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Drug treatment

Ophthalmology. 2015 Sep 14. [Epub ahead of print]

Association of Baseline Characteristics and Early Vision Response with 2-Year Vision Outcomes in the Comparison of AMD Treatments Trials (CATT).

Ying GS, Maguire MG, Daniel E, Ferris FL, Jaffe GJ, Grunwald JE, Toth CA, Huang J, Martin DF; Comparison of Age-Related Macular Degeneration Treatments Trials (CATT) Research Group.

PURPOSE: To evaluate the association of baseline characteristics and early visual acuity (VA) response with visual outcomes at years 1 or 2 in the Comparison of Age-Related Macular Degeneration (AMD) Treatments Trials (CATT).

DESIGN: Secondary analysis of CATT.

PARTICIPANTS: The 1185 CATT participants with baseline VA of 20/25 to 20/320.

METHODS: Participants were assigned to ranibizumab or bevacizumab and to 1 of 3 dosing regimens. Associations of baseline characteristics and early VA response (week 4 or 12) with VA response at years 1 or 2 were assessed by R2 from linear regression analyses. Patients who had a poor initial response (VA 20/40 or worse with persistent fluid and without ≥1-line VA gain) were defined as candidates for changing treatment.

MAIN OUTCOME MEASURES: Visual acuity change from baseline.

RESULTS: Statistically significant ($P < 0.05$) baseline predictors for less VA gain at year 2 were older age, VA of 20/40 or better, larger choroidal neovascularization area, presence of geographic atrophy, total foveal thickness ≤325 μm or ≥425 μm, and elevation of retinal pigment epithelium. Among 176 eyes gaining ≥3 lines at week 12, 78% had a ≥3-line gain at year 2, whereas among 113 eyes losing ≥1 line at week 12, 27% improved to a ≥1-line gain at year 2. Visual acuity response at week 12 was more predictive of VA response at year 2 ($R2 = 0.30$) than VA response at week 4 ($R2 = 0.17$) and baseline predictors ($R2 = 0.13$; $P < 0.0001$). Among 126 candidates for changing treatment drug at week 12, mean VA improved by 2.8 letters ($P = 0.050$), mean total retinal thickness decreased 53 μm ($P < 0.0001$), and fluid resolved in 33% ($P < 0.0001$) between week 12 and year 1 with continued use of the same drug and regimen. Similar improvements were observed among 83 candidates for changing drugs at week 24.

CONCLUSIONS: Visual acuity response at week 12 is more predictive of 2-year vision outcomes than either several baseline characteristics or week 4 response. Eyes with poor initial response may benefit from continued treatment without switching to another drug.

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Int J Clin Exp Med. 2015 Jul 15;8(7):11572-8. eCollection 2015.

Intravitreal ranibizumab therapy for retinal arterial macroaneurysm.

Erol MK, Dogan B, Coban DT, Toslak D, Cengiz A, Ozel D.

AIM: To evaluate the anatomic and functional results of intravitreal ranibizumab injection for treatment of symptomatic retinal arterial macroaneurysm (RAM).

MATERIALS AND METHODS: A series of seven patients (seven eyes) who had been diagnosed with symptomatic RAM were assessed by comprehensive ophthalmologic examination, fluorescein angiography (FA), optical coherence tomography (OCT), and indocyanine green angiography (ICGA). All patients were treated by intravitreal ranibizumab injection within one week of diagnosis and retreated upon evidence of persistent serous detachment or hemorrhage involving the macula on OCT. Anatomical recovery was examined by FA, OCT, and ICGA. Best-corrected visual acuity (BCVA) and central macular thickness (CMT) were evaluated using the Snellen chart and optical coherence tomography, respectively, at baseline; at 1, 3, and 6 months; and at the final visit. The BCVA and CMT values at baseline and the final visit were compared using the Wilcoxon signed rank test and determination of logarithm of the minimal angle of resolution (logMAR) of BCVA value.

RESULTS: Over a mean follow-up period of 10.86 ± 5.4 months, significant visual and anatomical recovery was observed, with visual acuity improving by three or more lines in all seven patients. The mean logMAR of BCVA improved from 1.09 ± 0.60 to 0.16 ± 0.16 (p = 0.018) and mean CMT decreased from 427.5 ± 132.4 μm to 208.7 ± 23.1 μm (P = 0.018). No complications were observed with intravitreal ranibizumab injection.

CONCLUSION: İntravitreal ranibizumab is an effective therapy for symptomatic RAM, improving BCVA and decreasing CMT.

KEYWORDS: Anti-vascular endothelial growth factor; best-corrected visual acuity; central macular thickness; ranibizumab; retinal arterial macroaneurysm

PMID: 26379984 [PubMed] PMCID: PMC4565367

PLoS One. 2015 Sep 14;10(9):e0137866. eCollection 2015.

Treatment as Required versus Regular Monthly Treatment in the Management of Neovascular Age-Related Macular Degeneration: A Systematic Review and Meta-Analysis.

Schmucker CM, Rücker G, Sommer H, Virgili G, Loke YK, Oeller P, Agostini H, Ehlken C.

BACKGROUND: To investigate whether treatment as required 'pro re nata' (PRN) versus regular monthly treatment regimens lead to differences in outcomes in neovascular age-related macular degeneration (nAMD). Regular monthly administration of vascular endothelial growth factor (VEGF) inhibitors is an established gold standard treatment, but this approach is costly. Replacement of monthly by PRN treatment can only be justified if there is no difference in patient relevant outcomes.

METHODS: Systematic review and meta-analysis. The intervention was PRN treatment and the comparator was monthly treatment with VEGF-inhibitors. Four bibliographic databases were searched for randomised controlled trials comparing both treatment regimens directly (head-to-head studies). The last literature search was conducted in December 2014. Risk of bias assessment was performed after the Cochrane Handbook for Systematic Reviews of Interventions.

FINDINGS: We included 3 head-to-head studies (6 reports) involving more than 2000 patients. After 2 years, the weighted mean difference in best corrected visual acuity (BCVA) was 1.9 (95% CI 0.5 to 3.3) ETDRS letters in favour of monthly treatment. Systemic adverse events were higher in PRN treated patients, but these differences were not statistically significant. After 2 years, the total number of intravitreal injections required by the patients in the PRN arms were 8.4 (95% CI 7.9 to 8.9) fewer than those having monthly treatment. The studies were considered to have a moderate risk of bias.

CONCLUSIONS: PRN treatment resulted in minor but statistically significant decrease in mean BCVA which may not be clinically meaningful. There is a small increase in risk of systemic adverse events for PRN treated patients. Overall, the results indicate that an individualized treatment approach with anti-VEGF using visual acuity and OCT-guided re-treatment criteria may be appropriate for most patients with nAMD.

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Exp Eye Res. 2015 Sep 11. [Epub ahead of print]

Topical Application of a G-Quartet Aptamer Targeting Nucleolin Attenuates Choroidal Neovascularization in a Model of Age-Related Macular Degeneration.

Leaderer D, Cashman SM, Kumar-Singh R.

Abstract: Choroidal neovascularization (CNV) associated with the 'wet' form of age related macular degeneration (AMD) is one of the most common causes of central vision loss among the elderly. The 'wet' form of AMD is currently treated by intravitreal delivery of anti-VEGF agents. However, intravitreal injections are associated with complications and long-term inhibition of VEGF leads to macular atrophy. Thus, there is currently an unmet need for the development of therapies for CNV that target molecules other than VEGF. Here, we describe nucleolin as a novel target for the 'wet' form of AMD. Nucleolin was found on the surface of endothelial cells that migrate from the choroid into the subretinal space in the laser-induced model of 'wet' AMD. AS1411 is a previously described G-quartet oligonucleotide that has been shown to bind nucleolin. We found that AS1411 inhibited the formation of tubes by human umbilical vein endothelial cells (HUVECs) by approximately 27.4% in vitro. AS1411 co-localized with the site of laser induced CNV in vivo. Intravitreally injected AS1411 inhibited laser-induced CNV by 37.6% and attenuated infiltration of macrophages by 40.3%. Finally, topical application of AS1411 led to a 43.4% reduction in CNV. Our observations have potential implications for the development of therapies for CNV and specifically for the 'wet' form of AMD.

PMID: 26368850 [PubMed - as supplied by publisher]

Arq Bras Oftalmol. 2015 Aug;78(4):257-9. doi: 10.5935/0004-2749.20150067.

Drastic effect of ranibizumab on choroidal neovascularization in idiopathic angioid streaks.

Yolcu U, Gundogan FC, Diner O.

Abstract: A 28-year-old man presented with bilateral vision loss. His best-corrected visual acuity (BCVA) was 0.3 in the right eye (OD) and 0.6 in the left eye (OS). Fundoscopy and fluorescein angiography showed angioid streaks encircling the optic discs of both eyes (OU). Spectral Domain Optical Coherence Tomography (SD-OCT) showed bilateral macular serous detachment. Systemic and ocular screening tests showed no specific cause for the angioid streaks. The patient had previously received pegaptanib sodium injection on three occasions, photodynamic therapy in OS, and no treatment in OD. Upon intravitreal injection of ranibizumab (twice in OU), subretinal fluid was nearly eliminated in OU. BCVA increased to 0.6 in OD and 0.9 in OS, and remained improved until 6 months after treatment.

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Graefes Arch Clin Exp Ophthalmol. 2015 Sep 19. [Epub ahead of print]

Polypoidal choroidal vasculopathy in patients aged less than 50 years: characteristics and 6-month treatment outcome.

Chang YS, Kim JH, Kim JW, Lee TG, Kim CG, Cho SW.

PURPOSE: To investigate the characteristics and 6-month treatment outcome of polypoidal choroidal vasculopathy (PCV) in patients aged <50 years.

METHODS: This retrospective study included 22 eyes from 22 patients who were <50 years old and had been diagnosed with treatment naïve PCV. Analyses of treatment outcome were performed in eyes treated with anti-vascular endothelial growth factor (VEGF) therapy. Eyes that exhibited submacular hemorrhage of ≥1 disc diameter and involving the fovea were included in the hemorrhage group. The remaining eyes were included in the no-hemorrhage group. The baseline best-corrected visual acuity (BCVA) was compared with that at 6 months within each group.

RESULTS: The mean age of the 22 patients was 46.5 ± 1.8 (range, 43-49) years. Submacular hemorrhage was noted in ten eyes (45.5 %). The presence of drusen was noted in one eye and pseudodrusen was not noted in any of the eyes included. Treatment outcome was analyzed in 18 eyes. A mean number of 2.9 ± 0.5 intravitreal anti-VEGF injections were administered during the 6-month follow-up period. In the no-hemorrhage group (n = 10), the BCVA at diagnosis and at 6 months was 0.55 ± 0.32 and 0.35 ± 0.22 respectively (P = 0.011). In the hemorrhage group (n = 8), the values were 0.99 ± 0.45 and 0.74 ± 0.63 respectively (P = 0.128).

CONCLUSIONS: A relatively high proportion of young PCV patients exhibited submacular hemorrhage at initial presentation. In those without submacular hemorrhage, intravitreal anti-VEGF therapy was found to be beneficial.

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J Chin Med Assoc. 2015 Sep 14. [Epub ahead of print]

Nanotechnology-based drug delivery treatments and specific targeting therapy for age-related macular degeneration.

Lin TC, Hung KH, Peng CH, Liu JH, Woung LC, Tsai CY, Chen SJ, Chen YT, Hsu CC.

Abstract: Nanoparticles combined with cells, drugs, and specially designed genes provide improved therapeutic efficacy in studies and clinical setting, demonstrating a new era of treatment strategy, especially in retinal diseases. Nanotechnology-based drugs can provide an essential platform for sustaining, releasing and a specific targeting design to treat retinal diseases. Poly-lactic-co-glycolic acid is the most widely used biocompatible and biodegradable polymer approved by the Food and Drug Administration. Many studies have attempted to develop special devices for delivering small-molecule drugs, proteins, and other macromolecules consistently and slowly. In this article, we first review current progress in the treatment of age-related macular degeneration. Then, we discuss the function of vascular endothelial growth factor (VEGF) and the pharmacological effects of anti-VEGF-A antibodies and soluble or modified VEGF receptors. Lastly, we summarize the combination of antiangiogenic therapy and nanomedicines, and review current potential targeting therapy in age-related macular degeneration.

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Other treatment & diagnosis

Retina. 2015 Sep 16. [Epub ahead of print]

TYPE 2 (SUBRETINAL) NEOVASCULARIZATION IN AGE-RELATED MACULAR DEGENERATION ASSOCIATED WITH PURE RETICULAR PSEUDODRUSEN PHENOTYPE.

Naysan J, Jung JJ, Dansingani KK, Balaratnasingam C, Freund KB.

PURPOSE: To report the association of pure type 2 neovascularization (NV) in age-related macular degeneration occurring almost exclusively in patients with reticular pseudodrusen.

METHODS: An observational retrospective cohort study of all eyes receiving antivascular endothelial growth factor therapy for newly diagnosed neovascular age-related macular degeneration by a single practitioner over a 6-year period. Only patients with treatment-naive, pure type 2 NV who also had either

pre-neovascular imaging of the study eye or imaging of a nonneovascular fellow eye available to determine baseline characteristics including drusen type and choroidal thickness were incuded.

RESULTS: Of 694 patients treated for neovascular age-related macular degeneration, only 8 met the inclusion criteria with pure type 2 NV. Of these, 7 (88%) had exclusively reticular pseudodrusen (5 in the nonneovascular fellow eye, 2 in the study eye before developing NV). Six (75%) patients in the affected neovascular eye and 6 (75%) in the fellow nonneovascular eye had choroidal thickness <120 μm. Mean follow-up was 46 months (range, 3.0-63.3). Best-corrected vision improved from 20/89 (range, 20/30-20/796) at baseline to 20/60 (range, 20/20-20/399) at last follow-up.

CONCLUSION: Pure type 2 NV is rare in age-related macular degeneration, occurring almost exclusively in patients with reticular pseudodrusen and thin choroids.

PMID: 26383711 [PubMed - as supplied by publisher]

Retina. 2015 Sep 16. [Epub ahead of print]

EVALUATION OF A TELEMEDICINE MODEL TO FOLLOW UP PATIENTS WITH EXUDATIVE AGE-RELATED MACULAR DEGENERATION.

Andonegui J, Aliseda D, Serrano L, Eguzkiza A, Arruti N, Arias L, Alcaine A.

PURPOSE: To evaluate a telemedicine model to follow up patients with exudative age-related macular degeneration and compare the time spent using this model with the time spent conducting office examinations.

METHODS: Results of office and telemedicine evaluations were compared to determine whether patients with exudative age-related macular degeneration previously treated with intravitreal injections needed additional treatment. The office examinations included visual acuity measurement, fundus examination, and optical coherence tomography. The telemedicine evaluation included evaluation of retinography images, optical coherence tomography images, and visual acuity data obtained in the office. We also measured the time spent on telemedicine evaluations and compared it with the time spent on office examinations.

RESULTS: Twenty-one patients were included. A comparison of office and remote diagnostic decisions showed the same results in 181 cases. Among the 20 remaining patients and considering office diagnostic decisions as the gold standard, 17 (8%) patients had false-positive diagnoses and 3 (1%) had false-negative diagnoses. The sensitivity and specificity of the telemedicine evaluations were 96% and 85%, respectively. The average time spent on remote evaluations was 1 minute 21 seconds compared with 10 minutes spent on office examination ($P < 0.001$).

CONCLUSION: The telemedicine model can be a useful alternative for following up patients with age-related macular degeneration.

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Med Sci Monit. 2015 Sep 14;21:2734-42.

Serum MicroRNAs as Potential Biomarkers of AMD.

Szemraj M, Bielecka-Kowalska A, Oszajca K, Krajewska M, Goś R, Jurowski P, Kowalski M, Szemraj J.

BACKGROUND: Age-related macular degeneration (AMD) is a major cause of blindness worldwide. Circulating microRNAs (miRNAs) in serum have emerged as novel candidate biomarkers for many diseases. The aim of the present study was to identify a serum microRNA (miRNA) expression profile specific for dry and wet forms of AMD.

MATERIAL AND METHODS: Serum miRNA expression was first screened using TaqMan® Human MicroRNA Array A (Applied Biosystems). An extensive, self-validated, individual, quantitative RT-PCR (qRT-PCR) study was then performed on a cohort of 300 AMD patients (150 wet form and 150 dry form) and

200 controls. The Mann-Whitney U test and nonparametric Spearman's rank correlation coefficient were used for statistical analysis.

RESULTS: miRNA expression analysis revealed increased expression of miR661 and miR3121 in serum of patients with dry AMD and miR4258, miR889, and Let7 in patients with wet form. Expression of analyzed miRNA was not observed or remained at low level in controls.

CONCLUSIONS: Differences in miRNA serum profile exist between patients with wet and dry form of AMD, which indicates miRNAs as potential biomarkers of AMD. Further studies should be performed to confirm its significance in clinical practice.

PMID: 26366973 [PubMed - in process]

Clin Ophthalmol. 2015 Sep 3;9:1519-22. eCollection 2015.

Comparative analysis of the development of collateral vessels in macular edema due to branch retinal vein occlusion following grid laser or ranibizumab treatment.

Kokolaki AE, Georgalas I, Koutsandrea C, Kotsolis A, Niskopoulou M, Ladas I.

PURPOSE: To evaluate the differences in the development of collateral vessels in patients with macular edema due to branch retinal vein occlusion (BRVO) after treatment with either grid laser or ranibizumab (RNB).

METHODS: Comparative study including patients with macular edema due to acute BRVO and best-corrected visual acuity (BCVA) between 20/40 and 20/200. The sample was divided into two groups according to the treatment applied: laser group, including eyes treated with Argon laser when retinal hemorrhages were sufficiently absorbed to perform the treatment, and RNB group, including patients treated initially with one monthly intravitreal injection for a period of 3 months of RNB and more injections according to need thereafter. Before treatment patients in both groups, received a complete ophthalmic examination, including BCVA, fundus examination, optical coherence tomography, fundus color photography, and fundus fluorescein angiography (FA). This same protocol of examination was repeated in every visit after treatment, except FA that was only repeated every 3 months. The detection of the collateral vessels was done by two experienced examiners based on the analysis of the early phase of the FA. If there was a discrepancy in their judgment, the criterion of a third examiner evaluating the FA was considered.

RESULTS: Mean baseline BCVA was 0.86±0.26 and 0.82±0.25 (logMAR [logarithm of the minimum angle of resolution]) in the RNB and laser groups, respectively (P=0.83). At the end of the follow-up, mean BCVA was 0.38±0.18 and 0.64±0.33 (logMAR) in the RNB and laser groups, respectively. The difference in the final BCVA between both groups was statistically significant (P=0.002). Collaterals developed in both groups; 66.67% of patients (14 out of 21 patients) developed collaterals at a mean time of 6.14±2.60 months after diagnosis in the RNB group, and 68.18% (16 out of 22 patients) developed collaterals in the laser group at a mean time of 6.2±1.97 months after diagnosis. No statistically significant differences between groups were found in the number of cases developing collateral vessels (P=1.00) as well as in the time required for such development (P=0.947).

CONCLUSION: The use of RNB for the treatment of macular edema due to BRVO does not seem to alter the development of collateral vessels. Future studies with larger samples are required to confirm these outcomes.

PMID: 26366053 [PubMed] PMCID: PMC4562744

Arq Bras Oftalmol. 2015 Aug;78(4):241-5.

Optical coherence tomography in patients undergoing cataract surgery.

Moreira Neto CA, Moreira Júnior CA, Moreira AT.

PURPOSE: To assess the ability of spectral domain optical coherence tomography (SD-OCT) to diagnose macular changes pre- and post-cataract surgery and to identify changes in central foveal thickness (CFT) relative to age, sex, and presence of concomitant ophthalmic pathologies, for a period of 6 months post-surgery.

METHODS: A prospective study of patients evaluated by SD-OCT within 5 h before surgery at 7, 30, 60, 90, and 180 days post-op, with respect to CFT and presence of maculopathy.

RESULTS: Ninety-eight eyes of 98 patients were evaluated, with the following mean results: age = 71.4 years, pre-op VA = 0.27 logMAR, and final VA = 0.73 logMAR. There were 21 eyes in patients with diabetes mellitus (DM) and 10 eyes with age-related macular degeneration (AMD), three with epiretinal membrane, and four with glaucoma. Sixty eyes had no other ophthalmic-related pathologies (NOO), and had a mean pre-op CFT of 222 μm, which progressively increased up to the 60thday post-op, reaching a mean of 227.2 μm. No pseudophakic cystoid macular edema was observed. The mean CFT was statistically significantly different ($p<0.001$) between NOO and diabetic patients from 30 days post-op. Four eyes presented with preoperative diagnosis of AMD as measured by ophthalmoscopy. After completion of the OCT, which was performed within 5 h before surgery, six additional patients were found to have AMD. Of the 98 total eyes, 10 were diagnosed with maculopathy only by OCT exam. Binocular indirect ophthalmoscopy (BIO) was unable to detect such changes.

CONCLUSION: OCT diagnosed preoperative maculopathies in 21.4% of the patients, and was more effective than BIO (11.2%). OCT showed a progressive increase in CFT in diabetics up to 180 days post-operatively, as well as greater CFT in male patients and patients older than 70 years.

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J Gene Med. 2015 Sep 15. [Epub ahead of print]

Adenovirus mediated delivery of factor H attenuates complement C3 induced pathology in the murine retina: a potential gene therapy for AMD.

Cashman SM, Gracias J, Adhi M, Kumar-Singh R.

BACKGROUND: Age related macular degeneration (AMD) is the most common cause of blindness in the elderly with no therapy available for 90% of patients. Recent genetic evidence implicates activation of complement in the pathogenesis of AMD. We have recently discovered that adenovirus (Ad) mediated expression of complement component C3 (AdCMVC3) in the murine retina recapitulates many of the pathological features found in human AMD. Utilizing a gene therapy approach, here we examine whether Ad mediated expression of complement Factor H (AdCAGfH) attenuates AdCMVC3-mediated retinal pathology.

METHODS: AdCMVC3 was co-injected with either AdCAGfH or a negative control virus expressing GFP (AdCMVGFP) into the subretinal space of adult mice. The resulting retinal pathology was analyzed by histology and immunocytochemistry and retinal function was quantified by electroretinography (ERG).

RESULTS: Morphological and functional analyses indicated that AdCMVC3 mediated retinal pathology could be attenuated by AdCAGfH. Specifically, endothelial cell proliferation was reduced by 91% and RPE atrophy could be attenuated by 69%. AdCAGfH injected eyes exhibited 90 to 150% greater A-wave and 120 to 180% greater B-wave amplitudes relative to control eyes. Immunocytochemical analysis of rhodopsin and RPE65 was consistent with the rescue of photoreceptors and RPE in AdCAGfH injected eyes.

CONCLUSIONS: C3-induced pathology in murine retina can be attenuated by Ad mediated expression of Factor H. Expression of Factor H is worthy of further study as a potential gene therapy for AMD. This article is protected by copyright. All rights reserved.

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Ageing Res Rev. 2015 Sep 11. [Epub ahead of print]

RPE Necroptosis in Response to Oxidative Stress and in AMD.

Hanus J, Anderson C, Wang S.

Abstract: Age-related macular degeneration (AMD) is the leading cause of irreversible blindness in the elderly. The underlying mechanism of non-neovascular AMD (dry AMD), also named geographic atrophy (GA) remains unclear and the mechanism of retinal pigment epithelial (RPE) cell death in AMD is controversial. We review the history and recent progress in understanding the mechanism of RPE cell death induced by oxidative stress, in AMD mouse models, and in AMD patients. Due to the limitation of toolsets to distinguish between apoptosis and necroptosis (or necrosis), most previous research concludes that apoptosis is a major mechanism for RPE cell death in response to oxidative stress and in AMD. Recent studies suggest necroptosis as a major mechanism of RPE cell death in response to oxidative stress. Moreover, ultrastructural and histopathological studies support necrosis as major mechanism of RPE cells death in AMD. In this review, we discuss the mechanism of RPE cell death in response to oxidative stress, in AMD mouse models, and in human AMD patients. Based on the literature, we hypothesize that necroptosis is a major mechanism for RPE cell death in response to oxidative stress and in AMD.

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Acta Ophthalmol. 2015 Sep 19. [Epub ahead of print]

The concept of virtual clinics in monitoring patients with age-related macular degeneration.

Tsaousis KT, Empeslidis T, Konidaris VE, Kapoor B, Deane J.

PURPOSE: To present clinical results regarding the treatment of patients with age-related macular degeneration (neovascular form) after the implementation of a 'virtual' type of follow-up in a single retina service centre.

METHODS: Retrospective study based on the clinical records of the Leicester Royal Infirmary Retina department. Two periods were compared, the 2-year period of 2011-2012 and the following one of 2012-2013 when the 'virtual' clinics model applied in the department. Primary outcomes were as follows: the time between two appointments, follow-up or treatment and the number of patients with significant (>15 letters) improvement of their best corrected distance visual acuity. Secondary parameters of interest were as follows: mean number of injections per patient/year and the average duration of a 'virtual' vs. a regular visit.

RESULTS: The mean time interval between two appointments was 5.3 weeks following the implementation of the 'virtual' clinics compared to 6.9 weeks in the previous period of regular appointments. Mean visual acuity improvement >15 letters was achieved in 6.9% of the patients compared to 23.1% of the 'virtual' appointments period. The results regarding injections/patient/year were as follows: 5.6 before the model of 'virtual' appointments and 5.9 after the implementation. The average time a patient spent for a conventional visit was 71.4 ± 24.1 min, and the respective time needed in the virtual clinic was 47.3 ± 18.6 min.

CONCLUSION: The model of 'virtual' (without actual consultation) follow-up appointments assisted our service to contend with the increased number of patient. In general, the specific pattern of patients' management could be widely considered obviously after comprehensive and all-embracing assessment of its safety and efficiency.

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Pathogenesis

Exp Eye Res. 2015 Sep 11. pii: S0014-4835(15)30024-5. doi: 10.1016/j.exer.2015.09.003. [Epub ahead of print]

Selective Accumulation of the Complement Membrane Attack Complex in Aging Choriocapillaris.

Chirco KR, Tucker BA, Stone EM, Mullins RF.

Abstract: The complement membrane attack complex (MAC) shows increased abundance in the choriocapillaris during normal aging and is especially prevalent in age-related macular degeneration (AMD). While perivascular MAC accumulation occurs in the choroid, it is not well understood whether similar deposition occurs in other aging tissues. In this study we examined the abundance of MAC across multiple human tissues. For studies on fixed tissues, paraffin sections were obtained from six human donor eyes and a commercially available tissue array containing 19 different tissues. Immunohistochemical labeling was performed using antibodies directed against the MAC and intercellular adhesion molecule-1 (ICAM-1), as well as the lectin Ulex europaeus agglutinin-I (UEA-I). The choriocapillaris was the only tissue with high levels of the MAC, which was not detected in any of the 38 additional samples from 19 tissues. ICAM-1 was abundantly expressed in the majority of tissues evaluated, and UEA-I labeled the vasculature in all tissues. A second experiment was performed using unfixed frozen sections of RPE-choroid and 7 extraocular tissues, which confirmed the relatively limited localization of the MAC to the choriocapillaris. In comparison to other tissues assessed, the restricted accumulation of MAC in the choriocapillaris may, in part, explain the specificity of AMD to the neural retina, RPE and choroid, and the relative absence of systemic pathology in this disease.

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Biochem J. 2015 Sep 18. [Epub ahead of print]

The trimeric serine protease HtrA1 forms a cage-like inhibition complex with an anti-HtrA1 antibody.

Ciferri C, Lipari MT, Liang WC, Estevez A, Hang J, Stawicki S, Wu Y, Moran P, Elliott M, Eigenbrot C, Katschke K, Van Lookeren Campagne M, Kirchhofer D.

Abstract: HtrA1 is a trypsin-fold serine protease implicated in the progression of age-related macular degeneration (AMD). Our interest in an antibody therapy to neutralize HtrA1 faces the complication that the target adopts a trimeric arrangement, with three active sites in close proximity. Here we describe antibody 94, obtained from a human antibody phage display library, which forms a distinct macromolecular complex with HtrA1 and inhibits the enzymatic activity of recombinant and native HtrA1 forms. Using biochemical methods and negative staining electron microscopy (EM) we were able to elucidate the molecular composition of the IgG94 and Fab94 complexes and the associated inhibition mechanism. The 246 kDa complex between the HtrA1 catalytic domain trimer (HtrA1_Cat) and Fab94 had a propeller-like organization with one Fab bound peripherally to each protomer. Low-resolution EM structures and epitope mapping indicated that the antibody binds to the surface-exposed loops B and C of the catalytic domain, suggesting an allosteric inhibition mechanism. The HtrA1_Cat:IgG94 complex (636 kDa) is a cage-like structure with three centrally located IgG94 coordinating two HtrA1_Cat trimers and the six active sites pointing into the cavity of the cage. In both complexes, all antigen-recognition regions (paratopes) are found binding one HtrA1 protomer, and all protomers are bound by a paratope, consistent with the complete inhibition of enzyme activity. Therefore, in addition to its potential therapeutic usefulness, antibody 94 establishes a new paradigm of multimeric serine protease inhibition.

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Epidemiology

Ophthalmology. 2015 Sep 14. [Epub ahead of print]

The Incidence and Progression of Age-Related Macular Degeneration over 15 Years: The Blue Mountains Eye Study.

Joachim N, Mitchell P, Burlutsky G, Kifley A, Wang JJ.

PURPOSE: To assess the 15-year incidence and progression of age-related macular degeneration (AMD) in an older Australian population.

DESIGN: Population-based cohort study.

PARTICIPANTS: Blue Mountains Eye Study (BMES) participants (n = 3654) aged 49+ years were examined during 1992-1994. Of these, 2334 (75.8% of survivors) were reexamined after 5 years (1997-1999), 1952 (76.7% of survivors) after 10 years (2002-2004), and 1149 (56.1% of survivors) after 15 years (2007-2010).

METHODS: Color retinal photographs were taken, and comprehensive questionnaires were administered at each visit and DNA was genotyped. Retinal photographic grading was performed by the same graders following the Wisconsin AMD grading protocol. Side-by-side comparisons were used to confirm newly developed AMD lesions. Incidence was estimated using Kaplan-Meier estimates. Associations of AMD incidence with age, sex, smoking status, presence of the complement factor H (CFH)-rs1061170 and age-related maculopathy susceptibility 2 (ARMS2)-rs10490924 polymorphisms, and fish consumption were analyzed using discrete logistic regression models. Generalized estimation equation models were used to assess the risk of incident late AMD associated with baseline AMD lesion characteristics.

MAIN OUTCOME MEASURES: The 15-year incidence and progression of AMD, and associated factors.

RESULTS: The 15-year incidence was 22.7% for early AMD and 6.8% for late AMD. After adjusting for competing risks, early and late AMD incidence were 15.1% and 4.1%, respectively. Age was strongly associated with early and late AMD incidence (both $P < 0.0001$). After age standardization to the Beaver Dam Eye Study (BDES) population, early and late AMD incidence in the BMES were 13.1% and 3.3%, respectively. Female sex and the presence of both risk alleles of CFH-rs1061170 or ARMS2-rs10490924 were independently associated with early AMD incidence, whereas current smoking and presence of ≥1 risk allele of CFH-rs1061170 or ARMS2-rs10490924 were associated with late AMD incidence. Fish consumption was inversely associated with late but not early AMD incidence. Severity of early AMD lesion characteristics was a strong predictor of progression to late AMD.

CONCLUSIONS: We documented the 15-year incidence of early and late AMD in an older Australian population that were comparable to BDES observations. Risk of progression to late AMD was strongly associated with severity of early AMD lesions.

PMID: 26383995 [PubMed - as supplied by publisher]

Diet, lifestyle and low vision

Eye (Lond). 2015 Sep 18. [Epub ahead of print]

Understanding the patient's lived experience of neovascular age-related macular degeneration: a qualitative study.

McCloud C, Lake S.

Purpose: In industrialised populations age-related macular degeneration (ARMD) is the leading cause of visual disability of the elderly. Successful new treatment with anti-endothelial growth factors for neovascular -classified ARMD has led to a divergence in treatment and experiences of people ARMD. This study aimed to understand the participant's experience of neovascular ARMD, including ongoing treatment with anti-vascular endothelial growth factor.

Methods: Twenty-five participants from one clinical site were qualitatively interviewed to elicit their experiences of treatment for neovascular ARMD.

Results: Two major themes were identified. A life negotiated by neovascular ARMD captures the participants' experience of living with the condition and treatment regime for neovascular ARMD. The second major theme: Uncertainty displayed their appraisal of life, treatment and their perceived future.

Conclusions: Anxieties concerning the injections, new limitations to lifestyles, and an uncertain future all emerged from the data analysis. However, thankfulness for the treatment, the importance of familiar patterns in treatments and recovery and a guarded optimism also emerged. Knowledge of the experiences,

anxieties and concerns of this patient population can be used to inform clinical practice and lead to patient-centred care.

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Health Qual Life Outcomes. 2015 Sep 15;13:142.

Validation and cross-cultural adaptation of the National Eye Institute Visual Function Questionnaire (NEI VFQ-25) in Serbian patients.

Kovac B, Vukosavljevic M, Djokic Kovac J, Resan M, Trajkovic G, Jankovic J, Smiljanic M, Grgurevic A.

PURPOSE: To test the validity and reliability of the Serbian version of the interviewer-administered format of the National Eye Institute Visual Functioning Questionnaire (NEI VFQ-25).

METHODS: The Serbian version of NEI VFQ-25 was translated in accordance with standard methods that have been adopted internationally. In order to assess the reliability and validity of the translated NEI VFQ-25, we used a sample of 105 patients with four different chronic ocular diseases. Cronbach's alpha coefficient was used to assess internal consistency for each subscale. To assess test-retest reliability, intraclass correlation coefficients were used. The test-retest data were obtained from clinically stable patients with age-related cataracts, in surveys performed 2 weeks apart. Rasch analysis was also applied as a modern methods of psychometric assessment of the questionnaire.

RESULTS: Four groups of patients were studied and the most prevalent were patients with cataract 40 (38.1%), followed by diabetic retinopathy 31 (29.5%), age related macular degeneration 22 (21.0%) and glaucoma 12 (11.4%). The overall index score on the NEI VFQ-25 ranged from 65.3 to 67.8 with a mean of 67.4 ± 15.0. Cronbach's alpha coefficient (index of internal consistency reliability) ranged from 0.643 to 0.889 for the subscales. Evaluation of the validity of the Serbian version of NEI VFQ-25 is presented in the multi-trait-multi-method matrix and all items passed the convergent and discriminant validity tests. Rasch analysis showed a good measurement precision, but also demonstrated misfitting items and multidimensionality of the questionnaire.

CONCLUSION: Although traditional validation method indicates that the Serbian version of NEI VFQ-25 is a valid and reliable instrument for the assessment of vision specific QoL in Serbian populations aged 40 years or older, Rasch analysis revealed a substantial weakness of the questionnaire that should be taken into consideration when interpreting the results.

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Author reply: approach to micronutrition in age-related macular degeneration.

Şahin M, Şahin A, Türkcü FM.

PMID: 26375347 [PubMed - in process]