

Issue 318

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This free weekly bulletin lists the latest published research articles on macular degeneration (MD) and some other macular diseases as indexed in the NCBI, PubMed (Medline) and Entrez (GenBank) databases.

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Drug treatment

Ophthalmologica. 2017 Mar 1. [Epub ahead of print]

Retinal Nerve Fiber Loss in Anti-VEGF Therapy for Age-Related Macular Degeneration Can Be Decreased by Anterior Chamber Paracentesis.

Enders P, Sitniska V, Altay L, Schaub F, Muether PS, Fauser S.

PURPOSE: To analyze peripapillary retinal nerve fiber layer thickness (RNFLT) change after long-term intravitreal anti-VEGF therapy. Patients with regular anterior chamber paracentesis (ACP) prior to intravitreal injections (IVIs) were compared to those without ACP.

METHODS: Neovascular age-related macular degeneration (nAMD) was treated in a pro re nata regimen with a minimum of 9 IVIs. RNFLT change was determined in spectral domain optical coherence tomography.

RESULTS: In 32 patients without ACP, mean RNFLT loss ($-2.16 \pm 3.60 \mu\text{m}$) was significantly higher than in 44 patients with regular ACP (0.16 ± 3.60 ; $p = 0.029$). Both groups were comparable in age (75.0 vs. 76.8 years; $p = 0.35$), number of IVIs (16.2 vs. 16.6; $p = 0.98$), and observational time (30.0 vs. 32.3 months; $p = 0.32$). In patients without ACP, RNFLT loss was higher compared to IVI-naïve fellow eyes ($p = 0.005$), whereas in ACP patients, no difference was detected ($p = 0.5$).

CONCLUSIONS: A moderate RNFLT loss is found in nonglaucomatous patients after injection therapy for nAMD. As it is decreased with regular ACP, tight management of intraocular pressure seems advisable.

PMID: 28245446

Graefes Arch Clin Exp Ophthalmol. 2017 Feb 25. [Epub ahead of print]

Switching therapy from bevacizumab to aflibercept for the management of persistent diabetic macular edema.

Bahrami B, Hong T, Zhu M, Schlub TE, Chang A.

PURPOSE: To evaluate the visual and anatomical outcomes following switching therapy from bevacizumab to aflibercept in patients with persistent diabetic macular edema (DME).

METHODS: Patients with DME and central macular thickness (CMT) $>300 \mu\text{m}$ on spectral domain optical coherence tomography (SD-OCT) despite at least 4 intravitreal bevacizumab injections in the prior 6 months were recruited for this prospective, single-armed, single centre, open-label clinical trial. Five loading

doses of intravitreal aflibercept were administered every 4 weeks until week 16, at which point the treatment interval was extended to 8 weeks. All participants were reviewed every 4 weeks. At each visit, examination included best-corrected visual acuity (BCVA) measured with an Early Treatment of Diabetic Retinopathy Study chart and CMT measured with SD-OCT. Primary outcome measures were change in CMT and BCVA at week 24 compared with baseline.

RESULTS: A total of 43 eyes from 43 patients were recruited for the study. At enrolment, study eyes had a mean $\pm$ standard deviation of 16.6 ± 11.5 previous intravitreal anti-VEGF injections over a period of 26.9 ± 23.8 months. Mean CMT reduced from 417 ± 91 μ m at baseline to 380 ± 102 μ m at 24 weeks (mean reduction 37 μ m, $p < 0.01$). Mean BCVA improved from 67.8 ± 10.3 letters at baseline to 71.0 ± 10.1 letters at 24 weeks (mean 3.2 letter gain, $p < 0.01$). Eyes improving by ≥ 5 letters at 4 weeks following the first injection had improved vision outcomes at 24 weeks (6.8 ± 7.1 letters vs. 1.0 ± 4.7 letters, $p < 0.01$).

CONCLUSION: Intravitreal aflibercept was effective in improving anatomical and visual outcomes among patients with incomplete response to intravitreal bevacizumab with 24 weeks of follow up.

PMID: 28238195

Mol Ther. 2017 Feb 21. [Epub ahead of print]

Targeted Intraceptor Nanoparticle for Neovascular Macular Degeneration: Preclinical Dose Optimization and Toxicology Assessment.

Zhang X, Bohner A, Bhuvanagiri S, Uehara H, Upadhyay AK, Emerson LL, Bondalapati S, Muddana SK, Fang D, Li M, Sandhu Z, Hussain A, Carroll LS, Tiem M, Archer B, Kompella U, Patil R, Ambati BK.

Abstract: Neovascular age-related macular degeneration (AMD) is treated with anti-VEGF intravitreal injections, which can cause geographic atrophy, infection, and retinal fibrosis. To minimize these toxicities, we developed a nanoparticle delivery system for recombinant Flt23k intraceptor plasmid (RGD.Flt23k.NP) to suppress VEGF intracellularly within choroidal neovascular (CNV) lesions in a laser-induced CNV mouse model through intravenous administration. In the current study, we examined the efficacy and safety of RGD.Flt23k.NP in mice. The effect of various doses was determined using fluorescein angiography and optical coherence tomography to evaluate CNV leakage and volume. Efficacy was determined by the rate of inhibition of CNV volume at 2 weeks post-treatment. RGD.Flt23k.NP had peak efficacy at a dose range of 30-60 μ g pFlt23k/mouse. Using the lower dose (30 μ g pFlt23k/mouse), RGD.Flt23k.NP safety was determined both in single-dose groups and in repeat-dose (three times) groups by measuring body weight, organ weight, hemoglobin levels, complement C3 levels, and histological changes in vital organs. Neither toxicity nor inflammation from RGD.Flt23k.NP was detected. No side effect was detected on visual function. Thus, systemic RGD.Flt23k.NP may be an alternative to standard intravitreal anti-VEGF therapy for the treatment of neovascular AMD.

PMID: 28236576

Acta Ophthalmol. 2017 Mar 2. [Epub ahead of print]

Head-to-head comparison of ranibizumab PRN versus single-dose dexamethasone for branch retinal vein occlusion (COMRADE-B).

Hattenbach LO, Feltgen N, Bertelmann T, Schmitz-Valckenberg S, Berk H, Eter N, Lang GE, Rehak M, Taylor SR, Wolf A, Weiss C, Paulus EM, Pielen A, Hoerauf H; COMRADE-B Study Group.

PURPOSE: To compare the efficacy and safety of ranibizumab 0.5 mg versus dexamethasone 0.7 mg according to their European labels in macular oedema secondary to branch retinal vein occlusion (BRVO) in a 6-month, phase IIIb, randomized trial.

METHODS: Patients received either monthly ranibizumab for 3 months followed by Pro re nata (PRN) treatment (n = 126) or a sustained-release dexamethasone implant followed by PRN sham injections (n = 118). Main outcomes were mean average change in best-corrected visual acuity (BCVA) from baseline to month 1 through month 6, mean changes in BCVA and foveal centre point thickness (FCPT), and adverse events (AEs).

RESULTS: There was no difference in BCVA gains between the treatments prior to month 3. Best-corrected visual acuity (BCVA) gain with dexamethasone declined thereafter. From month 3 to month 6, mean BCVA change from baseline was significantly higher with ranibizumab than with dexamethasone [raw means (standard deviation): +16.2 (±11) letters versus +9.3 (±10.1) letters]. At month 6, the difference in BCVA gains from baseline was +17.3 letters in the ranibizumab versus +9.2 letters in the dexamethasone group. Patients in the ranibizumab group received a mean of 2.94 loading injections and 1.74 PRN retreatment injections, while those in the dexamethasone group received a single loading injection. Elevated intraocular pressure (IOP) and AEs were more frequent with dexamethasone than ranibizumab treatment.

CONCLUSION: Ranibizumab PRN resulted in greater visual acuity (VA) gains in macular oedema following BRVO compared with single-dose dexamethasone over a 6-month study period, observed from month 3, when administered according to their European label. In clinical practice, retreatment with dexamethasone may be required prior to this point.

PMID: 28251811

Arch Soc Esp Oftalmol. 2017 Feb 18. [Epub ahead of print]

Delay in age-related macular degeneration treatment in Spain. [Article in English, Spanish]

Abreu-González R, Alberto-Pestano M, Rubio-Rodríguez G, Abreu Reyes P.

PMID: 28238369

Int J Ophthalmol. 2017 Feb 18;10(2):271-276. eCollection 2017.

Characteristics of retinal vein occlusion with final vision better than 78 letters after sequential therapy with ranibizumab and triamcinolone acetate.

Qin YW, Yu J, Zhang Q.

AIM: To analyze the reasons that may lead to the different vision result by combining the ranibizumab and triamcinolone acetate (TA) in sequence to treat macular edema in retinal vein occlusion (RVO).

METHODS: Ranibizumab and TA were combined in sequence to treat 43 patients with macular edema secondary to RVO. Six months after the treatment, patients with central fovea thickness (CFT) less than 300 µm in optical coherence tomography (OCT) were collected into Groups I and II, based on vision acuity (VA) better than 78 letters or less than 60 letters. The age, baseline VA, duration from onset to treatment, CFT at the baseline, sub-retinal fluid (SRF), sub-foveal exudates and injection times of TA and ranibizumab were taken into comparison.

RESULTS: The mean age of the subjects was 46.4y in Group I but 57.5y in Group II. The difference of age was significant between groups (P<0.01). The mean baseline VA was 51.4 letters in Group I and 43.9 letters in Group II (P<0.05). The baseline CFT were 670.9 µm in Group I with SRF in 54.3% patients and 678.1 µm in Group II with SRF in 52.9% (P>0.05). The mean number of injections of TA was 0.9 and the mean number of injections of ranibizumab was 2.3 in Group I but 1.7 and 2.9 respectively in Group II. The treatment times of ranibizumab had no difference between the 2 groups (P>0.05) but the difference of TA

injection times was significant, $P < 0.05$. Subfoveal exudates at final stage happened in no subjects in Group I but in 45.83% subjects in Group II.

CONCLUSION: This combined treatment is safer than TA injection and cheaper than ranibizumab injection alone. Younger patients and earlier treatment will help to get better vision outcome. Subfoveal exudates at the final stage have significant relationship with vision outcome. No relationship existed between the baseline CFT, SRF and the vision outcome.

PMID: 28251088 PMCID: PMC5313552

Retina. 2017 Feb 28. [Epub ahead of print]

RANIBIZUMAB FOR RETINAL VEIN OCCLUSION: Predictive Factors and Long-Term Outcomes in Real-Life Data.

Chatziralli I, Theodossiadis G, Chatzirallis A, Parikakis E, Mitropoulos P, Theodossiadis P.

PURPOSE: The purpose of the study was to evaluate the long-term anatomical and functional outcomes in patients with retinal vein occlusion (RVO), either central retinal vein occlusion or branch retinal vein occlusion, treated with intravitreal ranibizumab and to determine the predictive factors of the final visual outcome.

METHODS: This retrospective study included 54 treatment-naïve patients with macular edema due to RVO (25 with central retinal vein occlusion and 29 with branch retinal vein occlusion), who were treated with intravitreal ranibizumab (3 monthly injections and pro re nata). Predictive factors for visual outcome were assessed. In addition, the best-corrected visual acuity change and the percentage of patients with edema resolution were evaluated.

RESULTS: The mean follow-up time was 47.4 ± 11.1 months. At the end of the follow-up, patients with central retinal vein occlusion gained +6.9 letters (~ 1 Snellen line), whereas patients with branch retinal vein occlusion gained +15.1 letters (3 Snellen lines). Forty-eight percent of patients in central retinal vein occlusion group and 69.0% in branch retinal vein occlusion group presented resolution of macular edema. Negative predictive factors for the final visual outcome were found to be increasing age, increasing macular thickness, the presence of intraretinal fluid, the duration of RVO > 3 months, the ischemic type of RVO, the cystoid type of edema, and the external limiting membrane and ellipsoid zone disruption.

CONCLUSION: The various predictive factors that determine the visual outcome and possibly define the patients' prognosis after ranibizumab treatment in RVO have been studied. The long follow-up period showed that ranibizumab seems to be safe and effective in the treatment of the disease.

PMID: 28248827

Clin Ophthalmol. 2017 Feb 15;11:331-336. eCollection 2017.

Anti-VEGF treatment and peripheral retinal nonperfusion in patients with central retinal vein occlusion.

Abri Aghdam K, Reznicek L, Soltan Sanjari M, Klingenstein A, Kernt M, Seidensticker F.

PURPOSE: To evaluate the association between the size of peripheral retinal nonperfusion and the number of intravitreal ranibizumab injections in patients with treatment-naïve central retinal vein occlusion (CRVO).

METHODS: Fifty-four patients with treatment-naïve CRVO and macular edema were included. Each patient underwent a full ophthalmologic examination including optical coherence tomography imaging and ultrawide-field fluorescein angiography. Monthly intravitreal ranibizumab injections were applied according

to the recommendations of the German Ophthalmologic Society. Two ophthalmologists quantified the areas of peripheral retinal nonperfusion (group 1= less than five disc areas, group 2= more than five disc areas). Correlation analyses between the size of nonperfusion with best-corrected visual acuity, central subfield thickness, and the number of intravitreal injections were performed.

RESULTS: Best-corrected visual acuity improved significantly after intravitreal injections ($P < 0.001$, both groups). Final central subfield thickness after treatment did not significantly differ between both groups ($P = 0.92$, $P = 0.96$, respectively). Mean number of injections in group 1 and group 2 was 4.12 ± 2.73 and 9.32 ± 3.84 , respectively ($P < 0.001$). There was a significant positive correlation between areas of nonperfusion and the number of injections in each group. ($R = 0.97$, $P < 0.001$; $R = 0.94$, $P < 0.001$, respectively).

CONCLUSION: Peripheral retinal nonperfusion in patients with CRVO correlates significantly with the number of needed intravitreal ranibizumab injections. Ultrawide-field fluorescein angiography is a useful tool for detection of peripheral retinal ischemia, which may have direct implications in the diagnosis, follow-up, and treatment of these patients.

PMID: 28243056 PMCID: PMC5317345

Invest Ophthalmol Vis Sci. 2017 Feb 1;58(2):1246-1255.

Changes in Retinal Microcirculation After Intravitreal Ranibizumab Injection in Eyes With Macular Edema Secondary to Branch Retinal Vein Occlusion.

Fukami M, Iwase T, Yamamoto K, Kaneko H, Yasuda S, Terasaki H.

PURPOSE: To evaluate the effects of an intravitreal ranibizumab (IVR) injection on the retinal microcirculation of eyes with macular edema secondary to a branch retinal vein occlusion (BRVO).

METHODS: Twenty-six eyes of 26 patients with macular edema due to a BRVO that had received a single IVR injection (0.5 mg/0.05 mL) were studied. The retinal microcirculation was assessed by laser speckle flowgraphy (LSFG) using the mean blur rate (MBR) and relative flow volume (RFV). The size of the retinal arteries and veins surrounding the optic nerve head were measured separately. All of the examinations were made before, and at 1 week, and 1 and 2 months after the IVR.

RESULTS: The visual acuity improved significantly, and the mean central macular thickness decreased significantly during the follow-up period (both $P < 0.001$). The mean MBRall and MBRTissue decreased significantly at 1 week and 1 month after the IVR (both $P < 0.001$). The total RFV of the arteries and veins decreased significantly at 1 week and 1 month after the IVR injection in the occluded and nonoccluded quadrants (all $P < 0.001$). The width of the arteries and veins in the LSFG images decreased significantly at 1 week and 1 month after the IVR injection ($P < 0.001$).

CONCLUSIONS: An IVR injection leads to a transient vasoconstriction of the retinal arteries and veins and a reduction of the retinal blood flow and velocity in both the occluded and nonoccluded quadrants. The changes in retinal microcirculation might be related to the improvement of the macular edema and vision.

PMID: 28241312

Clin Ophthalmol. 2017 Feb 16;11:355. eCollection 2017.

Erratum: Worsening anatomic outcomes following aflibercept for neovascular age-related macular degeneration in eyes previously well controlled with ranibizumab [Corrigendum].

[No authors listed]

Abstract

[This corrects the article on p. 1053 in vol. 10, PMID: 27354759].

PMID: 28243059 PMCID: PMC5317329

Can J Ophthalmol. 2017 Feb;52(1):137. Epub 2017 Jan 5.

Effect of aflibercept on refractory macular edema associated with central retinal vein occlusion.

Călugăru D, Călugăru M.

PMID: 28237141

Can J Ophthalmol. 2017 Feb;52(1):137-138.

Re: Effect of Aflibercept on Refractory Macular Edema Associated with Central Retinal Vein Occlusion.

Chiang A, Cohen MN, Houston SK, Juhn A, Ho AC, Regillo CD, Vander JF.

PMID: 28237140

Other treatment & diagnosis

Retina. 2017 Mar 1. [Epub ahead of print]

VITRECTOMY FOR INTERMEDIATE AGE-RELATED MACULAR DEGENERATION ASSOCIATED WITH TANGENTIAL VITREOMACULAR TRACTION: A CLINICOPATHOLOGIC CORRELATION.

Ziada J, Hagenau F, Compera D, Wolf A, Scheler R, Schaumberger MM, Priglinger SG, Schumann RG.

PURPOSE: To describe the morphologic characteristics of the vitreomacular interface in intermediate age-related macular degeneration associated with tangential traction due to premacular membrane formation and to correlate with optical coherence tomography (OCT) findings and clinical data.

METHODS: Premacular membrane specimens were removed sequentially with the internal limiting membrane from 27 eyes of 26 patients with intermediate age-related macular degeneration during standard vitrectomy. Specimens were processed for immunocytochemical staining of epiretinal cells and extracellular matrix components. Ultrastructural analysis was performed using transmission electron microscopy. Spectral domain optical coherence tomography images and patient charts were evaluated in retrospect.

RESULTS: Immunocytochemistry revealed hyalocytes and myofibroblasts as predominant cell types. Ultrastructural analysis demonstrated evidence of vitreoschisis in all eyes. Myofibroblasts with contractile properties were observed to span between folds of the internal limiting membrane and vitreous cortex collagen. Retinal pigment epithelial cells or inflammatory cells were not detected. Mean visual acuity (Snellen) showed significant improvement from 20/72 ± 20/36 to 20/41 ± 20/32 ($P < 0.001$) after a mean follow-up period of 19 months (median, 17 months). During this period, none of the eyes required anti-vascular endothelial growth factor therapy.

CONCLUSION: Fibrocellular premacular proliferation in intermediate age-related macular degeneration predominantly consists of vitreous collagen, hyalocytes, and myofibroblasts with contractile properties. Vitreoschisis and vitreous-derived cells appear to play an important role in traction formation of this subgroup of eyes. In patients with intermediate age-related macular degeneration and contractile

premacular membrane, release of traction by vitrectomy with internal limiting membrane peeling results in significantly functional and anatomical improvement.

PMID: 28257377

Eye (Lond). 2017 Mar 3. [Epub ahead of print]

Microperimetry in age-related macular degeneration.

Midena E, Pilotto E.

Abstract: Age-related macular degeneration (AMD) is one of the major causes of visual loss and legal blindness in people over 55. Visual function tests are the cornerstone of visual function investigation and any therapeutic approach to AMD implies, as primary endpoint, the maintenance or improvement of visual function. The progression of visual impairment and the quantification of final residual visual function are currently determined by means of visual acuity quantification. The quantification of high-contrast visual acuity though has many drawbacks and cannot be considered a complete functional examination. Microperimetry is a non-invasive method used to analyse fixation and central visual field defects in a topographic related manner. The introduction of mesopic and more recently scotopic microperimetry, in research and clinical practice of macular disorders, now allows us to better investigate macular function as it strictly relates to macular morphology. We therefore can monitor the functional natural history and quantify the beneficial or detrimental effects of different therapies. The application of microperimetry in clinical studies has provided interesting diagnostic and prognostic information on functional macular changes in AMD patients. The present review brings new updates on the correlation between macular changes, mainly described with optical coherence tomography, and microperimetry changes in patients with AMD.

PMID: 28257134

Int Ophthalmol. 2017 Mar 2. [Epub ahead of print]

Effect of cataract surgery in patients with neovascular age-related macular degeneration: further evidence from disciform scars.

Arikan Yorgun M, Toklu Y, Kar ME, Çakmak BH.

PURPOSE: To evaluate the effect of cataract surgery on disease activation and visual outcomes in neovascular age-related macular degeneration (AMD).

METHODS: In this retrospective case-control study, study arm consisted of neovascular AMD patients, who underwent phacoemulsification surgery. Patients did not have any disease activation at least 6 months before the inclusion, and all had at least 12-month follow-up thereafter. Control group consisted of phakic patients, who did not undergo eye surgery during the study period. Primary outcomes were the presence of the disease activation and the change in best-corrected visual acuity (BCVA).

RESULTS: A total of 114 neovascular AMD patients [55 (48%) in exudative group and 59 (52%) in disciform group] were included. Preoperative logMAR BCVA was significantly improved after cataract surgery [0.8 (0.6-1.0) vs. 0.4 (0.4-0.7), $P < 0.001$ in exudative AMD; 1.85 (1.1-1.9) vs. 1.09 (0.8-1.9), $P = 0.001$ in disciform scar], but this improvement was not maintained during the study period in patients with both exudative AMD and disciform scar [0.6 (0.3-1.1), $P = 0.313$ in exudative AMD; 1.30 (1-1.9), $P = 0.03$ in disciform scar]. The incidence of disease activation was not statistically significant between surgery and control groups in patients with exudative AMD [5 (25%) patients in surgery group and 8 (22%) patients in the control group, $P = 0.886$, Cox proportional hazards regression analysis]. In disciform scar, disease activation was observed in 4 (17%) patients in the surgery group; however, no patient in the control group

had disease activation ($P = 0.009$, HRs could not be estimated, 95% CI 0.001-43.49, Cox proportional hazards regression analysis).

CONCLUSION: Cataract surgery has benefit on early postoperative visual improvement in patients with neovascular AMD. The incidence of disease activation was not affected after surgery in exudative AMD.

PMID: 28255836

Invest Ophthalmol Vis Sci. 2017 Mar 1;58(3):1378-1386.

Long-term Characterization of Retinal Degeneration in Royal College of Surgeons Rats Using Spectral-Domain Optical Coherence Tomography.

Ryals RC, Andrews MD, Datta S, Coyner AS, Fischer CM, Wen Y, Pennesi ME, McGill TJ.

PURPOSE: Prospective treatments for age-related macular degeneration and inherited retinal degenerations are commonly evaluated in the Royal College of Surgeons (RCS) rat before translation into clinical application. Historically, retinal thickness obtained through postmortem anatomic assessments has been a key outcome measure; however, utility of this measurement is limited because it precludes the ability to perform longitudinal studies. To overcome this limitation, the present study was designed to provide a baseline longitudinal quantification of retinal thickness in the RCS rat by using spectral-domain optical coherence tomography (SD-OCT).

METHODS: Horizontal and vertical linear SD-OCT scans centered on the optic nerve were captured from Long-Evans control rats at P30, P60, P90 and from RCS rats between P17 and P90. Total retina (TR), outer nuclear layer+ (ONL+), inner nuclear layer (INL), and retinal pigment epithelium (RPE) thicknesses were quantified. Histologic sections of RCS retina obtained from P21 to P60 were compared to SD-OCT images.

RESULTS: In RCS rats, TR and ONL+ thickness decreased significantly as compared to Long-Evans controls. Changes in INL and RPE thickness were not significantly different between control and RCS retinas. From P30 to P90 a subretinal hyperreflective layer (HRL) was observed and quantified in RCS rats. After correlation with histology, the HRL was identified as disorganized outer segments and the location of accumulated debris.

CONCLUSIONS: Retinal layer thickness can be quantified longitudinally throughout the course of retinal degeneration in the RCS rat by using SD-OCT. Thickness measurements obtained with SD-OCT were consistent with previous anatomic thickness assessments. This study provides baseline data for future longitudinal assessment of therapeutic agents in the RCS rat.

PMID: 28253400

Graefes Arch Clin Exp Ophthalmol. 2017 Mar 1. [Epub ahead of print]

Prevalence and characteristics of pseudodrusen subtypes in advanced age-related macular degeneration.

Shijo T, Sakurada Y, Yoneyama S, Sugiyama A, Kikushima W, Tanabe N, Iijima H.

PURPOSE: The purpose of our study was to investigate the clinical and genetic characteristics of pseudodrusen subtypes and their incidence in advanced age-related macular degeneration (AMD).

METHODS: We studied 84 eyes from 84 patients with pseudodrusen associated with advanced AMD, including typical AMD, polypoidal choroidal vasculopathy (PCV), retinal angiomatous proliferation (RAP), and geographic atrophy (GA). Multiple imaging modalities, including color fundus photography, spectral-

domain optical coherence tomography (SD-OCT), near-infrared reflectance, and fundus autofluorescence, were employed to diagnose pseudodrusen and its subtypes. Subfoveal choroidal thickness was measured using SD-OCT. Subject eyes were classified into two subtypes, dot-dominant or ribbon-dominant, according to the maximum length of ribbon pseudodrusen. Genotyping was performed for ARMS2 A69S (rs10490924) and CFH I62V (rs800292) variants.

RESULTS: The percentage of ribbon-dominant type pseudodrusen was significantly higher in eyes with RAP (69.6%) and GA (78.6%) compared with those with typical AMD (31.1%) ($p = .0025$ and $.0017$, respectively). Multivariate logistic regression analysis disclosed that incidence of female patients and coexisting large soft drusen was significantly higher in ribbon- than dot-dominant types ($P = 0.014$ and $P = 0.008$, respectively), while age, subfoveal choroidal thickness, and risk allele frequency for both ARMS2 A69S (rs10490924) and CFH I62V (rs800292) were not different between the two pseudodrusen subtypes.

CONCLUSIONS: Among eyes with advanced AMD associated with pseudodrusen, ribbon-dominant type pseudodrusen were more prevalent in eyes with GA or RAP and were associated with large soft drusen and female patients.

PMID: 28251353

Int J Ophthalmol. 2017 Feb 18;10(2):246-253. eCollection 2017.

The vitreomacular interface in different types of age-related macular degeneration.

El-Hifnawy MA, Ibrahim HA, Gomaa AR, Elmasry MA.

AIM: To evaluate the vitreomacular interface in cases with wet age-related macular degeneration (AMD) and to compare them to eyes with dry AMD and normal eyes.

METHODS: This was a cross-sectional comparative study that included 87 eyes with wet AMD, 42 eyes with dry AMD and 40 eyes without AMD as a control group. Optical coherence tomography (OCT) examination was performed for all patients to assess the vitreomacular interface.

RESULTS: In the wet AMD group, 34.5% of cases had vitreomacular adhesion (VMA). Only 14.3% of dry AMD cases and 10% of control cases had VMA. There was a significant difference between the control group and the wet AMD group ($P=0.004$) as well as the dry and wet AMD group ($P=0.017$). There was also a significant difference between the incidence of VMA in patients with subretinal choroidal neovascularization (CNV, type 1) and intraretinal CNV (type 2 or type 3) ($P=0.020$).

CONCLUSION: There is an association between posterior vitreous attachment and AMD. There is also an increased incidence of VMA with intra-retinal CNV.

PMID: 28251084 PMCID: PMC5313548

Retina. 2017 Feb 28. [Epub ahead of print]

OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY REVEALS BLOOD FLOW IN CHOROIDAL NEOVASCULAR MEMBRANE IN REMISSION PHASE OF NEOVASCULAR AGE-RELATED MACULAR DEGENERATION.

Ichiyama Y, Sawada T, Ito Y, Kakinoki M, Ohji M.

PURPOSE: The aim of the study was to investigate blood flow in choroidal neovascular membrane in remission phase of neovascular age-related macular degeneration using optical coherence tomography (OCT) angiography.

METHODS: OCT angiography was obtained in eyes with remission phase of neovascular age-related macular degeneration after treatments, defined as no exudative change (such as macular edema, subretinal fluid, and subretinal hemorrhage) observed in eyes without any treatment for neovascular age-related macular degeneration within the previous 6 months. Irregular blood flows shown in the segmentation of outer retina detected by OCT angiography were considered as blood flows in choroidal neovascular membrane. The vascular area and vessel density were obtained from OCT angiography images.

RESULTS: Twenty eyes of 20 patients were included in this analysis. The blood flows in choroidal neovascular membrane were observed in all eyes (100%) using OCT angiography. The mean vascular area was 3.81 ± 3.41 mm and the mean vessel density of lesion was $28.9 \pm 8.2\%$. The vessel density was significantly correlated with best-corrected visual acuity and duration of remission (best-corrected visual acuity: $P = 0.008$, $r = -0.576$; duration of remission: $P = 0.017$, $r = -0.525$, respectively).

CONCLUSION: Optical coherence tomography angiography revealed that blood flows in choroidal neovascular membrane remained in eyes with clinically inactive neovascular age-related macular degeneration.

PMID: 28248824

Invest Ophthalmol Vis Sci. 2017 Feb 1;58(2):1337-1345.

Three-Dimensional Analysis of Morphologic Changes and Visual Outcomes in Neovascular Age-Related Macular Degeneration.

Lee H, Jo A, Kim HC.

PURPOSE: To investigate the association of three-dimensionally quantified lesions with best-corrected visual acuity (BCVA) in typical neovascular age-related macular degeneration (nAMD).

METHODS: We retrospectively analyzed 65 eyes of 61 typical nAMD patients. Lesions at baseline and month 12 were manually delineated in optical coherence tomography. The volume of intraretinal fluid (IRF), subretinal fluid (SRF), subretinal hyperreflective material (SHRM), and pigment epithelial detachment (PED) were measured. In addition, the areas of external limiting membrane (ELM) and ellipsoid zone (EZ) were calculated.

RESULTS: At baseline, poor baseline BCVA was associated with increased volume of IRF and SHRM and impaired area of ELM ($\beta = 0.34$, $P = 0.001$; $\beta = 0.46$, $P < 0.001$; and $\beta = -0.23$, $P = 0.03$, respectively). At month 12, poor BCVA was associated with increased volume of IRF, reduced intact ELM area, and decreased EZ area ($\beta = 0.24$, $P = 0.01$; $\beta = -0.30$, $P = 0.02$; and $\beta = -0.37$, $P = 0.004$, respectively). Baseline BCVA, volume of IRF, and intact area of ELM were significant predictors for BCVA at month 12 ($\beta = 0.29$, $P = 0.01$; $\beta = 0.30$, $P = 0.01$; and $\beta = -0.28$, $P = 0.01$). Changes of BCVA were associated with changes of SHRM volume, intact EZ area, and ELM area ($\beta = 0.35$, $P = 0.002$; $\beta = -0.28$, $P = 0.01$; and $\beta = -0.22$, $P = 0.048$, respectively). The predictive power of volumetric analysis was higher than that of qualitative analysis ($R^2 = 0.47$ vs. $R^2 = 0.37$). The volume of SRF and fibrovascular PED showed positive and negative effect on visual outcome each, but they were not strong enough to remain in multivariate model.

CONCLUSIONS: Best-corrected visual acuity could be explained by three-dimensional optical coherence tomography morphology to a fair degree. In addition, three-dimensional analysis could predict visual outcomes better than qualitative analysis.

PMID: 28241322

Retina. 2017 Feb 23. [Epub ahead of print]

CHOROIDAL BLOOD FLOW AND THICKNESS AS PREDICTORS FOR RESPONSE TO ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR THERAPY IN MACULAR EDEMA SECONDARY TO BRANCH RETINAL VEIN OCCLUSION.

Okamoto M, Yamashita M, Sakamoto T, Ogata N.

PURPOSE: To determine the choroidal blood flow and subfoveal choroidal thickness (SCT) in eyes with macular edema secondary to branch retinal vein occlusion (BRVO).

METHODS: Thirty-two eyes of 32 patients with macular edema secondary to a BRVO were treated with a single intravitreal injection of ranibizumab (IVR) and were followed for 2 months. The central retinal thickness and SCT, and the retinal and choroidal blood flows were evaluated, and they were compared between the recurrent and resolved groups.

RESULTS: At the baseline, the SCT of eyes with a BRVO was significantly thicker than that of the fellow eye ($P < 0.01$). It was also significantly thicker in the recurrent group than in the resolved group ($P = 0.03$). The reduction of the retinal blood flow was found only after 1 week in the resolved group. The SCT and choroidal blood flow were significantly reduced during the follow-up period in the resolved group but not in the recurrent group.

CONCLUSION: The choroid is involved in the pathology of BRVO and the SCT at the baseline may be a predictive factor in the treatment of intravitreal injection of ranibizumab for macular edema secondary to BRVO.

PMID: 28234806

Pathogenesis

Mol Immunol. 2017 Feb 27;85:137-147. [Epub ahead of print]

Ionic tethering contributes to the conformational stability and function of complement C3b.

López-Perrote A, Harrison RE, Subías M, Alcorlo M, Rodríguez de Córdoba S, Morikis D, Llorca O.

Abstract: C3b, the central component of the alternative pathway (AP) of the complement system, coexists as a mixture of conformations in solution. These conformational changes can affect interactions with other proteins and complement regulators. Here we combine a computational model for electrostatic interactions within C3b with molecular imaging to study the conformation of C3b. The computational analysis shows that the TED domain in C3b is tethered ionically to the macroglobulin (MG) ring. Monovalent counterion concentration affects the magnitude of electrostatic forces anchoring the TED domain to the rest of the C3b molecule in a thermodynamic model. This is confirmed by observing NaCl concentration dependent conformational changes using single molecule electron microscopy (EM). We show that the displacement of the TED domain is compatible with C3b binding to Factor B (FB), suggesting that the regulation of the C3bBb convertase could be affected by conditions that promote movement in the TED domain. Our molecular model also predicts mutations that could alter the positioning of the TED domain, including the common R102G polymorphism, a risk variant for developing age-related macular degeneration. The common C3b isoform, C3bS, and the risk isoform, C3bF, show distinct energetic barriers to displacement in the TED that are related to a network of electrostatic interactions at the interface of the TED and MG-ring domains of C3b. These computational predictions agree with experimental evidence that shows differences in conformation observed in C3b isoforms purified from homozygous donors. Altogether, we reveal an ionic, reversible attachment of the TED domain to the MG ring that may influence complement regulation in some mutations and polymorphisms of C3b.

PMID: 28254726

Neural Regen Res. 2017 Jan;12(1):35-38.

Endoplasmic reticulum-mitochondrial crosstalk: a novel role for the mitochondrial peptide humanin.

Sreekumar PG, Hinton DR, Kannan R.

Abstract: In this review, the interactive mechanisms of mitochondria with the endoplasmic reticulum (ER) are discussed with emphasis on the potential protective role of the mitochondria derived peptide humanin (HN) in ER stress. The ER and mitochondria are dynamic organelles capable of modifying their structure and function in response to changing environmental conditions. The ER and mitochondria join together at multiple sites and form mitochondria-ER associated membranes that participate in signal transduction pathways that are under active investigation. Our laboratory previously showed that HN protects cells from oxidative stress induced cell death and more recently, described the beneficial role of HN on ER stress-induced apoptosis in retinal pigment epithelium cells and the involvement of ER-mitochondrial cross-talk in cellular protection. The protection was achieved, in part, by the restoration of mitochondrial glutathione that was depleted by ER stress. Thus, HN may be a promising candidate for therapy for diseases that involve both oxidative and ER stress. Developing novel approaches for retinal delivery of HN, its analogues as well as small molecular weight ER stress inhibitors would prove to be a valuable approach in the treatment of age-related macular degeneration.

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Mol Neurobiol. 2017 Feb 25. [Epub ahead of print]

IGF-1-Mediated Survival from Induced Death of Human Primary Cultured Retinal Pigment Epithelial Cells Is Mediated by an Akt-Dependent Signaling Pathway.

Zheng W, Meng Q, Wang H, Yan F, Little PJ, Deng X, Lin S.

Abstract: Degeneration of the human retinal pigmented epithelium (hRPE) is involved in several eye disorders such as age-related macular degeneration (AMD). In this study, we investigated the protective effect of IGF-1 on human primary cultured RPE cells and its underlying mechanism. IGF-1 dose- and time-dependently promoted the survival of RPE cells from serum deprivation. Western blot showed that IGF-1 stimulated the activation of the PI3K/Akt and MAPK pathways in hRPE. Inhibition of the PI3K/Akt pathway by the PI3K-specific inhibitor, LY294002 or inhibition of Akt by Akt-specific inhibitors Akt inhibitor VIII or SN-38, or downregulation Akt with siRNA specific for Akt blocked the effect of IGF-1 on hRPE. In contrast, blockade of the MAPK pathway with a specific inhibitor PD98059 had no effect. Interestingly, vitreous IGF-1 injection reversed the inhibitory effect of light exposure (a dry AMD model) on both a wave and b wave. Immunocytochemistry showed that vitreous IGF-1 injections promoted the survival of RPE cells in rat retina and the expression of RPE65 in RPE cells from light injury. These results indicate that IGF-1 is able to protect hRPE cell from different insults in vivo and in vitro. Further detailed studies may lead the way to a therapeutic intervention for retinal diseases in which cell death is an underlying contributory mechanism.

PMID: 28238097

J Neurosci. 2017 Feb 24. [Epub ahead of print]

Tamoxifen provides structural and functional rescue in murine models of photoreceptor degeneration.

Wang X, Zhao L, Zhang Y, Ma W, Gonzalez SR, Fan J, Kretschmer F, Badea TC, Hua Qian H, Wong WT.

Abstract: Photoreceptor degeneration is a cause of irreversible vision loss in incurable blinding retinal

diseases including retinitis pigmentosa and atrophic age-related macular degeneration. We found in two separate mouse models of photoreceptor degeneration that tamoxifen, a selective estrogen receptor modulator and a drug previously linked with retinal toxicity, paradoxically provided potent neuroprotective effects. In a light-induced degeneration model, tamoxifen prevented onset of photoreceptor apoptosis and atrophy, and maintained near-normal levels of electroretinographic responses. Rescue effects were correlated with decreased microglial activation and inflammatory cytokine production in the retina in vivo, and a reduction of microglia-mediated toxicity to photoreceptors in vitro, indicating a microglia-mediated mechanism of rescue. Tamoxifen also rescued degeneration in a genetic (Pde6brd10) model of retinitis pigmentosa, significantly improving retinal structure, electrophysiological responses, and visual behavior. These prominent neuroprotective effects warrant the consideration of tamoxifen as a drug suitable for being repurposed to treat photoreceptor degenerative disease.

SIGNIFICANCE STATEMENT: Photoreceptor degeneration is a cause of irreversible blindness in a number of retinal diseases such as atrophic age-related macular degeneration and retinitis pigmentosa. Tamoxifen, a selective estrogen-receptor modulator approved for the treatment of breast cancer, and previously linked to a low incidence of retinal toxicity, was unexpectedly found to exert marked protective effects against photoreceptor degeneration. Structural and functional protective effects were found for an acute model of light-induced photoreceptor injury and for a genetic model for retinitis pigmentosa. The mechanism of protection involved the modulation of microglial activation and the production of inflammatory cytokines, highlighting the role of inflammatory mechanisms in photoreceptor degeneration. Tamoxifen may be suitable for clinical study as a potential treatment for diseases involving photoreceptor degeneration.

PMID: 28235894

J Neuroinflammation. 2017 Feb 23;14(1):42.

Peripheral blood mononuclear cells from neovascular age-related macular degeneration patients produce higher levels of chemokines CCL2 (MCP-1) and CXCL8 (IL-8).

Lechner J, Chen M, Hogg RE, Toth L, Silvestri G, Chakravarthy U, Xu H.

BACKGROUND: Infiltrating immune cells including monocytes/macrophages have been implicated in the pathogenesis of neovascular age-related macular degeneration (nAMD). The aim of this study was to investigate the cytokine and chemokine expression and secretion profile of peripheral blood mononuclear cells (PBMCs) from nAMD patients and the relationship between the cytokine/chemokine expression profile and clinical phenotype of nAMD, including macular fibrosis, macular atrophy or the responsiveness to anti-VEGF therapy.

METHODS: One hundred sixty-one nAMD patients and 43 controls were enrolled in this study. nAMD patients were divided into subgroups based on the presence/absence of (1) macular atrophy, (2) macular fibrosis and (3) responsiveness to anti-VEGF therapy; 25-30 ml of peripheral blood were obtained from all participants and 5 ml were used for serum collection, and the remaining were used for PBMC isolation using density gradient centrifugation. Intracellular cytokine expressions by PBMCs following phorbol 12-myristate 13-acetate (PMA) and ionomycin stimulation were examined using flow cytometry. Cytokine productions in lipopolysaccharides (LPS)-or 1% oxygen -treated PBMC were measured using cytometric bead array (CBA) assay. In addition, cytokine and chemokine levels in the serum were also measured by CBA assay.

RESULTS: PBMCs from nAMD patients secreted higher levels of IL-8, CCL2 and VEGF, especially following LPS and 1% oxygen stimulation, than those from controls. 60-80% of IL-8 producing cells were CD11b+CD3- monocytes. The percentage of CD11b+CD3- IL-8+ was significantly increased in nAMD patients compared to controls. PBMCs from nAMD patients without macular fibrosis produced the highest levels of IL-8 and CCL2, whilst PBMCs from nAMD patients with macular atrophy produced highest levels of VEGF. In addition, PBMCs from patients who partially responded to anti-VEGF produced higher levels of

IL-8 compared to the cells from complete responders. Interestingly, serum level of CCL2 was not increased in nAMD patients although there was a trend of increased IL-8 in nAMD patients.

CONCLUSIONS: PBMCs, in particular monocytes, may contribute to CNV development in nAMD through secreting elevated levels of IL-8, CCL2 and VEGF after they are recruited to the macula. Apart from VEGF, IL-8 and CCL2 may be additional targets for nAMD management.

PMID: 28231837 PMCID: PMC5324243

Genetics, gene therapy

Am J Ophthalmol. 2017 Feb 25. pii: S0002-9394(17)30085-5. [Epub ahead of print]

Gene Therapy in Neovascular Age-related Macular Degeneration: Three Year Follow-up of a Phase 1 Randomised Dose Escalation Trial.

Constable IJ, Lai CM, Magno AL, French MA, Barone SB, Schwartz SD, Blumenkranz MS, Degli-Esposti MA, Rakoczy EP.

PURPOSE: To assess the safety of rAAV.sFlt-1 subretinal injection in neovascular age-related macular degeneration (wet AMD) over 36 months.

DESIGN: Phase 1 dose escalation trial.

METHODS: Eight subjects with advanced, treatment-experienced wet AMD were randomly assigned (3:1) to treatment and non-gene therapy control groups. Eligible subjects were ≥ 65 years, had wet AMD and best corrected visual acuity (BCVA) 10/200 -20/80 in the study eye and 20/200 or better in the other eye. Three of the treatment group subjects received low dose (1X1010 vector genomes) and three high dose (1X1011 vector genomes) rAAV.sFLT-1 via subretinal injection. Study monitoring was monthly to the primary endpoint at month 12 and then protocol-driven follow-up study visits were conducted at months 18 and 36. All subjects received intravitreal ranibizumab at baseline and week 4, and retreatment injections at subsequent visits based on pre-specified criteria for active wet AMD. The primary end-point was ocular and systemic safety but exploratory data including BCVA, retinal centre point thickness and the number of ranibizumab retreatments at and between study visits were also analyzed.

RESULTS: Six (75%) of the 8 subjects completed the 36 month study. Subretinal injection with pars plana vitrectomy was well tolerated in this cohort. No ocular or systemic safety signals were observed during the long-term follow-up period. Exploratory data analysis suggests stability of wet AMD over the 36-month period.

CONCLUSIONS: Subretinal delivery of rAAV.sFLT-1 was well tolerated and demonstrated a favorable safety profile through month 36. Thus, rAAV.sFLT-1 could be safely considered for future evaluation in the treatment of wet AMD.

PMID: 28245970

Mol Ther. 2017 Mar 1;25(3):765-779.

AAV-Nrf2 Promotes Protection and Recovery in Animal Models of Oxidative Stress.

Liang KJ, Woodard KT, Weaver MA, Gaylor JP, Weiss ER, Samulski RJ.

Abstract: NRF2 is a transcription factor that drives antioxidant gene expression in multiple organ systems. We hypothesized that Nrf2 overexpression could be therapeutically applied toward diseases in which redox homeostasis is disrupted. In this study, adeno-associated virus (AAV)-Nrf2 was tested in a mouse model of

acute acetaminophen-induced liver toxicity and successfully conferred protection from hepatotoxicity, validating the vector design and early onset of NRF2-mediated protection. Furthermore, therapeutic potential of AAV-Nrf2 in chronic disease also was tested in a light-induced mouse model of age-related macular degeneration. Adult BALB/c mice were intravitreally injected with AAV-Nrf2 and subject to light damage following injection. Retinal thickness and function were monitored following light damage using optical coherence tomography and electroretinography, respectively. By 3 months post-damage, injected eyes had greater retinal thickness compared to uninjected controls. At 1 month post-damage, AAV-Nrf2 injection facilitated full functional recovery from light damage. Our results suggest a therapeutic potential for Nrf2 overexpression in acute and long-term capacities in multiple organ systems, opening up doors for combination gene therapy where replacement gene therapy requires additional therapeutic support to prevent further degeneration.

PMID: 28253482

Stem cells

Cell Mol Life Sci. 2017 Feb 28. [Epub ahead of print]

Technical approaches to induce selective cell death of pluripotent stem cells.

Jeong HC, Cho SJ, Lee MO, Cha HJ.

Abstract: Despite the recent promising results of clinical trials using human pluripotent stem cell (hPSC)-based cell therapies for age-related macular degeneration (AMD), the risk of teratoma formation resulting from residual undifferentiated hPSCs remains a serious and critical hurdle for broader clinical implementation. To mitigate the tumorigenic risk of hPSC-based cell therapy, a variety of approaches have been examined to ablate the undifferentiated hPSCs based on the unique molecular properties of hPSCs. In the present review, we offer a brief overview of recent attempts at selective elimination of undifferentiated hPSCs to decrease the risk of teratoma formation in hPSC-based cell therapy.

PMID: 28246701

Diet, lifestyle & low vision

Br J Ophthalmol. 2017 Feb 23. [Epub ahead of print]

Putative protective role of lutein and zeaxanthin in diabetic retinopathy.

Neelam K, Goenadi CJ, Lun K, Yip CC, Au Eong KG.

Abstract: Diabetic retinopathy (DR) is one of the most important microvascular complications of diabetes and remains the leading cause of blindness in the working-age individuals. The exact aetiopathogenesis of DR remains elusive despite major advances in basic science and clinical research. Oxidative damage as one of the underlying causes for DR is increasingly being recognised. In humans, three hydroxycarotenoids, lutein (L), zeaxanthin (Z) and meso-zeaxanthin (MZ), accumulate at the central retina (to the exclusion of all other dietary carotenoids), where they are collectively known as macular pigment. These hydroxycarotenoids by nature of their biochemical structure and function help neutralise reactive oxygen species, and thereby, prevent oxidative damage to the retina (biological antioxidants). Apart from their key antioxidant function, evidence is emerging that these carotenoids may also exhibit neuroprotective and anti-inflammatory function in the retina. Since the preliminary identification of hydroxycarotenoid in the human macula by Wald in the 1940s, there has been astounding progress in our knowledge of the role of these carotenoids in promoting ocular health. While the Age-Related Eye Disease Study 2 has established a clinical benefit for L and Z supplements in patients with age-related macular degeneration, the role of

these carotenoids in other retinal diseases potentially linked to oxidative damage remains unclear. In this article, we comprehensively review the literature germane to the putative protective role of two hydroxycarotenoids, L and Z, in the pathogenesis of DR.

PMID: 28232380

Invest Ophthalmol Vis Sci. 2017 Mar 1;58(3):1404-1410.

Visualization of Dietary Patterns and Their Associations With Age-Related Macular Degeneration.

Chiu CJ, Chang ML, Li T, Gensler G, Taylor A.

PURPOSE: We aimed to visualize the relationship of predominant dietary patterns and their associations with AMD.

METHODS: A total of 8103 eyes from 4088 participants in the baseline Age-Related Eye Disease Study (AREDS) were classified into three groups: control (n = 2739), early AMD (n = 4599), and advanced AMD (n = 765). Using principle component analysis, two major dietary patterns and eight minor dietary patterns were characterized. Applying logistic regression in our analysis, we related dietary patterns to the prevalence of AMD. Qualitative comparative analysis by operating Boolean algebra and drawing Venn diagrams was used to visualize our findings.

RESULTS: In general, the eight minor patterns were subsets or extensions of either one of the two major dietary patterns (Oriental and Western patterns) and consisted of fewer characteristic foods than the two major dietary patterns. Unlike the two major patterns, which were more strongly associated with both early and advanced AMD, none of the eight minors were associated with early AMD and only four minor patterns, including the Steak pattern (odds ratio comparing the highest to lowest quintile of the pattern score = 1.73 [95% confidence interval: 1.24 to 2.41; Ptrend = 0.02]), the Breakfast pattern (0.60 [0.44 to 0.82]; Ptrend = 0.004]), the Caribbean pattern (0.64 [0.47 to 0.89; Ptrend = 0.009]), and the Peanut pattern (0.64 [0.46 to 0.89; Ptrend = 0.03]), were significantly associated with advanced AMD. Our data also suggested several potential beneficial (peanuts, pizza, coffee, and tea) and harmful (salad dressing) foods for AMD.

CONCLUSIONS: Our data indicate that a diet of various healthy foods may be optimal for reducing AMD risk. The effects of some specific foods in the context of overall diet warrant further study.

PMID: 28253403

Invest Ophthalmol Vis Sci. 2017 Feb 1;58(2):1304-1313. doi: 10.1167/iovs.16-20404.

Loss of Binocular Vision in Monocularly Blind Patients Causes Selective Degeneration of the Superior Lateral Occipital Cortices.

Prins D, Jansonius NM, Cornelissen FW.

PURPOSE: Chronic ocular pathology, such as glaucoma and macular degeneration, is associated with neuroanatomic changes in the visual pathways. It is a challenge to determine the mechanism responsible for these changes. This could be functional deprivation or transsynaptic degeneration. Acquired monocular blindness provides a unique opportunity to establish which mechanism underlies neuroanatomic changes in ocular pathology in general, since the loss of input is well defined, and it causes selective functional deprivation due to the loss of stereopsis. Here, we assessed whether acquired monocular blindness is associated with neuroanatomic changes, and if so, where these changes are located.

METHODS: High-resolution T1-weighted magnetic resonance images were obtained in 15 monocularly blind patients and 18 healthy controls. We used voxel- and surface-based morphometry to compare gray and white matter volume, cortical thickness, mean curvature, and surface area between these groups.

Macular Disease Foundation Australia Suite 902, 447 Kent Street, Sydney, NSW, 2000, Australia.

Tel: +61 2 9261 8900 | Fax: +61 2 9261 8912 | E: research@mdfoundation.com.au | W: www.mdfoundation.com.au

RESULTS: The gray matter volume in the bilateral superior lateral occipital cortices was decreased in the monocular blind patients, in the absence of volumetric differences in their early visual cortex.

CONCLUSIONS: The volumetric decrease in the superior lateral occipital cortices is consistent with specific functional deprivation, as the superior lateral occipital cortices play an important role in depth perception. Moreover, in the absence of differences in the early visual cortex, the decrease is inconsistent with transsynaptic degeneration propagating from the degenerated retinal axons.

PMID: 28245486

J Nutr Health Aging. 2017;21(3):254-261.

Non-Dietary Correlates and Determinants of Plasma Lutein and Zeaxanthin Concentrations in the Irish Population.

Moran R, Nolan JM, Stack J, O'Halloran AM, Feeney J, Akuffo KO, Kenny RA, Beatty S.

OBJECTIVE: To investigate non-dietary correlates and determinants of plasma lutein (L) and zeaxanthin (Z) concentrations in The Irish Longitudinal Study on Ageing (TILDA) sample.

DESIGN: Cross-sectional study.

SETTING: Community dwelling adults in the Republic of Ireland (ROI).

PARTICIPANTS: 3,681 participants aged 50 years and older.

MEASUREMENTS: TILDA is a nationally representative prospective cohort study of community dwelling adults aged 50 years and over in the ROI. Demographic and health variables were collected during a face-to-face interview carried out in the home (n=8175), and a substantial proportion of these (n=5035; 62%) also attended a study visit in a health assessment centre. Blood samples collected at baseline (wave 1, the subject of the current study), were analysed for plasma concentrations of L and Z by reversed-phase high performance liquid chromatography, and macular pigment (MP) optical density was also measured (using customized heterochromatic flicker photometry).

RESULTS: After excluding participants with eye disease, data from 3,681 participants were available for analysis. For this group of participants, plasma L and Z were inversely and significantly associated with body mass index (BMI), and were positively and significantly associated with MP, total cholesterol, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) ($p < 0.001$, for all). Plasma L and Z were significantly lower in males, current smokers, participants reporting less physical exercise, and participants reporting lower levels of education ($p < 0.05$, for all). Plasma L was significantly higher in participants reporting a family history of age-related macular degeneration (AMD) ($p = 0.001$), and in the group of ≥ 75 years old ($p < 0.05$). For each of these variables, the significant associations remained after controlling for other potential confounding variables.

CONCLUSION: The findings of this large study indicate that plasma concentrations of L and Z were lower in association with indicators of a poor lifestyle (high BMI, tobacco use, and less physical exercise) and in association with lower education, indicating that modifying lifestyle in a positive way is likely to be reflected in higher concentrations of plasma carotenoids, with consequential and putative health benefits.

PMID: 28244563

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Nutritional Supplementation Inhibits the Increase in Serum Malondialdehyde in Patients with Wet Age-Related Macular Degeneration.

Macular Disease Foundation Australia Suite 902, 447 Kent Street, Sydney, NSW, 2000, Australia.

Tel: +61 2 9261 8900 | Fax: +61 2 9261 8912 | E: research@mdfoundation.com.au | W: www.mdfoundation.com.au

Matsuura T, Takayama K, Kaneko H, Ye F, Fukukita H, Tsunekawa T, Kataoka K, Hwang SJ, Nagasaka Y, Ito Y, Terasaki H.

Purpose: To compare serum levels of malondialdehyde (MDA) in patients with wet age-related macular degeneration (wAMD), patients with dry AMD (dAMD), and patients without AMD and to evaluate the efficacy of nutritional supplementation for treating elevated serum MDA in patients with wAMD.

Methods: MDA levels were measured in sera from 20 patients with wAMD, 20 with dAMD, and 24 without AMD. Patients with wAMD were randomized to receive or not receive nutritional supplementation (10 patients in each group), and MDA levels were measured after 3 months of treatment.

Results: MDA levels in patients with wAMD were significantly greater compared with patients without AMD. In eyes with wAMD, there was a significant correlation between MDA levels and choroidal neovascularization lesion area. Serum MDA levels decreased in most patients that received supplementation and significantly increased in those who did not.

Conclusion: Baseline serum MDA levels were elevated in patients with wAMD, and MDA levels were directly correlated with choroidal neovascularization lesion area. In addition, nutritional supplementation appeared to exert a protective effect against oxidative stress in patients with wAMD.

PMID: 28243361 PMCID: PMC5294377

Ger Med Sci. 2017 Feb 9;15:Doc04. eCollection 2017.

Prevalence of depression, anxiety, adjustment disorders, and somatoform disorders in patients with age-related macular degeneration in Germany.

Jacob L, Spiess A, Kostev K.

Aims: The purpose of this study was to analyze the prevalence of depression, anxiety, adjustment disorders, and somatoform disorders in patients diagnosed with age-related macular degeneration (AMD) in Germany.

Methods: This study included 7,580 patients between the ages of 40 and 90 diagnosed with AMD between January 2011 and December 2014 in 1,072 primary care practices (index date). The last follow-up was in July 2016. We also included 7,580 controls without AMD, which were matched (1:1) to the AMD cases by age, sex, type of health insurance (private or statutory), physician, and Charlson comorbidity score as a generic marker of comorbidity. The outcome of the study was the prevalence of depression, anxiety, adjustment disorders, and somatoform disorders recorded in the database between the index date and the end of follow-up.

Results: The mean age among subjects was 75.7 years (SD=10.1 years), 34.0% were men, and 7.8% had private health insurance coverage. The Charlson comorbidity index was 2.0 (SD=1.8). Depression was the most frequent disease (33.7% in AMD patients versus 27.3% in controls), followed by somatoform disorders (19.6% and 16.7%), adjustment disorders (14.8% and 10.5%), and anxiety disorders (11.7% and 8.2%). Depression (OR=1.37, 95% CI: 1.27-1.47), anxiety (OR=1.50, 95% CI: 1.35-1.67), adjustment disorders (OR=1.50, 95% CI: 1.36-1.65), and somatoform disorders (OR=1.22, 95% CI: 1.12-1.32) were all positively associated with AMD.

Conclusion: Overall, a significant association was found between AMD and depression, anxiety, adjustment disorders, and somatoform disorders.

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