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on ophthalmology

Multi-country real-life experience of anti-vascular endothelial growth factor therapy for wet age-related macular degeneration

British Journal of Ophthalmology, 2014 September 5; Epub ahead of print

The value of preoperative medical testing for vitreoretinal surgery

Retina, 2014 August 8; Epub ahead of print

Low-intensity/high-density subthreshold micropulse diode laser for chronic central serous chorioretinopathy

Retina, 2014 August 14; Epub ahead of print

Impact of duration of macula-off retinal detachment on visual outcome: a systematic review and meta-analysis of literature

Retina, 2014 October; 34(10):1917–25

Switch from intravitreal ranibizumab to bevacizumab for the treatment of neovascular age-related macular degeneration: clinical comparison

Ophthalmologica, 2014 August 29; Epub ahead of print

Visual and anatomical outcomes of macular epiretinal membrane peeling after previous rhegmatogenous retinal detachment repair

Retina, 2014 August 13; Epub ahead of print

Evaluation of visual acuity, macular status, and subfoveal choroidal thickness changes after cataract surgery in eyes with diabetic retinopathy

Retina, 2014 August 12; Epub ahead of print

Proposed lexicon for anatomic landmarks in normal posterior segment spectral-domain optical coherence tomography: the IN•OCT Consensus

Ophthalmology, 2014 August; 121(8):1572–8

and more…

ISSUE 3, 2014

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Framingham *on dermatology*

Framingham *on diabetes*

Framingham *on gastroenterology*

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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 Ricardo Faria, MD

This issue of Framingham on Ophthalmology illustrates and highlights some of the "hot topics" that all of us, as ophthalmologists, have to deal with in our practice day-to-day. Not surprisingly, 5 of the 11 abstracts have to do with the use of anti-vascular endothelial growth factor (anti-VEGF) agents, which are definitely important and which have led to dramatic improvements in the management of retinal diseases.

The perfect protocol for the management of wet age-related macular degeneration (AMD) has still to be established, as there remain significant differences between the results of major randomized studies and our everyday clinical experiences. This has been shown in many publications, and is illustrated in one of our articles ("Multi-country real life experience of anti-vascular endothelial growth factor therapy wet age related macular degeneration"), in which a decrease in visual outcomes was apparent after the first year of treatment with anti-VEGF agents. While there is unquestionably a benefit from such treatments, most of our patients end up with a visual acuity similar to the level they had at baseline, whether or not their medication has changed. It is a similar story with diabetic macular edema, in which treatment options fail to reverse the often-observed catastrophic downhill course of visual function, suggesting that there are many other factors that need to be considered and addressed.

The number of anti-VEGF treatments required for each patient represent a huge burden for clinics and heath services. Part of the economic burden can be dealt with by the use of bevacizumab, as long as legal issues and safety are considered. To date, studies have failed to demonstrate a better safety profile or improved clinical efficacy for bevacizumab compared with ranibizumab or aflibercept. Meeting the need for all the visits involved in prescribing these treatments is a real challenge for any clinic or ophthalmology department.

The article, "The value of preoperative medical testing for vitreoretinal surgery", is a reminder that many of the preoperative systemic general examinations undertaken may simply be increasing the cost unnecessarily. As has already been shown for outpatients undergoing cataract surgery, it seems useless, as a general rule, to do full blood screening for outpatients undergoing pars plana vitrectomy. Bearing this in mind could bring about savings in cost and time.

Although common sense demands prompt surgery for a macula-off retinal detachment, we do not yet know how long can we wait before visual outcome becomes compromised. This raises many issues with legal consequences, and, as proposed by van Bussel and colleagues in "Impact of duration of macular-of retinal detachment on visual outcome', 3 days may be a safe time limit to avoid a worsening prognosis.

An interesting report on macular changes after cataract surgery is presented by Brito and colleagues in "Evaluation of visual acuity, macular status and subfoveal choroidal thickness changes after cataract surgery in eyes with diabetic retinopathy". Inflammatory changes after cataract surgery have long been known, but we need to pay special attention to those patients with pre-existing conditions, such as diabetic macular edema, to be sure not to make the condition worse. Making use of anti-VEGF therapy as part of the procedure may be a better alternative than prescribing post-operative anti-inflammatory eye drops. This is something we need to investigate with some urgency.

The IN•OCT consensus document on nomenclature is of great importance. Not only is it educational, but, by defining a consensus terminology, it aims to standardize the way ophthalmologists examine OCT images. The development of OCT was an incredible breakthrough in ophthalmology, and the technique remains, without a doubt, the ophthalmologist's "stethoscope" and a powerful tool for the study of the macula.

We wish you all happy reading, and send our best wishes for a wonderful 2015!

MULTI-COUNTRY REAL-LIFE EXPERIENCE OF ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR THERAPY FOR WET AGE-RELATED MACULAR DEGENERATION

British Journal of Ophthalmology, 2014 September 5; Epub ahead of print

AUTHORS: Holz FG, Tadayoni R, Beatty S, Berger A, Cereda MG, Cortez R, Hoyng CB, Hykin P, Staurenghi G, Heldner S, Bogumil T, Heah T, Sivaprasad S
CENTRE FOR CORRESPONDENCE: King's College Hospital, London, UK

BACKGROUND & AIM: The vascular endothelial growth factor (VEGF) antibody fragment ranibizumab improves visual acuity in patients with neovascular (wet) age-related macular degeneration (wAMD). Although these improvements can be maintained with monthly intravitreal injections, such a regimen places a significant treatment burden on patients, caregivers and physicians and is therefore often unachievable in clinical practice. Less frequent dosing regimens produce slightly less favourable outcomes. The aim of this study was to assess changes in visual acuity in patients with wAMD treated with ranibizumab.

STUDY DESIGN: Retrospective, observational, multicentre study.

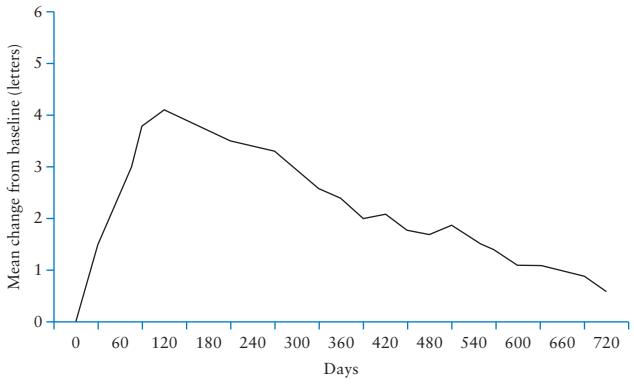
ENDPOINT: Change in visual acuity, and number of anti-VEGF injections.

METHOD: The study was conducted in clinical practice in 8 countries in Europe and the Americas. The medical records of patients with wAMD who began treatment with ranibizumab in 2009 were evaluated. Data were collected until the end of treatment and/or monitoring or until 31 August 2011. Patients evaluated (*n*=2227) were those who received ≥1 anti-VEGF injections and for whom visual acuity was assessed both at baseline and, for the treated eye, on at least one occasion post-baseline. Visual acuity was assessed from letter count on a visual acuity scoring system.

RESULTS: An improvement in visual acuity was observed until about day 120 but decreased noticeably thereafter (Figure). The mean change in visual acuity score from baseline to years 1 and 2 was +2.4 and +0.6 letters, respectively. The use of a loading scheme (first 3 injections within 90 days) maximized initial gain in visual acuity but did not seem to influence its subsequent decline. Patients received more injections in the first year than the second (mean 5.0 and 2.2, respectively). There were noticeable differences in visual outcomes and injection frequency between countries. More frequent injections and ophthalmologist visits were associated with greater improvements in visual acuity.

CONCLUSION: In patients with wAMD, ranibizumab treatment produced an initial improvement in visual acuity, but it was not maintained over time.

Mean change in visual acuity score for all patients, assessed using a last observation carried forward (LOCF) analysis



THE VALUE OF PREOPERATIVE MEDICAL TESTING FOR VITREORETINAL SURGERY

Retina, 2014 August 8; Epub ahead of print

AUTHORS: Shalwala A, Hwang RY, Tabing A, Sternberg P Jr., Kim SJ
CENTRE: Department of Ophthalmology, Vanderbilt University, Nashville, Tennessee, USA

BACKGROUND & AIMS: Patients scheduled for vitreoretinal surgery may have more complex indications for surgery than those undergoing other forms of intraocular surgery. Accordingly, they tend to undergo preoperative testing as a matter of course, even though there is a lack of evidence to suggest that it reduces the incidence of adverse systemic complications. The aims of this study were to identify risk factors associated with increased rates of postoperative adverse systemic events, and to determine whether these rates were influenced by preoperative testing.

STUDY DESIGN: Retrospective chart review.

ENDPOINTS: Baseline comorbidities, preoperative testing, type of anaesthesia during surgery, and postoperative systemic adverse events.

METHOD: The medical charts of 2215 patients who underwent vitreoretinal surgery between January 2002 and November 2011 were reviewed. Systemic adverse events were recorded from charts and hospital records if they had occurred within 30 days of surgery.

RESULTS: The commonest comorbidities were hypertension (53%), diabetes mellitus (37%) and coronary artery disease (18%). In total, 32.7% of patients had a positive smoking history. The commonest preoperative evaluation used was history-taking plus a physical examination (73%), followed by blood glucose testing (58%). Roughly half of patients underwent electrolyte, renal function and electrocardiographic evaluation; fewer patients underwent determination of a complete blood count (25%) or had a chest X-ray (4%). In all, 102 systemic adverse events occurred in 89 patients (4% of the total), most (72%) during the first 24 hours. The commonest adverse events were bradycardia (34%) and desaturation (25%). Patients with a history of coronary artery disease, asthma or chronic renal disease had increased odds of developing postoperative systemic adverse events (Table). In addition, patients receiving general anaesthesia were also at increased risk of these events (odds ratio 3.72, 95% confidence interval 2.29–6.14, $p<0.001$). Multivariate logistic regression revealed no significant correlation between preoperative testing and postoperative adverse events.

CONCLUSION: The incidence of postoperative systemic adverse events after vitreoretinal surgery was 4% and was not measurably affected by preoperative testing.

Logistic regression between preoperative comorbidities and postoperative adverse events

Preoperative comorbidity	Odds ratio	95% CI	*p*-value
Hypertension	0.67	0.39–1.16	0.16
Coronary artery disease	2.04	1.15–3.59	0.01
Arrhythmia	1.02	0.47–2.05	0.96
Chronic heart failure	0.97	0.40–2.20	0.95
Thromboembolic disease	0.31	0.02–1.59	0.27
Stroke	1.85	0.89–3.65	0.09
Asthma	2.18	1.07–4.15	0.03
Diabetes mellitus	1.67	0.82–3.25	0.14
Chronic renal failure	2.76	1.41–5.28	<0.01

LOW-INTENSITY/HIGH-DENSITY SUBTHRESHOLD MICROPULSE DIODE LASER FOR CHRONIC CENTRAL SEROUS CHORIORETINOPATHY

Retina, 2014 August 14; Epub ahead of print

AUTHORS: Malik KJ, Sampat KM, Mansouri A, Steiner JN, Glaser BM
CENTRE: National Retina Institute, Towson, Maryland, USA

BACKGROUND & AIM: Central serous chorioretinopathy is an idiopathic disorder characterized by neurosensory detachment with or without concomitant pigment epithelial detachment. Conventional focal laser treatment involves applying a thermal burn to the retina. It has been shown, however, that the risks associated with conventional laser therapy – scotoma, long-term focal scar expansion, choroidal neovascularization and potential new sites of leakage – can be avoided using a subthreshold MicroPulse laser. The aim of this study was to determine visual outcomes and macular thickness changes in patients with symptomatic chronic central serous chorioretinopathy who underwent treatment with a subthreshold MicroPulse diode laser.

STUDY DESIGN: Retrospective, interventional case series.

ENDPOINTS: Changes in visual acuity and maximum macular thickness.

METHOD: The records of patients with central serous chorioretinopathy of ≥3 months' duration were reviewed. These patients had symptomatic disease that may or may not have involved the foveal centre. A subthreshold 810-nm diode MicroPulse laser with a low duty cycle (5%) and a predetermined power of 750–1000 mW that obviated the need for a 'test burn' was applied to areas of leakage seen on a fluorescein angiogram, areas of clinical neurosensory detachment and/or pigment epithelial detachments.

RESULTS: Patients were excluded from the study for non-attendance at follow-up sessions (n=3), the use of steroid medications (n=1), and intravitreal injection of anti-vascular endothelial growth factor (n=1). Accordingly, the final sample consisted of 10 patients, one of whom was treated in both eyes. Mean pre- and post-treatment Early Treatment Diabetic Retinopathy Study visual acuity was 39.2±15.1 letters (range 8–58) and 45.5±12.0 letters (range 14–55), respectively. Mean maximum macular thickness was 414±137.0 µm at presentation and 316.2±96.5 µm at final follow-up, resulting in a significant (p=0.0046) mean decrease of 97.8 µm (range –7 to 213). In 7/11 eyes (63.6%), the reduction in maximum macular thickness was ≥88 µm, equivalent to a ≥25% reduction compared with the maximum macular thickness at initial presentation. Reductions in maximum macular thickness occurred in 8/11 eyes (72.7%) after a single treatment session.

CONCLUSIONS: The use of a subthreshold MicroPulse diode laser to treat patients with symptomatic chronic central serous chorioretinopathy produced a significant reduction in maximum macular thickness and some improvement in visual acuity.

IMPACT OF DURATION OF MACULA-OFF RETINAL DETACHMENT ON VISUAL OUTCOME:

A SYSTEMATIC REVIEW AND META-ANALYSIS OF LITERATURE

Retina, 2014 October; 34(10):1917–25

AUTHORS: van Bussel EM, van der Valk R, Bijlsma WR, La Heij EC
CENTRE: Department of Ophthalmology, University Medical Center Utrecht, Utrecht, the Netherlands

BACKGROUND & AIM: There is considerable variation in the visual outcomes of surgery for patients with macula-off retinal detachment, due to anatomical and functional damage occurring while the retina is detached. Postoperative visual acuity might therefore be improved by earlier surgical intervention, but it is not clear how critical the timing of surgery is in clinical practice, or whether or not macula-off retinal detachment should be considered a medical emergency. The aim of this study was to investigate the impact of time between macula-off retinal detachment and surgery on postoperative visual acuity.

STUDY DESIGN: Systematic review and meta-analysis.

ENDPOINT: Final visual acuity.

METHOD: Searches of Medline, Embase and the Cochrane database identified 14 eligible studies of patients with macula-off retinal detachment who were treated with scleral buckling or pars plana vitrectomy. Nine of these studies reported sufficient individual patient data on the duration of macular detachment and the final visual acuity to be suitable for meta-analysis. Macular detachment duration was categorized as ≤3, ≤4, ≤7 or ≤10 days, while a reasonable final visual acuity was defined as ≤0.4 logMAR. Meta-analysis using a random-effects model was performed to evaluate the impact of the duration of macular detachment on visual outcome, and the number needed to treat was calculated.

RESULTS: A total of 602 patients across the eligible studies were treated with scleral buckling. Within this group, those who underwent surgery no more than 3 days after macular detachment were significantly more likely to achieve a reasonable final visual acuity of ≤0.4 logMAR. The odds ratio for a duration of ≤3 days compared with 4–7 days was 2.86 (95% confidence interval 1.37–5.99), while the OR for a duration of ≤3 days compared with >3 days was 3.09 (95% CI 1.56–6.12). The number needed to treat was 4 for both odds ratios, implying that 4 patients need to be treated within 3 days instead of later to prevent one additional poor final visual acuity. No significant heterogeneity was identified in these pooled odds ratios, making the outcome similar for either random or fixed effects models. There were insufficient data to perform a meta-analysis of patients who underwent pars plana vitrectomy.

CONCLUSION: Scleral buckling should be performed within 3 days of macular detachment to maximize the likelihood of achieving a reasonable visual outcome.

SWITCH FROM INTRAVITREAL RANIBIZUMAB TO BEVACIZUMAB FOR THE TREATMENT OF NEOVASCULAR AGE-RELATED MACULAR DEGENERATION:

CLINICAL COMPARISON

Ophthalmologica, 2014 August 29; Epub ahead of print

AUTHORS: Pinheiro-Costa J, Freitas-da-Costa P, Falcão MS, Brandão EM, Falcão-Reis F, Carneiro AM
CENTRES: Department of Ophthalmology, Hospital de São João; Department of Anatomy; Department of Sense Organs, Faculty of Medicine, University of Porto, Porto, Portugal

BACKGROUND & AIM: Two recent clinical trials have shown improvements in the visual acuity of patients with choroidal neovascularization secondary to age-related macular degeneration (AMD) after monthly intravitreal injections of ranibizumab. As ranibizumab is not available in all centres, off-label use of bevacizumab, a similar anti-VEGF agent, has been initiated by some clinicians. However, the treatment equivalence of these agents is unclear, due to differences in their molecular weights, affinity to VEGF and pharmacokinetic properties. The aim of this study was to compare clinical outcomes after switching from intravitreal ranibizumab to bevacizumab in patients with neovascular AMD.

STUDY DESIGN: Retrospective chart review.

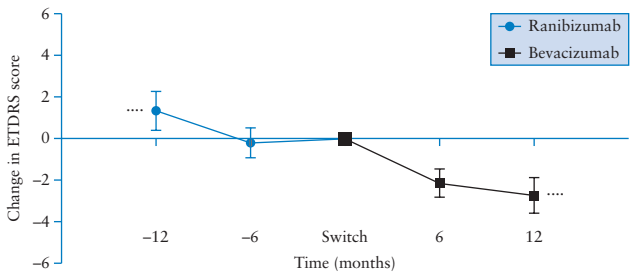
ENDPOINTS: Changes in Early Treatment Diabetic Retinopathy Study (ETDRS) best-corrected visual acuity (BCVA), retinal thickness, and frequency of injections.

METHOD: A total of 110 eyes of 104 consecutive patients with neovascular AMD (mean age 79.6±6.8 years; 60.9% women) were included in the study. All eyes were treated with a 1+pro re nata (1+PRN) regimen in a clinical setting with ranibizumab (at least 3 intravitreal injections), and were subsequently switched to bevacizumab (at least 3 intravitreal injections).

RESULTS: Mean duration of treatment was 18.1 months for ranibizumab, followed by a mean bevacizumab treatment duration of 12.2 months. Mean injection rates per month were similar between the treatments (0.54 and 0.56, respectively; p=0.230). At baseline, mean BCVA was 52.4 letters, and the mean at the time of the switch was a non-significant 3.1 letters higher than the mean (54.8 letters) at the last follow-up visit for bevacizumab (p=0.059). Following the switch to bevacizumab, a statistically significant decrease in BCVA to 51.7 letters (p<0.001) was observed. The Figure shows the change in BCVA around the switch. An increase in central retinal thickness in 51 eyes (46.4%) was observed after the switch.

CONCLUSION: Switching patients with AMD to bevacizumab may have a minor negative effect on the initial gain obtained with ranibizumab.

Change in BCVA (mean ETDRS score) before and after the switch, with standard error bars



VISUAL AND ANATOMICAL OUTCOMES OF MACULAR EPIRETINAL MEMBRANE PEELING AFTER PREVIOUS RHEGMATOGENOUS RETINAL DETACHMENT REPAIR

Retina, 2014 August 13; Epub ahead of print

AUTHORS: Weng CY, Gregori NZ, Moysidis SN, Shi W, Smiddy WE, Flynn HW Jr.
CENTRES: Department of Ophthalmology, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine; Department of Ophthalmology, Miami Veterans Affairs Medical Center, Miami, Florida, USA

BACKGROUND & AIM: The development of an epiretinal membrane is a common cause of visual impairment after rhegmatogenous retinal detachment (RRD) surgery. Pars plana vitrectomy with membrane peeling can restore macular anatomy and improve visual acuity in the majority of cases. However, approximately 12% of patients who undergo membrane peeling after RRD do not achieve improvement in vision despite the apparent anatomical success of the procedure. The aim of this study was to evaluate the visual and anatomical outcomes of membrane peeling in patients with previous RRD repair, and identify prognostic factors for a positive outcome.

STUDY DESIGN: Retrospective, consecutive case series.

ENDPOINTS: Best-corrected visual acuity (BCVA) and optical coherence tomography (OCT) characteristics.

METHOD: Data from consecutive patients who had attended the Bascom Palmer Eye Institute and undergone epiretinal membrane peeling after RRD repair (either macula-sparing or macula-involving) were identified from medical records. Analysis was undertaken of Snellen BCVA data and OCT data on foveal thickness from the clinic visits preceding and 1, 3, 6 and 12 months after epiretinal membrane peeling surgery.

RESULTS: The study included data from 53 eyes (53 patients, mean age 60 years). Following epiretinal membrane peeling, BCVA improved from baseline by a mean of 10 letters at 1 month (n=45; p=0.001), 15 letters at 3 months (n=42; p<0.001), 11 letters at 6 months (n=35; p=0.001), and 16 letters at 12 months (n=33; p<0.001). Mean central foveal thickness decreased by 141 µm (n=22; p<0.001), 185 µm (n=24; p<0.001), 180 µm (n=17; p=0.001), and 151 µm (n=9; p=0.017) after 1, 3, 6, and 12 months, respectively. Analysis revealed that better preoperative BCVA was correlated with better postoperative BCVA at each follow-up visit (p≤0.001). An intact preoperative inner segment/outer segment junction and intact external limiting membrane line, but not the change in central foveal thickness or the presence of fluid in the inner nuclear layer, outer nuclear layer or outer plexiform layer, correlated with better postoperative BCVA at 1, 3 and 6 months.

CONCLUSIONS: Significant improvements in both visual acuity and central foveal thickness were observed following epiretinal membrane peeling surgery after RRD repair, even in eyes with previous RRD involving the macula. The main prognostic factors for good visual outcomes after epiretinal membrane peeling were better preoperative visual acuity and intact outer retinal layers.

EVALUATION OF VISUAL ACUITY, MACULAR STATUS, AND SUBFOVEAL CHOROIDAL THICKNESS CHANGES AFTER CATARACT SURGERY IN EYES WITH DIABETIC RETINOPATHY

Retina, 2014 August 12; Epub ahead of print

AUTHORS: Brito PN, Rosas VM, Coentrão LM, Carneiro AV, Rocha-Sousa A, Brandão E, Falcão-Reis F, Falcão MA

CENTRES: Department of Ophthalmology; Department of Sense Organs, Faculty of Medicine of Porto University, Hospital S João, Alameda Prof Hernâni Monteiro, Porto, Portugal

BACKGROUND & AIM: Diabetic retinopathy leading to macular oedema is a common cause of visual loss in patients with uncontrolled diabetes, and it also causes the accelerated development of visually significant cataracts. The role of the choroidal layer in the pathogenesis of the disease is not well understood, despite the fact that it is responsible for the blood supply to the outer retina. The aim of this study was to assess any possible relationship between postoperative macular and subfoveal choroidal thickness after cataract surgery in eyes with diabetic retinopathy.

STUDY DESIGN: Prospective interventional study.

ENDPOINTS: Best-corrected visual acuity (BCVA), maximum macular thickness and mean foveal or subfoveal choroidal thickness one month after cataract surgery.

METHOD: The study included 35 eyes with clinically significant cataracts from 35 patients with diabetic retinopathy, and 14 age-matched controls. Spectral domain OCT was undertaken one week before cataract surgery and was repeated one month after surgery. In patients, eyes were classified into 3 groups based on clinical and optical coherence tomography (OCT): patients with no macular oedema (Group 1), patients with macular thickening detected using OCT (Group 2), and patients with clinically significant macular oedema who were treated with intravitreal bevacizumab after surgery (Group 3).

RESULTS: In all 3 groups, there was a significant increase in BCVA one month after surgery ($p<0.001$). Postoperative BCVA was best in patients without preoperative macular oedema (Group 1). Postoperatively, mean foveal thickness increased significantly in all diabetic retinopathy groups, except in the Group 3 patients treated with intravitreal bevacizumab (Table). An increase in maximum macular thickness of ≥11% was found in 25.7% of the eyes of the diabetic retinopathy patients, but in none of the control eyes. No significant change in subfoveal choroidal thickness was identified in any of the groups studied.

CONCLUSIONS: The surgical inflammation associated with cataract surgery resulted in a significant increase in macular thickness in eyes of diabetic retinopathy patients not treated with intravitreous bevacizumab, and in controls. However, these macular changes were not accompanied by changes in subfoveal choroidal thickness.

Foveal and maximum macular thickness by study group

	Foveal thickness (µm)			Maximum macular thickness (µm)		
	Preoperative	Postoperative	*p*-value	Preoperative	Postoperative	*p*-value
Group 1	274.55	296.72	0.003	333.66	353.38	0.004
Group 2	320.55	367.11	0.008	371.88	423.00	0.008
Group 3	472.50	474.12	0.933	542.12	540.50	0.889
Controls	242.71	247.57	0.013	336.85	346.28	0.001

PROPOSED LEXICON FOR ANATOMIC LANDMARKS IN NORMAL POSTERIOR SEGMENT SPECTRAL-DOMAIN OPTICAL COHERENCE TOMOGRAPHY:

THE IN•OCT CONSENSUS

Ophthalmology, 2014 August; 121(8):1572–8

AUTHORS: Staurenghi G, Sadda S, Chakravarthy U, Spaide RF; for the International Nomenclature for Optical Coherence Tomography (IN•OCT) Panel
CENTRES: Eye Clinic, Department of Biomedical and Clinical Sciences "Luigi Sacco", Luigi Sacco Hospital University of Milan, Milan, Italy; Department of Ophthalmology, Keck School of Medicine of the University of Southern California, Los Angeles, California; Vitreous Retina Macula Consultants of New York, New York, New York, USA; Queens University, Belfast, UK

BACKGROUND & AIM: Optical coherence tomography (OCT) is a valuable technique that allows imaging of the various structures of the retina. With recent advances in resolution, scan density, speed and the signal-to-noise ratio, it is now possible to discriminate the multiple layers comprising the vitreous face, retina, retinal pigment epithelium (RPE), Bruch's membrane and inner choroid. However, the nomenclature used to describe specific anatomical landmarks was derived from that in use by individual research centres at the time of the introduction of OCT, and is therefore inconsistent and often differs from known anatomy. The International Nomenclature for OCT Panel was established to define a consensus terminology for images of the normal eye obtained by spectral-domain OCT.

ARTICLE TYPE: Consensus document.

FINDINGS: A set of 3 high-quality B-scan images obtained from a normal eye were circulated among a panel of retina specialists. Selected features of the vitreous, retina and choroid were marked and tagged on each image, and panellists were asked to assign their preferred nomenclature for each tagged feature. In a roundtable meeting, the most frequently used term in each case was selected as a candidate label, and a process of open discussion and negotiation was used to arrive at a unanimous consensus name for each feature.

The panel agreed to number each of the 18 reflective bands from the vitreous to the choroid, and to provide a definition for each of these based on the anatomical correlate. The terms 'band' and 'layer' were used to describe discrete and defined lamina. The term 'zone' was introduced for features that were localized to a particular anatomical region but not associated with a proven reflective structure, and examples include the ellipsoid, myoid and the interdigitation zones. The consensus nomenclature for each of the respective OCT layers was as follows: posterior cortical vitreous, pre-retinal space, nerve fibre layer, ganglion cell layer, inner plexiform layer, inner nuclear layer, outer plexiform layer, Henle's nerve fibre layer and outer nuclear layer (for the inner and outer halves of this layer), external limiting membrane, myoid zone of the photoreceptors, ellipsoid zone of the photoreceptors, outer segments of the photoreceptors, cone interdigitation with RPE, RPE/Bruch's membrane complex, choriocapillaris, Sattler's layer, Haller's layer, and choroidal-scleral juncture.

CONCLUSIONS: This consensus nomenclature for OCT findings in normal eyes provides a consistent and pragmatic glossary of terms which will aid communication in this field and allow for the integration of future developments.

A PROSPECTIVE AND NATIONWIDE STUDY INVESTIGATING ENDOPHTHALMITIS FOLLOWING PARS PLANA VITRECTOMY:

CLINICAL PRESENTATION, MICROBIOLOGY, MANAGEMENT AND OUTCOME

British Journal of Ophthalmology, 2014 August; 98(8):1080–6

AUTHORS: Park JC, Ramasamy B, Shaw S, Ling RH, Prasad S
CENTRES: West of England Eye Unit, Royal Devon and Exeter NHS Foundation Trust, Exeter, Devon; Wirral University Teaching Hospital NHS Foundation Trust, Arrowe Park Hospital, Wirral; School of Computing and Mathematics, Plymouth University, Plymouth, Devon, UK

BACKGROUND & AIM: Endophthalmitis is a devastating intraocular infection which can occur as a rare complication following pars plana vitrectomy. Although much information is available on the presentation and treatment of endophthalmitis following cataract surgery, there are few prospective data on endophthalmitis after vitrectomy. The aim of this study was to provide epidemiological data relating to the presentation, microbiology, management and outcomes of endophthalmitis following pars plana vitrectomy.

STUDY DESIGN: Prospective, nationwide surveillance study.

ENDPOINT: Occurrence of infectious endophthalmitis within 6 weeks of pars plana vitrectomy.

METHOD: The study included data acquired during a 2-year surveillance period for cases of presumed infectious endophthalmitis (defined as any case diagnosed and managed as having infectious endophthalmitis in this time period, regardless of microbiology status) after pars plana vitrectomy. Ophthalmologists who reported cases were sent questionnaires to obtain information on preoperative clinical features, operation details and any operative complications, clinical presentation, initial management strategy, and outcome. All data had been stored as case reports in the British Ophthalmological Surveillance Unit (BOSU).

RESULTS: A total of 37 cases of presumed infectious endophthalmitis within 6 weeks of pars plana vitrectomy were reported, and 28 cases met the inclusion criteria. The mean age of patients was 61 years, and 67% were men. Twenty-two cases (78.6%) had surgery performed by a consultant, and the mean time from surgery to endophthalmitis was 5 days (range 1–28). Nineteen surgeries were carried out using 23/25 gauge ports, and 9 surgeries used 20 gauge ports. The most common presenting symptoms were blurred vision (85.2%), pain (77.8%), increasing eye redness (55.6%) and lid swelling (25.9%). Hypopyon was noted in 77.8% of cases. Seventeen cases (60.7%) had a positive microbial culture. Subgroup analysis comparing culture-positive endophthalmitis to culture-negative endophthalmitis revealed no significant differences in time to presentation, clinical symptoms or visual outcome. Final visual acuity after 6 months was poor, and 29.6% of eyes were eviscerated or had no perception of light.

CONCLUSIONS: The data obtained from this nationwide prospective study can help ophthalmic surgeons to promptly identify cases of endophthalmitis following vitrectomy. The results highlight the poor visual outcome associated with this rare complication.

AFLIBERCEPT TREATMENT FOR PATIENTS WITH EXUDATIVE AGE-RELATED MACULAR DEGENERATION WHO WERE INCOMPLETE RESPONDERS TO MULTIPLE RANIBIZUMAB INJECTIONS (TURF TRIAL)

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BACKGROUND & AIM: The management of neovascular age-related macular degeneration (AMD) has improved substantially with the advent of agents that block vascular endothelial growth factor (VEGF). Nevertheless, the eyes of many patients treated with ranibizumab or similar anti-VEGF agents contain recalcitrant fluid. In the SAVE trial, intravitreal ranibizumab led to significant visual and anatomic gains for patients with recalcitrant wet AMD, yet pro re nata (PRN) retreatments were required at almost every monthly visit. The aim of this study was to investigate whether aflibercept 2.0 mg could maintain or improve upon the clinical gains seen in the SAVE trial in patients with recalcitrant exudative AMD.

STUDY DESIGN: Prospective, multicentre, open-label, single-arm trial.

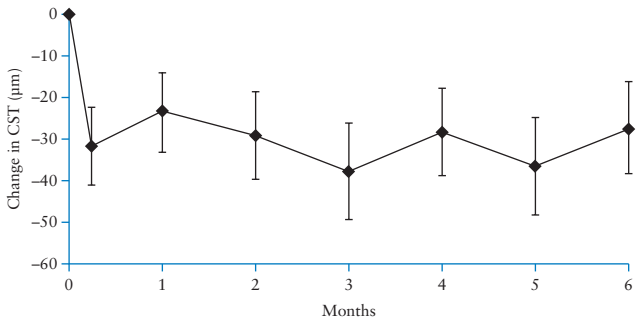
ENDPOINTS: Key outcomes included the mean change in Early Treatment Diabetic Retinopathy Study (ETDRS) best-corrected visual acuity (BCVA), and mean change in central subfield thickness (CST).

METHOD: A total of 46 patients with exudative AMD who had been incomplete responders to ranibizumab 2.0 mg in the SAVE trial were included in the study. All patients received 0.05 mL intravitreal injections of aflibercept 2.0 mg administered every 28 days for the first 3 months, and one mandatory dose at month 4. At 3 and 5 months, PRN retreatment was performed if there was evidence of disease.

RESULTS: At baseline, mean BCVA was 74.2 ETDRS letters (Snellen equivalent 20/32), and no significant change was observed at 6 months (mean BCVA change +0.2 letters, range −10 to +13, p=0.71). The baseline mean CST was 347 µm, and CST improved significantly from baseline at each study visit (−23.6 µm at 1 month and −27.3 µm at 6 months, p=0.018; Figure). Overall, 79% of possible PRN injections were required, and a mean 5.6 aflibercept injections were administered out of a possible maximum of 6 injections. At 6 months, 22% of patients had no retinal fluid, and no patient had experienced a loss of >15 ETDRS letters.

CONCLUSION: In patients with recalcitrant wet AMD, treatment with aflibercept 2.0 mg maintained the mean visual acuity improvements previously achieved with injections of high-dose ranibizumab 2.0 mg.

Change in central subfield thickness over 6 months, with standard error bars



PROFILE OF INTRAOCULAR IMMUNE MEDIATORS IN PATIENTS WITH AGE-RELATED MACULAR DEGENERATION AND THE EFFECT OF INTRAVITREAL BEVACIZUMAB INJECTION

Retina, 2014 September; 34(9):1811–8

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BACKGROUND & AIM: Ocular fluid levels of vascular endothelial growth factor (VEGF) are markedly elevated in patients with age-related macular degeneration (AMD). Bevacizumab has been successfully used to treat patients with AMD, but acute intraocular inflammation has been observed in some patients after intravitreal injection of the drug. However, inflammation is also a characteristic feature of AMD, and different types of cytokines participate in angiogenesis. The aim of this study was to determine changes in intraocular cytokine levels in patients with exudative AMD after intravitreal bevacizumab injection.

STUDY DESIGN: Prospective case–control study.

ENDPOINTS: Intraocular cytokine levels.

METHOD: The study included 37 patients (37 eyes) with AMD, and 28 age-matched patients (28 eyes) who underwent cataract surgery (controls). Undiluted aqueous humour samples were collected prior to intravitreal bevacizumab injection and also 2 days later prior to commencement of cataract surgery in some patients (10 eyes). Levels of 23 cytokines were determined using flow cytometry. The level of statistical significance was set at 0.0022 (0.05/23).

RESULTS: At baseline, the mean aqueous humour concentrations of a number of cytokines differed significantly ($p<0.0022$ for all) between the AMD and control groups, respectively, including VEGF (66.8±42.8 versus 13.6±25.3 pg/mL), angiogenin (7141.7±4303.0 versus 379.2±1422.0 pg/mL), macrophage inflammatory protein (MIP)-1β (16.1±19.4 versus 7.14±31.3 pg/mL), and monocyte chemotactic protein (MCP)-1 (456.9±313.7 versus 176.5±206.4 pg/mL). An exploratory multivariate analysis using all the measured cytokines as independent variables revealed that elevated angiogenin level (odds ratio 1.0007, 95% confidence interval 1.0003–1.0011, $p=0.0004$) and VEGF level (OR 1.0632, 95% CI 1.0202–1.1079, $p=0.0036$) differentiated between the groups. Two days after intravitreal bevacizumab injection, levels of interleukin (IL)-6 and IL-8 had increased significantly; non-significant increases in levels of MIP-1β and MCP-1 were observed; and VEGF levels tended to be reduced, albeit non-significantly (Table).

CONCLUSION: In patients with exudative AMD, intravitreal bevacizumab injection increased intraocular levels of inflammatory cytokines.

Changes in cytokine levels (pg/mL) 2 days after intravitreal bevacizumab injection

Cytokine	Baseline (n=10)	After intravitreal bevacizumab (n=10)	p-value
VEGF	91.4±50.1	29.6±31.2	0.049
IL-6	8.3±16.6	111.4±127.7	0.0020
IL-8	20.4±42.7	32.9±44.2	0.0020
MIP-1β	5.4±7.2	32.9±20.0	0.007
MCP-1	338.7±173.7	733.4±379.5	0.014

AGORA COM 3 INDICAÇÕES APROVADAS:

✓DMI[a] ✓OVCR[b] ✓EMD[c]

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ESPETRO DE AÇÃO ALARGADO (VEGF-A / VEGF-B / PIGF)[5]
MAIOR DURABILIDADE (actividade biológica de 83 dias)[6,7]

[a] DMI - Degenerescência Macular relacionada com a Idade neovascular (húmida)
[b] OVCR - Edema Macular Secundário à Oclusão da Veia Central da Retina
[c] DME - Perda de visão devida a Edema Macular Diabético

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RESUMO DAS CARACTERÍSTICAS DO MEDICAMENTO

▼ 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). Perda da visão devida a edema macular diabético (EMD). **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. ***Edema Macular Diabético:*** 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 cinco 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. O esquema de monitorização deve ser determinado pelo médico assistente. Se os resultados visuais e anatómicos indicarem que o doente não está a beneficiar com a continuação do tratamento, Eylea deve ser interrompido. 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 do frasco para injetáveis poderá resultar em sobredosagem. ***Populações especiais:*** **Compromisso hepático e/ou compromisso renal:** Não foram realizados estudos específicos com Eylea em doentes com compromisso hepático 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 regmatogénico 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. **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; Acuidade visual reduzida; Dor ocular; Rasgadura do epitélio pigmentado da retina; Descolamento do epitélio pigmentado da retina; Degenerescência retiniana; Hemorragia do vítreo; Catarata; Catarata nuclear; Catarata subcapsular; Catarata cortical; 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; Queratite puntiforme; Hiperemia conjuntival; Hiperemia ocular; Hipersensibilidade; Cegueira; Endoftalmite; Descolamento da retina; Rasgadura da retina; Irite; Uveíte; Iridociclite; Opacidades do cristalino; Deficiência do epitélio da córnea; Irritação no local da injeção; Sensação anormal no olho; Irritação palpebral; Flare da câmara anterior; Vitrite; 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 2014.

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

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