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on ophthalmology

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The Framingham series of publications is designed to meet clinical specialists' need for a reliable guide to the most important articles appearing in their field.

Each issue presents an authoritative selection from the recently published literature, with the emphasis on evidence-based medicine. Articles are recommended for inclusion by Framingham's editorial office and an advisory board headed by key opinion leaders in the relevant clinical area.

Framingham's team of medical writers prepares original abstracts of these articles, in a structured format that presents the main points at a glance. Our aim is to convey the essence of each article in a concise but readable style.

Issues are published every three to four months.

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Framingham *on ophthalmology*
is supported by an unrestricted educational grant from
Bayer Portugal S.A.
Carnaxide, Portugal

COMMENTARY PAGE OPHTHALMOLOGY

By Nuno Gomes, MD

It is an absolute pleasure to write the commentary page for the first edition of 2014 of Framingham on Ophthalmology. We start this edition with an excellent review of the pathophysiology of retinal detachment written by two leading experts in the field. Understanding the mechanisms involved in retinal detachment and the importance of dynamic tractions as pointed out by the authors, can help us to choose the most adequate treatment for this pathology, leading to better functional and anatomical results.

Long-term results of therapy with aflibercept seem very promising in Age-related macular degeneration, as shown by the paper written by Professor Ursula Schmidt-Erfurth et al.. It is important to stress out the fact that a very high percentage of patients were able to maintain their improvement in visual acuity over a long period of time even with an 8-week treatment regimen. This is one of the major concerns when starting therapy for these patients, and recent reports have shown a loss of visual acuity over the long run with "real-life" treatments, outside of clinical trials. This remains to be seen with aflibercept but so far the results seem very interesting.

Dr Steel and Dr Lotery present an interesting review on vitreo-macular traction and macular holes. Vitreo-macular tractions are in the spotlight at the moment as new advances have finally opened the door for pharmacological vitreolysis, with the advent of a new drug already approved for their treatment. It is important to point out that adequate patient selection is the key to success and, as knowledge of these drugs advances, important prognostic factors are emerging that can greatly contribute to augmenting the efficacy of these agents.

Two well designed studies about the use of anti-VEGF drugs for the treatment of myopic choroidal neovascularization confirmed our thoughts from everyday practice: ranibizumab is more effective than PDT and bevacizumab and ranibizumab seem to be equally effective for the treatment of this condition. The gain in visual acuity is remarkable and apparently well maintained over a long period of time.

A very interesting review paper by Dr. Simao about OCT in Neurodegenerative diseases confirms that in Ophthalmology there really is "much more than meets the eye", and we can learn a lot about different disorders of the central nervous system just by analyzing the retina and optic nerve with the latest imaging technology. As the author states, "…consider the eye as a window to the central nervous system…".

A final word for two papers that are proof that advances in imaging technology have transformed the way we look at our patients and pathologies. The paper by Mrejen et al. shows us that modern imaging techniques allow for a full understanding of disease mechanisms and disease activity providing us with something similar to a "histological" exam without the need for a biopsy as they review pigment epithelial detachment using multimodal imaging. Ko et al. provide evidence that changes in OCT can be used to predict the outcomes of treatment in patients with CRVO.

With new emerging treatments and new imaging modalities, these are indeed exciting times for Ophthalmology!

RHEGMATOGENOUS RETINAL DETACHMENT:
A REAPPRAISAL OF ITS PATHOPHYSIOLOGY AND TREATMENT

Ophthalmic Research, 2014; 51(1):15–31

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BACKGROUND & AIM: This article reviews the pathogenesis and treatment of rhegmatogenous retinal detachment, and is based on a literature review and the authors' own experience.

ARTICLE TYPE: Review.

FINDINGS: Retinal adhesion and attachment is due mainly to two factors: the retinal pigment epithelium pumping fluid out of the subretinal space, and the presence of interphotoreceptor matrix glue. However, the vitreous gel and the anatomy of the vitreoretinal interface also play a role. The hyaluronic acid content of the gel decreases with age, causing some of the collagen fibres to release water. This syneresis means that the vitreous volume comprises both gel and fluid, and is the first step in the development of retinal detachment. Rapid movement of the gel as a result of movement of the head or eyeball creates dynamic traction at the point of vitreoretinal adhesion, and this force is countered by the suction of the retinal pigment epithelium, interphotoreceptor matrix glue and resistance of the retina. However, the dynamic traction may be sufficient to cause a retinal tear. The retina will remain attached if the defensive forces are strong enough, but if they are overcome by the dynamic traction and shear stress, the retina will become elevated, allowing unbound fluid to enter the subretinal space. Once the amount of this fluid exceeds the ability of the retinal pigment epithelium to drain it, a rhegmatogenous retinal detachment will develop.

While the treatment of retinal detachment has traditionally focused on repairing the retinal tear, and this is still important, the primary therapeutic goal should actually be to weaken or eliminate the dynamic traction. Scleral buckling works by indenting the wall of the eye, which changes the direction of the force pulling on the retina and thereby weakening its effect. Pneumatic retinopexy reduces the flow of fluid through the retinal tear, and may also weaken the vitreoretinal traction, although this procedure is associated with a 30% occurrence of new retinal breaks. In contrast, pars plana vitrectomy eliminates the traction by removing the syneretic vitreous, and it is essential that vitreous removal is complete (including a surgically induced posterior vitreous detachment, if one is not already present, and the removal of the vitreous immediately behind the lens). The procedure is followed by the creation of a chorioretinal scar around the tear, and intraocular tamponade to prevent fluid entry.

CONCLUSION: Rhegmatogenous retinal detachment is due to syneresis and the development of dynamic traction, which should therefore be the primary target of surgery.

INTRAVITREAL AFLIBERCEPT INJECTION FOR NEOVASCULAR AGE-RELATED MACULAR DEGENERATION:

NINETY-SIX–WEEK RESULTS OF THE VIEW STUDIES

Ophthalmology, 2014 January; 121(1):193–201

AUTHORS: Schmidt-Erfurth U, Kaiser PK, Korobelnik JF, Brown DM, Chong V, Nguyen QD, Ho AC, Ogura Y, Simader C, Jaffe GJ, Slakter JS, Yancopoulos GD, Stahl N, Vitti R, Berliner AJ, Soo Y, Anderesi M, Sowade O, Zeitz O, Norenberg C, Sandbrink R, Heier JS
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BACKGROUND & AIM: Antiangiogenic therapies such as ranibizumab and bevacizumab, which target vascular endothelial growth factor (VEGF), are potentially effective in the treatment of neovascular age-related macular degeneration (AMD). However, while clinical trials have demonstrated improvements in visual acuity, these benefits are limited in clinical practice because of the required frequency of office visits and intravitreal injections. Aflibercept has been designed to inhibit intraocular VEGF with improved binding affinity and better pharmacokinetics than existing drugs, and administration every 2 months has proved to be as effective as monthly delivery of ranibizumab in maintaining visual acuity up to 52 weeks. The aim of this study was to assess the efficacy and safety of intravitreal aflibercept for neovascular AMD up to 96 weeks.

STUDY DESIGN: Two randomized phase III trials.

ENDPOINTS: Best-corrected visual acuity (BCVA), and arterial thromboembolic events.

METHOD: This analysis pooled data from 2 similarly designed randomized trials in which a total of 2457 patients with neovascular AMD were treated for 52 weeks with intravitreal ranibizumab 0.5 mg every 4 weeks (the standard of care), aflibercept 2 mg every 4 weeks, aflibercept 0.5 mg every 4 weeks, or aflibercept 2 mg every 8 weeks. The aflibercept regimens were preceded by 3 initial monthly doses. From weeks 52 to 96, patients continued on the same treatment arms, receiving a dose at least every 12 weeks, and with interim doses as required, based on the results of monthly evaluations. Maintenance of BCVA was defined as a loss of <15 letters compared with baseline.

RESULTS: The proportion of patients maintaining their baseline BCVA ranged from 94.4–96.1% across all treatment groups at week 52. Similar proportions of patients (91.5–92.4%) maintained visual acuity across all treatment groups at week 96, with the mean increase in BCVA from baseline largely similar among treatment groups (range 6.6–7.9 letters) throughout the 96 weeks of the study. By the end of extended treatment, the proportion of eyes without retinal fluid had decreased (from 60.3–72.4% at week 52 to 44.6–54.4% at week 96), and the number of eyes without fluid was 9.0% higher in those who received aflibercept 2 mg every 4 weeks than in those on ranibizumab. The incidence of arterial thromboembolic events was similar across treatment groups.

CONCLUSION: The aflibercept regimens were as effective as ranibizumab in maintaining BCVA up to 96 weeks.

IDIOPATHIC VITREOMACULAR TRACTION AND MACULAR HOLE:

A COMPREHENSIVE REVIEW OF PATHOPHYSIOLOGY, DIAGNOSIS, AND TREATMENT

Eye (London, England), 2013 October; 27 Suppl 1:S1–21

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BACKGROUND & AIM: This article reviews the pathophysiology, diagnosis and treatment of idiopathic vitreomacular traction (VMT) and macular holes.

ARTICLE TYPE: Review.

FINDINGS: Ageing is often accompanied by the development of posterior vitreous detachment (PVD) as a result of liquefaction of the vitreous gel and the creation of fluid-filled pockets, leading to weakened adhesion between the vitreous and retina, and their gradual separation over time. This state can also be complicated by persistent vitreomacular adhesions between the vitreous cortex and macular area, which may exert tractional forces on the macula. This VMT can cause the development of an epiretinal membrane as well as idiopathic macular holes (IMHs), which may lead to visual disturbances such as metamorphopsia, photopsia, blurred vision and decreased visual acuity. IMHs are full-thickness, vertical defects in the foveal neurosensory retina, and recent ultrasound and optical coherence tomography (OCT) findings indicate they occur as a result of anteroposterior and dynamic VMT during perifoveal PVD. VMT has a prevalence in the general population of approximately 22.5 per 100,000 persons, and tends to affect individuals between 65 and 75 years old. IMHs also occur in older individuals, and have a prevalence of 0.1 to 0.8% of adults over the age of 40 years.

While a number of technologies are available to visualize the vitreous and retina, and can help in the identification of VMT and IMH, the most accurate method is OCT. In particular, the recent development of spectral-domain OCT has increased the resolution of images and allowed more accurate staging of IMH, as well as the potential identification of impending macular holes. Pars plana vitrectomy is the main treatment option for patients with VMT or IMH. High success rates are reported for both conditions, and peeling of the inner limiting membrane of the retina can improve clinical outcomes in IMH; peeling is also practised in VMT, although its additional benefit is unclear. Non-invasive treatment options include pharmacological vitreolysis with ocriplasmin, which degrades laminin and fibronectin at the vitreoretinal interface. Clinical trial results indicate its efficacy in some patients, and success appears to be associated with the presence of a full-thickness IMH, a vitreomacular adhesion diameter no greater than 1500 mm, phakic lens, absence of epiretinal membrane, and age younger than 65 years.

CONCLUSIONS: VMT and IMH are common complications of PVD. Their assessment is aided greatly by OCT, while pars plana vitrectomy is currently the primary treatment option.

RADIANCE:

A RANDOMIZED CONTROLLED STUDY OF RANIBIZUMAB IN PATIENTS WITH CHOROIDAL NEOVASCULARIZATION SECONDARY TO PATHOLOGIC MYOPIA

Ophthalmology, 2014 March; 121(3):682–692.e2

AUTHORS: Wolf S, Balciuniene VJ, Laganovska G, Menchini U, Ohno-Matsui K, Sharma T, Wong TY, Silva R, Pilz S, Gekkieva M; for the RADIANCE Study Group
CENTRE FOR CORRESPONDENCE: Department of Ophthalmology, Inselspital, University Hospital, University of Berne, Berne, Switzerland

BACKGROUND & AIM: There is a need for effective, well-tolerated treatments for choroidal neovascularization (CNV) secondary to pathological myopia (myopic CNV). Although verteporfin photodynamic therapy (vPDT) can stabilize vision in the short term, its longer-term benefits are limited. The aim of this study was to compare the efficacy and safety of the humanized monoclonal antibody ranibizumab and vPDT in patients with visual impairment due to myopic CNV.

STUDY DESIGN: Randomized, multicentre phase III trial.

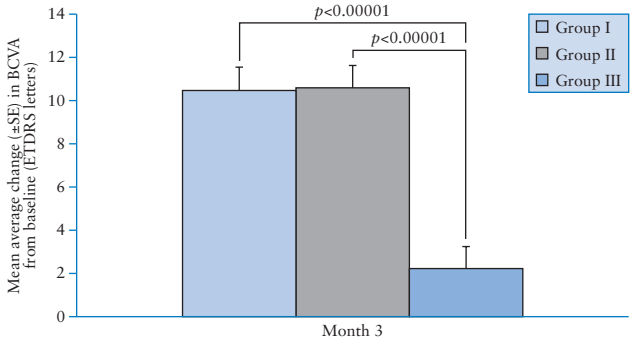
ENDPOINT: The primary endpoint was the change in mean average best-corrected visual acuity (BCVA) from baseline to months 1–3, assessed using Early Treatment Diabetic Retinopathy Study (ETDRS) letters.

METHOD: Patients with visual impairment due to myopic CNV (*n*=277) were randomly assigned to receive either 0.5 mg ranibizumab on day 1, month 1 and thereafter as needed guided by visual acuity (VA) stabilization criteria (Group I, *n*=106), 0.5 mg ranibizumab on day 1 and thereafter as needed guided by disease activity criteria (Group II, *n*=116), or vPDT on day 1 and disease activity treated with 0.5 mg ranibizumab or vPDT at the investigators' discretion from month 3 (Group III, *n*=55).

RESULTS: Ranibizumab was superior to vPDT with regard to the primary endpoint: Group I, +10.5 ETDRS letters; Group II, +10.6 ETDRS letters; and Group III, +2.2 ETDRS letters (Figure). Based on change in mean average BCVA from baseline to months 1–6, ranibizumab treatment guided by disease activity was non-inferior to VA stabilization-guided retreatment (+11.9 versus +11.7 ETDRS letters for Groups I and II, respectively; $p<0.00001$). Mean change in BCVA from baseline to month 12 was +13.8, +14.4 and +9.3 ETDRS letters in Groups I, II and III, respectively. Resolution of myopic CNV leakage was apparent in 63.8–65.7% of patients at month 12. Ocular serious adverse events occurred in one patient in Group I (0.9%) and one in Group II (0.8%). No deaths and no cases of endophthalmitis, retinal detachment, myocardial infarction or cerebrovascular events were reported.

CONCLUSIONS: In patients with myopic CNV, ranibizumab was more effective than vPDT, and was generally well tolerated.

Results for the primary endpoint



INTRAVITREAL ANTI-VEGF THERAPY FOR CHOROIDAL NEOVASCULARISATION SECONDARY TO PATHOLOGICAL MYOPIA:

4-YEAR OUTCOME

British Journal of Ophthalmology, 2013 November; 97(11):1447–50

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BACKGROUND & AIM: Although the standard treatment for myopic choroidal neovascularization (CNV) is photodynamic therapy (PDT) with verteporfin, antivascular endothelial growth factor (anti-VEGF) drugs such as ranibizumab and bevacizumab have had promising results when used off-label to treat CNV secondary to severe myopia. The aim of this study was to evaluate changes in best-corrected visual acuity (BCVA) during a 4-year follow-up period in a large series of highly myopic eyes with CNV treated with ranibizumab or bevacizumab.

STUDY DESIGN: Retrospective, non-randomized case series.

ENDPOINTS: The primary endpoint was change in BCVA. Secondary endpoints included the effect on visual outcome of age (<50 versus ≥50 years), spherical equivalent, anti-VEGF drug and previous PDT.

METHOD: The study sample consisted of 92 highly myopic eyes with subfoveal CNV. The treating drug (0.5 mg intravitreal ranibizumab, *n*=24; or 1.25 mg intravitreal bevacizumab, *n*=68) and initial protocol (loading dose of either one injection, *n*=77; or 3 injections, *n*=15) were dictated by surgeons' preferences and followed by an as-needed monthly regimen. BCVA was evaluated at baseline and then monthly for 4 years.

RESULTS: The mean age of the patients was 57±14 years (range 30–93 years). The mean±SD number of Early Treatment Diabetic Retinopathy Study (ETDRS) letters read was 46.1±16.8 at baseline, 55.5±18.6 at 12 months, 50.1±20.1 at 24 months, 54.2±21.9 at 36 months and 53.1±22.5 at 48 months (p=0.000 for baseline versus 12, 24 and 36 months; and p=0.01 for baseline versus 48 months). The mean±SD number of re-injections after the loading dose was 3.6±5.4, and the mean total number of injections was 4.9±5.4. The type of drug injected had no significant effect on BCVA: +5.3±19.3 ETDRS letters with bevacizumab and +4.3±14.8 with ranibizumab. Previous PDT had no significant effect on BCVA or number of injections required, although PDT treatment-naïve eyes had better initial and final visual acuity than previously PDT-treated eyes. Multiple regression analysis revealed a significant correlation between gain in BCVA and age (R^2=0.220, p<0.001). Spherical equivalent and type of treating drug had no influence on final BCVA or number of injections required, and the number of injections was not related to visual gain.

CONCLUSION: For highly myopic patients with CNV, intravitreal bevacizumab and ranibizumab produced similar statistically significant improvements in BCVA, which were maintained at 4 years.

THE CONTRIBUTION OF OPTICAL COHERENCE TOMOGRAPHY IN NEURODEGENERATIVE DISEASES

Current Opinion in Ophthalmology, 2013 November; 24(6):521–7

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BACKGROUND & AIM: Some patients with neuromyelitis optica (NMO), Alzheimer's disease or Parkinson's disease report visual problems despite having normal findings on ophthalmological examination. Optical coherence tomography (OCT) allows the direct imaging of the non-myelinated peripapillary retinal nerve fibre layer (RNFL), retinal ganglion cells (RGCs) and inner retinal layers (IRLs), and the technique may therefore aid investigation of the mechanisms underlying abnormalities in the visual pathway. This article reviews the role of OCT in assessing neurodegenerative diseases.

ARTICLE TYPE: Review.

FINDINGS: The pathological changes that occur in the eye in neurodegenerative diseases are very similar to those that occur in the brain. It is therefore possible to consider the eye as a window to the central nervous system, and to use OCT findings as surrogate biomarkers in these conditions. Several OCT studies have reported RNFL thinning and RGC loss in patients with NMO (to a greater extent than that seen in multiple sclerosis), and these measures have also been correlated with the results of visual function tests, visual acuity and disability status. Other studies have used Fourier domain OCT to correlate RNFL and macular thickness with visual field loss, and to detect IRL abnormalities in both NMO and multiple sclerosis. One hypothesis is that visual pathway abnormalities in NMO are due to trans-synaptic neurodegeneration, and this could be confirmed in future studies combining OCT with magnetic resonance imaging techniques.

Retinal degeneration has also been reported in patients with Alzheimer's disease, and OCT findings include reductions in RNFL thickness and in RGCs. Furthermore, RNFL and macular thinning, and axonal loss can occur in early stages of the disease while visual acuity and visual fields are still normal. One study in early Alzheimer's found RNFL reduction in the superior quadrant of the disc, as well as a corresponding visual field defect, narrowing of the retinal venous blood column, and secondary retinal hypoxia. In contrast, Fourier domain OCT in patients with Parkinson's disease has not shown any overall abnormalities in IRL or RNFL thickness. However, one study has found that the IRL is thinner than the outer retinal layer in Parkinson's disease, while another showed that RNFL thickness was more prominent in akinetic rigid patients than in those in whom tremor was dominant. In addition, the foveal pit appears to be thinner and broader in Parkinson's disease.

CONCLUSION: OCT has a valuable role in the assessment of neurodegenerative diseases such as NMO, Alzheimer's disease and Parkinson's disease.

RETINAL AND CHOROIDAL THICKNESS EVALUATION BY SD-OCT IN ADULTS WITH OBSTRUCTIVE SLEEP APNEA-HYPOPNEA SYNDROME (OSAS)

Eye (London, England), 2014 January 10; Epub ahead of print

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BACKGROUND & AIM: Obstructive sleep apnoea–hypopnoea syndrome (OSAS) may act as an independent risk factor for primary open-angle glaucoma, and may also affect the physiological structure of the optic nerve. The aim of this study was to assess changes to macular retina and choroidal thickness in patients with OSAS but without significant symptoms or pathological changes in the fundus using spectral domain-optical coherence tomography (OCT).

STUDY DESIGN: Prospective, observational case–control study.

ENDPOINTS: Macular and choroidal thickness.

METHOD: The study included 53 eyes from 53 patients with OSAS and 12 eyes from 12 age-matched controls. Macular and choroidal thickness was measured by OCT. All patients and controls underwent sleep monitoring, and patients' oxygen desaturation index (ODI) was determined during the sleep evaluation. An OCT scan was performed on each patient following mydriasis with Mydrin-P.

RESULTS: In the control group with no OSAS, foveal thickness was significantly thinner than in patients with severe OSAS (p=0.000). Similarly nasal macular thickness was significantly thinner in the control group than in patients with severe OSAS (p=0.008). There was a significant correlation between the ODI and the macular centre thickness (r=0.357, p=0.004), with an ODI coefficient of 0.457. In addition, there was a significant correlation between ODI and nasal macular thickness (r=0.265, p=0.033), with an ODI coefficient of 0.233. After correcting for age and diopter, the subfoveal choroidal thickness was found to differ significantly with degree of OSAS (Table), and a pairwise comparison revealed the subfoveal choroidal thickness of patients with the most severe OSAS to be significantly thinner than that of patients with no, mild or moderate disease (p=0.023, p=0.006, and p=0.036, respectively). The nasal choroidal thickness was significantly thinner in the patients with severe OSAS than in the control group and in patients with mild OSAS (p=0.013 and p=0.010, respectively). Choroidal thickness was found to be significantly correlated with diopter (r=0.520, p<0.001) and ODI (r=0.520, p=0.001).

CONCLUSION: In patients with OSAS, chronic intermittent hypoxia appears to lead to changes in the structure of the retina and choroid.

Mean±SD subfoveal choroidal thickness (μm), and the thickness 1 mm nasal and temporal to the fovea, in patients with various degrees of OSAS (* p<0.05)

	Degree of OSAS				
	None (control)	Mild	Moderate	Severe	p-value
Subfovea	254±32	260±48	242±50	213±58	0.024*
Nasal	237±27	230±38	212±35	201±46	0.038*
Temporal	243±38	239±30	233±31	219±40	0.186

SAFETY, EFFICACY, AND QUALITY OF LIFE FOLLOWING SUTURELESS VITRECTOMY FOR SYMPTOMATIC VITREOUS FLOATERS

Retina, 2013 December 31; Epub ahead of print

AUTHORS: Mason JO 3rd, Neimkin MG, Mason JO 4th, Friedman DA, Feist RM, Thomley ML, Albert MA
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BACKGROUND & AIM: Symptomatic vitreous floaters are a consequence of vitreous opacities that occur secondary to posterior vitreous detachment (PVD), asteroid hyalosis or vitreous syneresis. These can interfere with important activities of daily living and can be physically and psychologically debilitating for some patients. There is some evidence from smaller studies that pars plana vitrectomy (PPV), the preferred treatment option for symptomatic vitreous floaters, can improve quality of life (QOL). The aim of this study, however, was to assess safety, outcomes and QOL in the largest consecutive operative series of eyes to have undergone sutureless vitrectomy for symptomatic vitreous floaters.

STUDY DESIGN: Retrospective study.

ENDPOINTS: QOL, postoperative outcomes, and complications.

METHOD: The study sample consisted of 168 eyes of 143 patients who had undergone sutureless 25-gauge PPV for symptomatic vitreous floaters between January 2008 and January 2011. The efficacy of PPV was assessed using Snellen visual acuity. Postoperative complications were recorded, and QOL was assessed from a 9-item survey.

RESULTS: Mean Snellen visual acuity was 20/40 preoperatively and improved to 20/25 postoperatively ($p<0.0001$). Only 4/168 eyes (2.2%) had decreased postoperative visual acuity owing to transient complications. The QOL questionnaire was completed by 127/143 patients (88.8%). Preoperatively, most patients (73%) described their subjective severity of daily symptoms as either "severe" or "very severe". Activities most affected were reading (50%), driving (30%), occupational tasks (12%) and leisure activities (8%). Postoperatively, 96% of patients were "satisfied" with the outcome of PPV and 94% rated it a "complete success". Approximately 92% of patients reported that they had either no symptoms or only extremely mild symptoms after their operation. Iatrogenic retinal breaks were found in 12/168 eyes (7.1%) undergoing the surgical procedure. There was no significant correlation between retinal breaks and PVD induction ($p=1.00$). The commonest postoperative complication was cataract formation, which occurred in 9/40 phakic eyes (22.5%). Transient postoperative complications occurred in 3 eyes: 2 had vitreous haemorrhage and one had cystoid macular oedema. No patients developed a rhegmatogenous retinal detachment or a retinal tear postoperatively.

CONCLUSIONS: Visual acuity and QOL were improved with sutureless 25-gauge PPV for symptomatic vitreous floaters, and the rate of postoperative complications was low.

CHOROIDAL AND MACULAR THICKNESS CHANGES INDUCED BY CATARACT SURGERY

Clinical Ophthalmology, 2014; 8:55–60

AUTHORS: Falcão MS, Gonçalves NM, Freitas-Costa P, Beato JB, Rocha-Sousa A, Carneiro A, Brandão EM, Falcão-Reis FM
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BACKGROUND & AIM: Phacoemulsification is a form of cataract surgery that usually improves visual outcome. However, it represents an inflammatory insult to the eye, and postoperative inflammatory changes occur in the retina and choroid. There has been very little investigation of the morphologic changes that occur in the choroid as a result of this inflammatory insult, but cataract surgery may lead to increases in choroidal and retinal thickness at the posterior pole, and the increases in choroidal thickness may be related to previously observed changes in retinal macular thickness. The aim of this study was to evaluate the effect of uneventful phacoemulsification on the morphology and thickness of the macula, submacular choroid and peripapillary choroid.

STUDY DESIGN: Prospective interventional case series.

ENDPOINTS: Thickness of ocular tissues.

METHOD: Fourteen eyes of 14 patients undergoing routine cataract surgery were studied. Retinal macular thickness, choroidal submacular thickness and choroidal peripapillary thickness were measured preoperatively and then one week and one month after phacoemulsification using enhanced depth imaging spectral domain optical coherence tomography.

RESULTS: There was a statistically significant increase in mean retinal macular thickness one week after cataract surgery in horizontal scans (p=0.015) and even greater increases in both horizontal (p<0.001) and vertical (p=0.001) scans one month after surgery (Table). Choroidal thickness decreased in horizontal scans one week after surgery and increased in vertical scans, but neither of these changes were statistically significant. One month after surgery, there was a non-significant increase in choroidal thickness in vertical scans (+4.21 µm) and a non-significant decrease (–9.11 µm) in horizontal scans (Table). In peripapillary scans, statistically significant increases in choroidal thickness in the superonasal and inferotemporal quadrants were observed after one week: +13.27±17.83 µm (p=0.033) and +11.18±11.47 µm (p=0.009), respectively. However, these changes were no longer significant one month after surgery.

CONCLUSION: Phacoemulsification surgery induced non-pathologic increases in retinal macular thickness but no significant changes in choroidal thickness.

Mean±SD change in retinal and choroidal thickness (µm)

	Preoperative	After one week	*p*-value	After one month	*p*-value
Horizontal macular scans					
Retinal thickness	304.49±15.37	+3.45±4.59	0.015	+8.67±6.75	0.000
Choroidal thickness	239.28±79.08	–1.27±37.17	0.90	–9.11±39.59	0.41
Vertical macular scans					
Retinal thickness	308.77±14.69	+1.69±4.18	0.17	+8.80±7.07	0.001
Choroidal thickness	238.63±76.12	+0.47±25.81	0.95	+4.21±20.23	0.47

MULTIMODAL IMAGING OF PIGMENT EPITHELIAL DETACHMENT:
A GUIDE TO EVALUATION

Retina, 2013 October; 33(9):1735–62

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BACKGROUND & AIM: Retinal pigment epithelial detachment (PED) can occur in a number of retinal disorders, most commonly in age-related macular degeneration (AMD). PEDs can be classified as drusenoid, serous, vascularized or mixed, and it is important to be able to distinguish between them because each is associated with a specific pathogenesis, natural history, prognosis and optimal treatment. This article reviews the variety of PEDs occurring in AMD and other retinal disorders, as well as their presentation, classification and natural history. This summary focuses on imaging findings in drusenoid and vascularized PEDs.

ARTICLE TYPE: Review.

FINDINGS: Drusenoid PEDs take the form of yellow/white elevations of the retinal pigment epithelium (RPE), often surrounded by large soft drusen. They tend to show hyperfluorescence on fluorescein angiography, but are hypofluorescent on indocyanine green angiography (ICGA) because of a blocking effect. Fundus autofluorescence imaging typically shows isofluorescence or hyperautofluorescence, the degree of which may indicate the stage of progression and can help predict which PEDs will become atrophic. On optical coherence tomography (OCT), drusenoid PEDs are often hyper-reflective with posterior shadowing because of pigment clumping, and may have an undulating appearance. An increase in hyporeflectivity under the PED may be due to the presence of subretinal or intraretinal fluid, indicating choroidal neovascularization (CNV), or may correspond to a small pocket of benign subretinal fluid or an acquired vitelliform lesion.

A vascularized PED is the most common type of CNV found in AMD. It occurs as a separation between the RPE monolayer and Bruch membrane, and the assessment of its presence, location and nature requires a multimodal imaging approach. On clinical examination, a vascularized PED appears as an irregular elevation of the RPE, while fluorescein angiography shows irregular hyperfluorescence that increases over several minutes. ICGA findings may be either a well-defined focal area of hyperfluorescence, or a larger, variably delineated area (plaque), and can help confirm the presence of CNV in cases where fluorescein angiography provides only poor visualization. No large studies have been conducted to evaluate fundus autofluorescence imaging in vascularized PEDs. OCT can provide good visualization of the relationship between neovascular membranes and PEDs, while enhanced-depth OCT allows better assessment of the contents of PEDs, and has shown that they are filled with hyper-reflective material, partly composed of fibrovascular proliferation.

CONCLUSION: Multimodal imaging including enhanced depth OCT and ICGA allows a better assessment of the sub-RPE compartment in PEDs.

OPTICAL COHERENCE TOMOGRAPHY PREDICTS VISUAL OUTCOME IN ACUTE CENTRAL RETINAL VEIN OCCLUSION

Retina, 2013 December 27; Epub ahead of print

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BACKGROUND & AIM: Vision loss in acute central retinal vein occlusion (CRVO) is predominantly caused by macular ischaemia and macular oedema. The introduction of optical coherence tomography (OCT) has facilitated the measurement of macular oedema, but evaluating macular ischaemia remains challenging. The aim of this study was to investigate the clinical features of CRVO in relation to the presence of the novel prominent middle limiting membrane (p-MLM) sign on OCT at clinical presentation.

STUDY DESIGN: Retrospective case review.

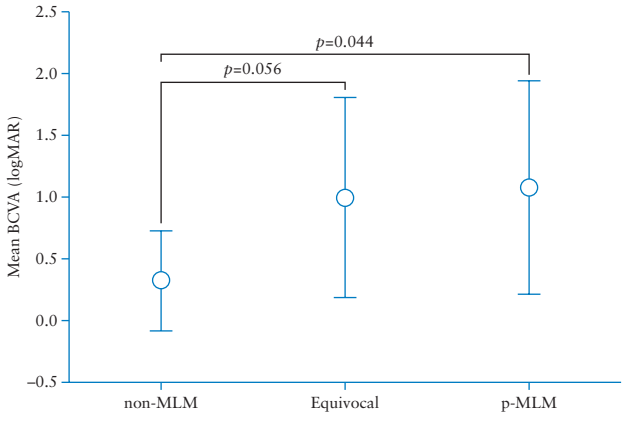
ENDPOINT: Clinical features of CRVO, such as visual acuity, central fovea thickness and CRVO type.

METHOD: The study retrospectively reviewed 50 consecutive eyes from patients diagnosed with acute CRVO at Yonsei University Hospital between December 2008 and December 2011. On OCT, the p-MLM sign was defined as a hyper-reflective line located in the inner synaptic portion of the outer plexiform layer. Presence of the p-MLM sign was interpreted as a sign of acute ischaemia. Eyes that had a p-MLM sign on presentation OCT (p-MLM group) were compared with eyes for which no p-MLM sign was identified (non-MLM group) and eyes in which there was uncertainty about the p-MLM sign (equivocal group).

RESULTS: In total, 14 (28%) eyes were found to have the p-MLM sign, 21 (42%) eyes did not, and the remaining 15 (30%) eyes were classed as equivocal. Compared with the non-MLM group, the eyes with p-MLM sign had a best-corrected visual acuity (BCVA) that was significantly worse at both initial screening and final visit. The mean initial BCVA was 1.10±0.72 versus 0.47±0.49 logMAR in the p-MLM and non-MLM groups, respectively (p=0.007), while it was 1.08±0.86 versus 0.32±0.41 logMAR, respectively, in patients at the final visit (p=0.044; Figure). The eyes with a p-MLM sign were more likely to be classified as ischaemic type CRVO compared with the eyes in the non-MLM group (57.1 versus 4.8%, p=0.001).

CONCLUSIONS: Eyes with CRVO which exhibited a p-MLM sign on OCT were more likely to have a worse visual outcome and to be classified as ischaemic type CRVO.

Mean BCVA of patients with CRVO at the final visit



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[a] DMI - Degenerescência Macular relacionada com a Idade neovascular (húmida)
[b] OVCR - Oclusão da Veia Central da Retina

Referências: **1.** Lanzetta P, Mitchell P, Wolf S, Veritti D. Different antivascular endothelial growth factor treatments and regimens and their outcomes in neovascular age-related macular degeneration: a literature review. Br J Ophthalmol. 2013 Dec;97(12):1497-507. **2.** Heier JS, et al. Intravitreal Aflibercept (VEGF Trap-Eye) in Wet Age-Related Macular Degeneration. Ophthalmology 2012; 119: 2537-2548. **3.** Stewart MW. Aflibercept (VEGF Trap-eye): the newest anti-VEGF drug. Br J Ophthalmol. 2012 Sep;96(9):1157-8. **4.** Resumo das Características do Medicamento EYLEA®.

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Neste caso o esquema de monitorização deve ser determinado pelo médico assistente e pode ser mais frequente do que o esquema de injeções. *Edema macular secundário a OVCR:* A dose recomendada para EYLEA® é de 2 mg de aflibercept, equivalente a 50 microlitros. Após a injeção inicial, o tratamento é administrado mensalmente. O intervalo entre duas doses não deve ser inferior a um mês. Se não se verificar uma melhoria nos resultados visuais e anatómicos ao longo das três primeiras injeções, não é recomendada a continuação do tratamento. O tratamento mensal continua até que os resultados visuais e anatómicos sejam estáveis durante as três avaliações mensais. Posteriormente, a necessidade de continuar o tratamento deve ser reconsiderada. Se necessário, pode continuar-se o tratamento, aumentando gradualmente os intervalos de tratamento a fim de manter os resultados visuais e anatómicos estáveis. Se o tratamento for interrompido, os resultados visuais e anatómicos devem ser monitorizados e o tratamento deve ser retomado caso estes se deteriorem. Normalmente, a monitorização deve ser feita nas consultas de administração de injeção. Durante o prolongamento do intervalo de tratamento até à conclusão da terapêutica, o esquema de monitorização deve ser determinado pelo médico assistente com base na resposta individual do doente e pode ser mais frequente do que o esquema de injeções. Cada frasco para injetáveis deve ser utilizado apenas para o tratamento de um olho. O frasco para injetáveis contém mais do que a dose recomendada de 2 mg de aflibercept. O volume extraível do frasco para injetáveis (100 microlitros) não é para ser utilizado no total. O excesso de volume deve ser eliminado antes de injetar. Injetar a totalidade do volume poderá resultar em sobredosagem. *Populações especiais:* Afeção hepática e/ou compromisso renal: Não foram realizados estudos específicos com EYLEA® em doentes com afeção hepática e/ou compromisso renal. Os dados disponíveis não sugerem a necessidade de ajustes posológicos com EYLEA® nestes doentes. População idosa: Não são necessárias considerações especiais. População pediátrica: A segurança e a eficácia em crianças e adolescentes não foram estabelecidas. *Contraindicações:* Hipersensibilidade à substância ativa aflibercept ou a qualquer um dos excipientes. Infeção ocular ou periocular ativa ou suspeita. Inflamação intraocular ativa grave. *Advertências e precauções especiais de utilização:* Endoftalmite; Aumento da pressão intraocular; Imunogenicidade; Efeitos sistémicos; Doentes com fatores de risco associados ao desenvolvimento de rasgadura do epitélio pigmentado da retina; Doentes com descolamento regmatogênico da retina ou com buracos maculares de fase 3 ou 4; Doentes com descolamento da retina; Nos casos de uma redução na acuidade visual corrigida (BCVA) de ≥30 letras em comparação com a última avaliação da acuidade visual, de uma hemorragia subretiniana envolvendo o centro da fóvea, ou, se a dimensão da hemorragia for ≥50% da área total da lesão, de uma cirurgia intraocular realizada nos 28 dias anteriores ou planeada para os próximos 28 dias. EYLEA® não deve ser utilizado durante a gravidez, a menos que o potencial benefício justifique o potencial risco para o feto. As mulheres com potencial para engravidar têm de utilizar métodos contracetivos eficazes durante o tratamento e durante pelo menos 3 meses após a última injeção intravítrea de aflibercept. A experiência é limitada no tratamento de doentes com OVCR crónica e isquémica. Não é recomendado o tratamento, em doentes que apresentem sinais clínicos da perda da função visual isquémica irreversível. Os dados clínicos com EYLEA® em doentes com retinopatia diabética são limitados. *Interações medicamentosas:* Não foram realizados estudos de interação. A utilização adjuvante de terapêutica fotodinâmica (TFD) com verteporfina e EYLEA® não foi estudada, por este motivo o perfil de segurança não está estabelecido. *Efeitos indesejáveis:* Hemorragia conjuntival; Dor ocular; Rasgadura do epitélio pigmentado da retina; Descolamento do epitélio pigmentado da retina; Degenerescência retiniana; Hemorragia do vítreo; Catarata; Catarata nuclear; Catarata subcapsular; Erosão da córnea; Abrasão da córnea; Aumento da pressão intraocular: Visão turva; Flocos vítreos; Edema da córnea; Descolamento do vítreo; Dor no local de injeção; Sensação de corpo estranho nos olhos; Aumento da lacrimação; Edema palpebral; Hemorragia no local de injeção; Hiperemia conjuntival; Hiperemia ocular; Hipersensibilidade; Endoftalmite; Descolamento da retina; Rasgadura da retina; Irite; Iridociclite; Catarata cortical; Opacidades do cristalino; Deficiência do epitélio da córnea; Irritação no local da injeção; Sensação anormal no olho; Irritação palpebral; Flare da câmara anterior; Vitrite; Uveíte; Hipópio; Acontecimentos tromboembólicos arteriais (enfarte do miocárdio não fatal, acidente vascular cerebral não fatal ou morte vascular (incluindo mortes de causa desconhecida)); Potencial imunogenicidade. *Número da A.I.M.:* Frasco para injetáveis: 5487376. *Data de revisão do texto:* Agosto 2013.

L.PT.SM.03.2014.0281