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MD Research News

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Drug treatment

Clin Ophthalmol. 2014 Apr 15;8:755-761. eCollection 2014.

Transformational change: nurses substituting for ophthalmologists for intravitreal injections - a quality-improvement report.

Michelotti MM, Abugreen S, Kelly SP, Morarji J, Myerscough D, Boddie T, Haughton A, Nixon N, Mason B, Sioras E.

BACKGROUND: The dramatic increase in need for anti-vascular endothelial growth factor (anti-VEGF) intravitreal therapy in the treatment of retinal disease and the absence of an equivalent increase in ophthalmologists to undertake such intravitreal injections created a patient-safety risk. Timing of intravitreal therapy (IVT) is critical to prevent vision loss and local clinics lacked capacity to treat patients appropriately. We aimed to improve capacity for IVT by nurse injections.

MATERIALS AND METHODS: A multidisciplinary prospective service-improvement process was undertaken at two adjacent general hospitals in the northwest of England. IVT injections by nurses were a principal component of solution development. After we had obtained appropriate institutional approval, experienced ophthalmic nurses were trained, supervised, and assessed to undertake IVT. Ophthalmologists directly supervised the first 200 injections, and a retina specialist was always on site.

RESULTS: Nurses undertook 3,355 intravitreal injections between June 2012 and November 2013, with minor adverse events (0.3% subconjunctival hemorrhage and corneal abrasion). There were no patient complaints at either hospital.

CONCLUSION: Experienced ophthalmic nurses quickly learned how to perform such injections safely. IVT by nurses was well accepted by patients and staff. Hospital A trained three nurses sequentially for improved flexibility in scheduling. Novel use of appropriately trained non-medical staff can improve efficiency and access in an overburdened service with time-sensitive disease. Retinal assessment was undertaken by ophthalmologists only. Improved access to IVT is important, as treatment with anti-VEGF therapy reduces blindness at population levels.

PMID: 24790403 [PubMed - as supplied by publisher]

Cochrane Database Syst Rev. 2014 May 1;5:CD007325. [Epub ahead of print]

Anti-vascular endothelial growth factor for macular oedema secondary to central retinal vein occlusion.

Braithwaite T, Nanji AA, Lindsley K, Greenberg PB.

BACKGROUND: Central retinal vein occlusion (CRVO) is a relatively common retinal vascular disorder in which macular oedema may develop, with a consequent reduction in visual acuity. Until recently there has been no treatment of proven benefit, but growing evidence supports the use of anti-vascular endothelial growth factor (anti-VEGF) agents.

OBJECTIVES: To investigate the effectiveness and safety of anti-VEGF therapies for the treatment of macular oedema secondary to CRVO.

SEARCH METHODS: We searched CENTRAL (which contains the Cochrane Central Register of Controlled Trials (CENTRAL) and the Cochrane Eyes and Vision Group Trials Register) (The Cochrane Library 2013, Issue 10), Ovid MEDLINE (January 1950 to October 2013), EMBASE (January 1980 to October 2013), Latin American and Caribbean Health Sciences Literature Database (LILACS) (January 1982 to October 2013), Cumulative Index to Nursing and Allied Health Literature (CINAHL) (January 1937 to October 2013), OpenGrey, OpenSIGLE (January 1950 to October 2013), the metaRegister of Controlled Trials (mRCT) (www.controlled-trials.com), ClinicalTrials.gov (www.clinicaltrials.gov), the WHO International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en) and Web of Science Conference Proceedings Citation Index-Science (CPCI-S). There were no language or date restrictions in the electronic search for trials. The electronic databases and clinical trials registers were last searched on 29th October 2013.

SELECTION CRITERIA: We considered randomised controlled trials (RCTs) that compared intravitreal anti -VEGF agents of any dose or duration to sham injection or no treatment. We focused on studies that included individuals of any age or gender and a minimum of six months follow-up.

DATA COLLECTION AND ANALYSIS: Two review authors independently assessed trial quality and extracted data. The primary outcome was the proportion of participants with a gain in best-corrected visual acuity (BCVA) from baseline of greater than or equal to 15 letters (3 lines) on the Early Treatment of Diabetic Retinopathy Study (ETDRS) chart. Secondary outcomes included the proportion of participants with a loss of 15 letters or more of BCVA, the mean change from baseline BCVA, the mean change in central retinal thickness (CRT), the number and type of complications or adverse outcomes, and the number of additional interventions administered. Where available, we also presented quality of life and economic data.

MAIN RESULTS: We found six RCTs that met the inclusion criteria after independent and duplicate review of the search results. These RCTs included 937 participants and compared outcomes at six months to sham injection for four anti-VEGF agents: aflibercept (VEGF Trap-Eye, Eylea), bevacizumab (Avastin), pegaptanib sodium (Macugen) and ranibizumab (Lucentis). Three trials were conducted in Norway, Sweden and the USA, and three trials were multicentre, one including centres in the USA, Canada, India, Israel, Argentina and Columbia, a second including centres in the USA, Australia, France, Germany, Israel, and Spain, and a third including centres in Austria, France, Germany, Hungary, Italy, Latvia, Australia, Japan, Singapore and South Korea. We performed meta-analysis on three key visual outcomes, using data from up to six trials. High-quality evidence from six trials revealed that participants receiving intravitreal anti-VEGF treatment were 2.71 times more likely to gain at least 15 letters of visual acuity at six months compared to participants treated with sham injections (risk ratio (RR) 2.71; 95% confidence intervals (CI) 2.10 to 3.49). High-quality evidence from five trials suggested anti-VEGF treatment was associated with an 80% lower risk of losing at least 15 letters of visual acuity at six months compared to sham injection (RR 0.20; 95% CI 0.12 to 0.34). Moderate-quality evidence from three trials (481 participants) revealed that the mean reduction from baseline to six months in central retinal thickness was 267.4 µm (95% CI 211.4 µm to 323.4 µm) greater in participants treated with anti-VEGF than in participants treated with sham. The meta-analyses demonstrate that treatment with anti-VEGF is associated with a clinically meaningful gain in vision at six months. One trial demonstrated sustained benefit at 12 months compared to sham. No significant ocular or systemic safety concerns were identified in this time period.

AUTHORS' CONCLUSIONS: Compared to no treatment, repeated intravitreal injection of anti-VEGF agents in eyes with CRVO macular oedema improved visual outcomes at six months. All agents were relatively well tolerated with a low incidence of adverse effects in the short term. Future trials should address the relative efficacy and safety of the anti-VEGF agents and other treatments, including intravitreal corticosteroids, for longer-term outcomes.

PMID: 24788977 [PubMed - as supplied by publisher]

Int J Ophthalmol. 2014 Apr 18;7(2):355-364. eCollection 2014.

Comparison of bevacizumab and ranibizumab in age-related macular degeneration: a systematic review and meta-analysis.

Zhang XY, Guo XF, Zhang SD, He JN, Sun CY, Zou Y, Bi HS, Qu Y.

AIM: To compare the effectiveness and safety between bevacizumab and ranibizumab in the treatment of age-related macular degeneration (AMD) through a systematic review and meta-analysis.

METHODS: We performed a comprehensive search of randomized controlled trials (RCTs), non-RCTs, case-control and cohort studies that compared bevacizumab and ranibizumab using PubMed and the Cochrane Library. After the related data were extracted by two investigators independently, pooled weighted mean differences (WMDs) and risk ratios (RRs) with 95% confidence intervals (CIs) were estimated using a random-effects or a fixed-effects model.

RESULTS: A total of four RCTs involving 1927 patients and eleven retrospective case series involving 2296 patients were included. For the primary outcomes, no significant differences were found between ranibizumab group and bevacizumab group in visual acuity (WMD: -0.04; 95%CI: -0.08 to 0.00; P=0.06), best corrected visual acuity (WMD: -0.05; 95%CI: -0.10 to 0.00; P=0.05), retina thickness (WMD: -4.69; 95%CI: -13.15 to 3.76; P=0.86) and foveal thickness (WMD: 10.91; 95%CI: -14.73 to 36.56; P=0.40). The pooled analyses in the evaluation of safety showed that compared to bevacizumab, ranibizumab was associated with decreased risks of ocular inflammation (RR: 0.45; 95% CI: 0.23 to 0.89; P=0.02) and venous thrombotic events (RR: 0.27; 95%CI: 0.08 to 0.89; P=0.03). However, there were no significant differences observed in deaths (P=0.69) and arterial thromboembolic events (P=0.71) between the two groups.

CONCLUSION: With equal clinical efficacy, ranibizumab was found to be associated with less adverse events compared to bevacizumab, indicating that ranibizumab might be a safer management.

PMID: 24790885 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2014 Apr 29. doi: 10.1136/bjophthalmol-2013-304775. [Epub ahead of print]

Functional and anatomical outcome of eyes with neovascular age-related macular degeneration treated with intravitreal ranibizumab following an exit strategy regimen.

Menke MN, Zinkernagel MS, Ebneter A, Wolf S.

AIMS: To assess the functional and morphological outcome of eyes with neovascular AMD treated with intravitreal ranbizumab following an exit strategy treatment regime.

METHODS: The Bern treatment regime for neovascular AMD has a fixed injection schedule, even in the non-active stage of the disease. The regimen has been adapted from the PIER study treatment protocol. Eyes with non-active AMD will receive 4 injections in the first year, and 2 injections in the second year of follow-up before treatment stops. Patients that received ranibizumab for treatment and reached the exit criteria were identified, and charts were reviewed to assess functional and morphological outcome.

RESULTS: Only 2.6% of all patients (15 out of 575 patients) reached the exit criteria. Mean change in best corrected ETDRS visual acuity (VA) was 4.5±16.9 letters when comparing baseline VA to 4 weeks after the last injection (p=0.32). OCT mean foveal thickness was significantly thinner after last treatment (247.9±43.0 µm) compared to baseline (332.5±83.1 µm, p=0.002). The mean total number of ranibizumab injections was 15.6±8.0, and the mean total treatment period was 40.9±18.3 months. Twenty percent of eyes had geographic atrophy present at baseline versus 46.6% at the end of treatment.

CONCLUSIONS: Even with a fixed treatment regime and a defined treatment exit strategy, only a small percentage of patients reach exit criteria. Retinal thickness has been significantly reduced by repeated intravitreal ranibizumab injections, and geographic atrophy became more frequent.

PMID: 24782472 [PubMed - as supplied by publisher]

Graefes Arch Clin Exp Ophthalmol. 2014 Apr 29. [Epub ahead of print]

The cost-utility of aflibercept for the treatment of age-related macular degeneration compared to bevacizumab and ranibizumab and the influence of model parameters.

Elshout M, van der Reis MI, Webers CA, Schouten JS.

BACKGROUND: Age-related macular degeneration (AMD) is a blinding disease placing considerable burden on society due to blindness-associated costs. Intravitreal anti-vascular endothelial growth factors (anti-VEGFs) are effective in reducing the incidence of blindness, but at potentially high costs, depending on the cost of the drug used. Aflibercept has been introduced as an anti-VEGF equally effective to ranibizumab, but less costly. For this new drug, new cost-effectiveness analyses are needed, and AMD models used today give biased results. We investigated the cost-effectiveness of aflibercept compared to bevacizumab, ranibizumab, and no treatment and studied the influence of commonly used model parameters.

METHODS: A patient-level, visual acuity-based, 2-eye model was developed. Data on effectiveness were derived from randomized controlled trials evaluating the outcomes of aflibercept, bevacizumab, and ranibizumab. Utility and resource utilization were assessed in interviews with AMD patients. Costs were based on standard health care cost prices. Time horizons were two and five years. A societal perspective was employed.

RESULTS: Over five years, costs associated with aflibercept treatment were <euro>36,030, with 2.15 QALYs. Costs associated with the bevacizumab regimens, ABC study as-needed (PRN); CATT study PRN; and CATT study 1×/month, were <euro>19,367; <euro>26,746; and <euro>30,520, with 2.16; 2.17; and 2.15 QALYs, respectively. Costs associated with ranibizumab PRN and 1×/month were <euro>45,491 and <euro>74,837 with 2.16 and 2.15 QALYs, respectively. 'No treatment' was associated with <euro>9530 and 1.96 QALYs. The incremental cost-effectiveness ratios versus 'no treatment' were: aflibercept-<euro>140,274; bevacizumab-<euro>51,062 (ABC PRN), <euro>83,256 (CATT PRN) and <euro>110,361 (1×/month); ranibizumab-<euro>181,667 (PRN) and <euro>349,773 (1×/month). Results were highly dependent on whether only one or both eyes were included, length of time horizon, and whether the costs of blindness and low-vision were included in the analysis.

CONCLUSIONS: Aflibercept is a cost-effective treatment for AMD over ranibizumab. However, aflibercept is not a cost-effective treatment when compared to bevacizumab. Application of inappropriate model assumptions leads to a biased cost-saving estimate of the cost-effectiveness of aflibercept. Therefore, cost-effectiveness analyses should be conducted with appropriate models.

PMID: 24777708 [PubMed - as supplied by publisher]

Ophthalmology. 2014 Apr 23. pii: S0161-6420(14)00245-0. doi: 10.1016/j.ophtha.2014.03.021. [Epub ahead of print]

Neutralization of Vascular Endothelial Growth Factor Slows Progression of Retinal Nonperfusion in Patients with Diabetic Macular Edema.

Campochiaro PA, Wykoff CC, Shapiro H, Rubio RG, Ehrlich JS.

OBJECTIVE: To determine the effect of suppression of vascular endothelial growth factor (VEGF) by monthly injection of ranibizumab on posterior retinal nonperfusion (RNP) in patients with diabetic macular edema (DME).

DESIGN: Unplanned retrospective analysis of prospectively collected data from 2 randomized, sham injection-controlled, double-masked, multicenter clinical trials.

PARTICIPANTS: Six hundred sixty-six patients with DME.

METHODS: An independent reading center measured the area of RNP on fluorescein angiograms obtained in the phase 3 RISE and RIDE trials.

MAIN OUTCOME MEASURES: The percentage of patients with no posterior RNP.

RESULTS: The percentage of patients with no posterior RNP decreased in the sham group between baseline and month 24, but remained relatively stable in the 2 ranibizumab groups. After month 24, the sham group crossed over to receive monthly injections of ranibizumab 0.5 mg, and the differences between the sham and ranibizumab groups were reduced. The percentage of patients who showed an increase in posterior RNP from baseline increased over time in all 3 groups, but at a faster rate in the sham group, resulting in statistically significant differences at every time point between months 3 (9.6% vs. 18.5%; P = 0.016) and 24 (16.1% vs. 37.6%; P<0.0001) for ranibizumab 0.5 mg versus sham and from months 6 (12.3% vs. 23.0%; P = 0.013) through 24 (15.0% vs. 37.6%; P<0.0001) for ranibizumab 0.3 mg. Initiation of ranibizumab in the sham group at month 24 was followed by reduction in the percentage of patients with an increase in posterior RNP from baseline at months 30 and 36, whereas the 2 ranibizumab groups continued their gradual rise.

CONCLUSIONS: Just as high VEGF levels contribute to progression of retinal nonperfusion in retinal vein occlusion, the same is true in patients with DME, suggesting that regardless of the underlying disease process, high levels of VEGF can cause closure of retinal vessels. However, our data also suggest that VEGF-induced worsening of retinal perfusion in DME is superimposed on another cause of more gradually worsening perfusion, possibly glucotoxicity. Thus, monthly injections of ranibizumab can slow, but not completely prevent, retinal capillary closure in patients with DME.

PMID: 24768239 [PubMed - as supplied by publisher]

Klin Monbl Augenheilkd. 2014 Apr;231(4):432-435. Epub 2014 Apr 25.

Retinal Pigment Epithelium Rips After Ranibizumab in Neovascular Age-Related Macular Degeneration: Incidence, Risk Factors and Long-Term Outcome.

Guber J, Praveen A, Saeed MU.

Background: Retinal pigment epithelium (RPE) rips after ranibizumab for wet age related macular degeneration (AMD) with a pigment epithelial detachments (PED) are a dreaded complication. Aim of this study was to analyse the incidence, the risk factors and long-term outcome after a PED tear.

Patients and Methods: 401 patients with wet AMD were analysed. A total of 33 eyes with PED were identified. Mean follow up time was 635 days (SD ± 311).

Results: PED tears occurred in 8 (24 %) patients. Most RPE rips (40 %) occurred within the first three months. Mean visual loss was 13 letters (range -57-9). The PED tear group had a mean PED height of 521 µm. The PED group without a tear had a mean height of 300 µm ($p \leq 0.001$). Patients with a PED height over 300 µm had more than twice the risk to develop a RPE rip compared to patients with PED height smaller than 300 µm ($p \leq 0.001$).

Conclusions: PED height is a relevant factor for the incidence of RPE rips after treatment with ranibizumab. Owing to the close time relationship with the therapy, this complication must be taken into account before treatment as it may lead to significant vision loss.

PMID: 24771185 [PubMed - as supplied by publisher]

Klin Monbl Augenheilkd. 2014 Apr;231(4):427-431. Epub 2014 Apr 25.

Ranibizumab Treatment in Age-Related Macular Degeneration: A Meta-Analysis of One-Year Results.

Gerding H.

Background: Although ranibizumab is widely used in age-related macular degeneration there is no

systematic data available on the relation between treatment frequency and functional efficacy within the first 12 months of follow-up.

Material and Methods: A meta-analysis was performed on available MEDLINE literature. 47 relevant clinical studies (54 case series) could be identified covering 11706 treated eyes. Non-linear and linear regressions were calculated for the relation between treatment frequency and functional outcome (average gain in visual acuity, % of eyes losing less than 15 letters of visual acuity, % of eyes gaining ≥ 15 letters) within the first year of care.

Results: Mean improvement of average visual gain was + 4.9 ± 3.6 (mean ± 1 standard deviation) letters (case-weighted: 3.3 letters). The average number of ranibizumab injections until month 12 was 6.3 ± 2.0 (case-weighted: 5.9). 92.4 ± 3.9% of eyes (case-weighted: 91.9%) lost less than three lines of visual acuity and 24.5 ± 8.2% (case-weighted: 23.3) gained more than 3 lines within the first year. Analysis of the relation between the number of injections and functional improvement indicated best fit for non-linear equations. A nearly stepwise improvement of functional gain occurred between 6.8 and 7.2 injections/year. A saturation effect of treatment occurred at higher injection frequency.

Conclusions: The results of this meta-analysis clearly indicate a non-linear relation between the number of injections and functional gain of ranibizumab within the first 12 months of treatment. Treatment saturation seems to occur at a treatment frequency > 7.2 injections within the first 12 months.

PMID: 24771184 [PubMed - as supplied by publisher]

Klin Monbl Augenheilkd. 2014 Apr;231(4):423-426. Epub 2014 Apr 25.

Preliminary Results of Aflibercept in Treatment-Naive Choroidal Neovascularization of Wet Age-Related Macular Degeneration.

Gambon R, Barthelmes D, Amstutz C, Fleischhauer J, Kurz-Levin M, Zweifel S.

Background: The aim of this study was to evaluate the early response of aflibercept as first-line therapy in treatment-naive patients with newly diagnosed choroidal neovascularization (CNV) in age-related macular degeneration (AMD).

Patients and Methods: An analysis of 35 eyes (35 patients, 28 female, 7 male) with treatment-naive active CNV was undertaken. Lesion activity was determined based on fluorescein angiography, clinical and optical coherence tomography (OCT) findings, including the presence of sub-, intraretinal fluid, retinal pigment epithelial (RPE) detachment and hemorrhage. Logarithm of the minimum angle of resolution (LogMAR) charts were used for testing best corrected or best available visual acuity (BCVA). Treatment response was evaluated based on changes in BCVA and lesion activity.

Results: Classic or predominantly classic CNV was diagnosed in 7 eyes (20.0%), occult or minimally classic in 21 eyes (60.0%), retinal angiomatous proliferation in 5 eyes (14.3%) and polypoidal choroidal vasculopathy in 2 eyes (5.7%). Lesion activity was evaluated as unchanged in only one eye. In all other eyes, a definite treatment response was observed with complete resolution of fluid in 20 eyes after a single injection. Three eyes did not show improved sub-RPE fluid with smaller pigment epithelial detachments. A rip of the RPE was seen in 3 eyes. All patients maintained vision, 7 patients (7 eyes) gained > 15 letters from baseline to month 2 follow-up, of whom 4 reached this level of visual acuity after one injection. The visual acuity gains in this study were maintained through 6 months.

Conclusion: There seems to be a rapid treatment response to aflibercept independent of the underlying CNV. Aflibercept may be beneficial even in eyes with large pigment epithelial detachments due to exudative AMD.

PMID: 24771183 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Am J Ophthalmol. 2014 Apr 28. pii: S0002-9394(14)00220-7. doi: 10.1016/j.ajo.2014.04.017. [Epub ahead of print]

Reduction in mean deviation values in automated perimetry in eyes with multifocal compared to monofocal intraocular lens implants.

Farid M, Chak G, Garg S, Steinert RF.

PURPOSE: To evaluate differences in mean deviation values in automated perimetry in healthy eyes with multifocal compared to monofocal intraocular lens (IOL) implants.

DESIGN: Prospective, age-matched, comparative analysis.

METHODS: SETTING: Single-center, tertiary referral academic practice. PATIENT POPULATION: A total of 37 healthy eyes in 37 patients with bilateral multifocal (n = 22) or monofocal (n = 15) IOL implants were studied. INTERVENTION/OBSERVATION PROCEDURE: Humphrey Visual Field 10-2 (Zeiss Meditec, Dublin CA) testing was performed on all patients.

MAIN OUTCOME MEASURES: Mean Deviation (MD) and Pattern Standard Deviation (PSD) numerical values were evaluated and compared between groups.

RESULTS: The average MD was -2.84 dB (SD 2.32) for the multifocal IOL group and -0.97 dB (SD 1.58) for the monofocal IOL group (p = 0.006). There was no significant difference in PSD between the two groups (p = 0.99). Eyes that had the visual field 10-2 testing >6 months from time of IOL placement showed no improvement in MD when compared to eyes that were tested within 6 months from IOL placement.

CONCLUSION: Multifocal IOL implants cause significant non-specific reduction in MD values on Humphrey Visual Field 10-2 testing that does not improve with time or neuroadaptation. Multifocal IOL implants may be inadvisable in patients where central visual field reduction may not be tolerated, such as macular degeneration, retinal pigment epithelium changes, and glaucoma.

PMID: 24784872 [PubMed - as supplied by publisher]

Eye (Lond). 2014 May 2. doi: 10.1038/eye.2014.104. [Epub ahead of print]

Diagnostic accuracy of the Amsler grid and the preferential hyperacuity perimetry in the screening of patients with age-related macular degeneration: systematic review and meta-analysis.

Faes L, Bodmer NS, Bachmann LM, Thiel MA, Schmid MK.

Objective: To clarify the screening potential of the Amsler grid and preferential hyperacuity perimetry (PHP) in detecting or ruling out wet age-related macular degeneration (AMD).

Evidence acquisition: Medline, Scopus and Web of Science (by citation of reference) were searched. Checking of reference lists of review articles and of included articles complemented electronic searches. Papers were selected, assessed, and extracted in duplicate.

Evidence synthesis: Systematic review and meta-analysis. Twelve included studies enrolled 903 patients and allowed constructing 27 two-by-two tables. Twelve tables reported on the Amsler grid and its modifications, twelve tables reported on the PHP, one table assessed the MCPT and two tables assessed the M-charts. All but two studies had a case-control design. The pooled sensitivity of studies assessing the Amsler grid was 0.78 (95% confidence intervals; 0.64-0.87), and the pooled specificity was 0.97 (95% confidence intervals; 0.91-0.99). The corresponding positive and negative likelihood ratios were 23.1 (95% confidence intervals; 8.4-64.0) and 0.23 (95% confidence intervals; 0.14-0.39), respectively. The pooled sensitivity of studies assessing the PHP was 0.85 (95% confidence intervals; 0.80-0.89), and specificity was 0.87 (95% confidence intervals; 0.82-0.91). The corresponding positive and negative likelihood ratios were 6.7 (95% confidence intervals; 4.6-9.8) and 0.17 (95% confidence intervals; 0.13-0.23). No pooling

was possible for MCPT and M-charts.

Conclusion: Results from small preliminary studies show promising test performance characteristics both for the Amsler grid and PHP to rule out wet AMD in the screening setting. To what extent these findings can be transferred to a real clinic practice still needs to be established.

PMID: 24788016 [PubMed - as supplied by publisher]

Eye (Lond). 2014 May 2. doi: 10.1038/eye.2014.102. [Epub ahead of print]

Influence of image compression on the interpretation of spectral-domain optical coherence tomography in exudative age-related macular degeneration.

Kim JH, Kang SW, Kim JR, Chang YS.

Purpose: To evaluate the effect of image compression of spectral-domain optical coherence tomography (OCT) images in the examination of eyes with exudative age-related macular degeneration (AMD).

Methods: Thirty eyes from 30 patients who were diagnosed with exudative AMD were included in this retrospective observational case series. The horizontal OCT scans centered at the center of the fovea were conducted using spectral-domain OCT. The images were exported to Tag Image File Format (TIFF) and 100, 75, 50, 25 and 10% quality of Joint Photographic Experts Group (JPEG) format. OCT images were taken before and after intravitreal ranibizumab injections, and after relapse. The prevalence of subretinal and intraretinal fluids was determined. Differences in choroidal thickness between the TIFF and JPEG images were compared with the intra-observer variability.

Results: The prevalence of subretinal and intraretinal fluids was comparable regardless of the degree of compression. However, the chorio-scleral interface was not clearly identified in many images with a high degree of compression. In images with 25 and 10% quality of JPEG, the difference in choroidal thickness between the TIFF images and the respective JPEG images was significantly greater than the intra-observer variability of the TIFF images (P=0.029 and P=0.024, respectively).

Conclusions: In OCT images of eyes with AMD, 50% of the quality of the JPEG format would be an optimal degree of compression for efficient data storage and transfer without sacrificing image quality.Eye advance online publication, 2 May 2014; doi:10.1038/eye.2014.102.

PMID: 24788012 [PubMed - as supplied by publisher]

World J Stem Cells. 2014 Apr 26;6(2):111-119.

Progress of mesenchymal stem cell therapy for neural and retinal diseases.

Ng TK, Fortino VR, Pelaez D, Cheung HS.

Abstract: Complex circuitry and limited regenerative power make central nervous system (CNS) disorders the most challenging and difficult for functional repair. With elusive disease mechanisms, traditional surgical and medical interventions merely slow down the progression of the neurodegenerative diseases. However, the number of neurons still diminishes in many patients. Recently, stem cell therapy has been proposed as a viable option. Mesenchymal stem cells (MSCs), a widely-studied human adult stem cell population, have been discovered for more than 20 years. MSCs have been found all over the body and can be conveniently obtained from different accessible tissues: bone marrow, blood, and adipose and dental tissue. MSCs have high proliferative and differentiation abilities, providing an inexhaustible source of neurons and glia for cell replacement therapy. Moreover, MSCs also show neuroprotective effects without any genetic modification or reprogramming. In addition, the extraordinary immunomodulatory properties of MSCs enable autologous and heterologous transplantation. These qualities heighten the clinical applicability of MSCs when dealing with the pathologies of CNS disorders. Here, we summarize the latest progress of MSC experimental research as well as human clinical trials for neural and retinal diseases. This review article will focus on

multiple sclerosis, spinal cord injury, autism, glaucoma, retinitis pigmentosa and age-related macular degeneration.

PMID: 24772238 [PubMed - as supplied by publisher]

J Ophthalmol. 2014;2014:287893. doi: 10.1155/2014/287893. Epub 2014 Mar 23.

Age macular degeneration: etiology, prevention, individualized therapies, cell therapy, and tissue engineering.

García-Layana A, Thumann G, Groll J.

PMID: 24778866 [PubMed]

Pathogenesis

Br J Pharmacol. 2014 May 2. doi: 10.1111/bph.12737. [Epub ahead of print]

Histamine receptor h4 as a new therapeutic target for choroidal neovascularization in age-related macular degeneration.

Kaneko H, Ye F, Ijima R, Kachi S, Kato S, Nagaya M, Higuchi A, Terasaki H.

BACKGROUND AND PURPOSE: To examine the therapeutic efficacy of reducing histamine receptor h4 (HRH4) expression in choroidal neovascularizations (CNVs) for the treatment of age-related macular degeneration (AMD).

EXPERIMENTAL APPROACH: HRH4 expression was examined in CNVs from patients with AMD. In mice, laser photocoagulation was performed in the retina to induce experimental CNV (laser-CNV). Protein and mRNA expression levels were examined and CNV volume was measured in wild-type and Hrh4-/- mice after inducing laser-CNV. JNJ7777120, a HRH4 antagonist, was administrated intravitreously after inducing laser-CNV. CNV volume and pathological vessel leakage were subsequently compared between mice that were injected and controls. Fundus imaging, retinal histology and electroretinography were carried out on the eyes injected with JNJ7777120 to evaluate retinal toxicity.

KEY RESULTS: Human HRH4 was confirmed only in CNV samples from AMD patients and not in the other subretinal tissues. Mouse HRH4 was expressed in the retinal pigment epithelium (RPE) only after inducing laser-CNV in wild-type mice, and it was co-localized with the macrophage marker F4/80. Laser-CNV volume was reduced in Hrh4-/- mice compared with that in wild-type mice, and JNJ7777120 successfully suppressed laser-induced CNV volume and pathological CNV leakage in wild-type mice. The eyes injected with JNJ7777120 did not show retinal degeneration.

CONCLUSIONS AND IMPLICATIONS: HRH4 was expressed in macrophages that accumulated around CNVs. Suppressing HRH4 expression led to the prevention of pathological vessel leakage without showing retinal toxicity, indicating that HRH4 has potential as a novel therapeutic target in AMD.

PMID: 24787705 [PubMed - as supplied by publisher]

Int J Ophthalmol. 2014 Apr 18;7(2):256-263. eCollection 2014.

Comparative proteomic analysis of plasma proteins in patients with age-related macular degeneration.

Xu XR, Zhong L, Huang BL, Wei YH, Zhou X, Wang L, Wang FQ.

AIM: To find the significant altered proteins in age-related macular degeneration (AMD) patients as

potential biomarkers of AMD.

METHODS: A comparative analysis of the protein pattern of AMD patients versus healthy controls was performed by means of proteomic analysis using two-dimensional gel electrophoresis followed by protein identification with MALDI TOF/TOF mass spectrometry.

RESULTS: We identified 28 proteins that were significantly altered with clinical relevance in AMD patients. These proteins were involved in a wide range of biological functions including immune responses, growth cytokines, cell fate determination, wound healing, metabolism, and anti-oxidance.

CONCLUSION: These results demonstrate the capacity of proteomic analysis of AMD patient plasma. In addition to the utility of this approach for biomarker discovery, identification of alterations in endogenous proteins in the plasma of AMD patient could improve our understanding of the disease pathogenesis.

PMID: 24790867 [PubMed - as supplied by publisher]

Int J Ophthalmol. 2014 Apr 18;7(2):194-197. eCollection 2014.

Interleukin-6 receptor blockade suppresses subretinal fibrosis in a mouse model.

Cui W, Zhang H, Liu ZL.

AIM: To determine the involvement of the interleukin (IL)-6 with the development of experimental subretinal fibrosis in a mouse model.

METHODS: Subretinal fibrosis was induced by subretinal injection of macrophage-rich peritoneal exudate cells and the local expression of IL-6 was assessed by quantitative real-time reverse transcription-polymerase chain reaction (RT-PCR) and enzyme-linked immunosorbent assay (ELISA) at various time points. In addition, we investigated the effect of IL-6 receptor (IL-6R) monoclonal antibody (MR16-1) on subretinal fibrosis development.

RESULTS: IL-6 mRNA level was significantly elevated at 1d after subretinal fibrosis induction and increased further to about 12-fold at 2d, reaching the peak. The result of ELISA showed that IL-6 protein was not detected in naive mice. At 2d after subretinal fibrosis induction, IL-6 protein level was upregulated to 67.33±14.96 pg/mg in subretinal fibrosis mice. MR16-1 treatment resulted in a reduced subretinal fibrosis area by 48% compared to animals from control group at 7d.

CONCLUSION: Our results indicated that IL-6 signaling may contribute to the pathogenesis of subretinal fibrogenesis and IL-6R inhibition may provide an effective, novel treatment of advanced and late-stage neovascular age-related macular degeneration.

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Eye (Lond). 2014 May 2. doi: 10.1038/eye.2014.104. [Epub ahead of print]

Diagnostic accuracy of the Amsler grid and the preferential hyperacuity perimetry in the screening of patients with age-related macular degeneration: systematic review and meta-analysis.

Faes L, Bodmer NS, Bachmann LM, Thiel MA, Schmid MK.

Objective: To clarify the screening potential of the Amsler grid and preferential hyperacuity perimetry (PHP) in detecting or ruling out wet age-related macular degeneration (AMD).

Evidence acquisition: Medline, Scopus and Web of Science (by citation of reference) were searched. Checking of reference lists of review articles and of included articles complemented electronic searches. Papers were selected, assessed, and extracted in duplicate.

Evidence synthesis: Systematic review and meta-analysis. Twelve included studies enrolled 903 patients

and allowed constructing 27 two-by-two tables. Twelve tables reported on the Amsler grid and its modifications, twelve tables reported on the PHP, one table assessed the MCPT and two tables assessed the M-charts. All but two studies had a case-control design. The pooled sensitivity of studies assessing the Amsler grid was 0.78 (95% confidence intervals; 0.64-0.87), and the pooled specificity was 0.97 (95% confidence intervals; 0.91-0.99). The corresponding positive and negative likelihood ratios were 23.1 (95% confidence intervals; 8.4-64.0) and 0.23 (95% confidence intervals; 0.14-0.39), respectively. The pooled sensitivity of studies assessing the PHP was 0.85 (95% confidence intervals; 0.80-0.89), and specificity was 0.87 (95% confidence intervals; 0.82-0.91). The corresponding positive and negative likelihood ratios were 6.7 (95% confidence intervals; 4.6-9.8) and 0.17 (95% confidence intervals; 0.13-0.23). No pooling was possible for MCPT and M-charts.

Conclusion: Results from small preliminary studies show promising test performance characteristics both for the Amsler grid and PHP to rule out wet AMD in the screening setting. To what extent these findings can be transferred to a real clinic practice still needs to be established.

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Eye (Lond). 2014 May 2. doi: 10.1038/eye.2014.102. [Epub ahead of print]

Influence of image compression on the interpretation of spectral-domain optical coherence tomography in exudative age-related macular degeneration.

Kim JH, Kang SW, Kim JR, Chang YS.

Purpose: To evaluate the effect of image compression of spectral-domain optical coherence tomography (OCT) images in the examination of eyes with exudative age-related macular degeneration (AMD).

Methods: Thirty eyes from 30 patients who were diagnosed with exudative AMD were included in this retrospective observational case series. The horizontal OCT scans centered at the center of the fovea were conducted using spectral-domain OCT. The images were exported to Tag Image File Format (TIFF) and 100, 75, 50, 25 and 10% quality of Joint Photographic Experts Group (JPEG) format. OCT images were taken before and after intravitreal ranibizumab injections, and after relapse. The prevalence of subretinal and intraretinal fluids was determined. Differences in choroidal thickness between the TIFF and JPEG images were compared with the intra-observer variability.

Results: The prevalence of subretinal and intraretinal fluids was comparable regardless of the degree of compression. However, the chorio-scleral interface was not clearly identified in many images with a high degree of compression. In images with 25 and 10% quality of JPEG, the difference in choroidal thickness between the TIFF images and the respective JPEG images was significantly greater than the intra-observer variability of the TIFF images (P=0.029 and P=0.024, respectively).

Conclusions: In OCT images of eyes with AMD, 50% of the quality of the JPEG format would be an optimal degree of compression for efficient data storage and transfer without sacrificing image quality.Eye advance online publication, 2 May 2014; doi:10.1038/eye.2014.102.

PMID: 24788012 [PubMed - as supplied by publisher]

Exp Eye Res. 2014 Apr 25. pii: S0014-4835(14)00108-0. doi: 10.1016/j.exer.2014.04.012. [Epub ahead of print]

Hyperglycemia promotes vasculogenesis in choroidal neovascularization in diabetic mice by stimulating VEGF and SDF-1 expression in retinal pigment epithelial cells.

Cai Y, Li X, Wang YS, Shi YY, Ye Z, Yang GD, Dou GR, Hou HY, Yang N, Cao XR, Lu ZF.

Abstract: To investigate the influence of hyperglycemia on the severity of choroidal neovascularization (CNV) in diabetic mice, especially the involvement of bone marrow-derived cells (BMCs) and underlying

molecular mechanisms. The mice were randomly divided into control group, diabetes group and diabetes treated with insulin group, which were laser treated to induce CNV. The CNV severity was evaluated by fundus fluorescein angiography, HE staining and choroidal flatmount. The BMCs recruitment and differentiation in CNV were examined in GFP chimeric mice by choroidal flatmount and immunofluorescence. The bone marrow-derived mesenchymal stem cells (BMSCs) recruitment and migration were tested in vivo and in vitro. VEGF and SDF-1 production in vivo and in vitro were tested by realtime PCR and ELISA. The CNV severity and expression of VEGF and SDF-1 were enhanced in DM mice compared with control mice and that insulin treatment decreased CNV severity in DM mice. The DM mice demonstrated more BMCs and bone marrow-derived mesenchymal stem cells (BMSCs) recruited and incorporated into CNV, increased ratio of BMCs expressing endothelial cell marker or macrophage marker, and upregulated expression of VEGF and SDF-1 in CNV. Human BMSCs migration and expression of VEGF and SDF-1 in retinal pigment epithelial (RPE) cells increased when cultured under high glucose. This study suggested that hyperglycemia enhanced the expression of VEGF and SDF-1 in RPE cells, and promoted recruitment and incorporation of BMCs and affected differentiation of BMCs in CNV, which led to more severe CNV in diabetic mice.

PMID: 24780853 [PubMed - as supplied by publisher]

J Control Release. 2014 Apr 25. pii: S0168-3659(14)00246-6. doi: 10.1016/j.jconrel.2014.04.028. [Epub ahead of print]

Protein polymer nanoparticles engineered as chaperones protect against apoptosis in human retinal pigment epithelial cells.

Wang W, Sreekumar PG, Valluripalli V, Shi P, Wang J, Lin YA, Cui H, Kannan R, Hinton DR, Mackay JA.

Abstract: αB-crystallin is a protein chaperone with anti-apoptotic and anti-inflammatory activity that is apically secreted in exosomes by polarized human retinal pigment epithelium. A 20 amino acid mini-peptide derived from residues 73-92 of αB-crystallin protects human retinal pigment epithelial (RPE) cells from oxidative stress, a process involved in the progression of age related macular degeneration (AMD). Unfortunately, due to its small size, its development as a therapeutic requires a robust controlled release system. To achieve this goal, the αB-crystallin peptide was re-engineered into a protein polymer nanoparticle/macromolecule with the purpose of increasing the hydrodynamic radius/molecular weight and enhancing potency via multivalency or an extended retention time. The peptide was recombinantly fused with two high molecular weight (~40 kD) protein polymers inspired by human tropoelastin. These elastin-like -polypeptides (ELPs) include: i) a soluble peptide called S96; and ii) a diblock copolymer called SI that assembles multivalent nanoparticles at physiological temperature. Fusion proteins, cryS96 and crySI, were found to reduce aggregation of alcohol dehydrogenase and insulin, which demonstrates that ELP fusion did not diminish chaperone activity. Next their interaction with RPE cells was evaluated under oxidative stress. Unexpectedly, H2O2-induced stress dramatically enhanced cellular uptake and nuclear localization of both cryS96 and crySI ELPs. Accompanying uptake, both fusion proteins protected RPE cells from apoptosis, as indicated by reduced caspase 3 activation and TUNEL staining. This study demonstrates the in vitro feasibility of modulating the hydrodynamic radius for small peptide chaperones by seamless fusion with protein polymers; furthermore, they may have therapeutic applications in diseases associated with oxidative stress, such as AMD.

PMID: 24780268 [PubMed - as supplied by publisher]

J Nanopart Res. 2013 Dec 1;15(12):2126.

Titanium-doped cerium oxide nanoparticles protect cells from hydrogen peroxide-induced apoptosis.

Clark A, Zhu A, Petty HR.

Abstract: To develop new nanoparticle materials possessing anti-oxidative capacity with improved physical

characteristics, we have studied titanium-doped cerium oxide (CeTiO2) nanoparticles. CeTiO2 nanoparticles had a mode diameter of 15-20 nm. These nanoparticles demonstrated catalase activity, and did not promote the activation of hemolytic or cytolytic pathways in living cells. Using surface plasmon resonance enhanced microscopy, we find that these nanoparticles associate with cells. Transmission electron microscopy studies demonstrated that these nanoparticles accumulate within the vacuolar compartment of cells. Importantly, CeTiO2 nanoparticles decrease hydrogen peroxide-mediated apoptosis of cells as judged by the reduced cleavage of a caspase 3-sensitive label. CeTiO2 nanoparticles may contribute to deflecting tissue damage in a broad spectrum of oxidant-mediated diseases, such as macular degeneration and Alzheimer's disease.

PMID: 24791147 [PubMed]

Epidemiology

Eye (Lond). 2014 May 2. doi: 10.1038/eye.2014.103. [Epub ahead of print]

How many people in England and Wales are registered partially sighted or blind because of age-related macular degeneration?

Rees A, Zekite A, Bunce C, Patel PJ.

Purpose: The purpose of the study was to determine what proportion of new certifications between 1 April 2007 and 31 March 2008 could be attributed to age-related macular degeneration (AMD) and to describe the AMD-certified population in England and Wales.

Methods: An electronic version of the Certificate of Vision Impairment form (CVI), the ECVI, was used at the certifications office to transfer information from the paper-based certificates into a database. The electronic certifications data set was queried for all certificates completed between 1 April 2007 and 31 March 2008 with the main cause of certifiable visual loss being AMD or with the main cause of certifiable visual loss being multiple pathology but a contributory cause being AMD. The electronic data set was adapted so that a distinction could be made between geographic atrophy (GA) and neovascular AMD (nAMD).

Results: The Certifications Office received 23 185 CVIs between April 2007 and March 2008, of whom 9823 (42%) were people registered severely sight impaired (SSI) and 12 607 (52%) were certified as sight impaired (SI). AMD contributed to 13 000 causes of registration on the CVI forms during this period and was the main cause in 11 015 people. In these 11 015 people, GA accounted for 49.3%, nAMD 35.1%, and AMD not specified 15.7%.

Conclusions: The data in this report provide detailed information on CVI registration due to AMD before the widespread adoption of ranibizumab therapy in NHS practice and provide an insight into the burden of vision loss due to AMD at a time of great change in the management of nAMD.

PMID: 24788009 [PubMed - as supplied by publisher]

Ophthalmology. 2014 Apr 23. pii: S0161-6420(14)00237-1. doi: 10.1016/j.ophtha.2014.03.013. [Epub ahead of print]

Five-Year Incidence, Progression, and Risk Factors for Age-related Macular Degeneration: The Age, Gene/Environment Susceptibility Study.

Jonasson F, Fisher DE, Eiriksdottir G, Sigurdsson S, Klein R, Launer LJ, Harris T, Gudnason V, Cotch MF.

OBJECTIVE: To investigate the incidence and progression of age-related macular degeneration (AMD) and associated risk factors.

DESIGN: Population-based, prospective, cohort study.

PARTICIPANTS: We included 2868 participants from the Age Gene/Environment Susceptibility-Reykjavik Study with retinal data at baseline and 5-year follow-up.

METHODS: Digital macular photographs were graded for presence of AMD. Participants completed a questionnaire and extensive clinical battery. Biomarkers were assessed. Risk factors for AMD were analyzed using multivariate regression analysis with odds ratios (ORs) and 95% CIs.

MAIN OUTCOME MEASURES: We assessed AMD, defined as early or late.

RESULTS: Among 2196 participants free of AMD at baseline, 14.9% developed incident AMD. In multivariate models, incident AMD was significantly associated with age (OR per year, 1.14; 95% CI, 1.11-1.17), current smoking (OR, 2.07; 95% CI, 1.38-3.11), former smoking (OR, 1.36; 95% CI, 1.04-1.79), plasma high-density lipoprotein (HDL) cholesterol level (OR, 1.62 per mmol/L; 95% CI, 1.19-2.22), and body mass index (BMI; OR, 1.04 per kg/m2; 95% CI, 1.01-1.07). Among 563 participants with early AMD at baseline, 22.7% progressed to late AMD (11.0% pure geographic atrophy [GA] and 11.7% exudative AMD). On multivariate analyses, age was significantly associated with progression to GA (OR 1.14; 95% CI, 1.07-1.21) and exudative AMD (OR, 1.08; 95% CI, 1.01-1.14). Adjusting for age, female sex was associated with exudative AMD (OR, 2.10; 95% CI, 1.10-3.98) and plasma HDL cholesterol with GA (OR, 2.03 per mmol/L; 95% CI, 1.02-4.05).

CONCLUSIONS: By age 85, 57.4% of participants had signs of AMD. Age, smoking, plasma HDL cholesterol, BMI, and female sex are associated with AMD. Elevated HDL cholesterol is associated with GA development.

PMID: 24768241 [PubMed - as supplied by publisher]

Expert Opin Drug Saf. 2014 Apr 30. [Epub ahead of print]

Aspirin and age-related macular degeneration: positives versus negatives.

Nowak JZ.

Abstract: The anti-inflammatory, analgesic, antipyretic and antithrombotic activities of aspirin confer its wide therapeutic application. The three former activities require higher doses of aspirin, whereas the latter can be achieved through a lower, thus safer dose of the drug. Low-dose, long-term aspirin is used as an antithrombotic therapy to prevent cardiovascular disease. Such therapy is used by millions of people worldwide, including those suffering from age-related macular degeneration (AMD); thus, questions have arisen as to whether such treatment has any impact on the development and course of AMD. This editorial addresses the important issue of possible beneficial and adverse effects of long-term, low-dose aspirin treatment of AMD patients. Special emphasis is given to the ability of aspirin to acetylate cyclooxygenases (especially COX-2) and thus to initiate a biochemical pathway leading to the generation of anti-inflammatory pro-resolving mediators synthesized from both ω-3 and ω-6 long-chain polyunsaturated fatty acids. Such mediators (e.g., resolvins, lipoxins) may be of therapeutic value in retarding the development of dry form AMD.

PMID: 24783984 [PubMed - as supplied by publisher]

Expert Opin Drug Saf. 2014 Apr 29. [Epub ahead of print]

Does aspirin increase the risk of age-related macular degeneration?

Chong EW, Guymer RH, Robman LD.

Abstract: This commentary on the review by Christen and Chew discusses the controversy surrounding aspirin use and its association with age-related macular degeneration (AMD). We address the strength of evidence between low-dose aspirin use and AMD and also discuss the risks and benefits of aspirin use in primary versus secondary prevention of cardiovascular diseases in these cases. We also highlight an

ongoing randomized controlled trial in this area.

PMID: 24773275 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2014 Apr 29. doi: 10.1136/bjophthalmol-2014-305318. [Epub ahead of print]

Polypoidal choroidal vasculopathy in Caucasian patients with presumed age-related macular degeneration.

Tan CS, Ngo WK, Cheong KX, Lim TH.

PMID: 24782471 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2014 Apr 29. pii: iovs.14-14059v1. doi: 10.1167/iovs.14-14059. [Epub ahead of print]

Choroidal Neovascularization in Eyes with Choroidal Vascular Hyperpermeability.

Miyake M, Tsujikawa A, Yamashiro K, Ooto S, Oishi A, Nakata I, Tamura H, Matsuda F, Yoshimura N.

Purpose: To describe the clinical and genetic characteristics of choroidal neovascularization (CNV) in eyes with choroidal vascular hyperpermeability (CVH).

Methods: This cross-sectional study consisted of 438 consecutive patients who underwent fluorescein and indocyanine green angiography for macular disease. We used the genotypes of 1,576 age-related macular degeneration (AMD) cases and 3,248 general population controls as reference groups for genetic association analyses.

Results: Of 871 eyes (438 patients) examined, CVH was found in 227 eyes (26.1%). Of these 227 eyes, 52 (22.6%) had CNV in the macular area. The proportion of patients with drusen and the choroidal thickness were not different between eyes with and without CNV, after adjusting for age (P = 0.21, and 0.95). Of the 52 eyes with CNV, 51 had type 1 CNV and only one eye had pure type 2 CNV. Of the 51 eyes with type 1 CNV, polypoidal lesions were observed in 17 eyes (33.3%). Genotype distributions of ARMS2 (A69S) and CFH (I62V) in patients with CVH and type 1 CNV significantly differed from those of AMD cases (P = 0.0014 and 0.0098, respectively), but not from general population controls (P = 0.33 and 0.82; statistical power of 88.5% and 72.9%, respectively).

Conclusions: In patients with CVH, type 1 CNV may occur frequently and sometimes accompanies type 2 CNV or polypoidal lesions. In terms of ARMS2 and CFH, genetic background of patients with CVH and type 1 CNV was different from those with AMD, but rather similar to the general Japanese population.

PMID: 24781946 [PubMed - as supplied by publisher]

Genetics

Annu Rev Genomics Hum Genet. 2014 Apr 16. [Epub ahead of print]

Age-Related Macular Degeneration: Genetics and Biology Coming Together.

Fritsche LG, Fariss RN, Stambolian D, Abecasis GR, Curcio CA, Swaroop A.

Abstract: Genetic and genomic studies have enhanced our understanding of complex neurodegenerative diseases that exert a devastating impact on individuals and society. One such disease, age-related macular degeneration (AMD), is a major cause of progressive and debilitating visual impairment. Since the pioneering discovery in 2005 of complement factor H (CFH) as a major AMD susceptibility gene, extensive investigations have confirmed 19 additional genetic risk loci, and more are anticipated. In addition to

common variants identified by now-conventional genome-wide association studies, targeted genomic sequencing and exome-chip analyses are uncovering rare variant alleles of high impact. Here, we provide a critical review of the ongoing genetic studies and of common and rare risk variants at a total of 20 susceptibility loci, which together explain 40-60% of the disease heritability but provide limited power for diagnostic testing of disease risk. Identification of these susceptibility loci has begun to untangle the complex biological pathways underlying AMD pathophysiology, pointing to new testable paradigms for treatment. Expected final online publication date for the Annual Review of Genomics and Human Genetics Volume 15 is September 01, 2014. Please see http://www.annualreviews.org/catalog/pubdates.aspx for revised estimates.

PMID: 24773320 [PubMed - as supplied by publisher]

PLoS One. 2014 Apr 29;9(4):e95900. doi: 10.1371/journal.pone.0095900. eCollection 2014.

Interleukin-17 retinotoxicity is prevented by gene transfer of a soluble interleukin-17 receptor acting as a cytokine blocker: implications for age-related macular degeneration.

Ardeljan D, Wang Y, Park S, Shen D, Chu XK, Yu CR, Abu-Asab M, Tuo J, Eberhart CG, Olsen TW, Mullins RF, White G, Wadsworth S, Scaria A, Chan CC.

Abstract: Age-related macular degeneration (AMD) is a common yet complex retinal degeneration that causes irreversible central blindness in the elderly. Pathology is widely believed to follow loss of retinal pigment epithelium (RPE) and photoreceptor degeneration. Here we report aberrant expression of interleukin-17A (IL17A) and the receptor IL17RC in the macula of AMD patients. In vitro, IL17A induces RPE cell death characterized by the accumulation of cytoplasmic lipids and autophagosomes with subsequent activation of pro-apoptotic Caspase-3 and Caspase-9. This pathology is reduced by siRNA knockdown of IL17RC. IL17-dependent retinal degeneration in a mouse model of focal retinal degeneration can be prevented by gene therapy with adeno-associated virus vector encoding soluble IL17 receptor. This intervention rescues RPE and photoreceptors in a MAPK-dependent process. The IL17 pathway plays a key role in RPE and photoreceptor degeneration and could hold therapeutic potential in AMD.

PMID: 24780906 [PubMed - in process]

Diet, lifestyle & low vision

J Clin Exp Ophthalmol. 2014 Jan 22;5(1):320.

Improved Adherence to Vision Self-monitoring with the Vision and Memory Stimulating (VMS) Journal for Non-neovascular Age-related Macular Degeneration during a Randomized Controlled Trial.

Bittner AK, Torr-Brown S, Arnold E, Nwankwo A, Beaton P, Rampat R, Dagnelie G, Roser M.

OBJECTIVE: An educational, interactive journal [Vision and Memory Stimulating (VMS) journal] was developed to boost patient confidence and promote long-term adherence with weekly vision self-monitoring in age-related macular degeneration (AMD) patients at risk for vision loss from new-onset neovascularization.

METHODS: In a multicenter randomized controlled trial, 198 subjects with intermediate stage, non-neovascular AMD received the VMS journal or followed usual care (e.g. their doctor's instructions for vision monitoring; Amsler grid). At 6 and/or 12 months post-enrollment, 157 subjects completed a questionnaire on vision self-monitoring.

RESULTS: At 6 and 12 months, respectively, 85% and 80% of the VMS journal subjects reported vision monitoring at least weekly, which represent statistically significant 7.1 and 4.2 times greater odds than the 50% of controls who monitored weekly at both follow-up times ($p<0.001$). At 6 and 12 months, respectively,

29% and 25% of controls indicated that they had not checked their vision in the past 6 months, while only 1.5% and 5% of the VMS journal subjects reported no vision self-monitoring. At 6 and 12 months, respectively, only 15% and 13% of the VMS journal subjects vs. 53% and 44% of the controls reported that they did not feel confident that they were taking care of their sight by self-monitoring ($p<0.001$). Usual care controls had statistically significant 6.7 and 5.0 times greater odds of reporting non-confidence at 6 and 12 months, respectively. There was no statistically significant change in weekly vs. less frequent self-monitoring between the groups ($p=0.68$), with 81% of all subjects reporting no change in frequency between 6 and 12 months.

CONCLUSIONS: These findings support the efficacy of the VMS journal for increasing vision self-monitoring adherence and confidence, in addition to promoting persistence in weekly monitoring over the course of a year in AMD subjects at risk for exudative retinal changes.

PMID: 24791222 [PubMed]

J Optom. 2014 Apr-Jun;7(2):100-5. doi: 10.1016/j.optom.2013.12.003. Epub 2014 Jan 24.

Residual stereopsis in age-related macular degeneration patients and its impact on vision-related abilities: A pilot study.

Cao KY, Markowitz SN.

OBJECTIVE: To determine the effect of residual stereopsis on vision-related abilities of low vision (LV) patients with age-related macular degeneration (AMD).

METHODS: Prospective non-randomized observational case series. Inclusion criteria included documented AMD, LV with best corrected visual acuity (BCVA) of 20/50-20/400 in the better eye, and ages between 50 and 90 years. Stereoacuity was measured using the near Frisby Stereotest. Vision related abilities were documented with the VA LV VFQ-48 questionnaire.

RESULTS: Twenty-seven subjects with mean age of 84±6 years old were recruited, of which 59.3% (16/27) were female. 59.3% (16/27) of the subjects were not able to see any stereoacuity plate, 25.9% (7/27) had stereoacuity of 340s of arc (SOA), 11.1% (3/27) had stereoacuity of 170 SOA and 3.7% (1/27) had stereoacuity of 85 SOA. The mean Overall Functional Visual Abilities (OFVA) score was significantly higher in those with stereopsis (2.25±0.99) than those without stereopsis (1.50±0.92) ($P=0.028$).

CONCLUSIONS: LV patients with stereopsis have better OFVA than those without. Stereopsis should be considered as a component of LV rehabilitation and considered as an outcome measure in research and clinical practice.

PMID: 24766867 [PubMed - in process]