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on ophthalmology

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Evaluating the safety of air travel for patients with scleral buckles and small volumes of intraocular gas

British Journal of Ophthalmology, 2014 April 29; Epub ahead of print

Femtosecond laser-induced macular changes and anterior segment inflammation in cataract surgery

Journal of Refractive Surgery, 2014 April; 30(4):222–6

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Retina, 2014 May 14; Epub ahead of print

and more…

ISSUE 2, 2014

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OUR PURPOSE

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

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COMMENTARY PAGE OPHTHALMOLOGY

By Teresa Quintão, MD

This issue of Framingham on Ophthalmology focuses on excellent scientific articles, published between January and May 2014, concerning medical and surgical aspects of retinal disease.

John VJ *et al.* followed up patients with vitreomacular adhesion and found that spontaneous resolution had occurred in 32% of cases, indicating the need for caution when making decisions about the optimal management of these cases.

An interesting report by Chang *et al.* showed aflibercept to be an effective therapy for patients with neovascular age-related macular degeneration resistant to other anti-vascular endothelial growth factor agents.

Patel *et al.* have shown that fluorescein angiography using ultra-wide-field imaging can improve the angiographic evaluation of the peripheral retina. This development has increased the utility of a relatively old technique.

The review by Rasmussen *et al.* of long-term (>2 years) treatment with ranibizumab has shown that most age-related macular degeneration patients preserve baseline visual acuity, validating the use of long-term ranibizumab treatment.

A retrospective study from Coimbra in Portugal by Farinha *et al.* on the progression of myopic maculopathy after treatment of choroidal neovascularization supports the view that changes were more likely to be related to the natural progression of the disease than to the treatment given.

Noble *et al.* compared intraocular pressures of the eyes of intraocular-gas patients, with or without scleral buckling, during simulated flight, finding that buckled eyes were less susceptible to spikes in intraocular pressure.

A prospective randomized trial by Conrad-Hengerer *et al.* found no significant differences in macular oedema and anterior segment inflammation when femtosecond laser-assisted cataract surgery was compared with standard phacoemulsification.

In patients with macular oedema due to retinal vein occlusion, Kuppermann *et al.* showed that treatment with a dexamethasone intravitreal implant led to a rapid improvement BCVA compared with sham treatment, confirming the usefulness of the procedure.

The use of spectral domain optical coherence tomography and angiography to evaluate focal choroidal excavation is described by Shinojima *et al.* This entity is probably underdiagnosed, and is more prevalent in patients from Asia.

Kubicka-Trzaska *et al.* determined serum antiretinal antibodies in patients with exudative age-related macular degeneration undergoing therapy with anti-vascular endothelial growth factor, concluding that serum antibody titre may be a biomarker of the efficacy of therapy.

Ooto *et al.* describes outer 'retinal corrugations' which can be identified by spectral-domain optical coherence tomography and which are associated with age-related macular degeneration.

All these scientific reports, and many others that have not been selected, are examples of the continuing advances in ophthalmology that contribute to improvements in the care of our patients.

CLINICAL COURSE OF VITREOMACULAR ADHESION MANAGED BY INITIAL OBSERVATION

Retina, 2014 March; 34(3):442–6

AUTHORS: John VJ, Flynn HW Jr, Smiddy WE, Carver A, Leonard R, Tabandeh H, Boyer DS
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BACKGROUND & AIM: Vitreous adhesion and presumed traction have been hypothesized to play a role in the pathogenesis of many macular conditions, such as neovascular age-related macular degeneration, macular hole and diabetic macular oedema. Spectral-domain optical coherence tomography (SD-OCT) is a technique that allows documentation of changes in the effects and extent of vitreomacular adhesion (VMA) over time. The aim of this study was to investigate the clinical course of patients with VMA defined by SD-OCT who were followed-up during non-interventional management.

STUDY DESIGN: Cohort study.

ENDPOINTS: Best-corrected visual acuity (BCVA) and grade of VMA.

METHOD: A total of 106 eyes of 81 patients (mean age 72.7 years) were identified as having VMA based on clinical symptoms and SD-OCT findings. Based on SD-OCT findings, VMA was graded as follows: Grade 1, incomplete cortical vitreous separation with attachment at the fovea; Grade 2, Grade 1 findings plus any intraretinal cysts or clefts; and Grade 3, Grade 2 findings plus the presence of subretinal fluid. The mean length of follow-up was 23 months.

RESULTS: At the initial visit, 43 eyes (41%) had Grade 1 VMA, 56 (52%) had Grade 2 VMA and 7 (7%) had Grade 3 VMA. The Table shows that spontaneous release of VMA had occurred in 13 Grade 1 eyes (30%), 17 Grade 2 eyes (30%) and 4 Grade 3 eyes (57%) after the follow-up period. At the final examination, 34 eyes overall (32%) had spontaneously resolved VMA, 25 (23%) had Grade 1 VMA, 38 (36%) had Grade 2 VMA, 4 (4%) had Grade 3 VMA, and 5 (5%) underwent pars plana vitrectomy. There were no significant differences in spontaneous resolution rates for the various grades (p=0.35). Overall, mean BCVA was 20/37 at baseline and 20/35 at the last examination. Grade 3 VMA patients had the worst visual acuity at the initial visit; however, in each of the VMA grades, there were no significant differences between changes from initial to final mean BCVA, and there were no significant differences in these changes between the VMA grades.

CONCLUSION: The findings suggest that patients with VMA diagnosed by SD-OCT but with minimal or non-progressive symptoms can be considered for non-interventional management initially.

Final status of VMA in the patients managed by initial observation

Presenting VMA grade	Number of eyes	Improved (%)	Stable (%)	Worse (%)
Grade 1	43	13/43 (30)	23/43 (53)	7/43 (16)
Grade 2	56	17/56 (30)	31/56 (55)	8/56 (14)
Grade 3	7	4/7 (57)	1/7 (14)	2/7 (28)

INTRAVITREAL AFLIBERCEPT FOR TREATMENT-RESISTANT NEOVASCULAR AGE-RELATED MACULAR DEGENERATION

Ophthalmology, 2014 January; 121(1):188–92

AUTHORS: Chang AA, Li H, Broadhead GK, Hong T, Schlub TE, Wijeyakumar W, Zhu M
CENTRES: Sydney Institute of Vision Science; Save Sight Institute; Sydney School of Public Health, University of Sydney, Sydney, New South Wales, Australia

BACKGROUND & AIM: Neovascular age-related macular degeneration (AMD) can be treated with monoclonal antibodies, such as ranibizumab and bevacizumab, which target vascular endothelial growth factor (VEGF). Aflibercept, a new anti-VEGF agent with greater affinity for the molecule, has proved effective in treatment-naïve patients, and there is some evidence that it might also be effective in patients with treatment-resistant disease. The aim of this study was to investigate the efficacy of intravitreal aflibercept for the treatment of patients with AMD resistant to other anti-VEGF agents.

STUDY DESIGN: Prospective, open-label, non-controlled trial.

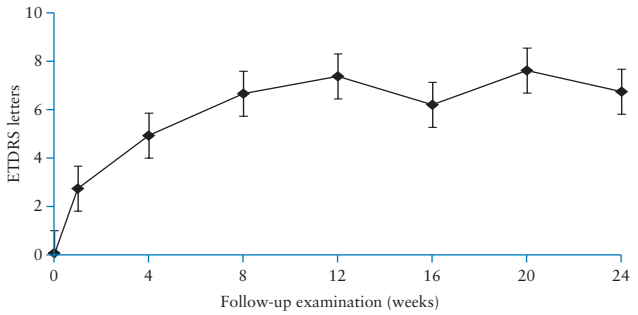
ENDPOINTS: Best-corrected visual acuity (BCVA) and central retinal thickness (CRT).

METHOD: The study included 49 patients with choroidal neovascularization secondary to AMD that had proved resistant to previous treatment. Treatment resistance was defined as persistent intraretinal or subretinal fluid, and a BCVA of between 35 and 90 Early Treatment Diabetic Retinopathy Study (ETDRS) chart letters. Participants were treated with intravitreal aflibercept 2 mg administered at weeks 0, 4, 8, 16 and 24, and were monitored every month with a full ophthalmic investigation, fundus photography and spectral-domain optical coherence tomography.

RESULTS: After 24 weeks of treatment, the mean BCVA of the cohort improved by 6.9±8.12 ETDRS letters ($p<0.001$; Figure). A total of 55% of eyes improved by at least 5 letters, while 26% improved by at least 10 letters and 10% by at least 15 letters. Increasing the spacing between injections from 4 to 8 weeks did not reduce BCVA. The mean CRT of the cohort decreased by 89.4 µm over 24 weeks of treatment ($p<0.001$). In 33% of eyes, the decrease in CRT was more than 100 µm, while 20% had a reduction of more than 150 µm, and 4% had an increase in CRT of more than 150 µm at week 24. Increasing the spacing between injections from every 4 weeks to 8 weeks resulted in an increase in CRT of 37.4 µm ($p<0.001$), but this did not cause a significant change in vision.

CONCLUSION: Aflibercept was found to be an effective therapy for patients with treatment-resistant neovascular AMD.

Change in mean BCVA over 24 weeks



ULTRA-WIDE-FIELD FLUORESCEIN ANGIOGRAPHY IN RETINAL DISEASE

Current Opinion in Ophthalmology, 2014 May; 25(3):213–20

AUTHORS: Patel M, Kiss S
CENTRE: Department of Ophthalmology, Weill Cornell Medical College, New York, New York, USA

BACKGROUND & AIM: Fluorescein angiography is a valuable tool in the investigation of retinal diseases. However, it has become increasingly important to examine the retinal periphery, and the development of ultra-wide-field fluorescein angiography (UWFA) now allows capture of up to 200° of the retina at a time. This means that it is now possible to visualize the periphery without a great deal of patient co-operation or technical expertise on the part of the operator. UWFA captures twice as much retinal area as conventional systems (although with some compromise in image quality), and is now used in the diagnosis and management of a number of retinal conditions. This article reviews the applications of UWFA in diabetic retinopathy, retinal vein occlusion, sickle cell retinopathy, uveitis and paediatric retinal disease.

ARTICLE TYPE: Review.

FINDINGS: In diabetic retinopathy, fluorescein angiography can be used to detect microaneurysms, non-perfusion, macular oedema and neovascularization, many of which may occur at the periphery of the retina. By revealing more of the retinal area, UWFA has the potential to detect more evidence of these abnormalities, thereby altering the assessment of the degree of retinopathy. Furthermore, UWFA may also detect positive findings missed by standard fluorescein angiography. Other applications include identifying peripheral non-perfusion or vascular leakage (which may indicate an increased risk of developing neovascularization or macular oedema), as well as targeting panretinal photocoagulation therapy directly to ischaemic areas rather than to the whole retina.

In patients with retinal vein occlusion, untreated peripheral non-perfusion detected with UWFA has been shown to be associated with macular oedema and neovascularization, indicating the potential value of the technique in identifying individuals who will need closer follow-up for these complications. In sickle cell retinopathy, UWFA has revealed peripheral vascular findings not detected by clinical examination or standard fluorescein angiography, while surveys of clinicians have shown that the use of UWFA can change the assessment of disease activity in patients with posterior uveitis or posterior vasculitis, as well as guiding the management of these conditions. Finally, UWFA can be helpful in the diagnosis and management of children with retinal conditions, partly because its use requires less co-operation, which can be an issue in the assessment of younger patients.

CONCLUSIONS: UWFA can be valuable in the diagnosis and management of a number of retinal conditions, and is likely to be used increasingly in future. It will be necessary, however, to reconcile practice guidelines founded on older studies with the new information made available by UWFA.

LONG-TERM LONGITUDINAL STUDY OF PATIENTS TREATED WITH RANIBIZUMAB FOR NEOVASCULAR AGE-RELATED MACULAR DEGENERATION

Current Opinion in Ophthalmology, 2014 May; 25(3):158–63

AUTHORS: Rasmussen A, Sander B
CENTRE: Research Department of Ophthalmology, Glostrup Hospital, Glostrup, Denmark

BACKGROUND & AIM: Ranibizumab is an antibody targeted against vascular endothelial growth factor (VEGF), and it has proved to be effective in the treatment of patients with choroidal neovascularization secondary to age-related macular degeneration (AMD). Monthly intravitreal injections improve the natural history of the disease and may also reduce the risk of blindness, and the effects of VEGF inhibition are well documented for up to 2 years of therapy. However, many patients are treated for longer than 2 years, and this article reviews recent findings on the efficacy of long-term ranibizumab for neovascular AMD.

ARTICLE TYPE: Review.

FINDINGS: Three major, prospective extension trials have examined ranibizumab treatment beyond 2 years, assessing the long-term tolerability, safety and efficacy of the drug. In all cases, therapy started with 3 loading doses, following which ranibizumab was administered at the discretion of the investigator, although the protocols of the studies differed. In general, most patients who received ranibizumab maintained a visual acuity that was at least as good as it was before initiating treatment. Around 20% of participants achieved an improvement of visual acuity by 15 letters or more. Between 20 and 30% of patients across the 3 trials did not respond to treatment and experienced a loss in visual acuity. In most cases, this was probably due to the natural progression of the disease, although there was evidence from one trial that the divergence in outcomes may have been due to under-treatment. Baseline visual acuity has proved to be a significant predictor of treatment outcome, although this effect has varied between studies.

A number of retrospective trials have also investigated the long-term efficacy of ranibizumab for neovascular AMD. They have generally reported similar results, with stable visual acuity (or a non-significant decrease) in patients treated for up to 48 months, although the outcome often depended on the starting acuity. The most common ocular adverse events associated with ranibizumab are subconjunctival haemorrhage, corneal abrasion and eye pain, although these are generally temporary and mild. The rates of retinal detachment, cataract and intraocular pressure rise are similar to those for shorter-term treatment. Around 5% of patients experience non-ocular adverse events, such as ischaemic cerebrovascular conditions, myocardial infarction and arterial embolic or thrombotic events.

CONCLUSION: Most patients receiving long-term ranibizumab treatment for neovascular AMD preserve their baseline visual acuity, with few ocular or systemic adverse events.

PROGRESSION OF MYOPIC MACULOPATHY AFTER TREATMENT OF CHOROIDAL NEOVASCULARIZATION

Ophthalmologica, 2014; 231(4):211–20

AUTHORS: Farinha CL, Baltar AS, Nunes SG, Figueira JP, Pires IA, Cachulo ML, Silva RM
CENTRES: Medical Retina Unit, Ophthalmology Department, Centro Hospitalar e Universitário de Coimbra; Association for Innovation and Biomedical Research on Light and Image and Faculty of Medicine, University of Coimbra, Coimbra, Portugal

BACKGROUND & AIM: Pathological myopia is one of the commonest causes of blindness and the primary cause of choroidal neovascularization (CNV) in individuals aged <50 years. Although myopic maculopathy is the primary cause of vision loss associated with severe myopia, few attempts have been made to assess either its pattern of progression or the long-term visual prognosis in patients. In addition, the impact of treatments such as photodynamic therapy (PDT) and intravitreal administration of ranibizumab (IVR) on the pattern of progression of myopic CNV or long-term visual prognosis remain unknown. The aim of this study was to investigate the functional and morphological progression of myopic maculopathy in eyes with myopic CNV.

STUDY DESIGN: Retrospective study.

ENDPOINTS: Functional and morphological progression of myopic maculopathy.

METHOD: Eyes with a history of myopic CNV were grouped according to treatment received during follow-up: PDT (n=15), IVR (n=10) or PDT plus IVR (n=13). A fourth group consisted of 16 contralateral highly myopic eyes, without a history of CNV, that had never required any treatment (dry maculopathy group). Functional and morphological progression of myopic maculopathy was assessed using best-corrected visual acuity, colour fundus photography and spectral-domain optical coherence tomography.

RESULTS: Mean follow-up was 80.6±28.0 months. The prevalence of diffuse and patchy atrophy increased during follow-up. Rates of tessellated fundus and lacquer cracks were lower and tended to either decrease or remain constant. The presence of active CNV decreased in all treatment groups, with a reciprocal increase in macular atrophy. A posterior staphyloma was identified in 29 eyes (54% of the total). Progression of total and central areas of macular atrophy was statistically significant in all 3 treatment groups during follow-up (p<0.05), but not in the dry maculopathy group. Final best-corrected visual acuity correlated inversely with total and central areas of macular atrophy (p<0.01). Multivariate regression analysis revealed that greater initial age (p=0.010), final axial length (p=0.014), presence of staphyloma (p<0.001) and a larger area of central atrophy in the initial evaluation (p=0.011) predicted a larger final area of macular atrophy. The type of treatment had no predictive value for macular atrophy.

CONCLUSION: Morphological and functional changes of eyes with myopic CNV were more likely to be related to natural progression of myopic maculopathy than to the type of treatment performed.

EVALUATING THE SAFETY OF AIR TRAVEL FOR PATIENTS WITH SCLERAL BUCKLES AND SMALL VOLUMES OF INTRAOCULAR GAS

British Journal of Ophthalmology, 2014 April 29; Epub ahead of print

AUTHORS: Noble J, Kanchanaranya N, Devenyi RG, Lam WC
CENTRES: Department of Ophthalmology and Vision Sciences, University of Toronto; Sunnybrook Health Sciences Centre; Toronto Western Hospital, University Health Network, Toronto, Ontario, Canada

BACKGROUND & AIM: Patients with intraocular gas bubbles are advised not to travel by air because of the risk of dangerously raised intraocular pressure (IOP). Scleral buckling is thought to reduce this risk by lowering ocular rigidity, though this has not been confirmed in clinical trials. The aim of this study was to compare IOP changes in buckled versus unbuckled eyes during simulated flight in a hypobaric chamber.

STUDY DESIGN: Clinical study.

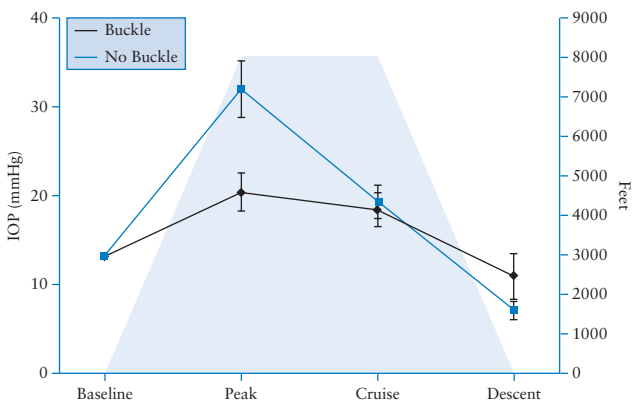
ENDPOINT: IOP.

METHOD: The study enrolled consecutive patients who had undergone recent pars plana vitrectomy with or without scleral buckling. Subjects were tested 4–6 weeks post-surgery when intravitreal gas volumes were estimated to be approximately 10% in size. IOP was measured at baseline and every 5 min in the hypobaric chamber by Goldmann applanation tomography, with the contralateral non-gas-containing eye as control. The chamber was decompressed at a rate corresponding to an ascent rate of 300 feet/min until an altitude of 8000 feet was reached. This was maintained for 15 min ("cruise phase") and the chamber was then repressurized at the same rate as during ascent.

RESULTS: The study tested 12 patients, 6 with and 6 without buckled eyes. Overall, the IOP in the gas-containing eyes rose from a mean baseline value of 13±3 mmHg to a peak of 26±9 mmHg during the cruise phase and returned to or below the baseline level after repressurization. The IOP in contralateral eyes did not change significantly. There was no difference in IOP between unbuckled and buckled eyes at baseline, but unbuckled eyes reached a higher mean peak IOP during the ascent phase than buckled eyes (32±8 versus 20±5 mmHg, p=0.013; Figure). Both the absolute and relative increase in IOP was greater in the unbuckled eyes (p=0.001). On repressurization, unbuckled eyes demonstrated IOPs significantly lower than baseline (7±3 versus 13±3 mmHg, p<0.001), but the final IOP in buckled eyes was not significantly lower than baseline.

CONCLUSION: There was evidence that buckled eyes were less susceptible to spikes in IOP than unbuckled eyes during simulated flight.

IOP during simulated flight



FEMTOSECOND LASER-INDUCED MACULAR CHANGES AND ANTERIOR SEGMENT INFLAMMATION IN CATARACT SURGERY

Journal of Refractive Surgery, 2014 April; 30(4):222–6

AUTHORS: Conrad-Hengerer I, Hengerer FH, Al Juburi M, Schultz T, Dick HB
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BACKGROUND & AIM: Reducing inflammation following cataract surgery is important for rapid recovery. Flare values in the anterior chamber are a sign of increased permeability of the blood–aqueous barrier, and reducing procedural inflammation is associated with improved outcomes. Femtosecond laser-assisted cataract surgery has recently been introduced for capsulotomy and nuclear fragmentation prior to phacoemulsification. The aim of this study was to compare macular oedema and post-operative inflammation of the anterior segment following laser-assisted cataract surgery or standard optimized phacoemulsification over a 6-month period.

STUDY DESIGN: Prospective randomized trial.

ENDPOINT: Laser flare counts from the anterior chamber, and changes in macular thickness and volume.

METHOD: One hundred and four patients (mean age 71.3 years) scheduled for elective bilateral cataract surgery and implantation of an intraocular lens were enrolled. A total of 104 eyes were randomized to laser-assisted cataract surgery (laser group). In the 104 fellow eyes, small-incision phacoemulsification using pulsed ultrasound and intraocular lens implantation was performed (standard group). Assessments of retinal thickness and laser flare were undertaken pre-operatively, and post-operatively at 2 hours, 3–4 days, 1 week and 1, 3 and 6 months.

RESULTS: The mean applied effective phacoemulsification time was 0.035±0.11 seconds in the laser group and 1.39±0.13 seconds in the standard group. Pre-operative mean centre thickness (minimal centre value of the fovea) was 210±23 µm in the laser group and 205±21 µm in the standard group. Six months post-operatively, these values were 215±22 µm and 209±30 µm, respectively. There was no significant difference in mean centre thickness between the groups pre-operatively or during the 6-month post-operative follow-up. Pre-operative laser flare photometry values were not significantly different between the standard and laser group. Post-operatively, a statistically significantly difference in laser flare values was seen at 2 hours (16.7±5.8 and 18.8±6.5 pc/ms in the laser and standard groups, respectively; p=0.033) but no significant difference was seen from day 3 onwards. Macular oedema occurred in 2 eyes in the laser group and 3 eyes in the standard group.

CONCLUSION: There were no significant differences in the mean centre thickness, laser flare photometry values, or the occurrence of macular oedema between femtosecond laser-assisted cataract surgery and standard phacoemulsification.

ONSET AND DURATION OF VISUAL ACUITY IMPROVEMENT AFTER DEXAMETHASONE INTRAVITREAL IMPLANT IN EYES WITH MACULAR EDEMA DUE TO RETINAL VEIN OCCLUSION

Retina, 2014 May 14; Epub ahead of print

AUTHORS: Kuppermann BD, Haller JA, Bandello F, Loewenstein A, Jiao J, Li XY, Whitcup SM
CENTRES: The Gavin Herbert Eye Institute, University of California; Allergan, Inc, Irvine, California; Wills Eye Institute, Philadelphia, Pennsylvania, USA; University of Udine, Udine, Italy; Department of Ophthalmology, Tel Aviv Medical Center and Sackler Facility of Medicine, Tel Aviv, Israel

BACKGROUND & AIM: Treatment with a controlled-release dexamethasone intravitreal implant reduces macular oedema-induced vision loss associated with branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO). However, the time of onset and duration of best-corrected visual acuity (BCVA) improvement has not been determined. The aim of this analysis was to characterize early improvement and duration of effect in those receiving an implant of 0.7 mg dexamethasone.

STUDY DESIGN: Post hoc analysis of 2 randomized phase III trials.

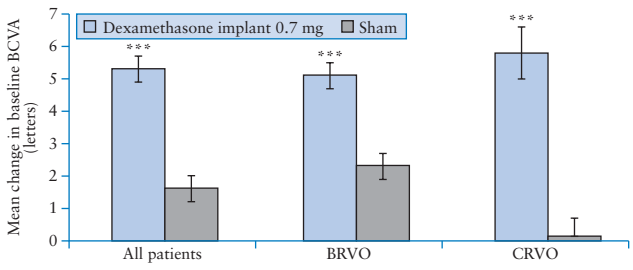
ENDPOINT: The primary endpoint was the percentage of patients with ≥15-letter improvement in BCVA at day 7 compared with baseline.

METHOD: The analysis compared outcomes in patients randomized to treatment with either an implant of 0.7 mg dexamethasone or a sham procedure, stratified by diagnosis (BRVO/CRVO). BCVA was evaluated at baseline and at post-implant day 1, 7, 30, 60, 90 and 180. In those achieving a 15-letter BCVA improvement, the duration of the effect was evaluated by several alternative methods.

RESULTS: The analysis encompassed 853 patients (67% diagnosed with BRVO), of whom 427 received the dexamethasone implant and 426 the sham treatment. The mean BCVA change from baseline was significantly greater in the implant group than the sham group at day 7 ($p<0.001$; Figure) and peaked at day 60. At day 7, 10.3% of patients in the implant group achieved a ≥15-letter improvement over baseline versus only 4.0% in the sham-treated group ($p<0.001$), with similar improvements seen in both BRVO and CRVO patients. At day 7, the mean BCVA improvement was 5.1 letters in BRVO patients given an implant versus 2.3 letters for those given sham treatment, while the mean improvements for the CRVO patients were 5.8 letters and 0.1 letters, respectively (Figure). Among those showing at least a 15-letter improvement during the study, 27.7% of patients maintained this improvement for >90 days, while in 17.4% the improvement lasted >135 days.

CONCLUSION: Compared with a sham procedure, treatment with a dexamethasone implant led to rapid improvements in vision in patients with macular oedema secondary to BRVO or CRVO.

Mean change in baseline BCVA from baseline to day 7 in all patients and subgroups (* $p<0.001$ versus sham)**



MORPHOLOGIC FEATURES OF FOCAL CHOROIDAL EXCAVATION ON SPECTRAL DOMAIN OPTICAL COHERENCE TOMOGRAPHY WITH SIMULTANEOUS ANGIOGRAPHY

Retina, 2014 July; 34(7):1407–14

AUTHORS: Shinojima A, Kawamura A, Mori R, Yuzawa M
CENTRE: Department of Ophthalmology, School of Medicine, Nihon University, Tokyo, Japan

BACKGROUND & AIM: Little is known about the aetiology and morphological characteristics of focal choroidal excavation (FCE). The aim of this study was to identify clinically relevant morphological changes in patients with FCE using enhanced depth imaging optical coherence tomography, a novel technique for evaluating choroidal status.

STUDY DESIGN: Observational study.

ENDPOINTS: FCE shape and morphological features of retinal pigment epithelial irregularities.

METHOD: The study included 31 FCE lesions in 29 eyes of 26 patients (23 eyes from 21 men and 6 eyes from 5 women) with a range of disorders including typical age-related macular degeneration, idiopathic neovascularization and idiopathic focal choroidal excavation. Between April 2008 and December 2012, fundus examinations were performed in all 26 patients using an indirect ophthalmoscope and slit-lamp biomicroscope with a contact lens. Mean refractive error and best-corrected visual acuity were determined and colour fundus photographs obtained. Fluorescein angiography and indocyanine green angiography with simultaneous enhanced depth imaging optical coherence tomography were then performed. In addition, angiographic video recording was carried out in 25 eyes.

RESULTS: FCE was identified in 21 eyes of patients with typical age-related macular degeneration, central serous chorioretinopathy, polypoidal choroidal vasculopathy, and idiopathic choroidal neovascularization. Idiopathic FCE was identified in 8 eyes. The FCE lesions were classified into 3 morphological types: cone-shaped, bowl-shaped, and mixed-type. Optical coherence tomography revealed the cone-shaped type in 17 FCE lesions, the bowl-shaped type in 8 lesions, and mixed-type in 6 lesions. All of the bowl-shaped and mixed-types had retinal pigment epithelial irregularities within the FCE lesion. The cone-type lesions appeared to be tethered to other structures and had a smooth retinal pigment epithelium. The cone-shaped type of FCE lesion was not observed in any of the eyes from patients with typical age-related macular degeneration. There was less angiographically detected atrophic change at the centre of FCE in cone-shaped FCE than in mix-type or bowl-shaped FCE.

CONCLUSIONS: FCE is present in a range of ocular diseases including typical age-related macular degeneration, central serous chorioretinopathy and idiopathic choroidal neovascularization. In some cases, the formation of FCE may be associated with the pathology of chorioretinal disease, although some eyes develop idiopathic FCE.

CIRCULATING ANTIRETINAL ANTIBODIES IN RESPONSE TO ANTI-ANGIOGENIC THERAPY IN EXUDATIVE AGE-RELATED MACULAR DEGENERATION

Acta Ophthalmologica, 2014 May 6; Epub ahead of print

AUTHORS: Kubicka-Trząska A, Wilańska J, Romanowska-Dixon B, Sanak M
CENTRES: Department of Ophthalmology and Ocular Oncology; Division of Molecular Biology and Clinical Genetics, Jagiellonian University Medical College, Krakow, Poland

BACKGROUND & AIMS: The presence of serum antiretinal antibodies (ARAs) may be an important disease marker in patients with age-related macular degeneration (AMD). However, no data have yet been published on the response of ARAs to treatment of AMD with anti-vascular endothelial growth factor (VEGF), and the aims of this study were to assess the changes in levels of ARAs during anti-VEGF therapy in patients with exudative AMD and to examine correlations with immunofluorescence patterns.

STUDY DESIGN: Cohort study.

ENDPOINT: Serum ARA titres.

METHOD: The study included 108 eyes from 98 patients with AMD, aged 55–93 years, who were treated with intravitreal bevacizumab, 1.25 mg/0.05 mL every 4 weeks for 3 months (loading period). Fifty age-and sex-matched healthy subjects were included as controls. Baseline ophthalmic examination included best-corrected visual acuity (BCVA), slit lamp biomicroscopy and fundoscopy, optical coherence tomography (OCT) and fluorescein angiography. After the loading period, a decision was taken regarding re-injection (maintenance period) based on results of BCVA and OCT assessment. Serum ARA levels were determined at baseline, and the immunohistochemical assessments were repeated every 4 weeks over an 8-month follow-up period.

RESULTS: At baseline, 94 (95.5%) of the 98 patients had positive ARA titres, and titres were significantly higher in the patients than the controls (p=0.0000). There was a positive correlation between ARA titres and the diameter of choroidal neovascularization (CNV) measured by fluorescein angiography and central retinal thickness (CRT) assessed by OCT (Table), and a positive correlation between the complexity of circulating ARAs and CNV diameter and CRT. During the 8-month follow-up, a significant reduction in ARA levels was observed, and at the end of the loading period the mean reduction in serum ARA titres was 21% compared with baseline (p=0.01). The reduction in ARA titres during follow-up also correlated with improvements in BCVA and reductions in CRT.

CONCLUSIONS: Anti-VEGF treatment reduced the serum levels of ARAs, with the greatest reduction occurring during the loading period of bevacizumab treatment. Serum ARA titres may represent an effective biomarker of the efficacy of anti-VEGF therapy.

Correlations between ARA measurement parameters and clinical parameters of disease activity in AMD patients (NS, correlation not significant)

Clinical parameter	ARA titre	ARA immunofluorescence patterns	Number of ARA immunofluorescence patterns
CNV type	p=0.0002	NS	NS
CNV diameter	p=0.0000	NS	p=0.0108
CRT	p=0.0000	NS	p=0.0210
BCVA	NS	NS	NS

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OUTER RETINAL CORRUGATIONS IN AGE-RELATED MACULAR DEGENERATION

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BACKGROUND & AIM: Age-related macular degeneration (AMD) is a leading cause of visual impairment in developed countries. There are 2 major phenotypes: neovascular AMD, manifested by the invasion of choroidal neovascularization (CNV) into the sub-retinal pigment epithelium (RPE) and sub-retinal space; and geographic atrophy (GA), manifested as an area of focal loss of the RPE and outer retina. The introduction of spectral-domain optical coherence tomography (SD-OCT) has improved the identification and management of AMD. However, the morphology of AMD is not well characterized, and the aim of this study was to use SD-OCT to investigate tomographic changes in AMD and define characteristic features.

STUDY DESIGN: Retrospective study.

ENDPOINT: Histopathological characteristics of AMD.

METHOD: After a retrospective review of medical records, 25 eyes of 16 patients (mean age 82.7 years) with severe atrophy associated with AMD were selected, along with 53 donor eyes of 53 patients with late AMD. Subjects underwent comprehensive ophthalmological examination, and the thickness of the hyper-reflective material was assessed. These findings were evaluated against histopathological findings in donor eyes with GA or CNV.

RESULTS: Of the 16 patients, 20 eyes had CNV and 5 eyes had GA. Examination of the SD-OCT images showed a curvilinear hyper-reflective material above the Bruch membrane line within the atrophic area. The material lay above the hyper-reflective tissue in the CNV eyes, suggesting fibrovascular scar, and just above the Bruch membrane line in GA eyes. The hyper-reflective material was contiguous with the outer portion of the RPE band, and there was a relatively hypo-reflective space below. Composite surface volume rendering images showed the hyper-reflective material to be thrown into folds within the atrophic area in the CNV eyes, and to have a different orientation to the underlying large choroidal vessels. In the GA eyes, there were drusen leading to a hollow appearance under the drusen, and composite surface volume rendering images revealed a sheet with numerous bumps in the material. Review of histopathologic findings of eyes with advanced GA and CNV revealed an undulating layer of basal laminar deposit in areas of RPE atrophy.

CONCLUSION: SD-OCT findings of an undulating sheet of hyper-reflective material above the Bruch membrane, termed outer retinal corrugations in this report, correlated with the basal laminar deposit seen in areas of RPE atrophy on histopathological findings.

AGORA TAMBÉM APROVADO PARA
EDEMA MACULAR SECUNDÁRIO À OVCR[b]

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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®.

Medicamento sujeito a receita médica restrita. Para mais informações deverá contactar o titular de AIM.

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▼ Este medicamento está sujeito a monitorização adicional. *Nome:* EYLEA® 40 mg/ml solução injetável num frasco para injetáveis. *Composição:* 1 ml de solução injetável contém 40 mg de aflibercept. *Forma Farmacêutica:* Solução injetável. *Indicações terapêuticas:* EYLEA® é indicado em adultos para o tratamento da degenerescência macular relacionada com a idade (DMI) neovascular (húmida). Perda da visão devida a edema macular secundário a oclusão da veia central retiniana (OVCR). *Posologia e modo de administração:* EYLEA® é apenas para injeção intravítrea. *DMI húmida:* A dose recomendada para EYLEA® é de 2 mg de aflibercept, equivalente a 50 microlitros. O tratamento com EYLEA® é iniciado com uma injeção por mês durante três doses consecutivas, seguido de uma injeção a cada dois meses. Não há necessidade de monitorização entre injeções. Após os primeiros 12 meses de tratamento com EYLEA®, o intervalo entre tratamentos pode ser prolongado com base nos resultados visuais e anatómicos. 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.

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