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MD Research News

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Drug treatment

Retina. 2015 Apr 20. [Epub ahead of print]

CHANGES IN VISUAL ACUITY IN PATIENTS WITH WET AGE-RELATED MACULAR DEGENERATION TREATED WITH INTRAVITREAL RANIBIZUMAB IN DAILY CLINICAL PRACTICE: The TWIN Study.

Souied EH, Oubraham H, Mimoun G, Cohen SY, Quere S, Derveloy A; TWIN Study Group.

PURPOSE: The real-life LUMIERE study on patients with wet age-related macular degeneration treated with intravitreal ranibizumab in 2006 to 2009 showed that failure to follow recommendations was associated with lower efficacy than had been observed in the development phase. The TWIN Study reviewed the situation in 2010 to 2011.

METHODS: Retrospective, descriptive purely observational study of data acquired after 12 months of treatment with intravitreal ranibizumab.

RESULTS: In 881 patients (68% women, mean age, 79 years) treated by 21 ophthalmologists, the mean gain in visual acuity was +4.3 ± 15.4 letters (up from 3.2 ± 14.8 in 2006-2009; NS). Significant improvements were documented in the mean interval between diagnosis and treatment initiation (down from 12.6 ± 26.4-7.7 ± 10.9 days; $P < 0.001$), and in the percentage of patients who received a full course of induction treatment (56.6 vs. 39.6%; $P < 0.001$). After induction, hardly any patients were monitored every month as recommended, although retreatment was more assiduous (5.6 ± 2.3 vs. 5.1 ± 2.1 injections; $P < 0.001$).

CONCLUSION: Despite improvements in key parameters, the effectiveness of intravitreal ranibizumab is still compromised by poor compliance with the guidelines, especially the frequency of postinduction monitoring that is now the most important determinant of successful treatment.

PMID: 25901835 [PubMed - as supplied by publisher]

Retina. 2015 May;35(5):841-58.

SUSTAINED ELEVATION OF INTRAOCULAR PRESSURE AFTER INTRAVITREAL ANTI-VEGF AGENTS: What Is the Evidence?

Dedania VS, Bakri SJ.

PURPOSE: To summarize the literature addressing sustained and delayed elevation of intraocular pressure (IOP) in patients with neovascular age-related macular degeneration being treated with intravitreal vascular endothelial growth factor (VEGF) inhibitors and to present possible mechanisms of effect.

METHODS: Analysis of current literature evaluating sustained and delayed elevation of IOP in patients

receiving intravitreal anti-VEGF therapy for neovascular age-related macular degeneration.

RESULTS: Studies have demonstrated that patients undergoing treatment with intravitreal anti-VEGF agents may experience sustained and delayed elevation of IOP. The incidence of sustained elevation of IOP in patients with neovascular age-related macular degeneration varied from 3.45% to 11.6%, and few patients required surgical management to control IOP. Possible risk factors associated with sustained and delayed elevation of IOP include, but are not limited to, history of glaucoma, phakia, history of glucocorticoid use, and/or extended treatment duration. There are multiple theories explaining the pathogenesis of sustained elevation of IOP, including microparticle obstruction of the trabecular meshwork, intraocular inflammation, and transient elevation of IOP.

CONCLUSION: Sustained and delayed elevation of IOP in patients undergoing treatment of neovascular age-related macular degeneration with intravitreal anti-VEGF agents is likely a multifactorial process. Further studies to prospectively investigate sustained elevation of IOP in large, randomized, controlled trials might lead to a better understanding of the long-term adverse events associated with intravitreal anti-VEGF therapy.

PMID: 25905784 [PubMed - in process]

Klin Monbl Augenheilkd. 2015 Apr;232(4):560-563. Epub 2015 Apr 22.

Functional and Anatomic Efficacy of a Conversion to Aflibercept in Eyes with Age-Related Macular Degeneration after Long-Term Ranibizumab Treatment.

Gerding H.

Background: It was the aim of this retrospective study to analyse the functional and anatomic efficacy of a conversion from ranibizumab to aflibercept treatment in eyes with exsudative age-related macular degeneration (AMD) with recently unsatisfactory response to a ranibizumab treatment.

Material, Patients and Methods: 40 eyes of 37 patients (age: 80.6 ± 7.7 years [mean ± 1 standard deviation (SD)] were included. The average visual acuity (VA) was 0.56 ± 0.33 logMAR [mean ± standard error (SE)] at the time of the first aflibercept injection. The eyes had received a mean of 21.5 ± 11.7 (mean ± SD) injections of ranibizumab within 3.15 ± 1.79 (mean ± SD) years. Follow-up covered 6 months in all patients. Before and after treatment and conversion of treatment, a PRN regimen with monthly visual acuity and OCT examinations was applied.

Results: After conversion to aflibercept the mean gain of VA was 0.45 ± 1.26 lines at month 1 (mean ± SE, $p = 0.04$), 0.26 ± 1.60 at months 3 ($p = 0.067$), and 0.65 ± 1.77 ($p = 0.03$) at month 6. Total OCT central foveal point thickness decreased from 417 ± 215 µm (mean ± 1 SD) before the first injection of aflibercept to 299 ± 139 ($p < 0.001$), 325 ± 174 at month 3 ($p < 0.001$), and 321 ± 150 µm at month 6 ($p < 0.001$). The average number of aflibercept injections was 4.0 ± 1.1 (mean ± SD). At the end of follow up 61% of eyes had gained ≥ 1 line, 22% ≥ 2 lines, and 12% ≥ 3 lines. 10% had lost ≥ 1 line, 5% ≥ 2 lines, and 2% ≥ 3 lines.

Conclusions: The results of this case series show that conversion from ranibizumab to aflibercept can significantly reduce retinal thickness and improve visual acuity in patients with age-related macular degeneration with increasingly unsatisfactory response to long-term ranibizumab treatment.

PMID: 25902122 [PubMed - as supplied by publisher]

Klin Monbl Augenheilkd. 2015 Apr;232(4):552-555. Epub 2015 Apr 22.

The Effect of Switching Ranibizumab to Aflibercept in Refractory Cases of Macular Edema Secondary to Ischemic Central Vein Occlusion.

Lehmann-Clarke L, Dirani A, Mantel I, Ambresin A.

Background: Macular edema resulting from central retinal vein occlusion is effectively treated with anti-vascular endothelial growth factor injections. However, some patients need monthly retreatment and still show frequent recurrences. The purpose of this study was to evaluate the visual and anatomic outcomes of refractory macular edema resulting from ischemic central retinal vein occlusion in patients switched from ranibizumab to aflibercept intravitreal injections.

Patients and Methods: We describe a retrospective series of patients followed in the Medical Retina Unit of the Jules Gonin Eye Hospital for macular edema due to ischemic central retinal vein occlusion, refractory to monthly retreatment with ranibizumab, and changed to aflibercept. Refractory macular edema was defined as persistence of any fluid at each visit one month after last injection during at least 6 months. All patients had to have undergone pan-retinal laser scan.

Results: Six patients were identified, one of whom had a very short-term follow-up (excluded from statistics). Mean age was 57 ± 12 years. The mean changes in visual acuity and central macular thickness from baseline to switch were + 20.6 ± 20.3 ETDRS letters and - 316.4 ± 276.6 µm, respectively. The additional changes from before to after the switch were + 9.2 ± 9.5 ETDRS letters and - 248.0 ± 248.7 µm, respectively. The injection intervals could often be lengthened after the switch.

Conclusions: Intravitreal aflibercept seems to be a promising alternative treatment for macular edema refractory to ranibizumab in ischemic central retinal vein occlusion.

PMID: 25902119 [PubMed - as supplied by publisher]

Klin Monbl Augenheilkd. 2015 Apr;232(4):538-541. Epub 2015 Apr 22.

Recurrent Macular Edema in Central Retinal Vein Occlusion Treated with Intravitreal Ranibizumab using a Modified Treat and Extend Regimen.

Dirani A, Mantel I, Ambresin A.

Background: The aim of this study was to evaluate the stability over time of the individually defined interval of intravitreal ranibizumab injection (IVR) for the treatment of recurrent macular edema (ME) in central retinal vein occlusion (CRVO).

Patients and Methods: A case series of treatment naïve patients followed in the Jules Gonin Eye Hospital for macular edema due to central retinal vein occlusion is presented. Patients were treated monthly with IVR until complete absence of fluid on qualitative SD-OCT with a minimum of 5 monthly IVR. Thereafter, they were followed according to a modified treat and extend regimen (mTER).

Results: Twelve eyes (12 patients) with ME due to CRVO were included. The mean follow-up period was 31.3 months. Analysis showed that best corrected visual acuity (BCVA), central macular thickness and qualitative spectral domain optical coherence tomography (SD-OCT) showed comparable results under monthly interval, after titration of an individualized interval and when performed in a series. 78% of treating intervals were within ± 2 weeks of the first individually adjusted interval. The mean first defined interval was 4.3 weeks and the mean interval over time was 5.5 weeks ($p = 0.003$). There was a trend towards longer interval over time.

Conclusion: The adjusted interval of retreatment of patients with ME due to CRVO showed a high stability with a trend toward longer duration over time. An mTER regimen seems to be valuable to follow patients with ME with good stabilization of VA.

PMID: 25902116 [PubMed - as supplied by publisher]

Klin Monbl Augenheilkd. 2015 Apr;232(4):533-7. Epub 2015 Apr 22.

[Long-Term Outcome in Patients with Intravitreal Anti-VEGF Therapy for Exudative AMD].[Article in

German]

Amstutz CA, Fleischhauer J, Zweifel S, Barthelmes D.

BACKGROUND: Randomized controlled phase III studies have shown that intravitreal anti-VEGF therapy is effective for exsudative age-related macular degeneration (AMD) over two years. Recently, the seven-year outcomes in ranibizumab-treated patients of the ranibizumab phase III studies have been published. Only a few other studies with such a long follow-up for intravitreal anti-VEGF therapy in patients with exsudative AMD have been published so far. We report on the outcome of patients receiving intravitreal anti-VEGF therapy for exudative AMD at the Department of Ophthalmology, University Hospital of Zurich with follow-up of 3 to 7 years.

PATIENTS: Retrospective chart review of all patients treated at our institution for exudative AMD with begin of treatment since 2006.

RESULTS: The numbers of patients with a follow-up of 3 to 4, 4 to 5, 5 to 6, 6 to 7, and more than 7 years were 430, 277, 151, 87, and 47, respectively. Mean follow-up time was 4.9 years, and median was 4.6 years. Changes in visual acuity for these patients were - 5.0, - 7.8, - 11.7, - 12.8, and - 19.2 ETDRS letters, respectively.

CONCLUSIONS: Whereas in patients with exudative AMD during the first two years of intravitreal anti-VEGF treatment visual acuity can at least be stabilised, after three and more years visual acuity decreases in spite of continued treatment.

PMID: 25902115 [PubMed - in process]

Int J Pharm Compd. 2015 Jan-Feb;19(1):70-2.

Stability assessment of repackaged bevacizumab for intravitreal administration.

Pereboom M, Becker ML, Amenchar M, Verweij SL, van der Hoeven RT, Mulder IJ.

Abstract: Intravitreal bevacizumab is frequently used off-label for the treatment of neovascular age-related macular degeneration, but there are concerns about the safety of intravitreal administered bevacizumab. It is suggested that repackaging bevacizumab in plastic syringes could affect the safety due to the unknown shelf life of the syringes. In this study, we analyzed the shelf life of the repackaged bevacizumab syringes, stored at 4 degrees C, at certain time intervals. Over the 32 days tested, bevacizumab concentration and the pH were stable. However, the number of particles in the repackaged bevacizumab syringes increased during storage at 4 degrees C and had exceeded the limits for intravitreal injections after 7 days. Since the number of particles seems to be the limitation of the shelf life of repackaged bevacizumab, it is necessary to quantify the number of particles in repackaged bevacizumab. Based on our results the maximum shelf life of repackaged bevacizumab should be 3 days.

PMID: 25902630 [PubMed - in process]

Klin Monbl Augenheilkd. 2015 Apr;232(4):525-8. Epub 2015 Apr 22.

[Disease perception in patients with wet age-related macular degeneration].[Article in German]

Kostadinov F, Valmaggia C.

BACKGROUND: The disease perception of the patients treated with intravitreal injections of anti-vascular endothelial growth factor due to wet age-related macular degeneration was investigated.

PATIENTS AND METHODS: 177 questionnaires focusing on the development of the perceived visual acuity and the quality of life were evaluated. The subgroup 1 included 125 patients (70.6%) with a unilateral wet age-related macular degeneration. The subgroup 2 included 52 patients (29.4%) with a bilateral wet

age-related macular degeneration.

RESULTS: Patients would almost always recommend the therapy to a friend (97.2%). The critical remarks are related to the uncertain course of the disease (22.8%) and the uncertain duration of the treatment (19 %). There was a discrepancy between the measured visual outcome and the perceived one in 5.6% in the subgroup 1, and in 38.5% in the subgroup 2. This difference was statistically significant (chi-square test with $p < 0.01$).

CONCLUSIONS: The treatment of wet age-related macular degeneration with intravitreal injections of anti-vascular endothelial growth factor is judged positively. Binocular affected patients have a higher disease perception and therefore a poorer self-assessment of their visual acuity and their quality of life compared with monocular affected patients.

PMID: 25902113 [PubMed - in process]

Am J Ophthalmol. 2015 Apr 17. [Epub ahead of print]

Impact of intravitreal ranibizumab on vessels functionality in patients with retinal vein occlusion.

Corvi F, La Spina C, Benatti L, Querques L, Lattanzio R, Bandello F, Querques G.

PURPOSE: To investigate the short-term effects of intravitreal ranibizumab on retinal vessels functionality in patients with retinal vein occlusion (RVO).

DESIGN: Prospective, interventional case series.

METHODS: We enrolled 11 eyes of 11 consecutive treatment-naïve patients with macular edema secondary to RVO. All patients underwent a complete ophthalmic evaluation, including optical coherence tomography and dynamic and static retinal vessel analysis using the Dynamic Vessel Analyzer (Imedos, Jena, Germany) before (baseline),1 week and 1 month after administration of intravitreal ranibizumab. Investigations of RVO patients were compared to 11 eyes of age- and sex-matched control subjects.

RESULTS: In RVO patients, dynamic analysis showed a significant increase of mean venous dilation from +2.46±1.03% at baseline to +3.96±1.3% at 1 week (p=0.001). At 1-week mean maximum venous and arterial dilations did not differ from control subjects. Static analysis showed a mean overall significant decrease of central retinal artery equivalent and central retinal vein equivalent from baseline to 1 week (from 174.8±22.5MU to 167.2±26.7MU [p=0.04], and from 228.4±20.7MU to 217.3±22.8 [p=0.0002]). Mean central retinal artery equivalent in healthy control subjects was 175.9±10.45MU, not significantly different from baseline, week-1 and month-1 of RVO eyes. Conversely, mean central retinal vein equivalent was 195.5±9.91 MU in healthy control subjects, significantly different from baseline, week 1 and month 1 of RVO eyes.

CONCLUSIONS: Using Dynamic Vessel Analyzer in patients with RVO we found that intravitreal ranibizumab increased veins dilation (dynamic analysis), and had a vasoconstrictive effect on both arteries and veins (static analysis).

PMID: 25896458 [PubMed - as supplied by publisher]

Ophthalmologica. 2015 Apr 17. [Epub ahead of print]

Switch to Aflibercept in the Treatment of Neovascular AMD: One-Year Results in Clinical Practice.

Pinheiro-Costa J, Costa JM, Beato JN, Freitas-da-Costa P, Brandão E, Falcão MS, Falcão-Reis F, Carneiro ÂM.

PURPOSE: To report the clinical outcomes of intravitreal aflibercept therapy in eyes with refractory and recurrent neovascular age-related macular degeneration (AMD) switched from intravitreal bevacizumab or

ranibizumab.

METHODS: This is a retrospective review of eyes with neovascular AMD switched to intravitreal aflibercept with at least 1 year of follow-up after the switch. All patients had had a minimum of 3 injections of bevacizumab or ranibizumab before the switch. Aflibercept was used in patients considered refractory to bevacizumab (group 1) and in recurrent patients on therapy with ranibizumab due to an institutional policy decision (group 2). Changes in best-corrected visual acuity, fluid on optical coherence tomography (OCT), central retinal thickness (CRT) and the frequency of injections were compared.

RESULTS: Eighty-five eyes of 69 patients were analyzed, 39 eyes in group 1 and 46 in group 2. The mean follow-up time was 31.6 months prior to the switch and 14.7 months on treatment with aflibercept. One year after the switch, there was a nonsignificant mean decrease of 2 letters in visual acuity in both groups (group 1: from 58.2 to 55.8 letters, $p = 0.086$; group 2: from 56.4 to 54.5 letters, $p = 0.168$), but the mean number of injections per month was significantly lower (from 0.76 to 0.57, $p < 0.001$). With the switch, 90.6% of the patients showed anatomic improvement with a reduction of fluid on OCT, and both groups presented significant improvement in CRT (group 1: 65.3 µm, $p = 0.051$; group 2: 91.0 µm, $p < 0.001$).

CONCLUSION: Aflibercept appears to be a valuable tool for the management of patients with poor responses to other anti-vascular endothelial growth factor drugs. These patients could have anatomic improvement, and the injection intervals could be extended.

PMID: 25896317 [PubMed - as supplied by publisher]

Ophthalmology. 2015 Apr 16. [Epub ahead of print]

Routine versus As-Needed Bevacizumab with 12-Weekly Assessment Intervals for Neovascular Age -Related Macular Degeneration: 92-Week Results of the GMAN Trial.

Mahmood S, Roberts SA, Aslam TM, Parkes J, Barugh K, Bishop PN; GMAN Study Group.

PURPOSE: To evaluate the efficacy and safety of intravitreal bevacizumab (Avastin; Genentech, South San Francisco, CA) in patients with neovascular age-related macular degeneration (nAMD) using 2 different treatment regimens in which patients were assessed clinically at up to 12-week intervals.

DESIGN: Randomized, controlled, noninferiority trial.

PARTICIPANTS: A total of 331 patients with nAMD.

METHODS: Patients were treated with 1.25 mg intravitreal bevacizumab and followed up to 92 weeks. They were randomized into 2 arms. All patients received 3 loading doses 4 weeks apart and thereafter were assessed every 12 weeks until the end of the study. One arm received a routine treatment at each 12-week assessment, and the other arm was treated at these assessments on an as-needed basis. After the loading doses, patients in either arm who showed signs of disease activity had an additional assessment after 6 weeks and at that visit had top-up treatments on an as-needed basis.

MAIN OUTCOME MEASURES: Mean best-corrected visual acuity (BCVA) at 92 weeks.

RESULTS: At 92 weeks, patients who had treatments every 12 weeks had superior BCVA to those treated on an as-needed basis every 12 weeks ($P = 0.008$), with the regular treatment arm gaining a mean BCVA of 5.5 letters and the as-needed treatment arm gaining 0.6 letters. The regular treatment arm of the study showed significantly improved outcomes with respect to 5-, 10-, and 15-letter changes in BCVA from baseline compared with the as-needed treatment arm, as well as superior reading speed. In patients who completed the study, up to but not including week 92, the mean number of treatments was 10.8 for the regular treatment arm and 9.1 for the as-needed treatment arm.

CONCLUSIONS: A treatment regimen with regular bevacizumab injections every 12 weeks after loading doses supplemented with as-needed top-up treatments produced a stable improvement in BCVA from

baseline. The improvement in BCVA was broadly similar to that obtained in other studies using anti-vascular endothelial growth factor drugs with more frequent assessments and treatments.

PMID: 25892016 [PubMed - as supplied by publisher]

Klin Monbl Augenheilkd. 2015 Apr;232(4):366. Epub 2015 Apr 22.

Editorial: Long Term Follow-Up of Visual Acuity After anti-VEGF Therapy in Neovascular Age-Related Macular Degeneration.

Guex-Crosier Y.

PMID: 25902076 [PubMed - as supplied by publisher]

Other treatment & diagnosis

BMJ Open. 2015 Apr 21;5(4):e007400.

Health professionals' and service users' perspectives of shared care for monitoring wet age-related macular degeneration: a qualitative study alongside the ECHoES trial.

Townsend D, Reeves BC, Taylor J, Chakravarthy U, O'Reilly D, Hogg RE, Mills N.

OBJECTIVES: To explore the views of eye health professionals and service users on shared community and hospital care for wet or neovascular age-related macular degeneration (nAMD).

METHOD: Using maximum variation sampling, 5 focus groups and 10 interviews were conducted with 23 service users and 24 eye health professionals from across the UK (consisting of 8 optometrists, 6 ophthalmologists, 6 commissioners, 2 public health representatives and 2 clinical eye care advisors to local Clinical Commissioning Groups). Data were transcribed verbatim and analysed thematically using constant comparative techniques derived from grounded theory methodology.

RESULTS: The needs and preferences of those with nAMD appear to be at odds with the current service being provided. There was enthusiasm among health professionals and service users about the possibility of shared care for nAMD as it was felt to have the potential to relieve hospital eye service burden and represent a more patient-centred option, but there were a number of perceived barriers to implementation. Some service users and ophthalmologists voiced concerns about optometrist competency and the potential for delays with referrals to secondary care if stable nAMD became active again. The health professionals were divided as to whether shared care was financially more efficient than the current model of care. Specialist training for optometrists, under the supervision of ophthalmologists, was deemed to be the most effective method of training and was perceived to have the potential to improve the communication and trust that shared care would require.

CONCLUSIONS: While shared care is perceived to represent a promising model of nAMD care, voiced concerns suggest that there would need to be greater collaboration between ophthalmology and optometry, in terms of interprofessional trust and communication.

PMID: 25900465 [PubMed - in process]

Acta Ophthalmol. 2015 Apr 20. [Epub ahead of print]

Quantifying metamorphopsia in patients with diabetic macular oedema and other macular abnormalities.

Achiron A, Lagstein O, Glick M, Gur Z, Bartov E, Burgansky-Eliash Z.

PURPOSE: To quantify subjective visual metamorphopsia in newly diagnosed patients suffering from diabetic macular oedema (DME) and other macular abnormalities and to evaluate anti-VEGF treatment effect.

METHODS: Patients with DME, subfoveal choroidal neovascularization (CNV) secondary to age-related macular degeneration (AMD) or retinal venous occlusion (RVO) were recruited. Metamorphopsia score (Mscore) was calculated using M-Charts at baseline and at the end of a series of anti-VEGF injections.

RESULTS: Fifteen eyes of 10 patients with DME, 14 eyes of 13 patients with AMD-CNV and five patients with RVO were included in this study. At baseline, positive Mscore was observed in 46.6% of eyes with DME, 50% of eyes with AMD-CNV and four of five eyes with RVO. Treatment led to a complete metamorphopsia reduction (Mscore = 0) in 71.4% of DME patients, 35.7% of AMD and 0% of RVO patients.

CONCLUSION: We suggest that the M-charts may serve as an additional test for diagnosis and follow-up, complementary to morphological evaluation by imaging, in diabetic patients facing their first anti-VEGF treatment.

PMID: 25899144 [PubMed - as supplied by publisher]

Eye (Lond). 2015 Apr 24. [Epub ahead of print]

The diagnostic accuracy of spectral-domain optical coherence tomography for neovascular age-related macular degeneration: a comparison with fundus fluorescein angiography.

Wilde C, Patel M, Lakshmanan A, Amankwah R, Dhar-Munshi S, Amoaku W; Medscape.

Purpose: To evaluate the diagnostic accuracy of spectral-domain optical coherence tomography (SD-OCT) for neovascular age-related macular degeneration (nAMD): a comparison against fundus fluorescein angiography (FFA).

Methods: A retrospective review of SD-OCT, colour fundus photographs (FP), and FFA of 411 consecutive patients referred to a rapid access Macular Clinic over a 4-year period was performed. FFA images were reviewed nonstereoscopically. SD-OCT images were acquired using the Topcon 3D OCT-1000 instrument. All FFA and OCT images were graded by at least two ophthalmologists independently. Side-by-side grading took place with immediate open discussion and adjudication. If there was disagreement between the two grading ophthalmologists or they were not 90% confident of their assigned grade, then adjudication by a third ophthalmologist was performed.

Results: A total of 278 eyes were graded as having choroidal neovascularisation (CNV) with SD-OCT and 231 diagnosed with FFA. The main diagnostic CNV classifications on FFA were: classic no occult in 27 eyes, predominantly classic in 16, minimally classic in 50, occult in 129, and 9 peripapillary membranes. There were a total of 47 false positives with SD-OCT: a rate of 16.9%. The sensitivity and specificity of SD-OCT alone for detecting CNV was 100 and 80.8%, respectively.

Conclusion: Our study confirms SD-OCT in comparison to the reference standard of nonstereoscopic FFA is highly sensitive at detecting newly presenting nAMD in the setting of a specialist AMD clinic where the investigations are interpreted by trained specialists. However, it does not seem accurate enough to replace FFA in the diagnosis on nAMD in current practice.

PMID: 25907206 [PubMed - as supplied by publisher]

J Clin Med. 2015 Mar;4(3):424-440.

Small Drusen and Age-Related Macular Degeneration: The Beaver Dam Eye Study.

Klein R, Myers CE, Lee KE, Gangnon RE, Sivakumaran TA, Iyengar SK, Klein BE.

Abstract: We tested the hypothesis that large areas of small hard drusen (diameter <63 μm) and intermediate drusen (diameter 63-124 μm) are associated with the incidence of age-related macular degeneration (AMD). Eyes of 3344 older adults with at least 2 consecutive visits spaced 5 years apart over a 20-year period were included. A 6-level severity scale including no drusen, 4 levels of increasing area (from minimal [<2596 μm2] to large [>9086 μm2]) of only small hard drusen, and intermediate drusen was used. The 5-year incidence of AMD was 3% in eyes at the start of the interval with no, minimal, small, and moderate areas of only small drusen and 5% and 25% for eyes with large area of only small drusen and intermediate drusen, respectively. Compared to eyes with a moderate area of small drusen, the odds ratio (OR) of developing AMD in eyes with a large area of only small drusen was 1.8 (P<.001). Compared to eyes with large area of only small drusen, eyes with intermediate drusen had an OR of 5.5 (P<0.001) of developing AMD. Our results are consistent with our hypothesis that large areas of only small drusen are associated with the incidence of AMD.

PMID: 25905023 [PubMed]

Surv Ophthalmol. 2015 May-Jun;60(3):204-215. Epub 2014 Nov 5.

The other CNVM: A review of myopic choroidal neovascularization treatment in the age of anti-vascular endothelial growth factor agents.

Adatia FA, Luong M, Munro M, Tufail A.

Abstract: Choroidal neovascular membranes (CNVM) associated with pathological myopia (PM) can result in significant vision loss and legal blindness. These membranes usually occur subfoveally and are a major complication of PM, developing in approximately 5-10% of such eyes. PM is the second most common cause of choroidal neovascularization after age-related macular degeneration (AMD), and accounts for nearly 60% of CNVM cases in patients younger than age 50. Vascular endothelial growth factor-A has been implicated as the major angiogenic stimulus responsible for choroidal neovascularization secondary to AMD and several major studies have proved the benefits of anti-VEGF treatment for AMD-related CNVM. Benefits have also been observed in a number of prospective and retrospective studies evaluating PM CNVM. Despite the small differences in molecular properties of ranibizumab and bevacizumab, both drugs showed similar therapeutic effects for CNVM associated with PM. Many studies also highlighted that patient age, previous photodynamic therapy treatment, axial length, and visual acuity prior to treatment may affect treatment prognosis. Although there is a paucity of large randomized controlled trials, this systematic review highlights the large numbers of individual trials that demonstrate a significant improvement in VA. The inferior long-term results of alternative therapies, combined with an excellent safety profile from anti-VEGF treatment, make anti-VEGF the current recommended first-line therapy.

PMID: 25890624 [PubMed - as supplied by publisher]

Reprod Biol Endocrinol. 2015 Feb 22;13(1):9.

Human embryonic stem cell cultivation: historical perspective and evolution of xeno-free culture systems.

Desai N, Rambhia P, Gishto A.

Abstract: Human embryonic stem cells (hESC) have emerged as attractive candidates for cell-based therapies that are capable of restoring lost cell and tissue function. These unique cells are able to self-renew indefinitely and have the capacity to differentiate in to all three germ layers (ectoderm, endoderm and mesoderm). Harnessing the power of these pluripotent stem cells could potentially offer new therapeutic treatment options for a variety of medical conditions. Since the initial derivation of hESC lines in 1998, tremendous headway has been made in better understanding stem cell biology and culture requirements for maintenance of pluripotency. The approval of the first clinical trials of hESC cells for

treatment of spinal cord injury and macular degeneration in 2010 marked the beginning of a new era in regenerative medicine. Yet it was clearly recognized that the clinical utility of hESC transplantation was still limited by several challenges. One of the most immediate issues has been the exposure of stem cells to animal pathogens, during hESC derivation and during in vitro propagation. Initial culture protocols used co-culture with inactivated mouse fibroblast feeder (MEF) or human feeder layers with fetal bovine serum or alternatively serum replacement proteins to support stem cell proliferation. Most hESC lines currently in use have been exposed to animal products, thus carrying the risk of xeno-transmitted infections and immune reaction. This mini review provides a historic perspective on human embryonic stem cell culture and the evolution of new culture models. We highlight the challenges and advances being made towards the development of xeno-free culture systems suitable for therapeutic applications.

PMID: 25890180 [PubMed - in process] PMCID: PMC4351689

Am J Ophthalmol. 2015 Apr 14. [Epub ahead of print]

Optical Coherence Tomography Angiography Signs of Vascular Abnormalization with Antiangiogenic Therapy for Choroidal Neovascularization.

Spaide RF.

PURPOSE: To investigate the vascular appearance of choroidal neovascularization (CNV) treated with recurrent intravitreous anti-vascular endothelial growth factor (VEGF) injections, which have been proposed to cause transient vascular normalization along with decreased vascularity and leakage.

DESIGN: Retrospective case series with Perspective on the topic.

METHODS: Patients with treated CNV secondary to age-related macular degeneration from a community based retinal referral practice were evaluated with optical coherence tomography angiography employing split-spectrum amplitude decorrelation. The choroidal neovascular morphology of the 17 eyes of 14 consecutive patients were described.

RESULTS: The mean age of the patients, 8 men and 6 women, was 78.4 (standard deviation [±] 9.3) years. The mean greatest linear dimension of the lesion was 3600 microns. The mean number of anti-VEGF injections was 47 (±21). The vascular diameter of the vessels in the CNV appeared large even in small lesions, with feeder vessels approaching the size of the major arcade vessels of the retina. The vessels had few branch points and many vascular anastomotic connections among larger vessels. There was a paucity of capillaries visualized within the lesions.

CONCLUSIONS: The findings of this study do not support the hypothesis of vascular normalization in eyes receiving recurrent periodic antiangiogenic treatment. The observed "abnormalization" of the vessels may be explained by periodic pruning of angiogenic vascular sprouts by VEGF withdrawal in the face of unimpeded arteriogenesis. As the eye is a readily accessible VEGF laboratory, features expressed therein may also apply to neovascularization elsewhere in the body, such as in tumors.

PMID: 25887628 [PubMed - as supplied by publisher]

Graefes Arch Clin Exp Ophthalmol. 2015 Apr 24. [Epub ahead of print]

In-vivo mapping of drusen by fundus autofluorescence and spectral-domain optical coherence tomography imaging.

Göbel AP, Fleckenstein M, Heeren TF, Holz FG, Schmitz-Valckenberg S.

PURPOSE: To determine fundus autofluorescence (FAF) signal variations and corresponding microstructural alterations on spectral-domain optical coherence tomography (SD-OCT) in areas of funduscopically visible drusen associated with age-related macular degeneration (AMD).

METHODS: Thirty eyes from 22 patients with geographic atrophy (GA) secondary to AMD (median age 74, range 64-87 years), who had undergone retinal imaging including color fundus photography (CFP), FAF and SD-OCT (Spectralis HRA+OCT; Heidelberg Engineering GmbH, Heidelberg, Germany) were retrospectively analyzed. In each eye, at least one druse (≥63 µm) in the perilesional zone of GA recorded on CFP was analyzed. Relative FAF intensities and alterations in SD-OCT bands at the site of each druse were evaluated.

RESULTS: A total of 73 drusen were analyzed, which were associated with heterogeneous corresponding alterations on FAF and SD-OCT. The FAF signal was normal, increased, decreased or not evaluable in 32 (44 %), 27 (37 %), 12 (16 %), and 2 (3 %) drusen, respectively. Focal hyperreflectivity overlying drusen was most frequently spatially confined to increased FAF (present in 9 (33 %) of 27 drusen with increased FAF). Outer nuclear layer thinning and choroidal hyperreflectivity were associated with decreased FAF (present in 7 [58 %] of 12 and 6 [50 %] of 12 drusen with decreased FAF, respectively).

CONCLUSIONS: The appearance of soft drusen on CFP does not allow for differentiation between preserved and markedly compromised outer retinal integrity, including incipient atrophy and focal neurosensory alterations of reflectivity overlying extracellular sub-retinal pigment epithelium (RPE) deposits. Multimodal imaging reveals a broad spectrum of microstructural changes, which may reflect different stages in the evolution of drusen.

PMID: 25904296 [PubMed - as supplied by publisher]

Proc Natl Acad Sci U S A. 2015 Apr 20. [Epub ahead of print]

Quantitative optical coherence tomography angiography of vascular abnormalities in the living human eye.

Jia Y, Bailey ST, Hwang TS, McClintic SM, Gao SS, Pennesi ME, Flaxel CJ, Lauer AK, Wilson DJ, Hornegger J, Fujimoto JG, Huang D.

Abstract: Retinal vascular diseases are important causes of vision loss. A detailed evaluation of the vascular abnormalities facilitates diagnosis and treatment in these diseases. Optical coherence tomography (OCT) angiography using the highly efficient split-spectrum amplitude decorrelation angiography algorithm offers an alternative to conventional dye-based retinal angiography. OCT angiography has several advantages, including 3D visualization of retinal and choroidal circulations (including the choriocapillaris) and avoidance of dye injection-related complications. Results from six illustrative cases are reported. In diabetic retinopathy, OCT angiography can detect neovascularization and quantify ischemia. In age-related macular degeneration, choroidal neovascularization can be observed without the obscuration of details caused by dye leakage in conventional angiography. Choriocapillaris dysfunction can be detected in the nonneovascular form of the disease, furthering our understanding of pathogenesis. In choroideremia, OCT's ability to show choroidal and retinal vascular dysfunction separately may be valuable in predicting progression and assessing treatment response. OCT angiography shows promise as a noninvasive alternative to dye-based angiography for highly detailed, in vivo, 3D, quantitative evaluation of retinal vascular abnormalities.

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Sci Rep. 2015 Apr 22;5:9595.

Functional optical coherence tomography enables in vivo physiological assessment of retinal rod and cone photoreceptors.

Zhang Q, Lu R, Wang B, Messinger JD, Curcio CA, Yao X.

Abstract: Transient intrinsic optical signal (IOS) changes have been observed in retinal photoreceptors,

suggesting a unique biomarker for eye disease detection. However, clinical deployment of IOS imaging is challenging due to unclear IOS sources and limited signal-to-noise ratios (SNRs). Here, by developing high spatiotemporal resolution optical coherence tomography (OCT) and applying an adaptive algorithm for IOS processing, we were able to record robust IOSs from single-pass measurements. Transient IOSs, which might reflect an early stage of light phototransduction, are consistently observed in the photoreceptor outer segment almost immediately (<4 ms) after retinal stimulation. Comparative studies of dark- and light-adapted retinas have demonstrated the feasibility of functional OCT mapping of rod and cone photoreceptors, promising a new method for early disease detection and improved treatment of diseases such as age-related macular degeneration (AMD) and other eye diseases that can cause photoreceptor damage.

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Clin Experiment Ophthalmol. 2015 Apr 20. [Epub ahead of print]

Clinical and molecular characterisation of females affected by X-linked retinoschisis.

Staffieri SE, Rose L, Chang A, De Roach JN, McLaren TL, Mackey DA, Hewitt AW, Lamey TM.

BACKGROUND: X-linked Retinoschisis (XLRS) is a leading cause of juvenile macular degeneration associated with mutations in the RS1 gene. XLRS has a variable expressivity in males and shows no clinical phenotype in carrier females.

DESIGN: Clinical and molecular characterisation of male and female individuals affected with XLRS in a consaguineous family.

PARTICIPANTS: Consanguineous Eastern European-Australian family METHODS: Four clinically affected and nine unaffected family members were genetically and clinically characterised. DNA analysis was conducted by the Australian Inherited Retinal Disease Register and DNA Bank (AIRDR).

MAIN OUTCOME MEASURES: Clinical and molecular characterisation of the causative mutation in a consanguineous family with X-linked retinoschisis RESULTS: By direct sequencing of the RS1 gene, one pathogenic variant, NM_000330.3: c.304C>T, p. R102W, was identified in all clinically diagnosed individuals analysed. The two females were homozygous for the variant whilst the males were hemizygous.

CONCLUSION: Clinical and genetic characterisation of affected homozygous females in x-linked retinoschisis affords the rare opportunity to explore the molecular mechanisms of XLRS and the manifestation of these mutations as disease in humans.

PMID: 25894957 [PubMed - as supplied by publisher]

ACS Med Chem Lett. 2015 Feb 12;6(4):445-9. eCollection 2015.

Applications of azo-based probes for imaging retinal hypoxia.

Uddin MI, Evans SM, Craft JR, Marnett LJ, Uddin MJ, Jayagopal A.

Abstract: We report the design and synthesis of an activatable molecular imaging probe to detect hypoxia in mouse models of retinal vascular diseases. Hypoxia of the retina has been associated with the initiation and progression of blinding retinal vascular diseases including age-related macular degeneration, diabetic retinopathy, and retinopathy of prematurity. In vivo retinal imaging of hypoxia may be useful for early detection and timely treatment of retinal diseases. To achieve this goal, we synthesized HYPOX-3, a near-infrared (NIR) imaging agent coupled to a dark quencher, Black Hole Quencher 3 (BHQ3), which has been previously reported to contain a hypoxia-sensitive cleavable azo-bond. HYPOX-3 was cleaved in hypoxic retinal cell culture and animal models, enabling detection of hypoxia with high signal-to-noise ratios without acute toxicity. HYPOX-3 fluorescences in hypoxic cells and tissues and was undetectable under normoxia.

These imaging agents are promising candidates for imaging retinal hypoxia in preclinical disease models and patients.

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Pathogenesis

Cytokine. 2015 Apr 15. [Epub ahead of print]

Resveratrol attenuates CXCL11 expression induced by proinflammatory cytokines in retinal pigment epithelial cells.

Kutty RK, Samuel W, Abay R, Cherukuri A, Nagineni CN, Duncan T, Jaworski C, Vijayasarathy C, Redmond TM.

Abstract: Dysfunction of the retinal pigment epithelium (RPE) resulting from chronic inflammation is implicated in the pathogenesis of age-related macular degeneration (AMD). RPE cells adjacent to drusen deposits in the AMD eye are known to contain CXCL11, a chemokine involved in inflammatory cell recruitment. We investigated the CXCL11 production by the human RPE (ARPE-19) cells under inflammatory conditions and tested its response to resveratrol, a naturally occurring anti-inflammatory antioxidant. A proinflammatory cytokine mixture consisting of IFN-γ, IL-1β and TNF-α highly increased CXCL11 mRNA expression and CXCL11 protein secretion by ARPE-19 cells. Resveratrol substantially inhibited the proinflammatory cytokines-induced CXCL11 production while partially blocking nuclear factor-κB activation. This inhibitory action of resveratrol was also observed for the cytokines-induced expression of chemokines CXCL9, CCL2 and CCL5. Our results indicate that resveratrol could potentially attenuate RPE inflammatory response implicated in the pathogenesis of AMD.

PMID: 25890876 [PubMed - as supplied by publisher]

BMC Med. 2015 Apr 23;13:95.

Thyroid function: a new road to understanding age-related macular degeneration?

Ittermann T, Jürgens C.

Abstract: Age-related macular degeneration (AMD) continues to be amongst the leading causes of blindness and visual impairment worldwide. AMD remains a degenerative disorder of unknown etiology with rising prevalence. It induces retinal changes and damages those parts of the retina which are essential for central vision. The risk of developing this condition is associated with increasing age. Early stages usually progress without warning signs over years. The major identified risk factors for AMD development are age, ethnicity, family history, and current smoking. Associations of other modifiable risk factors with AMD have been widely published but these studies have reported conflicting results and showed a lack of consistency. According to recent data published in BMC Medicine from the population-based Rotterdam study, thyroid hormones may contribute to a better characterization of AMD in clinical practice. In that study serum free thyroxine levels were positively associated with development of AMD. More studies are needed to validate these findings and to understand better the role of thyroid hormones in the pathogenesis of AMD disease.Please see related article: http://dx.doi.org/10.1186/s12916-015-0329-0.

PMID: 25903272 [PubMed - in process]

Nat Chem Biol. 2015 Apr 20. [Epub ahead of print]

Catalytic mechanism of a retinoid isomerase essential for vertebrate vision.

Kiser PD, Zhang J, Badiee M, Li Q, Shi W, Sui X, Golczak M, Tochtrop GP, Palczewski K.

Abstract: Visual function in vertebrates is dependent on the membrane-bound retinoid isomerase RPE65, an essential component of the retinoid cycle pathway that regenerates 11-cis-retinal for rod and cone opsins. The mechanism by which RPE65 catalyzes stereoselective retinoid isomerization has remained elusive because of uncertainty about how retinoids bind to its active site. Here we present crystal structures of RPE65 in complex with retinoid-mimetic compounds, one of which is in clinical trials for the treatment of age-related macular degeneration. The structures reveal the active site retinoid-binding cavity located near the membrane-interacting surface of the enzyme as well as an Fe-bound palmitate ligand positioned in an adjacent pocket. With the geometry of the RPE65-substrate complex clarified, we delineate a mechanism of catalysis that reconciles the extensive biochemical and structural research on this enzyme. These data provide molecular foundations for understanding a key process in vision and pharmacological inhibition of RPE65 with small molecules.

PMID: 25894083 [PubMed - as supplied by publisher]

Epidemiology

BMC Med. 2015 Apr 23;13:94.

Thyroid function and age-related macular degeneration: a prospective population-based cohort study - the Rotterdam Study.

Chaker L, Buitendijk GH, Dehghan A, Medici M, Hofman A, Vingerling JR, Franco OH, Klaver CC, Peeters RP.

BACKGROUND: In animal models, lack of thyroid hormone is associated with cone photoreceptor preservation, while administration of high doses of active thyroid hormone leads to deterioration. The association between thyroid function and age-related macular degeneration (AMD) has not been investigated in the general population.

METHODS: Participants of age ≥55 years from the Rotterdam Study with thyroid-stimulating hormone (TSH) and/or free thyroxine (FT4) measurements and AMD assessment were included. We conducted age- and sex-adjusted Cox proportional hazards models to explore the association of TSH or FT4 with AMD, in the full range and in those with TSH (0.4-4.0 mIU/L) and/or FT4 in normal range (11-25 pmol/L). Cox proportional hazards models were performed for the association of TSH or FT4 with retinal pigment alterations (RPA), as an early marker of retinal changes. Multivariable models additionally included cardiovascular risk factors and thyroid peroxidase antibodies positivity. We also performed stratification by age and sex. A bidirectional look-up in genome-wide association study (GWAS) data for thyroid parameters and AMD was performed. Single nucleotide polymorphisms (SNPs) that are significantly associated with both phenotypes were identified.

RESULTS: We included 5,573 participants with a median follow-up of 6.9 years (interquartile range 4.4-10.8 years). During follow-up 805 people developed AMD. TSH levels were not associated with increased risk of AMD. Within normal range of FT4, participants in the highest FT4 quintile had a 1.34-fold increased risk of developing AMD, compared to individuals in the middle group (95% confidence interval [CI] 1.07-1.66). Higher FT4 values in the full range were associated with a higher risk of AMD (hazard ratio 1.04, CI, 1.01-1.06 per 1 pmol/L increase). Higher FT4 levels were similarly associated with a higher risk of RPA. Restricting analyses to euthyroid individuals, additional multivariable models, and stratification did not change estimates. We found a SNP (rs943080) in the VEGF-A gene, associated with AMD, to be significant in the TSH GWAS (P = 1.2 x 10(-4)). Adding this SNP to multivariable models did not change estimates.

CONCLUSIONS: Higher FT4 values are associated with increased risk of AMD - even in euthyroid individuals - and increased risk of RPA. Our data suggest an important role of thyroid hormone in pathways leading to AMD.

PMID: 25903050 [PubMed - in process]

Genetics

Hum Genet. 2015 Apr 19. [Epub ahead of print]

A missense variant in CST3 exerts a recessive effect on susceptibility to age-related macular degeneration resembling its association with Alzheimer's disease.

Butler JM, Sharif U, Ali M, McKibbin M, Thompson JP, Gale R, Yang YC, Inglehearn C, Paraoan L.

Abstract: Age-related macular degeneration (AMD) and Alzheimer's disease (AD) are degenerative, multifactorial diseases involving age-related accumulation of extracellular deposits linked to dysregulation of protein homeostasis. Here, we strengthen the evidence that an nsSNP (p.Ala25Thr) in the cysteine proteinase inhibitor cystatin C gene CST3, previously confirmed by meta-analysis to be associated with AD, is associated with exudative AMD. To our knowledge, this is the first report highlighting a genetic variant that increases the risk of developing both AD and AMD. Furthermore, we demonstrate that the risk associated with the mutant allele follows a recessive model for both diseases. We perform an AMD-CST3 case-control study genotyping 350 exudative AMD Caucasian individuals. Bringing together our data with the previously reported AMD-CST3 association study, the evidence of a recessive effect on AMD risk is strengthened (OR = 1.89, P = 0.005). This effect closely resembles the AD-CST3 recessive effect (OR = 1.73, P = 0.005) previously established by meta-analysis. This resemblance is substantiated by the high correlation between CST3 genotype and effect size across the two diseases (R 2 = 0.978). A recessive effect is in line with the known function of cystatin C, a potent enzyme inhibitor. Its potency means that, in heterozygous individuals, a single functional allele is sufficient to maintain its inhibitory function; only homozygous individuals will lack this form of proteolytic regulation. Our findings support the hypothesis that recessively acting variants account for some of the missing heritability of multifactorial diseases. Replacement therapy represents a translational opportunity for individuals homozygous for the mutant allele.

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J Clin Med. 2015;4(2):304-317.

Association of OCT derived drusen measurements with AMD associated-genotypic SNPs in Amish population.

Chavali VR, Diniz B2, Huang J, Ying GS, Sadda SR, Stambolian D.

PURPOSE: To investigate the association of OCT derived drusen measures in Amish age-related macular degeneration (AMD) patients with known loci for macular degeneration.

METHODS: Members of the Old Order Amish community in Pennsylvania ages 50 and older were assessed for drusen area, volume and regions of retinal pigment epithelium (RPE) atrophy using a Cirrus High- Definition-OCT. Measurements were obtained in the macula region within a central circle (CC) of 3 mm diameter and a surrounding perifoveal ring (PR) of 3 to 5 mm diameter using the Cirrus OCT RPE analysis software. Other demographic information including age, gender and smoking status were collected. Study subjects were further genotyped to determine their risk for the AMD associated SNPs in SYN3, LIPC, ARMS2, C3, CFB, CETP, CFI and CFH genes using TaqMan genotyping assays. The association of genotypes with OCT measures were assessed using linear trend p-values calculated from univariate and multivariate generalized linear models.

RESULTS: 432 eyes were included in the analysis. Multivariate analysis (adjusted by age, gender and smoking status) confirmed the known significant association between AMD and macular drusen with the number of CFH risk alleles for drusen area (area increased 0.12 mm2 for a risk allele increase, p<0.01), drusen volume (volume increased 0.01 mm3 for a risk allele increase, p≤0.05) and area of RPE atrophy (area increased 0.43 mm2 for a risk allele increase, p=0.003). SYN3 risk allele G is significantly associated with larger area PR (area increased 0.09 mm2 for a risk allele increase, p=0.03) and larger drusen volume

in central circle (volume increased 0.01 mm3 for a risk allele increase, p=0.04).

CONCLUSION: Among the genotyped SNPs tested, the CFH risk genotype appears to play a major role in determining the drusen phenotype in the Amish AMD population.

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Curr Eye Res. 2015 Apr 21:1-7. [Epub ahead of print]

GSTM1 and GSTM5 Genetic Polymorphisms and Expression in Age-Related Macular Degeneration.

Hunter AA 3rd, Smit-McBride Z, Anderson R, Bordbari MH, Ying GS, Kim ES, Park SS, Telander DG, Dunaief JL, Hjelmeland LM, Morse LS.

PURPOSE: Previously, two cytosolic antioxidant enzymes, Glutathione S-transferase Mu 1 (GSTM1) and Mu 5 (GSTM5), were reduced in retinas with age-related macular degeneration (AMD). This study compared genomic copy number variations (gCNV) of these two antioxidant enzymes in AMD versus controls.

METHODS: Genomic copy number (gCN) assays were performed using Taqman Gene Copy Number Assays (Applied Biosystems, Darmstadt, Germany) in technical quadruplicate for both GSTM1 and GSTM5. Peripheral leukocyte RNA levels were compared with controls in technical triplicates. Statistical comparisons were performed in SAS v9.2 (SAS Institute Inc., Cary, NC).

RESULTS: A large percentage of patients in both AMD and age-matched control groups had no copies of GSTM1 (0/0). The mean gCN of GSTM1 was 1.40 (range 0-4) and 1.61 (range 0-5) for AMD and control, respectively ($p = 0.29$). A greater percentage of control patients had > 3 gCNs of GSTM1 compared with AMD, respectively (15.3% versus 3.0%, $p = 0.004$). The gCN of GSTM5 was 2 in all samples except one control sample. The relative quantification of GSTM1 and GSTM5 mRNA from peripheral blood leukocytes in patients showed significant differences in relative expression in AMD versus control ($p < 0.05$). Peripheral blood leukocyte mRNA and gCN were not significantly correlated ($p = 0.27$).

CONCLUSION: Since high copy numbers of GSTM1 are found more frequently in controls than in AMD, it is possible that high copy number leads to increased retinal antioxidant defense. Genomic polymorphisms of GSTM1 and GSTM5 do not significantly affect the peripheral blood leukocyte mRNA levels.

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Clin Experiment Ophthalmol. 2015 Apr 20. [Epub ahead of print]

Genotype-directed therapy and age-related-macular degeneration: a cautionary note.

Grosso A, Marchese C, Arias L, Panico C, Sigler E.

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Diet, lifestyle and low vision

J Exp Psychol Learn Mem Cogn. 2015 Apr 20. [Epub ahead of print]

Visual Memory for Objects Following Foveal Vision Loss.

Geringswald F, Herbik A, Hofmüller W, Hoffmann MB, Pollmann S.

Abstract: Allocation of visual attention is crucial for encoding items into visual long-term memory. In free vision, attention is closely linked to the center of gaze, raising the question whether foveal vision loss

entails suboptimal deployment of attention and subsequent impairment of object encoding. To investigate this question, we examined visual long-term memory for objects in patients suffering from foveal vision loss due to age-related macular degeneration. We measured patients' change detection sensitivity after a period of free scene exploration monocularly with their worse eye when possible, and under binocular vision, comparing sensitivity and eye movements to matched normal-sighted controls. A highly salient cue was used to capture attention to a nontarget location before a target change occurred in half of the trials, ensuring that change detection relied on memory. Patients' monocular and binocular sensitivity to object change was comparable to controls, even after more than 4 intervening fixations, and not significantly correlated with visual impairment. We conclude that extrafoveal vision suffices for efficient encoding into visual long-term memory.

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