most significant data were obtained for the macular thickness in the temporal subfield. The macular thickness in the temporal subfield after vitrectomy with ILM removal in our study was $295 \pm 43.1 \mu\text{m}$, which is significantly lower than the normative data ($313.4 \pm 18.5 \mu\text{m}$). It should be noted that we revealed the thinning of the temporal macula after vitrectomy with ILM removal not only in patients with DME but in those with tractional retinal detachment and vitreous hemorrhage, which we did not come across in the literature.

Yoshikawa et al. [17] believes that displacement of the fovea to the optic disc in DME patients after vitrectomy with ILM peeling leads also to the thinning of the temporal subfield and the thickening of the nasal subfield of the macula. According to the authors, after the ILM, which is a rigid basal membrane, is removed, other mechanical forces, in particular, axonal contractility, can be a cause of the shortening of papillofoveal distance and the appearing of asymmetric changes in the macular thickness.

Our data confirm once again the universal character of the asymmetric changes in the macular thickness in temporal and nasal subfields after vitrectomy with ILM removal for various pathological changes in the retina. However, to clarify the practical meaning of this phenomenon, the further functional investigations are required.

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Table 1. Characteristics of the patients and the operated on eyes

Patients (n,%)	Total	77	100%
	Male	37	48.1%
	Female	40	51.9%
Age, y		55.9±9.9	25-78 y/o
Type of diabetes mellitus (DM) (n, %)	Type 1	5	6.5%
	Type 2	72	93.5%
DM treatment	Insulin	65	84.4%
	Oral antidiabetic drugs	12	15.6%
HbA1c, %		8.1±0.9	5.9-10.5
DM duration, years		12.4±6.3	1-28 y/o
Eyes (n)		89	100%
Vitrectomy indication	Vitreous hemorrhage	18	20.2%
	Tractional retinal detachment	47	52.8%
	Vitreomacular traction	24	27.0%
The state of the lens	Phakic eyes	76	85.4%
	Pseudophakic eyes	13	14.6%
The volume of operative intervention	Vitrectomy only	52	58.4%
	Combined surgery (Phacovitrectomy)	37	41.6%
Inner limiting membrane	Removed during the surgery	59	66.3%
	Not removed during the surgery	30	33.7%
Vitreous tamponade	Silicone oil	28	31.5%
	Gas	43	48.3%
	Air	18	20.2%
Visual acuity (LogMAR units)	Before surgery	1.52±0.76	0.1-3
	At 12 months after surgery	0.76±0.49	0.3-3

Table 2. Macular thickness at 12 months after vitrectomy (µm)

Subfields	ILM removal (n=59)	No ILM removal (n=30)	p
Inner temporal	279±51.9	332±93.8	0.002
Foveal	285±96.6	288±120.6	0.936
Inner nasal	341±99.4	358±107.8	0.496

Table 3. Postoperative macular thickness in dependence on vitrectomy indications

The main vitrectomy indication	The subfield measured	Retinal thickness (μm)		p
Vitreous hemorrhage		ILM removal (n=10)	No ILM removal (n=8)	
	Inner temporal	258±54.2	345±47.9	0.008
	Foveal	273±103.8	313±77.7	0.377
	Inner nasal	271±125.5	366±61.1	0.099
Tractional retinal detachment		ILM removal (n=32)	No ILM removal (n=15)	
	Inner temporal	266±59.5	331±120.9	0.030
	Foveal	273±86.1	277±163.9	0.925
	Inner nasal	332±72.5	362±147.9	0.397
Tractional macular edema (vitreomacular traction)		ILM removal (n=17)	No ILM removal (n=7)	
	Inner temporal	295±43.1	338±103.8	0.161
	Foveal	292±78.7	296±90.8	0.634
	Inner nasal	377±102.5	331±53.8	0.360

Table 4. Retinal thickness in groups with vitreomacular traction before and after vitrectomy (μm)

	ILM removal (n=17)			No ILM removal (n=7)		
	Inner temporal	Foveal	Inner nasal	Inner temporal	Foveal	Inner nasal
Before surgery	464±97.7	520±167.9	495±191.8	443±140.1	498±87.3	440±138.0
At 12 months after surgery	295±43.1	292±78.7	377±102.5	338±103.8	296±90.8	331±53.8
p	<0.001	0.001	0.007	0.156	0.014	0.240

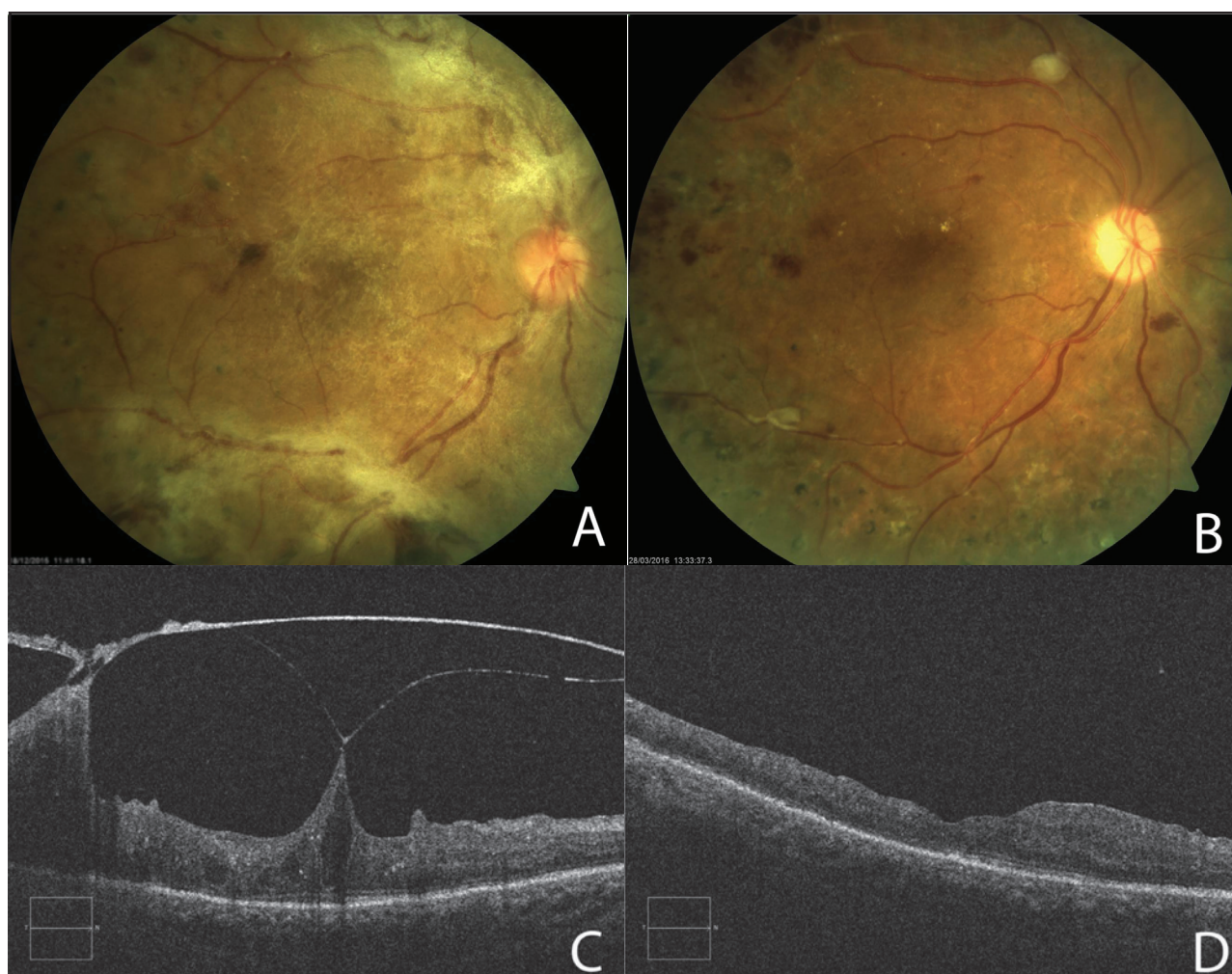


Fig. 1 . The right eye of a Patient G.S., 46 y/o. A: apparent epiretinal fibrosis can be seen before surgery; B: the state of the fundus after surgery; C: the OCT scan before surgery reveals vitreomacular traction and epiretinal membrane (the height of the fovea is 1390 μm); D: at 12 months after vitrectomy with ILM removal and gas tamponade, thinning in the inner temporal (254 μm) and central foveolar (239 μm) subfields and little thickening in the nasal subfield of the macula can be seen.

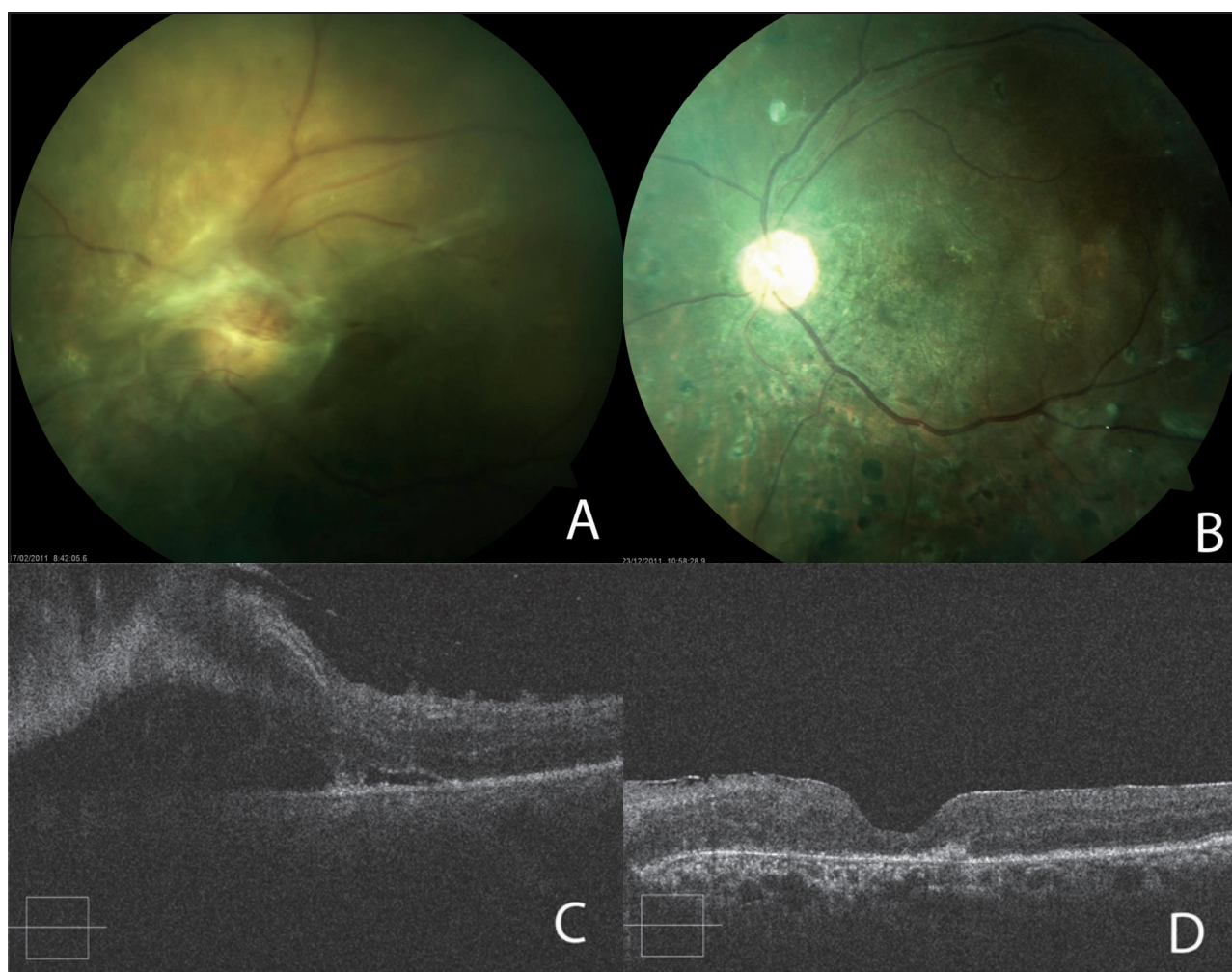


Fig. 2 . The left eye of a Patient S.N., 58 y/o. with tractional retinal detachment before (A) and after (B) vitrectomy without ILM removal. C: tractional retinal detachment can be seen on the OCT scan; D: at 12 months after surgery, the fovea is thinned (215 μm), the temporal and nasal macula preserves a normal thickness, 336 μm and 365 μm , respectively. A thin epiretinal membrane without traction signs can be observed.