

# Insights Into Epiretinal Membranes: Presence of Ectopic Inner Foveal Layers and a New Optical Coherence Tomography Staging Scheme



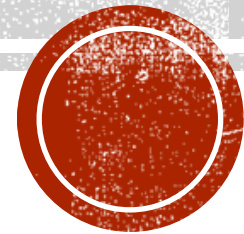
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**ANDREA GOVETTO, ROBERT A. LALANE, III, DAVID SARRAF, MARTA S. FIGUEROA, AND  
JEAN PIERRE HUBSCHMAN**

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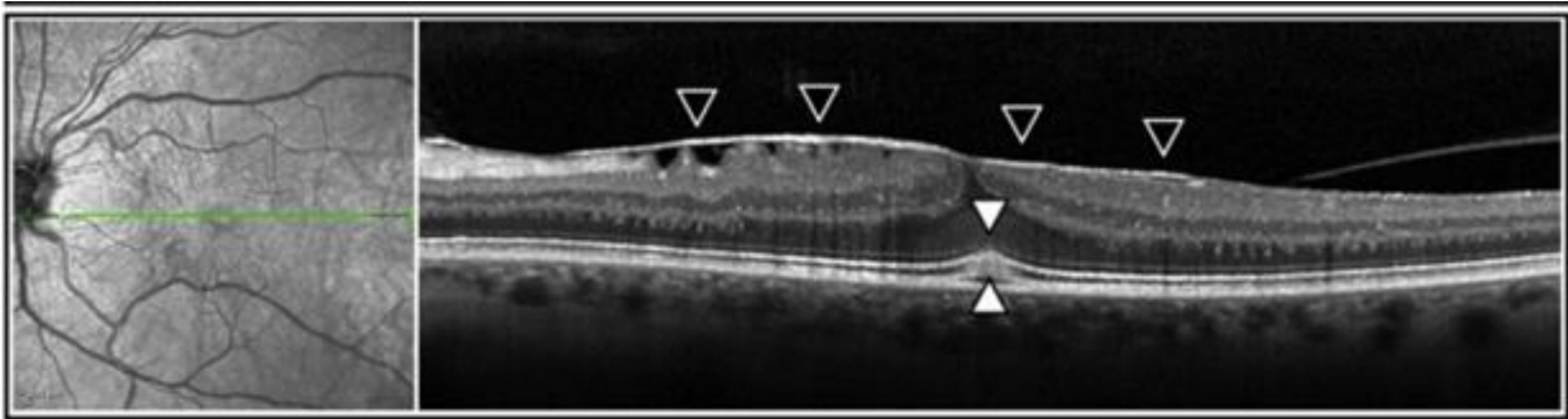
AMERICAN JOURNAL OF OPHTHALMOLOGY MARCH 2017



Residente Guilherme Rozza  
Hospital das Clinicas de Ribeirao Preto

# EXPLICANDO O ESTUDO

- MER



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**EXCLUI MER secundaria:**  
Inflamacao, vasculopatias,  
Traumas, Tumores, DR, Após Cirurgias



- MER
- Apenas Pacientes com MER Idiopática (784p>612p/194o>63p>131o)
- Usado OCT-B e OCT-A
- Agrupar Achados no OCT para uma possível Classificação
- Estudo Observacional e Retrospectivo
- Correlacionar estágios com desfechos funcionais e anatômicos

-Não analisa intervenções cirúrgicas

-Estudo descritivo

**TABLE 1.** Study of Ectopic Inner Foveal Layers in Epiretinal Membranes: Exclusion Criteria

Exclusion Criteria

- Any previous intraocular surgery with the exclusion of uncomplicated phacoemulsification
- History of retinal detachment
- Intermediate or advanced age-related macular degeneration
- History of choroidal neovascularization of any etiology
- Central serous chorioretinopathy
- Proliferative diabetic retinopathy
- Nonproliferative diabetic retinopathy with history of clinically significant diabetic macular edema
- Macular teleangiectasias
- Tractional and degenerative lamellar macular holes
- History of central or branch retinal vein occlusion and central or branch retinal artery occlusion
- Advanced glaucoma, or optic neuropathy of any kind
- History of inflammatory eye disorders
- History of Irvine-Gass syndrome
- Visually significant cataract
- History of endophthalmitis or any other intraocular infection
- Retinal dystrophies
- Foveal hypoplasia/fovea plana
- History of ocular trauma
- Any other potential cause of vision loss other than epiretinal membranes



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# 4 ESTAGIOS

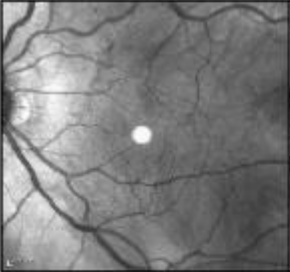
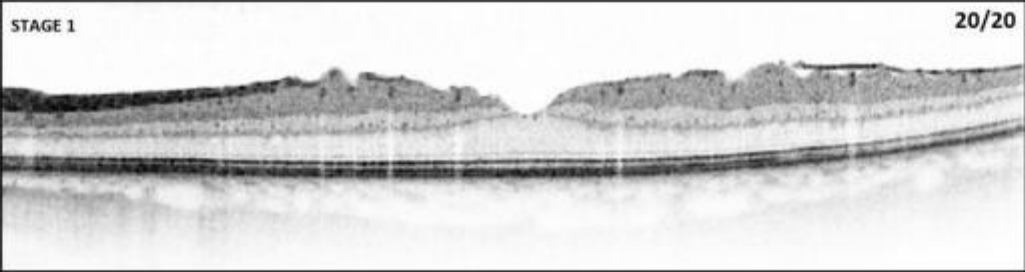

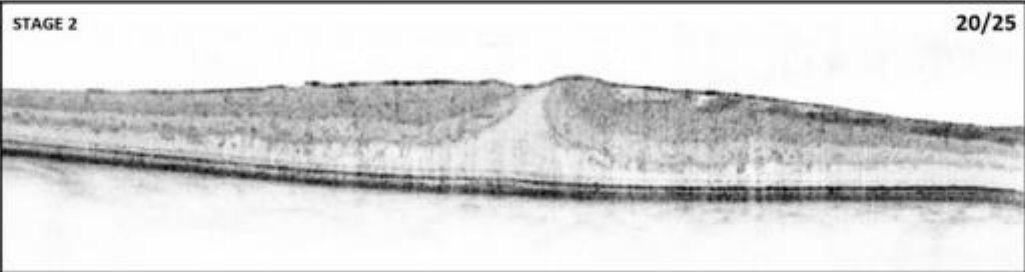
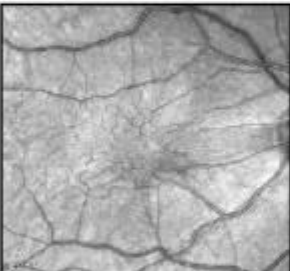
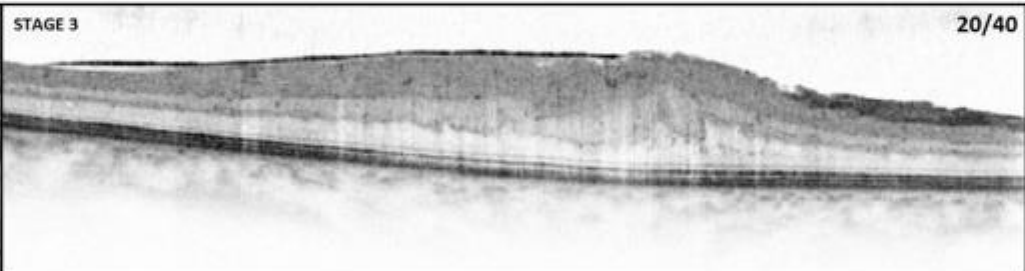

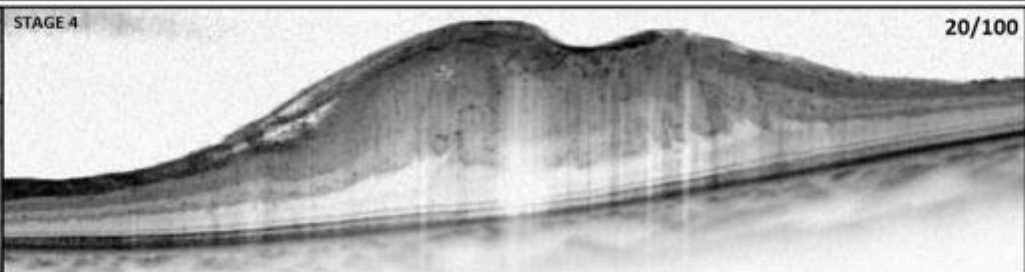
	<b>STAGE 1</b>  <b>20/20</b>	<b>STAGE 1</b> <ol style="list-style-type: none"><li>1. Presence of the foveal pit.</li><li>2. Well-defined retinal layers.</li></ol>
	<b>STAGE 2</b>  <b>20/25</b>	<b>STAGE 2</b> <ol style="list-style-type: none"><li>1. Absence of the foveal pit.</li><li>2. Well-defined retinal layers.</li></ol>
	<b>STAGE 3</b>  <b>20/40</b>	<b>STAGE 3</b> <ol style="list-style-type: none"><li>1. Absence of the foveal pit.</li><li>2. Well-defined retinal layers.</li><li>3. Presence of ectopic inner foveal layers.</li></ol>
	<b>STAGE 4</b>  <b>20/100</b>	<b>STAGE 4</b> <ol style="list-style-type: none"><li>1. Absence of the foveal pit.</li><li>2. Disrupted retinal layers.</li><li>3. Presence of ectopic inner foveal layers.</li></ol>

FIGURE 3. Proposed optical coherence tomography staging scheme of idiopathic epiretinal membranes.



# ACHADOS...

- Perda da Depressão Foveal
- Camada Foveal Interna Ectopica
- Preguilamento no Polo Posterior
- Regioes Fibroticas no Estagio 4

- \* Cotton Ball ( Tracao na Retina Externa )
- \* Ruptura na Elipsoide Interna Foveal
- \* EMC

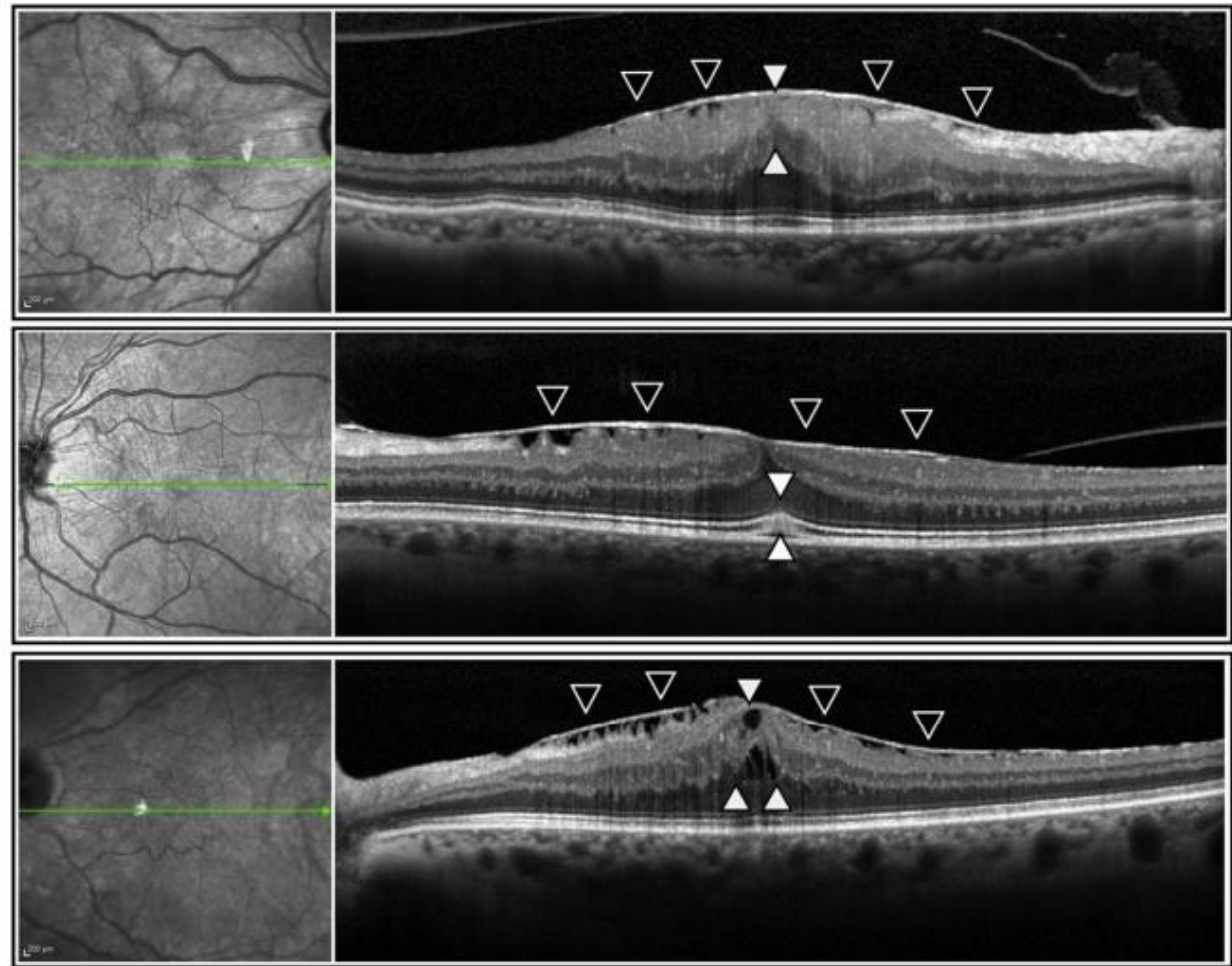
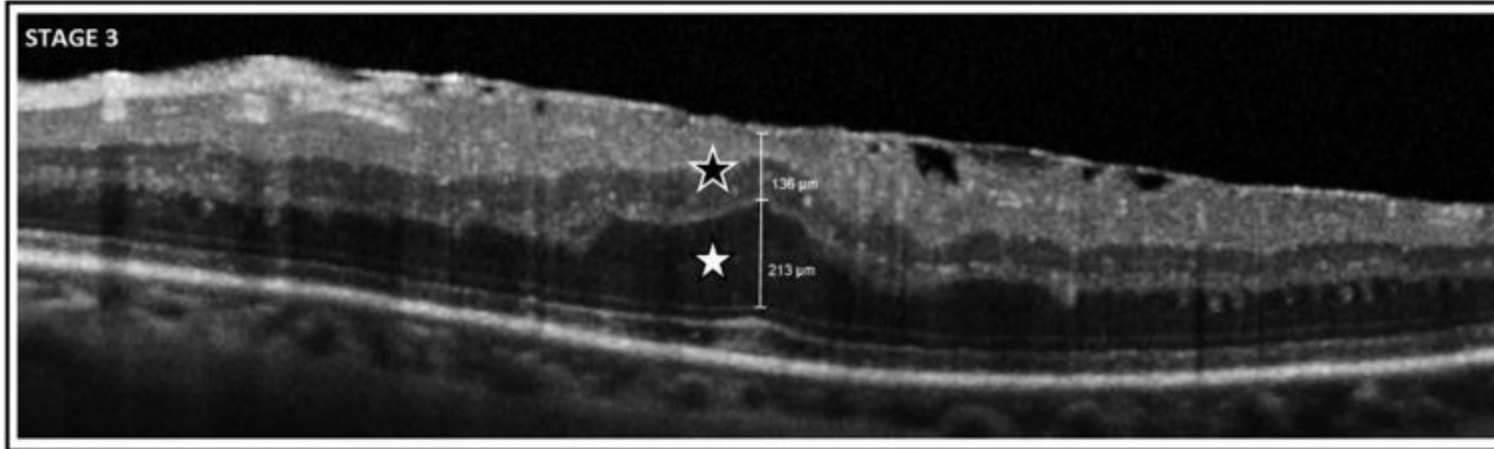
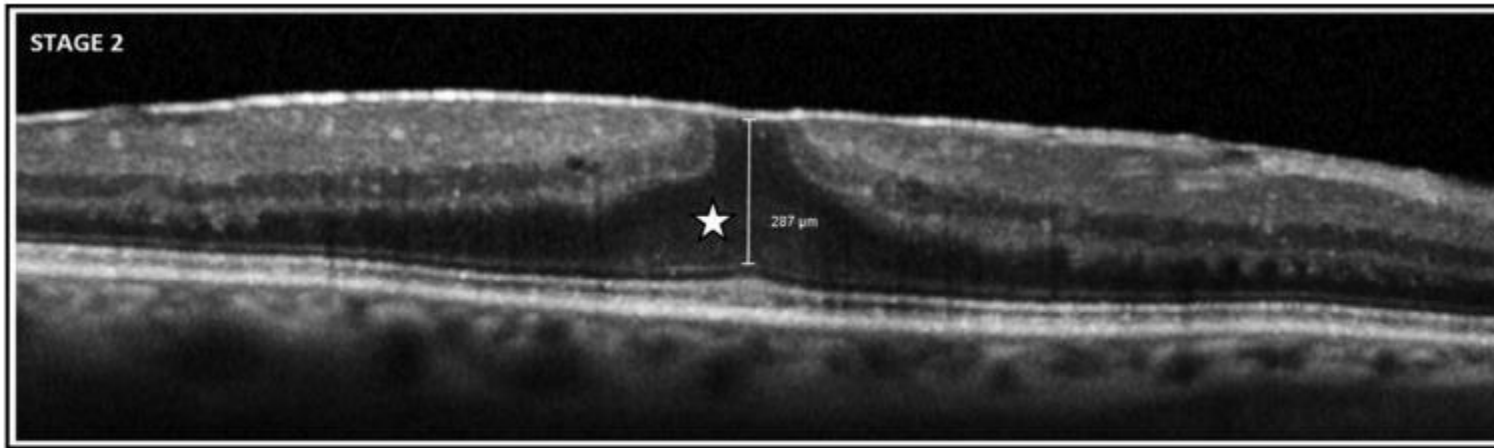


FIGURE 2. Morphologic characteristics of epiretinal membranes. (Top) Stage 3 epiretinal membrane (black arrows). The reflectivity of the ectopic inner foveal layers (white arrows) is similar to that of the inner nuclear layer (hyporeflective band over the outer plexiform layer) and that of the inner plexiform layer (hyperreflective band over the inner nuclear layer). The ectopic inner foveal layers appear continuous, cross the entire foveal area, and reside above the outer nuclear layer, which is not in apparent contact with the internal limiting membrane. (Center) Stage 2 epiretinal membrane (black arrows). Stretching of the outer nuclear layer is evident, and the foveal depression is absent. The inner nuclear and ganglion cell layers appear displaced, but a continuous layer of retinal tissue over the outer nuclear layer is absent. In the outer retina the cotton ball sign (white arrows) is identified as a hyperreflective area under the central ellipsoid zone, with poorly defined borders. (Bottom) Stage 3 epiretinal membrane (black arrows). Hyporeflective intraretinal cystoid spaces are illustrated between the outer nuclear and outer plexiform layers, and in the inner nuclear layer (white arrows).



# MEDIDA DA ESPESSURA...



Manualmente no Software

FIGURE 1. Optical coherence tomography measurements in epiretinal membranes. (Top) Measurement of the outer nuclear layer thickness in the central fovea (white star) in stage 2 epiretinal membrane. A straight line is traced with the caliper tool from the external limiting membrane to the internal limiting membrane. (Bottom) Measurement of the outer nuclear layer thickness in the central fovea (white star) in a stage 3 epiretinal membrane. The upper limit of the outer nuclear layer is the inferior border of the ectopic inner foveal layers. The thickness of the ectopic inner foveal layers (black star) is measured tracing a straight line from the upper limit of the outer nuclear layer to the internal limiting membrane.



# RESULTADOS E DISCUSSÃO...

**TABLE 2.** Baseline Characteristics of Studied Epiretinal Membranes (N = 194)

	Stage 1 (N = 43)	Stage 2 (N = 88)	Stage 3 (N = 51)	Stage 4 (N = 12)	P Value
Age (y)	69.1 ± 7.5	70.8 ± 9.4	70.2 ± 8.7	68.5 ± 8.7	.664 <sup>a</sup>
Central foveal thickness (μm)	321.6 ± 60.1	412.4 ± 49.8	497.37 ± 64	639.25 ± 93.5	<.001 <sup>a</sup>
Outer nuclear layer thickness (μm)	169.89 ± 66	267.47 ± 58	230.77 ± 61	-	<.001 <sup>a</sup>
Ectopic inner foveal layer thickness (μm)	-	-	161.55 ± 63	-	-
Cystoid macular edema	0/43 (0%)	2/88 (2.3%)	7/51 (13.7%)	5/12 (41.7%)	<.001 <sup>b</sup>
Ellipsoid disruption	1/43 (2.3%)	10/88 (11.4%)	11/51 (21.6%)	9/12 (75%)	<.001 <sup>b</sup>
Cotton ball sign	3/43 (7%)	21/88 (23.9%)	11/51 (21.6%)	0/12 (0%)	.034 <sup>b</sup>
BCVA, logMAR (Snellen)	0.02 ± 0.6 (20/21)	0.14 ± 0.13 (20/27)	0.33 ± 0.17 (20/43)	0.61 ± 0.26 (20/81)	<.001 <sup>c</sup>

Espessamento progressivo

BCVA = best-corrected visual acuity.

<sup>a</sup>Analysis of variance test.

<sup>b</sup>χ<sup>2</sup> test.

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Tração/Espessamento/Leve afilamento

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Fator de mau prognóstico

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Secundário a Tração

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Lesão em Cones, mau prognóstico

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Indicativo de Tração na CFR  
( ALARME !!! )

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Progressivamente Pior

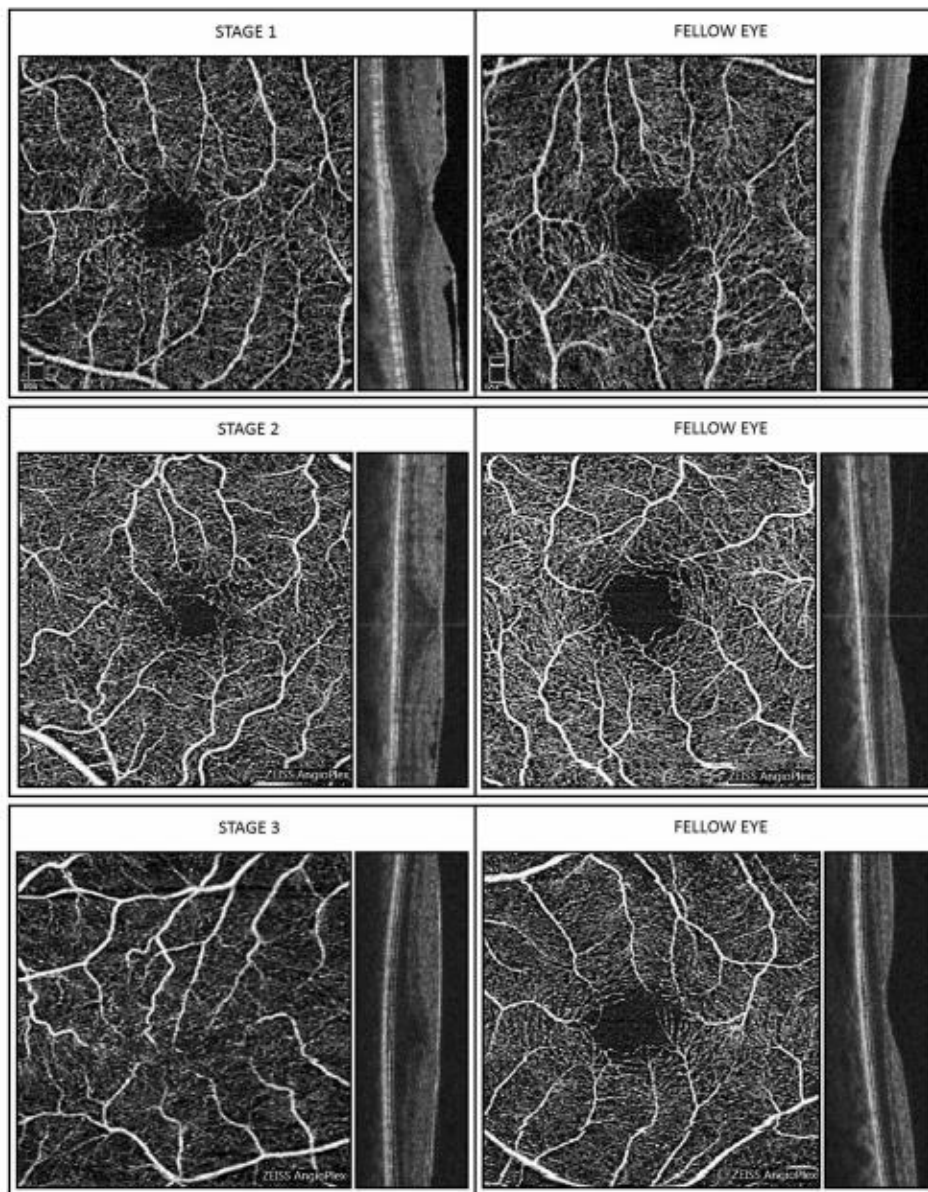
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**FIGURE 4.** Optical coherence tomography angiography of idiopathic epiretinal membranes and unaffected fellow eyes. Foveal avascular zone and deep and superficial retinal capillary plexus are imaged with  $3 \times 3$ -mm scans. (Top) Stage 1 epiretinal membrane. Variation of the foveal avascular zone is minimal, but is slightly reduced upon comparison to the unaffected fellow eye. Mild deformation of the vessels owing to epiretinal membrane traction is noted. (Center) Stage 2 epiretinal membrane. Reduction of the foveal avascular zone is evident, and is significantly decreased if compared with the fellow eye. The deformation of the vessels and their displacement toward the foveal center is remarkable. (Bottom) Stage 3 epiretinal membrane. The foveal avascular zone is nearly absent. Severe deformation and displacement of the vessels is noted.

# OCT-A

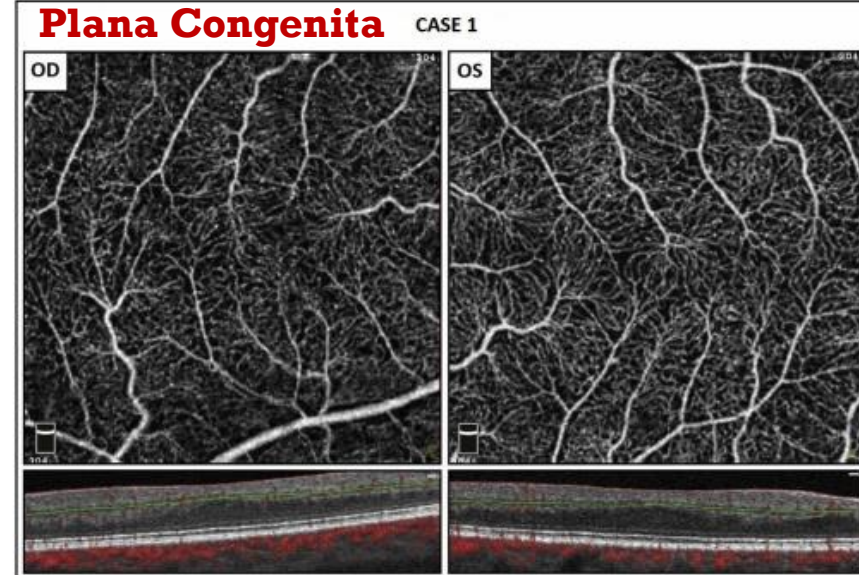
- Redução da ZAF
- Vasos tortuosos por tração
- Estagio 4 ( Não consegue plotar imagem )



# COMPARACAO ENTRE FOVEAS PLANAS...

Congenita ( Disgenesia – Bilateral )

- Possui anastomoses na região sem ZAF



AMBAS tem CAMADA FOVEAL INTERNA ECTOPICA  
(Mas a congênita Reduz menos a AV)

Aquirida ( Secundaria a MER – Assimetrica )

- Sem anastomoses na região de redução da ZAF

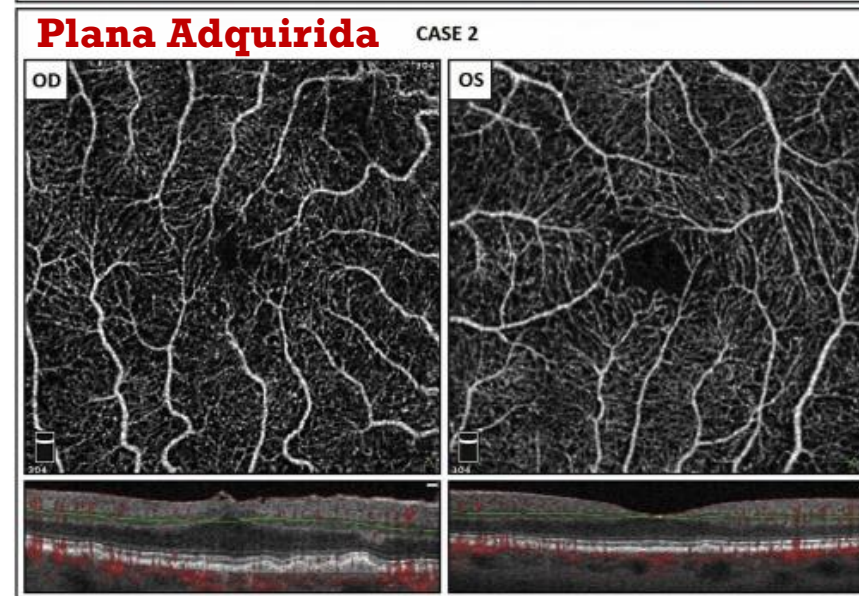


FIGURE 8. Morphologic differences between foveal microvasculature in fovea plana and idiopathic epiretinal membrane. Foveal avascular zone and deep and superficial retinal capillary plexus are imaged with  $3 \times 3$ -mm scans. (Top) Case 1: optical coherence tomography angiography in fovea plana. In both eyes, the foveal avascular zone is absent. Macular-foveal capillaries crossing the entire foveal area are identified. The morphology of the vessels is similar in both eyes. (Bottom) Case 2: optical coherence tomography angiography in stage 3 epiretinal membrane (right eye) and unaffected fellow eye (left eye). In the right eye, the foveal avascular zone is severely reduced, although still present. The ectopic layers are present across the entire foveal area, but no flow is seen in the center of the fovea. Macular foveal capillaries are absent and the vessels appear displaced and stretched, and their morphology is different from the fellow eye. The foveal avascular zone in the fellow eye is normal.



# EVOLUCAO NATURAL

**TABLE 3.** Natural History of Epiretinal Membranes During the Follow-up Period: Epiretinal Membranes Without Anatomic Signs of Progression to Later Stages

	Stage 1 (N = 23)	Stage 2 (N = 67)	Stage 3 (N = 15)	Stage 4 (N = 3)
Central foveal thickness ( $\mu\text{m}$ )				
Baseline	328.35 $\pm$ 67.7	401.9 $\pm$ 39.2	469.9 $\pm$ 73.6	690 $\pm$ 155
End of follow-up	334.13 $\pm$ 69.6	408.06 $\pm$ 44.3	480.13 $\pm$ 73.5	735 $\pm$ 129.7
P value <sup>a</sup>	.47	.1	.03	.1
Outer nuclear layer thickness ( $\mu\text{m}$ )				
Baseline	177.56 $\pm$ 71	257.45 $\pm$ 46	222.9 $\pm$ 70.3	-
End of follow-up	171.4 $\pm$ 67.5	268.4 $\pm$ 57.5	223.13 $\pm$ 70.3	-
P value <sup>a</sup>	.6	.04	.8	-
Ectopic inner foveal layer thickness ( $\mu\text{m}$ )				
Baseline	-	-	135.7 $\pm$ 52	-
End of follow-up	-	-	146.06 $\pm$ 51	-
P value <sup>a</sup>	-	-	.15	-
BCVA, logMAR (Snellen)				
Baseline	0.02 $\pm$ 0.07 (20/21)	0.13 $\pm$ 0.12 (20/27)	0.21 $\pm$ 0.17 (20/32)	0.9 $\pm$ 0.36 (20/158)
End of follow-up	0.02 $\pm$ 0.07 (20/21)	0.17 $\pm$ 0.13 (20/29)	0.27 $\pm$ 0.13 (20/37)	1 $\pm$ 0.27 (20/200)
P value <sup>a</sup>	.99	<.001	.018	.31

BCVA = best-corrected visual acuity.

<sup>a</sup>Wilcoxon signed rank test.

**CUIDADO ( ALARME !!!)**

**SEM PROGRESSÃO ANATÔMICA  
( 82,5% EM 18 MESES )**

# EVOLUCAO NATURAL

**TABLE 4.** Natural History of Epiretinal Membranes During the Follow-up Period: Epiretinal Membranes With Anatomic Signs of Progression to Later Stages<sup>a</sup>

	Stage 1 to Stage 2 (N = 9)	Stage 2 to Stage 3 (N = 10)
Central foveal thickness ( $\mu\text{m}$ )		
Baseline	330.7 $\pm$ 32.03	413 $\pm$ 55.2
End of follow-up	399 $\pm$ 56.8	442.4 $\pm$ 47
P value <sup>b</sup>	.012	.005
Outer nuclear layer thickness ( $\mu\text{m}$ )		
Baseline	153.11 $\pm$ 41.3	273 $\pm$ 79.7
End of follow-up	247.5 $\pm$ 55.8	213.4 $\pm$ 63.5
P value <sup>b</sup>	.008	.011
Ectopic inner foveal layer thickness ( $\mu\text{m}$ )		
Baseline	-	-
End of follow-up	-	120.9 $\pm$ 31.3
BCVA, logMAR (Snellen)		
Baseline	0.022 $\pm$ 0.04 (20/21)	0.09 $\pm$ 0.13 (20/24)
End of follow-up	0.08 $\pm$ 0.07 (20/24)	0.27 $\pm$ 0.14 (20/37)
P value <sup>b</sup>	.039	.012

BCVA = best-corrected visual acuity.

<sup>a</sup>Statistical analysis was performed only in epiretinal membranes progressing from stage 1 to 2, and from stage 2 to 3.

<sup>b</sup>Wilcoxon signed rank test.

**COM PROGRESSÃO ANATÔMICA  
(17,5 % EM 18 MESES )**



# ACUIDADE VISUAL COM A MELHOR CORREÇÃO...

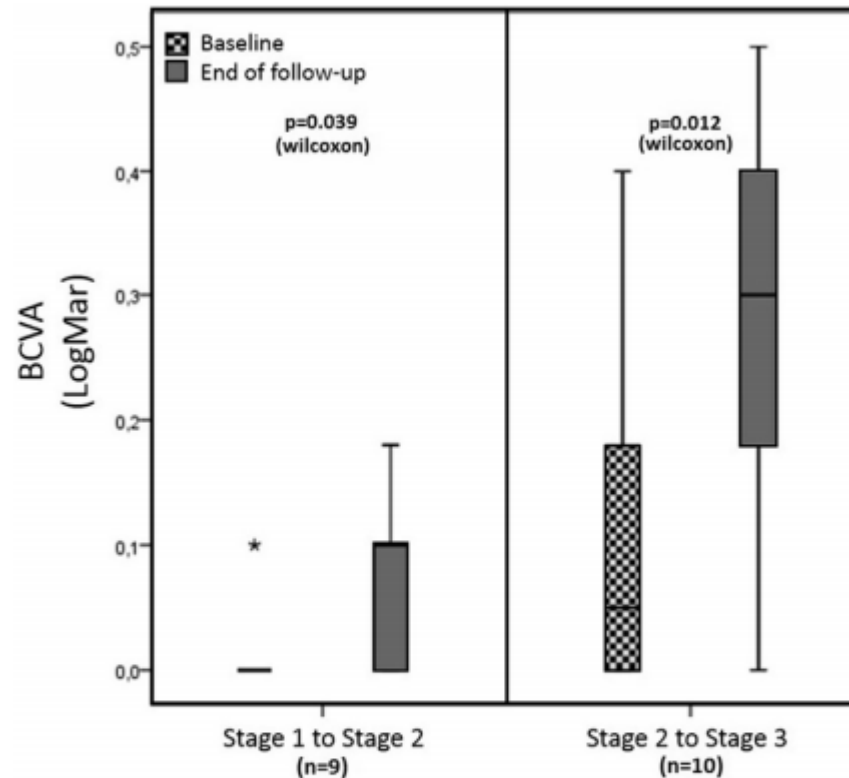
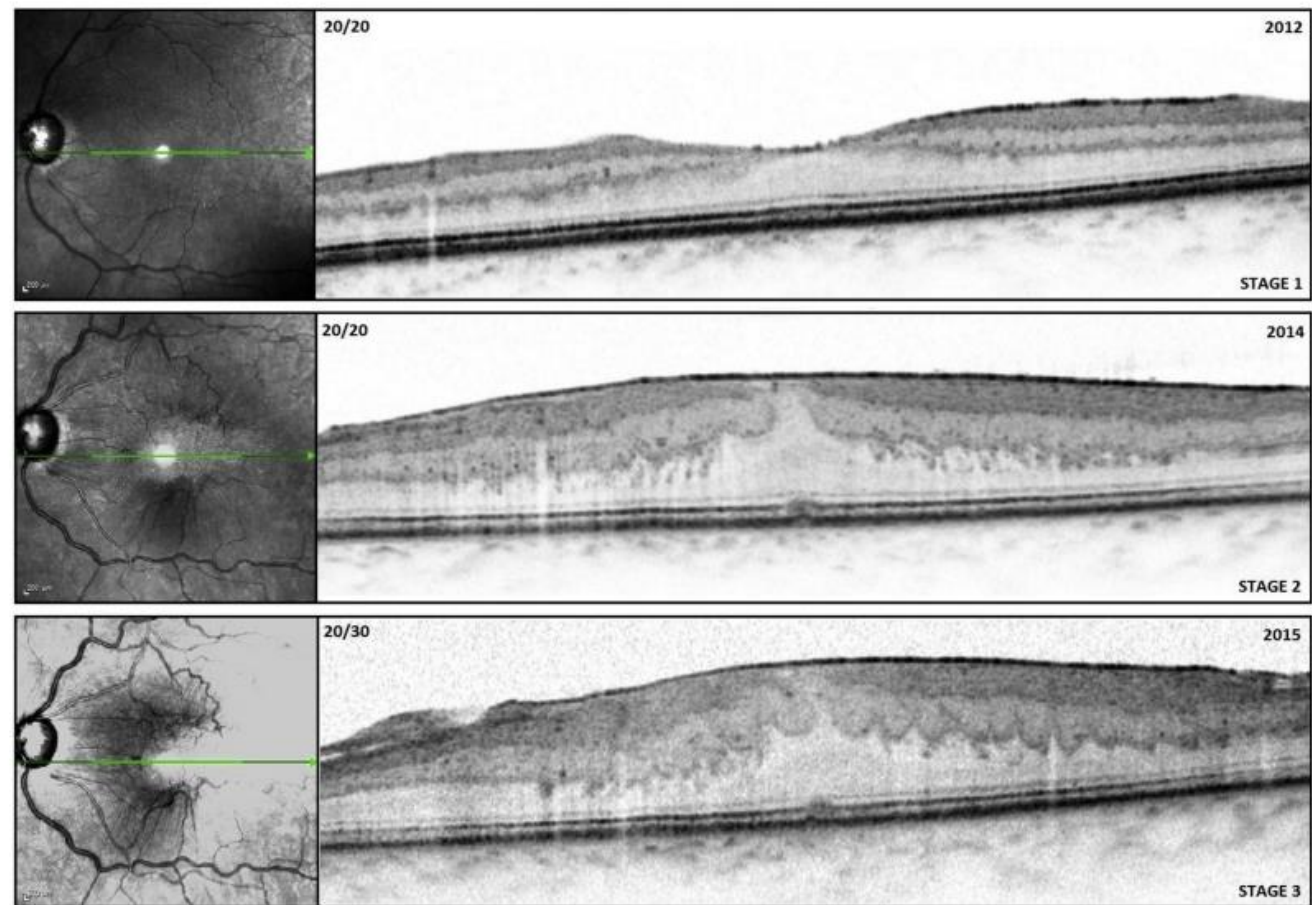
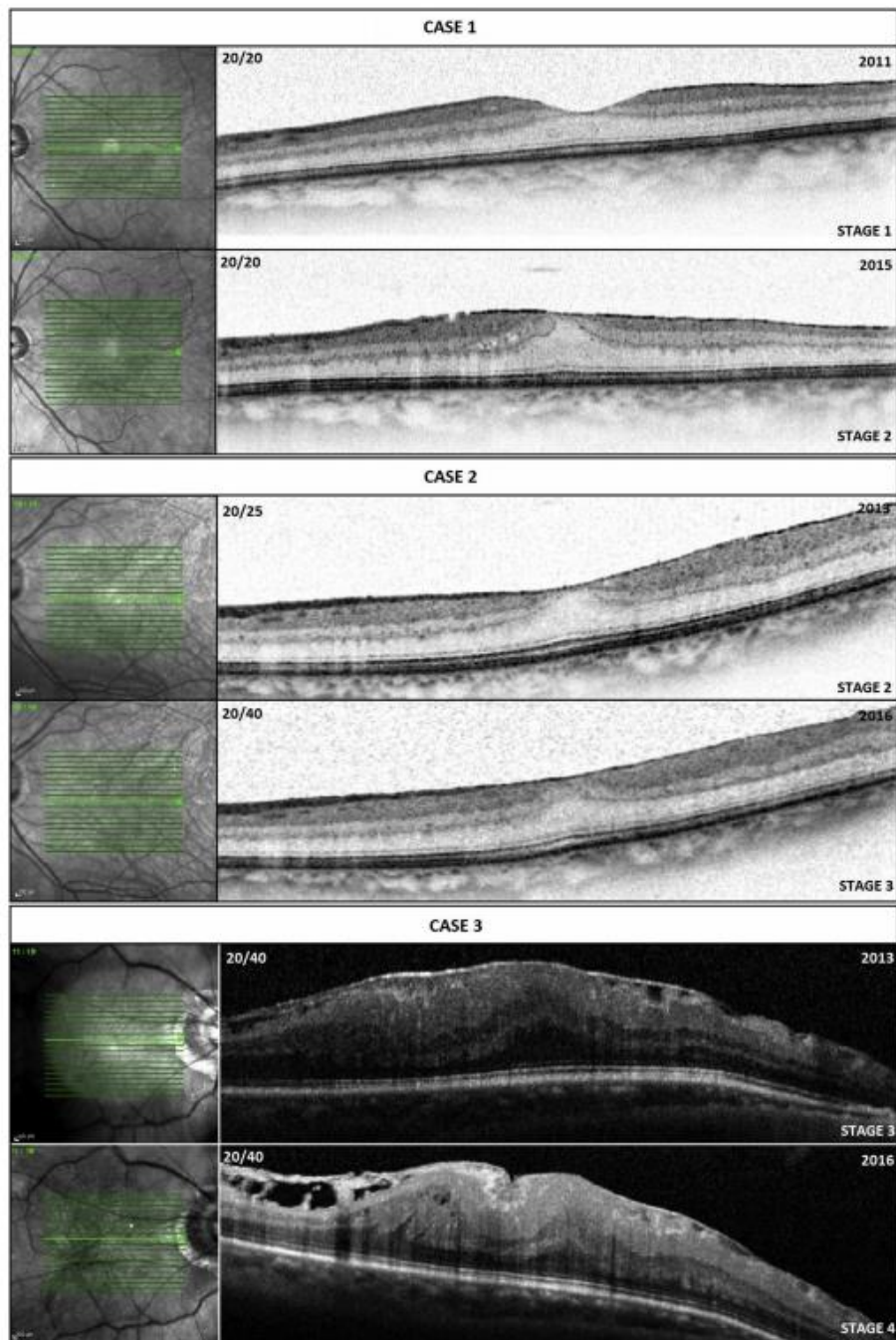


FIGURE 7. Best-corrected visual acuity correlations according to epiretinal membrane stage. Asterisks represents the maximum value of the BCVA in that subgroup (ie, 0.1 LogMAR).





**FIGURE 6.** A case of epiretinal membrane progression through stages 1, 2, and 3. (Top) At baseline a stage 1 epiretinal membrane is noted. The optic pit is present and no ectopic layers over the fovea are identified. Vision is 20/20 Snellen equivalent. (Center) Two years later, the optic pit is lost, the epiretinal membrane is thicker, and stretching of the outer nuclear layer is present. A cotton ball sign has developed but there are no ectopic inner layers across the fovea. Visual acuity remained stable. (Bottom) In the same eye-tracked optical coherence tomography scan, a continuous layer of ectopic retinal tissue across the fovea is illustrated. The ectopic inner foveal layers are continuous with the inner nuclear and inner plexiform layers (with similar reflectivity) and reside above the outer nuclear layer, which appears shallower. The cotton ball sign is still present. Visual acuity dropped to 20/30 Snellen equivalent.

**FIGURE 5.** Cases of epiretinal membrane progression to later stages. (Top) Case 1: progression from stage 1 to stage 2 epiretinal membrane. After 4 years of follow-up, the retina is thicker, and the foveal depression is lost. Small intraretinal cystoid spaces are



# PRE E POS RETIRADA DA MER...

- Estudo não seguiu pacientes que tiveram indicação de intervenção na primeira avaliação (63 Pacientes )

- Mas registra que, na pratica, quanto mais avançada a MER, menor a chance de bons resultados

- Estagios 3 e 4 já possuem CAMADA FOVEAL INTERNA ECTOPICA, e geralmente ela não tende a regredir após a CX

- Cotton Ball em um estagio 2 pode ser tão prejudicial quanto CAMADA ECOTOPICA dos estágios subsequentes

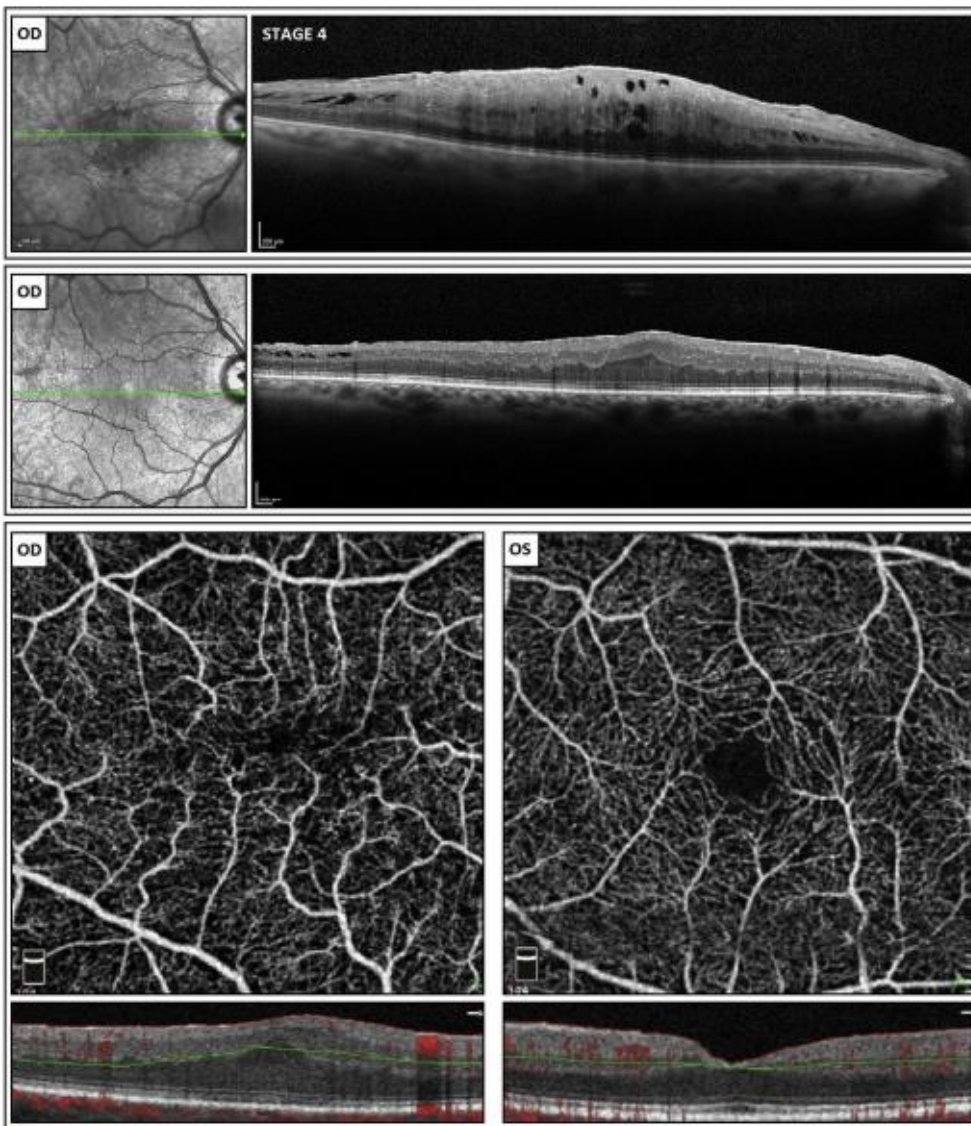


FIGURE 9. Postoperative multimodal imaging of a stage 4 epiretinal membrane. (Top) Preoperative optical coherence tomography. The retina is thickened, with disrupted retinal layers and the presence of intraretinal cystoid spaces. The ectopic inner foveal layers are continuous across the entire foveal area. (Center) Postoperative optical coherence tomography. Twelve months after pars plana vitrectomy with epiretinal membrane and internal limiting membrane peeling, the ectopic inner foveal layers are still present and continuous across the entire foveal area. The thickness of the retina and the ectopic inner foveal layers is decreased. (Bottom) Postoperative optical coherence tomography angiography of the vitrectomized eye (right eye) and the unaffected fellow eye (left eye). At 12 months from surgery, the foveal avascular zone of the vitrectomized eye is severely reduced but foveal capillaries are notably absent. The morphology of the retinal vessels appears distorted. The foveal avascular zone and the retinal vasculature in the fellow eye are normal.



**OBRIKADO !!**

