Drum treatment

Pharmacotherapy. 2017 Dec 29. [Epub ahead of print]

One Year Effectiveness Study of Intravitreous Ranibizumab in Neovascular Age-Related Macular Degeneration: A Meta-Analysis.

Guo M, Etmiman M, Cheng J, Zafari Z, Maberley D.

PURPOSE: The clinical efficacy of ranibizumab has been examined by a large number of prospective and retrospective studies to date. This meta-analysis was conducted to summarize the current body of evidence on visual acuity (VA) changes with use of ranibizumab in the treatment of neovascular age-related macular degeneration (wAMD).

METHODS: A literature review of multiple electronic databases (EMBASE, MEDLINE, MedMEME) was conducted to find randomized controlled trials (RCTs) and observational studies that reported changes in VA while patients with wAMD were on ranibizumab. Study factors analyzed were baseline patient characteristics, study type, sample size, and 12-month change in VA. Data were pooled in a meta-analysis with VA change as the main outcome. Data were then stratified by study design and a meta-regression was conducted to assess 12-month VA change against baseline VA and age.

RESULTS: A total of 42 studies were included for analysis. An overall increase of 5.58 letters (95% Confidence Interval:4.42-6.75; P heterogeneity, <0.001) was shown with use of ranibizumab compared to baseline. Improvements in VA were larger for RCTs, at 7.71 letters (95%CI:6.66-8.76; P heterogeneity, 0.013), compared to observational studies, at 4.85 letters (95%CI:3.32-6.38; P heterogeneity, <0.001). The meta-regression showed a significant decrease in effect size between baseline VA and 12-month VA change.

CONCLUSION: This meta-analysis suggests visual improvements at 12 months of 0.5-mg ranibizumab use in patients with wAMD. A higher gain in VA was observed when pooling results from RCTs compared to those in observational studies. This article is protected by copyright. All rights reserved.

PMID: 29286545

Int Ophthalmol. 2017 Dec 22. [Epub ahead of print]

Outcome of "treat and monitor" regimen of aflibercept and ranibizumab in macular edema secondary to non-ischemic branch retinal vein occlusion.

Pichi F, Elbarky AM, Ehamaky TR.

PURPOSE: To compare the efficacy of a modified PRN treatment regimen ("treat and monitor") of
aflibercept and ranibizumab in macular edema secondary to non-ischemic branch retinal vein occlusion.

METHODS: Seventy eyes of 70 patients with treatment naïve branch retinal vein occlusion were enrolled. All patients underwent a comprehensive ophthalmic examination, spectral-domain optical coherence tomography, and fluorescein angiography. Patients were randomized 1:1 to receive intravitreal aflibercept (34 eyes) and ranibizumab (36 eyes) with a "treat and monitor" treatment regimen with monthly follow-up for 12 months. Primary outcome measures included mean change in best corrected visual acuity (BCVA) and central foveal thickness (CFT) at month 12 compared to baseline.

RESULTS: At 12 months follow-up, the mean BCVA improved from 0.58 ± 0.13 to 0.20 ± 0.15 logMAR (P = 0.0003) in the aflibercept group (mean injections 2.6 ± 1.51) and from 0.52 ± 0.11 to 0.21 ± 0.1 logMAR (P = 0.0002) in the ranibizumab group (mean injections 2.8 ± 1.78). No statistical difference between the two groups in terms of the visual acuity gains in eyes with macular edema secondary to non-ischemic BRVO treated with either aflibercept or ranibizumab was observed. Mean CFT reduced from 498 ± 46 to 204 ± 23 µm (P < 0.0001) in the aflibercept group and from 488 ± 31 to 212 ± 29 µm (P < 0.0001) in the ranibizumab group.

CONCLUSION: "Treat and monitor" regimen is a real-life effective strategy in improving visual acuity after macular edema from branch vein occlusion and in reducing the number of injections.

PMID: 29274022


Outcome of the first year of treatment for exudative age-related macular degeneration under a treatment programme using aflibercept - own experience.

Pawlicka I, Hyjek-Ryś A, Kozak M.

STUDY OBJECTIVE: Anatomic and functional (function improvement) outcome of the aflibercept treatment for exudative age-related macular degeneration was analysed after the first year of treatment.

MATERIAL AND METHODS: 62 patients treated with intravitreal aflibercept injections according to the adapted regimen. The treatment efficacy was understood as a reduction in oedema (and the central retinal thickness), with an increase in or stabilisation of the best corrected visual acuity.

RESULTS: In nearly all patients, a reduction in the central retinal thickness was observed, with stabilisation of or improvement in the best corrected visual acuity.

CONCLUSION: The aflibercept treatment for exudative age-related macular degeneration is a promising and efficient treatment method.

PMID: 29263460


One-year outcomes of ziv-aflibercept for macular edema in central retinal vein occlusion.

Eldeeb M, Chan EW, Dedhia CJ, Mansour A, Chhablani J.

PURPOSE: To report the 12-month efficacy and safety outcomes of intravitreal ziv-aflibercept in macular edema secondary to central retinal vein occlusion (CRVO).

METHODS: Interventional case series documenting 12-month outcomes of intravitreal ziv-aflibercept (1.25 mg in 0.05 mL) in 6 patients with treatment-naive macular edema secondary to CRVO. All patients had comprehensive ophthalmic examination, spectral domain optical coherence tomography at baseline and all
follow-up visits, and fluorescein. Retreatment decisions were based on recurrence or persistence of intraretinal or subretinal fluid, deterioration in visual acuity (VA), increase in central subfield thickness (CST) by ≥ 50 μm from the previous visit, or lowest recorded CST.

RESULTS: Participants had (2 males, 4 females) an average age of 53.5 years. From baseline to 12 months, the mean logMAR VA improved from 0.86 (Snellen ≈ 20/145) to 0.33 (Snellen ≈ 20/40), central macular thickness decreased from 519 μm to 255 μm, and total macular volume decreased from 14.7 mm3 to 7.1 mm3. No eyes had uveitis, cataract progression, intraocular pressure (IOP) elevations, or systemic adverse events.

CONCLUSIONS AND IMPORTANCE: Ziv-aflibercept achieves favorable intermediate-term functional and structural outcomes in macular edema secondary to CRVO. No safety concerns were raised. Low-cost ziv-aflibercept may thus be useful for CRVO in resource-poor countries. Further prospective studies in larger cohorts are needed further establish the efficacy and safety of this agent.

PMID: 29260119 PMCID: PMC5731707


Acute Endophthalmitis Caused by Leuconostoc spp. following Intravitreal Bevacizumab Injection.

Singh S, Patel CV, Kishore K.

Abstract: We present a case of acute endophthalmitis caused by Leuconostoc spp. following intravitreal bevacizumab injection. An 86-year-old immunocompetent female developed acute endophthalmitis after intravitreal injection of bevacizumab for neovascular age-related macular degeneration. The patient presented with pain, visual acuity of hand motions, hypopyon, and dense vitritis 96 h after treatment. She was treated with vitreous and anterior chamber tap followed by intravitreal injections of 1 mg vancomycin, 2.25 mg ceftazidime, and 400 μg dexamethasone. Cultures revealed growth of Leuconostoc spp., a genus of gram-positive bacteria that is inherently resistant to vancomycin. Due to persistent inflammation, pars plana vitrectomy (PPV) with intravitreal injection of 0.4 mg amikacin was performed 16 days later, followed by resolution of endophthalmitis and return of vision to 20/40. In conclusion, the management of acute endophthalmitis caused by Leuconostoc spp., a gram-positive coccobacillus, can be particularly challenging due to its inherent resistance to vancomycin. PPV with intravitreal amikacin led to resolution of endophthalmitis. Our case expands the number of cases of endophthalmitis caused by Leuconostoc spp. and highlights the possibility of Leuconostoc-related endophthalmitis in an outpatient setting in an immunocompetent host.

PMID: 29282402 PMCID: PMC5731157

Retina. 2017 Dec 21. [Epub ahead of print]

CHANGES IN PLASMA VASCULAR ENDOTHELIAL GROWTH FACTOR LEVEL AFTER INTRAVITREAL INJECTION OF BEVACIZUMAB, AFLIBERCEPT, OR RANIBIZUMAB FOR DIABETIC MACULAR EDEMA.

Hirano T, Toriyama Y, Iesato Y, Imai A, Murata T.

PURPOSE: The aim of this study was to investigate the changes in plasma vascular endothelial growth factor (VEGF) level depending on the severity of diabetic retinopathy (DR) or diabetic macular edema (DME) and after intravitreal injection of bevacizumab, aflibercept, or ranibizumab for treatment of DME.

METHODS: Plasma VEGF level was evaluated in 72 patients with DR and changes were measured in 42 patients with DME receiving intravitreal injections of bevacizumab, aflibercept, or ranibizumab at the initial
injection.

RESULTS: There were no correlations between plasma VEGF level and the severity of DME or DR. Baseline plasma VEGF level (51.9 pg/mL) was significantly reduced using bevacizumab to 11.9 pg/mL after 1 week and 24.1 pg/mL after 4 weeks (P = 0.0130 and 0.0201, respectively). In aflibercept-treated eyes, plasma VEGF decreased from 52.2 pg/mL to 7.8 pg/mL and 12.6 pg/mL, respectively, at the same time points (both P < 0.001). No such reductions were observed in patients receiving ranibizumab.

CONCLUSION: Baseline plasma VEGF level showed no correlations with DR or DME severity, whereas intravitreal injection of bevacizumab or aflibercept significantly reduced plasma VEGF for up to 4 weeks and ranibizumab produced no such effects. Changes in plasma VEGF level seemed not to be critical in progression or treatment of DME and DR. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

PMID: 29280940

Prog Retin Eye Res. 2018 Jan 2. [Epub ahead of print]

Real-world outcomes in patients with neovascular age-related macular degeneration treated with intravitreal vascular endothelial growth factor inhibitors.

Mehta H, Tufail A, Daien V, Lee AY, Nguyen V, Ozturk M, Barthelmes D, Gillies MC.

Abstract: Clinical trials identified intravitreal vascular endothelial growth factor inhibitors (anti-VEGF agents) have the potential to stabilise or even improve visual acuity outcomes in neovascular age-related macular degeneration (AMD), a sight-threatening disease. Real-world evidence allows us to assess whether results from randomised controlled trials can be applied to the general population. We describe the development of global registries, in particular the Fight Retinal Blindness! registry that originated in Australia, the United Kingdom AMD Electronic Medical Records User Group and the IRIS registry in the USA. Real-world observations relating to efficacy, safety and resource utilisation of intravitreal anti-VEGF therapy for neovascular AMD are then summarised. Novel observations that would have been challenging to identify in a clinical trial setting are then highlighted, including the risk of late disease reactivation, outcomes in second versus first treated eyes, and the increased risk of posterior capsular rupture during cataract surgery in patients who have received intravitreal anti-VEGF therapy. We conclude by exploring future directions in the field. This includes the development of a global consensus on real-world outcome measures to allow greater comparison of results. Real-world neovascular AMD outcome registries can be linked with other databases to determine systemic safety or genetic predictors of treatment efficacy. Machine learning offers opportunities to extract useful insights from “Big Data” often collected in these registries. Real-world registries could be used by drug regulatory authorities and industry as an alternative to more costly and time-consuming phase 4 clinical trials, potentially allowing medication costs to be based on outcomes achieved.

PMID: 29305324

Retina. 2017 Dec 26. [Epub ahead of print]

EFFICACY AND SAFETY OF INTRAVITREAL AFLIBERCEPT AND RANIBIZUMAB IN ASIAN PATIENTS WITH NEOVASCULAR AGE-RELATED MACULAR DEGENERATION: Subgroup Analyses From the View Trials.

Wong TY, Cheung CMG, Lai TYY, Chen SJ, Lee WK, Yoon YH, Iida T, Tueckmantel C, Sowade O, Ogura Y.
PURPOSE: To assess the treatment effect of intravitreal aflibercept and ranibizumab in Asian patients with neovascular age-related macular degeneration.

METHODS: We evaluated data from VIEW 1 and VIEW 2, comparing functional and morphologic outcomes at Week 96 between intravitreal aflibercept 2 mg monthly (2q4) or 2 mg bimonthly after 3 initial monthly doses (2q8) versus ranibizumab 0.5 mg monthly among Asian patients (n = 269) and between Asian and white patients (n = 2044).

RESULTS: In Asian patients, there were no significant differences between intravitreal aflibercept 2q4 and 2q8 compared with ranibizumab in mean gain in best-corrected visual acuity (10.23 and 8.35 vs. 8.51 letters). Reduction in central retinal thickness was greater for intravitreal aflibercept 2q4 (150.43 μm, P = 0.0075) and 2q8 (148.15 μm, P = 0.0126) than ranibizumab (119.46 μm). The proportion of dry retinas was greater for intravitreal aflibercept 2q4 (65.7%, P < 0.01) than ranibizumab (41.7%). There were no differences in outcomes between Asian and white patients. Serious treatment-emergent ocular adverse events occurred in <8% of treated eyes, evenly distributed across subgroups.

CONCLUSION: In Asian patients with neovascular age-related macular degeneration, functional and morphologic outcomes were largely similar between intravitreal aflibercept and ranibizumab groups, and to results seen in white patients. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

PMID: 29280937


Fiebai B, Odogu V.

PURPOSE: The study aimed to describe our initial experience with the use of anti vascular endothelial growth factors (anti-VEGFs) in the treatment of retinal diseases.

METHODS: The case records of all patients who had received at least 3 doses of intravitreal anti-VEGF injections between January 2012 to December 2016 were reviewed. Information culled from the data was age, sex, indications for treatment, type of injection, presenting visual acuity, post injection visual acuity, systemic and ocular co morbidities. Results were analyzed using Statistical Package for Social Sciences (SPSS) 20.0 for Windows statistical software.

RESULTS: A total of 190 injections were given during the study period, to 58 eyes of 50 patients. Twenty-eight females (56.00%) and twenty-two males (44.00%) were seen with a mean age of 59.6± 11.66. Bevacizumab was the most frequently administered anti-VEGF, 142 (74.74%) while only 48(25.26%) injections of Ranibizumab were given. Three eyes had both bevacizumab and ranibizumab (1.58%). Retinal vein occlusion 61(32.11%) was the commonest indication for the injections followed by diabetic macular edema 43(22.63%) and proliferative diabetic retinopathy 42(22.11%). Others were neovascular age related macular degeneration, neovascular glaucoma, vitreous hemorrhage, myopic choroidal neovascularization and cystoid macular edema. There was an association between age and disease, (p = 0.001). There was an improvement in visual acuity after intervention in cases with retinal vein occlusion and diabetic macular edema, and this was statistically significant. Hypertension was the commonest systemic disorder in this series 81(42.36%) and the supero-temporal quadrant 131(68.95%) was the most preferred position to administer the injection. Floaters was the commonest complication seen.

CONCLUSION: Anti VEGFs have become an invaluable tool in the management of a number of retinal
diseases in our center. However, the cost implications are a hindrance to an increased uptake of this form of treatment. Cheaper alternative preparations should be made available to encourage the uptake. Government in developing countries should be encouraged to bear the health burden of the old aged pensioner (OAP).

PMID: 29299078 PMCID: PMC5725526


Antiplatelet and anticoagulant drugs do not affect visual outcome in neovascular age-related macular degeneration in the BRAMD trial.

Buitendijk GHS, Schauwvlieghe AME, Vingerling JR, Schlingemann RO, Klaver CCW; comparing Bevacizumab to Ranibizumab in Age-related Macular Degeneration (BRAMD) trial research group.

PURPOSE: To determine if use of antiplatelet or anticoagulant (AP/AC) medication influences visual acuity in patients with active neovascular age-related macular degeneration (N-AMD).

DESIGN: Retrospective analysis of data from a randomized controlled trial

METHODS: Setting: Multi-center

STUDY POPULATION: 330 patients with active N-AMD from the BRAMD study, a comparative trial between bevacizumab and ranibizumab in the Netherlands.

OBSERVATION PROCEDURES: Patients underwent an extensive ophthalmic examination. Visual acuity was categorized into functional vision (best corrected visual acuity (BCVA) >=0.5), visual impairment (BCVA < 0.5), and severe visual impairment (BCVA<0.3). Fundus photographs were graded for presence of retinal or subretinal hemorrhages. Information on AP/AC medication was obtained through interview. Logistic regression analysis was used to determine associations between AP/AC medication and outcomes. Frequency of hemorrhages in users and non-users stratified for visual acuity categories was analyzed with ANCOVA.

MAIN OUTCOME MEASURES: BCVA and presence of hemorrhages.

RESULTS: In total, 40.9% of the patients used AP/AC medication, of which 73.3% was aspirin. AP/AC use was not associated with visual impairment (adjusted odds ratio (OR) 0.79 (95% confidence interval (CI) 0.43-1.44), or severe visual impairment (adjusted OR 0.75 (95% CI 0.40-1.43). Patients on AP/AC presented with comparable frequencies of hemorrhages (27% versus 32%, P=0.29, respectively). Similar results were found when analyses were restricted to aspirin users only.

CONCLUSION: In our study, use of AP/AC medication was neither associated with visual decline nor with the occurrence of hemorrhages in patients with active N-AMD.

PMID: 29330064


[Role of genetic markers in personalization of anti-angiogenic therapy in patients with exudative age-related macular degeneration]. [Article in Russian]

Moshetova LK, Sychev DA, Osmanova ER, Turkina KI.

Abstract: The review presents data of clinical and pharmacogenetic research by Russian and foreign authors conducted within the last three years on the effectiveness of anti-angiogenic treatment against wet age-related macular degeneration (AMD). Scientific results on the association between angiogenesis-
related gene polymorphisms responsible for predisposition to AMD on the one hand and a positive response to anti-VEGF therapy on the other are presented. Particular attention is paid to the main regulator of angiogenesis - the VEGF-A gene.

PMID: 29319678


Observation of curative effect of intravitreal injection of conbercept in wet age-related macular degeneration: Optical coherence tomography analysis after injection.

Yang W, Tan Y, Li C, Liu Y, Lu G.

Abstract: To observe the clinical efficacy of intravitreal injection of conbercept in the treatment of wet age-related macular degeneration (wAMD), optical coherence tomography (OCT) and the best corrected visual acuity (BCVA) was observed to measure the changes of anatomical changes of central macular thickness (CMT) and the area and volume of retinal pigment epithelium (RPE) uplift. Fifteen patients (15 eyes) with wet AMD were enrolled in this study. All patients underwent intravitreal injection of conbercept of 0.05 mL once. After 1 week, 1 month, and 3 months, OCT and BCVA were used to examine and to compare with the preoperative and postoperative central macular thickness and RPE uplift area. BCVA (median) increased respectively from 0.12 ± 0.13 to 0.21 ± 0.15 at 1 week, to 0.90 ± 0.25 at 1 month, to 0.38 ± 0.17 at 3 months (p < .001). The thickness of central macular decreased from 500 ± 25 μm to 256 ± 19 μm, 221 ± 29 μm, and 215 ± 14 μm, respectively. The normal physiological structure and stratification of the macular area were clear gradually. Conbercept treatment of wet AMD can significantly improve visual acuity, after 1 month up to the plateau, 3 months of continuous drug injection can make the vision maintained at a high stage, and macular retinal normal structural morphology recovery is good, the treatment has no obvious adverse reactions, and with good security.

PMID: 29319204

Retina. 2018 Jan 10. [Epub ahead of print]

INCIDENCE AND LONG-TERM VISUAL ACUITY OUTCOMES OF RETINAL PIGMENT EPITHELIUM TEARS AFTER INTRAVITREAL ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR TREATMENT OF NEOVASCULAR AGE-RELATED MACULAR DEGENERATION.


PURPOSE: To report the incidence of retinal pigment epithelium tears in eyes treated with aflibercept for neovascular age-related macular degeneration and compare it with ranibizumab, and to describe long-term visual outcomes of retinal pigment epithelium tears after intensive anti-vascular endothelial growth factor treatment.

METHODS: Retrospective analysis of clinical charts, spectral domain optical coherence tomography and fundus fluorescein angiography imaging of consecutive naive patients treated with intravitreal aflibercept or ranibizumab for neovascular age-related macular degeneration.

RESULTS: Eight hundred consecutive eyes were included in the study (300 treated with ranibizumab and 500 with aflibercept) with 34.0 ± 9.1 months of follow-up. The incidence of tears in the aflibercept group was 3.2% and 2.3% after ranibizumab (P = 0.52). Twenty-nine eyes with retinal pigment epithelium tears were followed for a mean of 30.76 months. Visual acuity at baseline was 20/100 (50.7 ± 19.3 Early Treatment Diabetic Retinopathy Study letters) and 20/200 (36.1 ± 26.1 Early Treatment Diabetic Retinopathy Study letters) at the end of follow-up. The mean number of injection was 7.3 at 12 months and 13.9 ± 8.1 at the end of the study. The number of injections positively correlated with the final visual outcome.
CONCLUSION: There was a low rate of retinal pigment epithelium tears after aflibercept injections, similar to ranibizumab. The correlation between the number of anti-vascular endothelial growth factors received and visual outcomes supports the need for continuing anti-vascular endothelial growth factor therapy.

PMID: 29324593


Two-year outcomes of intravitreal ziv-aflibercept.


AIM: To assess the two-year outcome of intravitreal ziv-aflibercept (IVZ) in eyes with macular diseases.

METHODS: Consecutive subjects with various macular diseases that received six or more of 0.05 mL IVZ (1.25 mg) injections with at least 1 year follow-up were included. Outcome measures were best-corrected visual acuity (BCVA) (logarithm of the minimum angle of resolution) and central macular thickness (CMT) on spectral domain optical coherence tomography. Paired comparison was done using Wilcoxon signed-rank test calculator.

RESULTS: 107 eyes of 91 subjects received IVZ and were followed with mean±SD follow-up interval of 1.48±0.44 months following treat and extend or pro-re-nata protocol. The distribution included neovascular macular degeneration (42 eyes), diabetic macular oedema (32 eyes) and macular oedema secondary to retinal vein occlusion (11 eyes). Fifty eyes were naive, while 57 eyes were previously treated. Combining all disease categories, CMT decreased significantly by 133.0±153.0 µm at the 24-month follow-up (P<0.001) with BCVA gain of 0.35±0.37 at the 24-month follow-up (P<0.001) with mean number of injections of 8.5 at month 12, 2.4 between 12 and 18 month and 1.7 between 18 and 24 month. Ocular and systemic adverse effects included one episode of transient uveitis and one instance of central retinal artery occlusion after 1121 injections.

CONCLUSIONS: IVZ appears safe and efficacious in the therapy of macular diseases through 2 years.

PMID: 29317400

Other treatment & diagnosis


Long-term Progression of Type 1 Neovascularization in Age-related Macular Degeneration Using Optical Coherence Tomography Angiography.

Xu D, Dávila JP, Rahimi M, Rebhun CB, Alibhai AY, Waheed NK, Sarraf D.

PURPOSE: To analyze the long-term growth patterns of type 1 neovascularization (NV) in eyes with age-related macular degeneration (AMD) receiving anti-vascular endothelial growth factor (VEGF) therapy.

DESIGN: Retrospective cohort study.

METHODS: Patients were enrolled from two eye centers and underwent optical coherence tomography angiography (OCTA) imaging with follow-up greater than 1 year. Choroidal neovascularization (CNV) was manually segmented on OCTA images and compared between time points. CNV growth was sub-divided into three categories based on OCTA area measurement: CNV doubling, modest growth of less than 50%, and shrinkage. These growth rates were correlated with OCTA morphologic features.
RESULTS: Forty-one eyes were analyzed. Mean CNV area was $1.60 \pm 1.84 \text{mm}^2$ at baseline and $1.80 \pm 1.84 \text{mm}^2$ at 1 year. Thirty-three eyes (80%) displayed an increase in CNV area at 1 year with a mean increase of $0.20 \pm 0.38 \text{mm}^2 \ (p=0.001)$. Eleven eyes (27%) underwent CNV doubling, 19 eyes (46%) illustrated modest growth, and 6 (15%) showed shrinkage. Anatomic features including a capillary fringe (odds ratio [OR]=5.3, $p=0.036$) and immature lesion morphology (OR=4.2, $p=0.015$) were significantly associated with CNV doubling. CNV growth occurred in three predominant patterns: "symmetric" growth, "asymmetric" growth, and "finger-like projections" which reflected the orientation of expansion of CNV. "Symmetric" and "asymmetric" growth together correlated with greater frequency of CNV doubling (OR=15, $p=0.0048$).

CONCLUSION: OCTA provides noninvasive measurement of the area of neovascular lesions in AMD. Sustained growth of type 1 NV can be identified in the majority of lesions (80%) that display characteristic patterns of progression despite ongoing anti-VEGF therapy.

PMID: 29269100


Projection-resolved optical coherence tomography angiography exhibiting early flow prior to clinically observed retinal angiomatous proliferation.


PURPOSE: The purpose of this study is to analyze early retinal angiomatous proliferation (RAP) utilizing a novel imaging modality, Projection-Resolved Optical Coherence Tomography Angiography (PR-OCTA).

OBSERVATIONS: Five months prior to the diagnosis of a RAP lesion, cross-sectional PR-OCTA demonstrated flow in the outer retina contiguous with the deep retinal capillary plexus (DCP) and adjacent to a small pigment epithelial detachment. After development of a clinically visible RAP lesion, cross-sectional PR-OCTA demonstrated the RAP lesion connecting DCP and sub-retinal pigment epithelial neovascularization.

CONCLUSIONS & IMPORTANCE: This is the first report of PR-OCTA demonstrating abnormal flow in the outer retina prior to the development of a clinically detectable RAP lesion. PR-OCTA may be useful for surveillance and to help further characterize and stage RAP lesions.

PMID: 29260118 PMCID: PMC5731673


Retinal findings in membranoproliferative glomerulonephritis.

Mansour AM, Lima LH, Arevalo JF, Amaro MH, Lozano V, Ghannam AB, Chan EW.

PURPOSE: To assess the evolution of retinal findings in patients with membranoproliferative glomerulonephritis (MPGN) by funduscopy, intravenous fluorescein angiography and optical coherence tomography.

OBSERVATIONS: Three women and one man were followed for a period of 1.5-37 years. Four patients (8 eyes) had drusen detected at first fundus exam at age 24, 29, 50 and 55. Three patients (6 eyes) had diffuse thickening of Bruch’s membrane, and two patients (3 eyes) had detachment of the retinal pigment epithelium with serous retinal detachment. Drusen tended to widen over a period of 10-year follow-up in one case.

CONCLUSIONS AND IMPORTANCE: Drusen remain the ocular stigmata for MPGN occurring at an early age. The retinal disease is progressive with gradual thickening of Bruch’s membrane and occurrence of
Femtosecond laser-assisted cataract surgery and implantable miniature telescope.

Pham R, Worrell B, Nguyen P, Narain K.

PURPOSE: This paper is a case report of the use of femtosecond laser for cataract surgery to implant an implantable miniature telescope for a patient with large central areas of geographic atrophy.

OBSERVATIONS: On postoperative day 1 the patient's uncorrected visual acuity at near was 20/50. The cornea was clear and the patient reported no problem with navigation without occupational therapy training.

CONCLUSIONS AND IMPORTANCE: To our knowledge and confirmed by the manufacturer of the implantable miniature telescope this is the first case ever reported of a patient who has undergone femtosecond laser cataract surgery with corneal astigmatism correction and implantation of the implantable miniature telescope. This is also the first case report of the preoperative use of microperimetry and visual electrophysiology to evaluate a patient's postoperative potential visual acuity. The success of the procedure illustrated the importance of meticulous preoperative planning, the combined use of state-of-the-art technologies and the seamless teamwork in order to achieve the best clinical outcome for patients who undergo implantation of the implantable miniature telescope.

Mapping standard ophthalmic outcome sets to metrics currently reported in eight eye hospitals.

Michelotti M, de Korne DF, Weizer JS, Lee PP, Flanagan D, Kelly SP, Odergren A, Sandhu SS, Wai C, Klazinga N, Haripriya A, Stein JD, Hingorani M.

BACKGROUND: To determine alignment of proposed international standard outcomes sets for ophthalmic conditions to metrics currently reported by eye hospitals.

METHODS: Mixed methods comparative benchmark study, including eight eye hospitals in Australia, India, Singapore, Sweden, U.K., and U.S. All are major international tertiary care and training centers in ophthalmology. Main outcome measure is consistency of ophthalmic outcomes measures reported.

RESULTS: International agreed standard outcomes (ICHOM) sets are available for cataract surgery (10 metrics) and macular degeneration (7 metrics). The eight hospitals reported 22 different metrics for cataract surgery and 2 for macular degeneration, which showed only limited overlap with the proposed ICHOM metrics. None of the hospitals reported patient reported visual functioning or vision-related quality of life outcomes measures (PROMs). Three hospitals (38%) reported rates for uncomplicated cataract surgeries only. There was marked variation in how and at what point postoperatively visual outcomes following cataract, cornea, glaucoma, strabismus and oculoplastics procedures were reported. Seven (87.5%) measured post-operative infections and four (50%) measured 30 day unplanned reoperation rates.

CONCLUSIONS: Outcomes reporting for ophthalmic conditions currently widely varies across hospitals internationally and does not include patient-reported outcomes. Reaching consensus on measures and consistency in data collection will allow meaningful comparisons and provide an evidence base enabling improved sharing of "best practices" to improve eye care globally. Implementation of international standards is still a major challenge and practice-based knowledge on measures should be one of the inputs of the
Pathophysiological correlations between fundus fluorescein angiography and optical coherence tomography results in patients with idiopathic epiretinal membranes.


Abstract: The aim of the current study was to determine the association between fundus fluorescein angiography (FFA) image results, optical coherence tomography (OCT) imaging results and visual functions in patients with idiopathic epiretinal membranes (ERMs). A total of 80 eyes from 40 patients diagnosed with ERM were analyzed. Best-corrected visual acuity (BCVA) and metamorphopsia were measured using the Early Treatment Diabetic Retinopathy Study eye chart and M-charts, respectively. Macular thickness and volume were determined using OCT. Macular vascular leakage and distortion, and foveal avascular zone (FAZ) diameters were assessed using FFA. BCVA and M-chart results confirmed macular degeneration in the affected eyes. The area of macular vascular leakage was positively correlated with macular volume ($r=0.50$; $P=0.001$). The ratio of FAZ diameters was negatively correlated with central macular thickness ($r=-0.41$; $P=0.008$). The grade of macular vascular distortion was positively correlated with macular thickness (all $r\geq0.47$; $P<0.01$) and volume ($r=0.53$; $P<0.001$). The results of the current study demonstrated that FFA may effectively identify the degree of changes in retinal macular vasculature. Vascular distortion, measured by FFA, may reflect changes in macular structure and visual functions. These results suggest a potential application of FFA in the pre- and post-surgical evaluation of patients with ERMs.

PMID: 29285122 PMCID: PMC5740817

Color Doppler imaging of the retrobulbar circulation and plasmatic biomarkers of vascular risk in age-related macular degeneration: A pilot study.

Rodrigo F, Ruiz-Moreno JM, García JB, Torregrosa ME, Segura JV, Piñero DP.

PURPOSE: To evaluate preliminarily and compare the level of plasmatic biomarkers of vascular risk in patients with and without exudative age-related macular degeneration (ARMD) and to relate it to vascular resistance alterations in the ophthalmic artery (OA), central retinal artery (CRA), posterior temporal ciliary artery (PTCA), and posterior nasal ciliary artery (PNCA).

METHODS: Color Doppler imaging of the OA, CRA, PTCA, and PNCA was performed in 30 eyes of 30 cataract patients (control group) as well as in 30 eyes of 30 patients with naive exudative ARMD (study group), measuring the peak systolic velocity, end-diastolic velocity (EDV), and Pourcelot resistive index (RI). Likewise, in both groups, a blood test was performed to determine the plasmatic levels of homocysteine, C-reactive protein (CRP), B12 vitamin, and folic acid.

RESULTS: A positive and significant correlation was found between the level of CRP and RI of the OA in the ARMD group ($r = 0.498$, $P = 0.005$), with an increased RI in all arteries compared to controls, although differences only reached statistical significance for the PTCA ($P = 0.035$). Likewise, a significantly lower EDV for the CRA was found in ARMD eyes compared to controls ($P = 0.041$). In the study group, significantly higher plasmatic levels of homocysteine ($P = 0.042$) and CRP ($P = 0.046$) were found. In contrast, no significant differences were found between groups in the levels of folic acid ($P = 0.265$) and B12 vitamin ($P = 0.520$).
CONCLUSION: The decrease of the choroidal perfusion related to hyperhomocysteinemia, and increase in the CRP plasmatic levels may play an etiological role on the exudative ARMD. This should be investigated in future studies with larger samples of patients.

PMID: 29283130

J Biophotonics. 2017 Dec 28. [Epub ahead of print]

Measuring polarization changes in the human outer retina with polarization-sensitive optical coherence tomography.

Cense B, Miller DT, King BJ, Theelen T, Elsner AE.

Abstract: Morphological changes in the outer retina such as drusen are established biomarkers to diagnose age-related macular degeneration. However earlier diagnosis might be possible by taking advantage of more subtle changes that accompany tissues that bear polarization-altering properties. To test this hypothesis, we developed a method based on polarization-sensitive optical coherence tomography with which volumetric data sets of the macula were obtained from 10 young (<25 yr) and 10 older (>54 yr) subjects. All young subjects and five of the older subjects had retardance values induced by the retinal pigment epithelium and Bruch’s membrane (RPE-BM) complex that were just above the noise floor measurement (5°-13° at 840 nm). In contrast, elevated retardance, up to 180°, was observed in the other five older subjects. Analysis of the degree of polarization uniformity (DOPU) demonstrates that reduced DOPU (<0.4) in the RPE is associated with elevated double pass phase retardation (DPPR) below the RPE-BM complex, suggesting that the observed elevated DPPR in older subjects is the result of increased scattering or polarization scrambling. Collectively, our measurements show that the outer retina can undergo dramatic change in its polarization properties with age, and in some cases still retain its clinically normal appearance.

PMID: 29282883


Changes in Choroidal Thickness after Cataract Surgery.

Ibrahim AM, Elgouhary SM, Nassar MK, El Batanony AH.

OBJECTIVE: The aim of this study is to compare subfoveal choroidal thickness (SFCT) before and after uneventful phacoemulsification using enhanced depth imaging optical coherence tomography (EDI-OCT).

BACKGROUND: Cataract is a major cause of visual impairment in the elderly. Cataract surgery is the most common ophthalmic surgery and is performed simultaneously with glaucoma or vitreous surgery in many cases. However, according to the results in epidemiology studies, cataract surgery is associated with the onset of age-related macular degeneration (AMD) and cataract surgery increases visual acuity in these patients without an increased risk of progression to exudative AMD.

METHODS: A prospective study was conducted on 53 eyes of 53 patients who had phacoemulsification. Measurements of SFCT were performed preoperatively, 7 days (D7), 1 month (M1), and 3 months (M3) postoperative using the EDI-OCT technique. Central retinal thickness was also measured at the same time.

RESULTS: Twenty-seven male (50.9%) and 26 female (49.1%) with a mean age of 56.43 years ± 10.34 (SD) were analyzed. The mean choroidal thickness was 199.9 ± 60.74 µm. It significantly increased to 228.42 ± 59.77 µm at D7, then decreased to 210.78 ± 59.59 µm at M1, and then decreased to 200.63 ± 61 µm at M3. The mean retinal thickness was 260.79 ± 6.12 µm. It significantly increased to 294.09 ± 7.20 µm at D7 and then decreased to 274.70 ± 6.00 µm at M1 and 258.92 ± 5.89 µm at M3.
CONCLUSION: Mean SFCT increased after cataract surgery. The changes in SFCT return to near the baseline after 3 months.

PMID: 29278973


All Types of Age-related Macular Degeneration in One Patient.
Cebeci Z, Kır N.

Abstract: Herein, we describe a neovascular age-related macular degeneration patient with retinal angiomatous proliferation (RAP) and polypoidal choroidal vasculopathy (PCV) coexisting in the same eye at the time of diagnosis. A 55-year-old woman presented with a history of decreased vision in her left eye. Fundoscopy, fluorescein and indocyanine green angiography, and optical coherence tomography imaging revealed RAP and PCV lesions in her left eye at first diagnosis. The patient received intravitreal ranibizumab therapy but developed tachyphylaxis after the first dose despite having three monthly doses. Switching to intravitreal aflibercept injection in our case resulted in anatomic and functional improvement.

PMID: 29326855 PMCID: PMC5758773


[Development of en face optical coherence tomography and its application in ocular fundus diseases]. [Article in Chinese]
Zhou Y, Wang M.

Abstract: Optical coherence tomography (OCT) is able to obtain the cross-sectional image of the fundus noninvasively and quickly. The cross-sectional image in vivo almost matches the histological section of the retina. OCT has become the most important imaging tool in ophthalmology. Based on the latest OCT technology, en face OCT is a new imaging technique that reveals the structure of retinal and choroidal sections approximately paralleled to the retina surface. Compared to the conventional OCT, en face OCT provides more comprehensive information and makes more accurate diagnosis and assessment of the prognosis. En face OCT is widely used in ocular fundus diseases, such as macular epiretinal membrane, macular hole, macular edema, age-related macular degeneration and retinal vascular disease, glaucoma and neuro-ophthalmology. This article reviews the related concepts, principles and clinical applications of en face OCT. (Chin J Ophthalmol, 2017, 53: 956-960).

PMID: 29325389


An Evaluation of the Relationship Between Clinically Unilateral Pseudoexfoliation Syndrome and Age-Related Macular Degeneration.
Zengin MO, Karti O, Karahan E, Kusbeci T.

BACKGROUND AND OBJECTIVE: To evaluate the relationship between age-related macular degeneration (AMD) and clinically unilateral pseudoexfoliation syndrome (XFS).

PATIENTS AND METHODS: Seventy-six patients (152 eyes) with bilateral AMD and clinically unilateral XFS were included. Eyes with AMD were divided into three stages (early, intermediate, and late), based on the Beckman Initiative for Macular Research Classification Committee of fundus findings. The distribution of
AMD lesions was assessed in both groups, and the subfoveal choroidal thickness (SFCT) was measured using enhanced depth imaging spectral-domain optical coherence tomography (SD-OCT).

RESULTS: There were significantly more early and intermediate-stage AMD cases in eyes with XFS than in non-XFS fellow eyes (P < .05). In contrast, there were significantly fewer wet AMD cases in XFS eyes than in non-XFS fellow eyes (P < .05). SFCT in all AMD stages was significantly lower in eyes with XFS (P < .05).

CONCLUSION: XFS was associated with a lower prevalence of wet AMD. Further studies are required to elucidate this association. [Ophthalmic Surg Lasers Imaging Retina. 2018;49:12-19.].

PMID: 29304261


Optical coherence tomography angiography: a review of current and future clinical applications.

Ang M, Tan ACS, Cheung CMG, Keane PA, Dolz-Marco R, Sng CCA, Schmetterer L.

Abstract: Optical coherence tomography angiography is a non-invasive imaging technique that now allows for simultaneous in vivo imaging of the morphology as well as the vasculature in the eye. In this review, we provide an update on the existing clinical applications of optical coherence tomography angiography technology from the anterior to posterior segment of the eye. We also discuss the limitations of optical coherence tomography angiography technology, as well as the caveats to the interpretation of images. As current optical coherence tomography angiography systems are optimized for the retina, most studies have focused on interpreting images from conditions such as age related macular degeneration and retinal vascular diseases. However, the interpretation of these optical coherence tomography angiography images should be taken in consideration with other multi-modal imaging to overcome the limitations of each technique. In addition, there are a growing variety of clinical applications for optical coherence tomography angiography imaging in optic nerve head evaluation for glaucoma and optic neuropathies. Further developments in anterior optical coherence tomography angiography have now allowed for evaluation of anterior segment pathology such as glaucoma, ocular surface diseases, corneal vascularisation, and abnormal iris vasculature. Future developments in software could allow for improved segmentation and image resolution with automated measurements and analysis.

PMID: 29318383


Hyperpigmented spots after treatment for submacular hemorrhage secondary to polypoidal choroidal vasculopathy.

Kim JH, Chang YS, Kim CG, Lee DW, Han JI.

PURPOSE: To investigate the characteristics and clinical course of hyperpigmented spots after submacular hemorrhage secondary to polypoidal choroidal vasculopathy (PCV).

METHODS: This retrospective, observational study included 87 eyes initially treated with three anti-vascular endothelial growth factor (VEGF) injections for submacular hemorrhage secondary to PCV. Patients were divided into two groups according to the presence of multiple small, dark-gray or black, pigmented lesions after initial treatment: the hyperpigmented spots group and no-hyperpigmented spots group. Baseline characteristics and re-activation of the lesion were compared between the two groups.

RESULTS: The mean follow-up period was 30.6 ± 12.9 months, and 41 eyes (47.1%) were included in the hyperpigmented spots group. The hyperpigmented spots group exhibited greater extent of hemorrhage (P <
0.001) and greater central foveal thickness (P = 0.045) than did the no-hyperpigmented spots group. In the hyperpigmented spots group, re-activation of the lesion was noted in 17 eyes (41.5%) at a mean duration of 15.4 ± 12.7 months after the third anti-VEGF injection. In the no-hyperpigmented spots group, re-activation was noted in 28 eyes (60.9%) at a mean duration of 6.4 ± 4.0 months after the third injection. Kaplan-Meier analysis with log-rank test revealed a significant difference in the re-activation of the lesion between the two groups (P = 0.006).

CONCLUSIONS: Hyperpigmented spots were associated with a large amount of submacular hemorrhage in PCV. The low incidence of re-activation and late re-activation of the lesion in eyes with hyperpigmented spots suggest that a novel follow-up and treatment strategy is required for this condition.

PMID: 29302789

Polypoidal Choroidal Vasculopathy in Highly Myopic Eyes with Elongated Axial Length.
Kokame GT, Tom ES, Shantha JG, Kaneko KN.

PURPOSE: To retrospectively review the prevalence of myopia and elongated axial length in eyes with polypoidal choroidal vasculopathy (PCV) and to evaluate treatment response of PCV in highly myopic eyes. PCV has rarely been reported in myopic eyes.

METHODS: A retrospective review of all eyes diagnosed with PCV at the clinics of Retina Consultants of Hawaii and the Hawaii Macula and Retina Institute was performed between February of 2007 and April of 2017 to evaluate for eyes with significant myopia and elongated axial length.

RESULTS: A total of 282 eyes were diagnosed with PCV by ICG angiography. There were 144 males (59%) and 99 females (41%). 204 patients had unilateral PCV and 39 patients had bilateral PCV. A total of 3 patients with PCV had significant myopia less than -6 diopters or confirmed elongated axial length. One of these patients had bilateral PCV so there were 4 eyes noted with significant myopia and elongated axial length out of 282 eyes with PCV (1.4%). All 3 patients were Asian and presented with active leakage or bleeding related to PCV diagnosed on indocyanine green angiography and optical coherence tomography. Treatments typically used to treat PCV including intravitreal antiangiogenic medications and photodynamic therapy were utilized.

CONCLUSION AND IMPORTANCE: High myopia is rare in eyes diagnosed with PCV, even though choroidal neovascularization is a common cause of vision loss in myopic macular degeneration. However, even in highly myopic eyes, PCV may show signs of resistance to antiangiogenic medications.

PMID: 29299080 PMCID: PMC5725482

Multi-directional optical coherence tomography for retinal imaging.

Abstract: We introduce multi-directional optical coherence tomography (OCT), a technique for investigation of the scattering properties of directionally reflective tissue samples. By combining the concepts of multi-channel and directional OCT, this approach enables simultaneous acquisition of multiple reflectivity depth-scans probing a mutual sample location from differing angular orientations. The application of multi-directional OCT in retinal imaging allows for in-depth investigations on the directional reflectivity of the retinal nerve fiber layer, Henle’s fiber layer and the photoreceptor layer. Major ophthalmic diseases (such as glaucoma or age-related macular degeneration) have been reported to alter the directional reflectivity
properties of these retinal layers. Hence, the concept of multi-directional OCT might help to gain improved understanding of pathology development and progression. As a first step, we demonstrate the capabilities of multi-directional OCT in the eyes of healthy human volunteers.

PMID: 29296488 PMCID: PMC5745103


Use of a Neural Net to Model the Impact of Optical Coherence Tomography Abnormalities on Vision in Age-related Macular Degeneration.

Wan P, Long E.

PMID: 29290309

Pathogenesis


HtrA1 Mediated Intracellular Effects on Tubulin Using a Polarized RPE Disease Model.

Melo E, Oertle P, Trepp C, et al

Abstract: Age-related macular degeneration (AMD) is the leading cause of irreversible vision loss. The protein HtrA1 is enriched in retinal pigment epithelial (RPE) cells isolated from AMD patients and in drusen deposits. However, it is poorly understood how increased levels of HtrA1 affect the physiological function of the RPE at the intracellular level. Here, we developed hRPE (human fetal retinal pigment epithelial) cell culture model where cells fully differentiated into a polarized functional monolayer. In this model, we fine-tuned the cellular levels of HtrA1 by targeted overexpression. Our data show that HtrA1 enzymatic activity leads to intracellular degradation of tubulin with a corresponding reduction in the number of microtubules, and consequently to an altered mechanical cell phenotype. HtrA1 overexpression further leads to impaired apical processes and decreased phagocytosis, an essential function for photoreceptor survival. These cellular alterations correlate with the AMD phenotype and thus highlight HtrA1 as an intracellular target for therapeutic interventions towards AMD treatment.

PMID: 29269042


Polarized Human Retinal Pigment Epithelium Exhibits Distinct Surface Proteome on Apical and Basal Plasma Membranes.

Khristov V, Wan Q, Sharma R, Lotfi M, Maminishkis A, Bharti K.

Abstract: Surface proteins localized on the apical and basal plasma membranes are required for a cell to sense its environment and relay changes in ionic, cytokine, chemokine, and hormone levels to the inside of the cell. In a polarized cell, surface proteins are differentially localized on the apical or the basolateral sides of the cell. The retinal pigment epithelium (RPE) is an example of a polarized cell that performs a variety of functions that are dependent on its polarized state including trafficking of ions, fluid, and metabolites across the RPE monolayer. These functions are absolutely crucial for maintaining the health and integrity of adjacent photoreceptors, the photosensitive cells of the retina. Here we present a series of approaches to identify and validate the polarization state of cultured primary human RPE cells using immunostaining for RPE apical/basolateral markers, polarized cytokine secretion, electrophysiology, fluid transport,
phagocytosis, and identification of plasma membrane proteins through cell surface capturing technology. These approaches are currently being used to validate the polarized state and the epithelial phenotype of human induced pluripotent stem (iPS) cell derived RPE cells. This work provides the basis for developing an autologous cell therapy for age-related macular degeneration using patient specific iPS cell derived RPE.

PMID: 29264809


Involvement of Innate Immune System in Late Stages of Inherited Photoreceptor Degeneration.

Sudharsan R, Beiting DP, Aguirre GD, Beltran WA.

Abstract: Retinitis pigmentosa (RP) is a group of inherited retinal degenerations that lead to progressive vision loss. Over 200 mutations in 60 different genes have been shown to cause RP. Given the diversity of genes and mutations that cause RP, corrective gene therapy approaches currently in development may prove both time-consuming and cost-prohibitive for treatment of all forms of RP. An alternative approach is to find common biological pathways that cause retinal degeneration in various forms of RP, and identify new molecular targets. With this goal, we analyzed the retinal transcriptome of two non-allelic forms of RP in dogs, rcd1 and xlpra2, at clinically relevant advanced stages of the two diseases. Both diseases showed very similar trends in changes in gene expression compared to control normal dogs. Pathway analysis revealed upregulation of various components of the innate immune system in both diseases, including inflammasome and complement pathways. Our results show that the retinal transcriptome at advanced stages of RP is very similar to that of other retinal degenerative diseases such as age-related macular degeneration and diabetic retinopathy. Thus, drugs and therapeutics already in development for targeting these retinopathies may also prove useful for the treatment of many forms of RP.

PMID: 29263354 PMCID: PMC5738376


Diverse roles of macrophages in intraocular neovascular diseases: a review.


Abstract: Macrophages are involved in angiogenesis, and might also contribute to the pathogenesis of intraocular neovascular diseases. Recent studies indicated that macrophages exert different functions in the process of intraocular neovascularization, and the polarization of M1 and M2 phenotypes plays extremely essential roles in the diverse functions of macrophages. Moreover, a large number of cytokines released by macrophages not only participate in macrophage polarization, but also associate with retinal and choroidal neovascular diseases. Therefore, macrophage might be considered as a novel therapeutic target to the treatment of pathological neovascularization in the eye. This review mainly summarizes diverse roles of macrophages and discusses the possible mechanisms in retinal and choroidal neovascularization.

PMID: 29259911 PMCID: PMC5733520


Cigarette smoke-induced EGFR activation promotes epithelial mesenchymal migration of human retinal pigment epithelial cells through regulation of the FAK-mediated Syk/Src pathway.
Abstract: Epithelial-mesenchymal transition (EMT) of retinal pigment epithelial (RPE) cells is inevitable change of age-related macular degeneration (AMD). Smoking is a major risk factor for the development of EMT in several diseases, including lung cancer. Cigarette smoke-induced stress promotes the production of epidermal growth factor (EGF) in RPE cells. However, the underlying signaling pathways induced by aberrant EGF receptor (EGFR) expression in cigarette smoke-exposed RPE cells remain largely unknown. In the present study, the morphological transformation and production of EMT-associated cytokines were investigated to analyze the effect of smoking on the retina. Furthermore, EGF-treated or cigarette smoke-exposed RPE cells, as well as the downstream targets of EGFR, were investigated to identify the key molecules involved in EMT of cigarette smoke-stimulated RPE cells via immunoblotting. Exposure of RPE cells to cigarette smoke extract (CSE) induced secretion of VEGF and TGF-β1, and increased the expression of EMT markers. CSE-mediated focal adhesion kinase (FAK) activation resulted in the phosphorylation and activation of spleen associated tyrosine kinase (Syk)/Src proto-oncogene, non-receptor tyrosine kinase (Src), leading to migration and invasion of RPE cells. Knockdown of FAK or pharmacological inhibition of Syk/Src abrogated CSE-mediated VEGF and TGF-β1 production and blocked the phosphorylation of Smad2/3 in CSE-stimulated RPE cells. Erlotinib (an EGFR inhibitor) suppressed EGF and CSE-mediated switch from an epithelial to mesenchymal phenotype. Baicalein, an inhibitor of 12/15-lipoxygenase, also efficiently suppressed CSE-induced EMT processes by inhibiting EGFR-associated downstream signaling transduction. The results identified a novel signaling pathway mediated by EGFR in CSE-activated RPE cells, and suggest baicalein as a potential new therapeutic drug for CSE-associated retinopathy.

PMID: 29286114


Understanding AMD by analogy: systematic review of lipid-related common pathogenic mechanisms in AMD, AD, AS and GN.

Xu Q, Cao S, Rajapakse S, Matsubara JA.

RATIONALE: Age-related macular degeneration (AMD) is one of the leading causes of blindness among the elderly. Due to its complex etiology, current treatments have been insufficient. Previous studies reveal three systems closely involved in AMD pathogenesis: lipid metabolism, oxidation and inflammation. These systems are also involved in Alzheimer's disease, atherosclerosis and glomerulonephritis. Understanding commonalities of these four diseases may provide insight into AMD etiology.

OBJECTIVES: To understand AMD pathogenesis by analogy and suggest ideas for future research, this study summarizes main commonalities in disease pathogenesis of AMD, Alzheimer's disease, atherosclerosis and glomerulonephritis.

METHODS: Articles were identified through PubMed, Ovid Medline and Google Scholar. We summarized the common findings and synthesized critical differences.

RESULTS: Oxidation, lipid deposition, complement activation, and macrophage recruitment are involved in all four diseases shown by genetic, molecular, animal and human studies. Shared genetic variations further strengthen their connection. Potential areas for future research are suggested throughout the review.

CONCLUSIONS: The four diseases share many steps of an overall framework of pathogenesis. Various oxidative sources cause oxidative stress. Oxidized lipids and related molecules accumulate and lead to complement activation, macrophage recruitment and pathology. Investigations that arise under this structure may aid us to better understand AMD pathology.

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Exp Eye Res. 2017 Dec 25. [Epub ahead of print]

Efficacy of Lenvatinib, a multitargeted tyrosine kinase inhibitor, on laser-induced CNV mouse model of neovascular AMD.


Abstract: Neovascular age-related macular degeneration (AMD) is a leading cause of vision loss worldwide. Although intravitreal injection of anti-VEGF antibodies and VEGF Trap have significant clinical benefits, the complications of intravitreal injection, drug resistance and patient compliance still need to be concerned. In this study, the effects of an orally administered multi-targeted tyrosine kinase inhibitor (Lenvatinib, E7080) were evaluated in vitro and in vivo on neovascular AMD mouse model. The results showed that E7080 effectively inhibited the proliferation, migration and tubule formation of human choroidal microvascular endothelial cells (HCMECs), and suppressed the angiogenesis of zebrafish subintestinal vessels without causing malformation. The anti-angiogenic effect of E7080 on the laser-induced choroidal neovascularization (CNV) mouse model by oral administration of 10 mg/kg/day was observed. The fluorescein angiography showed CNV leakage area in treatment group vs control group was 3.407 ± 0.2939 vs 5.202 ± 0.9001 (P = .0133) at day 7th post laser-induced CNV, 1.138 ± 0.4334 vs 3.122 ± 0.3466 (P = .0064) at day 14th, 1.401 ± 0.6577 vs 2.781 ± 0.9815 (P = .00262) at day 21th respectively. Moreover, pharmacokinetics analysis in rat retina showed that E7080 rapidly penetrated the blood-retina barrier to retina through oral administration. The T1/2 in retina was 3.81 ± 0.77 h, the Tmax was 4.60 ± 0.73 h, the AUC0-∞ was 110448.51 ± 18532.51 h*ng/g after a single dose administration analyzed by liquid chromatography-tandem mass spectrometry (LC/MS/MS). In conclusion, our study suggested that orally administered E7080 can be a novel therapeutic strategy for neovascular AMD.

PMID: 29284110


Up-regulated Pro-inflammatory MicroRNAs (miRNAs) in Alzheimer's disease (AD) and Age-Related Macular Degeneration (AMD).

Pogue AI, Lukiw WJ.

Abstract: Alzheimer's disease (AD) of the brain neocortex and age-related macular degeneration (AMD) of the retina are two complex neurodegenerative disorders, which (i) involve the progressive dysregulation and deterioration of multiple neurobiological signaling pathways, (ii) exhibit the temporal accumulation of pro-inflammatory lesions including the amyloid beta (Aβ) peptide-containing senile plaques of AD and the drusen of AMD, and (iii) culminate in an insidious inflammatory neurodegeneration ending, respectively, in neural cell atrophy and death and progressive loss of cognition and central visual function. Recent independent research studies have indicated that AD and AMD share common, pathological signaling defects and disease mechanisms at the molecular genetic level. Using high-integrity total RNA samples pooled from AD brain and AMD retina, microfluidic hybridization miRNA arrays, and bioinformatics, the current study was undertaken to quantify microRNA (miRNA) speciation and complexity common to both AD and AMD. These small non-coding (sncRNAs) are known to post-transcriptionally regulate multiple neurobiological pathways and an abundance of research information has already been generated on the roles of these miRNAs in pathological situations involving inflammatory neuropathology and neural cell decline. Here, for the first time, we report the sequence and abundance of a septet of sncRNAs including miRNA-7, miRNA-9-1, miRNA-23a/miRNA-27a, miRNA-34a, miRNA-125b-1, miRNA-146a, and miRNA-155 that are significantly increased in abundance and common to both AD-affected superior temporal lobe neocortex (Brodmann A22) and the AMD-affected macular region of the retina. Bioinformatics, miRNA-mRNA complementarity, next-gen RNA sequencing, and feature alignment analysis further indicate that these 7 up-regulated miRNAs have the potential to interact with and down-regulate ~ 9460 target messenger RNAs (mRNAs; about 3.5% of the genome) involved in the synchronization of amyloid...
production and clearance, phagocytosis, innate-immune, pro-inflammatory, and neurotrophic signaling and/or synaptogenesis in diseased tissues.

PMID: 29302837


Apolipoprotein M Inhibits Angiogenic and Inflammatory Response by Sphingosine 1-Phosphate on Retinal Pigment Epithelium Cells.

Terao R, Honjo M, Aihara M.

Abstract: Sphingosine 1-phosphate (S1P) is a potent lipid mediator that modulates inflammatory responses and proangiogenic factors. It has been suggested that S1P upregulates choroidal neovascularization (CNV) and may be deeply involved in the pathogenesis of exudative age-related macular degeneration (AMD). Recent studies have suggested that apolipoprotein M (ApoM), a carrier protein for S1P, modulates the biological properties of S1P in the pathogenesis of atherosclerosis. However, the role of ApoM/S1P in AMD has not been explored. We investigated the effect of S1P on proangiogenic factors in human retinal pigment epithelium (RPE) cell lines in vitro. S1P promoted the expression of vascular endothelial growth factor in RPE cells. Hypoxia inducible factor-1α expression was also upregulated. These S1P-induced enhancements in growth factors and chemotactic cytokines in RPE cells were significantly inhibited by ApoM treatment. Additionally, in vivo experiments using a laser-induced CNV murine model demonstrated that intravitreal ApoM injection significantly reduced the progression of CNV formation. Although the detailed mechanisms remain to be elucidated, the present results provide a novel potential therapeutic target for AMD, and demonstrate a suppressive role for ApoM and S1P in the pathology of CNV progression.

PMID: 29301231


Evidence for the activation of pyroptotic and apoptotic pathways in RPE cells associated with NLRP3 inflammasome in the rodent eye.

Gao J, Cui JZ, To E, Cao S, Matsubara JA.

BACKGROUND: Age-related macular degeneration (AMD) is a devastating eye disease causing irreversible vision loss in the elderly. Retinal pigment epithelium (RPE), the primary cell type that is afflicted in AMD, undergoes programmed cell death in the late stages of the disease. However, the exact mechanisms for RPE degeneration in AMD are still unresolved. The prevailing theories consider that each cell death pathway works independently and without regulation of each other. Building upon our previous work in which we induced a short burst of inflammasome activity in vivo, we now investigate the effects of prolonged inflammasome activity on RPE cell death mechanisms in rats.

METHODS: Long-Evans rats received three intravitreal injections of amyloid beta (Aβ), once every 4 days, and were sacrificed at day 14. The vitreous samples were collected to assess the levels of secreted cytokines. The inflammasome activity was evaluated by both immunohistochemistry and western blot. The types of RPE cell death mechanisms were determined using specific cell death markers and morphological characterizations.

RESULTS: We found robust inflammasome activation evident by enhanced caspase-1 immunoreactivity, augmented NF-κB nuclear translocalization, increased IL-1β vitreal secretion, and IL-18 protein levels. Moreover, we observed elevated proteolytic cleavage of caspase-3 and gasdermin D, markers for apoptosis and pyroptosis, respectively, in RPE-choroid tissues. There was also a significant reduction in the
anti-apoptotic factor, X-linked inhibitor of apoptosis protein, consistent with the overall changes of RPE cells. Morphological analysis showed phenotypic characteristics of pyroptosis including RPE cell swelling.

CONCLUSIONS: Our data suggest that two cell death pathways, pyroptosis and apoptosis, were activated in RPE cells after exposure to prolonged inflammasome activation, induced by a drusen component, Aβ. The involvement of two distinct cell death pathways in RPE sheds light on the potential interplay between these pathways and provides insights on the future development of therapeutic strategies for AMD.

PMID: 29329580

Metallomics. 2018 Jan 12. [Epub ahead of print]

Transition metals and trace elements in the retinal pigment epithelium and choroid: correlative ultrastructural and chemical analysis by analytical electron microscopy and nano-secondary ion mass spectrometry.

Biesemeier A, Eibl O, Eswara S, Audinot JN, Wirtz T, Schraermeyer U.

Abstract: Understanding the localisation and abundance of structural elements, trace elements and especially transition metals like Cu and Zn in ocular tissue sections is important for physiology, and also for the characterisation of diseases related to oxidative stress like age-related macular degeneration. Transition metal abundances were investigated in an aged donor eye by nano-secondary ion mass spectrometry (nano-SIMS) elemental mapping using Cs+ and O- primary ions, respectively, and correlated to their respective mole fractions investigated by analytical electron microscopy (AEM). The ultrastructure of the tissue and the elemental composition of melanosomes of the choroid and RPE, and RPE lipofuscin and melanolipofuscin granules can adequately be investigated by nano-SIMS using the secondary ion maps. Melanosomes, 0.5-1 μm in size, yield sulphur maps and maps of stored metals like calcium, sodium and copper. Lipofuscin shows especially high phosphorus signals. Elements with mole fractions of about 0.1 at%, e.g. for P and Cu, as investigated by AEM before, can be validated using simultaneous SIMS maps with an estimated lateral resolution of 66 nm with typical acquisition times of 30 minutes for each area of interest. However, Zn (0.19 at%) was not detected by SIMS. Nano-SIMS imaging of CN-, PO2-, S-, Cu-, Ca+, Fe+ and Na+ ions provides excellent detection limits demonstrating the possibilities for chemical mapping with high-sensitivity trace element detection and reduced acquisition times. Quantification of nano-SIMS data was achieved by correlating mole fractions obtained by AEM to secondary ions per pixel obtained by nano-SIMS. Both methods yield the melanin type in melanosomes and trace metal storage.

PMID: 29327028


Comparison of the neuroinflammatory responses to selective retina therapy and continuous-wave laser photocoagulation in mouse eyes.


PURPOSE: This study investigated microglia and inflammatory cell responses after selective retina therapy (SRT) with microsecond-pulsed laser in comparison to continuous-wave laser photocoagulation (cwPC).

METHODS: Healthy C57BL/6 J mice were treated with either a train of short pulses (SRT; 527-nm, Q-switched, 1.7-μs pulse) or a conventional thermal continuous-wave (532-nm, 100-ms pulse duration) laser. The mice were sacrificed and their eyes were enucleated 1, 3, 7, and 14 days after both laser treatments. Pattern of cell death on retinal section was evaluated by TUNEL assay, and the distribution of activated inflammatory cells and glial cells were observed under immunohistochemistry. Consecutive changes for the expression of cytokines such as IL-1β, TNF-α, and TGF-β were also examined using
immunohistochemistry, and compared among each period after quantification by Western blotting.

RESULTS: The numbers of TUNEL-positive cells in the retinal pigment epithelium (RPE) layer did not differ in SRT and cwPC lesions, but TUNEL-positive cells in neural retinas were significantly less on SRT. Vague glial cell activation was observed in SRT-treated lesions. The population of inflammatory cells was also significantly decreased after SRT, and the cells were located in the RPE layer and subretinal space. Proinflammatory cytokines, including IL-1β and TNF-α, showed significantly lower levels after SRT; conversely, the level of TGF-β was similar to the cwPC-treated lesion.

CONCLUSIONS: SRT resulted in selective RPE damage without collateral thermal injury to the neural retina, and apparently produced negligible glial activation. In addition, SRT showed a markedly less inflammatory response than cwPC, which may have important therapeutic implications for several macular diseases.

PMID: 29322247

**Epidemiology**


**Development and Validation of a Risk Score for Age-Related Macular Degeneration: The STARS Questionnaire.**

Delcourt C, Souied E, Sanchez A, Bandello F; STARS Survey Group.

PURPOSE: To develop and validate a risk score for AMD based on a simple self-administered questionnaire.

METHODS: Risk factors having shown the most consistent associations with AMD were included in the STARS (Simplified Théa AMD Risk-Assessment Scale) questionnaire. Two studies were conducted, one in Italy (127 participating ophthalmologists) and one in France (80 participating ophthalmologists). During 1 week, participating ophthalmologists invited all their patients aged 55 years or older to fill in the STARS questionnaire. Based on fundus examination, early AMD was defined by the presence of soft drusen and/or pigmentary abnormalities and late AMD by the presence of geographic atrophy and/or neovascular AMD.

RESULTS: The Italian and French samples consisted of 12,639 and 6897 patients, respectively. All 13 risk factors included in the STARS questionnaire showed significant associations with AMD in the Italian sample. The area under the receiving operating characteristic curve for the STARS risk score, derived from the multivariate logistic regression in the Italian sample, was 0.78 in the Italian sample and 0.72 in the French sample. In both samples, less than 10% of patients without AMD were classified at high risk, and less than 13% of late AMD cases were classified as low risk, with a more intermediate situation in early AMD cases.

CONCLUSIONS: STARS is a new, simple self-assessed questionnaire showing good discrimination of risk for AMD in two large European samples. It might be used by ophthalmologists in routine clinical practice or as a self-assessment for risk of AMD in the general population.

PMID: 29260196

**Retina. 2017 Dec 27. [Epub ahead of print]**

**COLORADO AGE-RELATED MACULAR DEGENERATION REGISTRY: Design and Clinical Risk Factors of the Cohort.**

Lynch AM, Patnaik JL, Cathcart JN, Mathias MT, Siringo FS, Echalier LL, Wagner BD, Oliver SCN, Pecen
PE, Olson JL, Fine SL, Palestine AG, Mandava N.

PURPOSE: To study new and existing risk factors related to age-related macular degeneration (AMD) phenotypes in a Colorado cohort.

METHODS: Age-related macular degeneration was categorized into early, intermediate, or advanced forms. Controls (n = 180) were patients with cataract and no AMD. Demographic and clinical data were gathered by patient interview and verified by chart review. Image data were reviewed by vitreoretinal specialists. Statistical analysis included univariable and multivariate logistic regression analysis (P < 0.05).

RESULTS: Among the 456 patients with AMD, 157 (34.4%), 80 (17.6%), and 219 (48.0%) had the early/intermediate, geographic atrophy, and neovascular forms of the disease, respectively. Adjusted for age, African-American race was associated with a reduced risk of early/intermediate (adjusted odds ratio [AOR] = 0.08, confidence interval [CI] = 0.01-0.67) and neovascular AMD (AOR = 0.15, CI = 0.03-0.72). A family history of AMD was a risk factor for early/intermediate (AOR = 4.08, CI = 2.30-7.25), geographic atrophy (AOR = 8.62, CI = 3.77-19.7), and neovascular AMD (AOR = 3.76, CI = 2.16-6.56). A history of asthma was related to the early/intermediate form of AMD (AOR = 2.34, CI = 1.22-4.46).

CONCLUSION: Studying AMD in specific populations may reveal novel risk factors such as our finding of a relationship between asthma history and AMD.

PMID: 29283981


PURPOSE: To report research participants' baseline characteristics in the AMD2000 study, a prospective, multicenter, 5-year, observational cohort study of Japanese age-related macular degeneration (AMD). The characteristics were determined using multimodal imaging.

METHODS: Patients with AMD were recruited at 18 clinical sites in Japan between April 2006 and March 2009. Each patient underwent a complete ophthalmic examination, including measurement of best-corrected visual acuity (Landolt chart), indirect ophthalmoscopy, slit-lamp biomicroscopy with a contact lens, optical coherence tomography imaging, fundus photography, and fluorescein and indocyanine green angiography.

RESULTS: Four hundred sixty participants (326 men [70.9%]) were included in the study. At enrollment, 131 eyes (28.5%) had hard drusen and 125 eyes (27.2%) had soft drusen in the macular area. A total of 455 eyes (98.9%) were diagnosed as having wet AMD, and 5 eyes (1.1%), as having dry AMD. Of the 455 eyes with wet AMD, 209 eyes (45.4%) had typical AMD, 228 eyes (49.6%) had polyoidal choroidal vasculopathy (PCV), and 18 eyes (3.9%) had retinal angiomatous proliferation. The size of choroidal neovascularization (CNV) was significantly smaller with indocyanine green angiography than with fluorescein angiography (P < 0.001). Poor baseline visual acuity was associated with cystoid macular edema, older age, scar, extrafoveal macular edema, subfoveal CNV, large branching vascular network, and hard exudates.

CONCLUSION: Japanese patients with AMD are predominantly male, lack drusen, and have a high rate of PCV.

PMID: 29270814


PURPOSE: The purpose of this study is to provide a pooled estimate of moderate-to-severe visual impairment (MSVI) and blindness in Iran for people 50 years and over and to identify the major causes through systematic review.

MATERIALS AND METHODS: International (PubMed, ISI Web of Science, and Scopus) and national databases (Scientific Information Database, Barakat Knowledge Network System, Iran Databank of Ophthalmology Research, and Magiran) databases were searched. Following relevance assessment and critical appraisal, eight studies were included. A funnel plot was drawn to explore the stability for estimation. Single-variable meta-regression analysis was applied for heterogeneity assessment, and a random effect model was used (but no significant source for the observed heterogeneity was found).

RESULTS: Age-standardized pooled estimate of MSVI was 4.24% (95% confidence interval [CI]: 2.92-5.56); 3.98% (95% CI: 2.37-5.59) for men, and 4.08% (95% CI: 2.95-5.21) for women. Blindness (visual acuity <3/60) prevalence was 1.31% (95% CI: 1.23-1.39); 0.96% (95% CI: 0.89-1.03) for men, and 1.13% (95% CI: 1.06-1.20) for women. Causes of visual impairment (VI) were cataract (40.23%), amblyopia (12.03%), corneal opacity (9.63%), age-related macular degeneration (9.31%), diabetic retinopathy (4.94%), and glaucoma (3.67%).

CONCLUSION: VI prevalence in the 50 years and older population in Iran seems significantly better than the corresponding global estimates. A rough 60% rate of treatable VI was estimated, mostly attributable to unoperated cataract.

PMID: 29279656 PMCID: PMC5698990

Diabetes Care. 2018 Jan 9. [Epub ahead of print]

Markedly Decreasing Incidence of Blindness in People With and People Without Diabetes in Southern Germany.

Claessen H, Kvitkina T, Narres M, Trautner C, Zöllner I, Bertram B, Icks A.

OBJECTIVE: Studies comparing the incidence of blindness in persons with and without diabetes are scarce worldwide. In Germany, a decline in the incidence of blindness was found during the 1990s. The aim of this study was to analyze the recent time trend.

RESEARCH DESIGN AND METHODS: Data were based on administrative files in southern Germany to assess recipients of blindness allowance newly registered between 1 January 2008 and 31 December 2012. We estimated age- and sex-standardized incidence of blindness in people with and people without diabetes and the corresponding relative risk. Poisson regression was used to examine age- and sex-adjusted time trends.

RESULTS: We identified 1,897 new cases of blindness (23.7% of which were associated with diabetes). We observed a strong decrease in incidence in both the population with diabetes (2008, 17.3 per 100,000 person-years [95% CI 13.6-21.1], and 2012, 8.9 per 100,000 person-years [6.3-11.6]: 16% decrease [10-22] per year) and that without diabetes (2008, 9.3 per 100,000 person-years [8.3-10.3], and 2012, 6.6 [5.8-7.4]: 9% decrease [5-13] per year). The relative risk comparing those incidences was 1.70 (95% CI 1.32-2.16) and remained constant in the observation period. Regarding time trend, we found similar results for both sexes.

CONCLUSIONS: We found a significant reduction in incidence of blindness in the populations with and
without diabetes, which was more prominent among individuals with diabetes compared with the 1990s. Our findings may be explained by effective secondary prevention therapies and improved ophthalmologic care beyond diabetic retinopathy, particularly regarding macular degeneration, which means earlier detection and earlier and better treatment.

PMID: 29317450


**Polypoidal Choroidal Vasculopathy.**

Kim JB, Nirwan RS, Kuriyan AE.

**PURPOSE OF REVIEW:** The goal of this paper is to review the recent literature of polypoidal choroidal vasculopathy (PCV) and provide an update on the epidemiology, pathophysiology, clinical findings, and management.

**RECENT FINDINGS:** Although indocyanine-green angiography (ICGA) is still the gold standard for diagnosis of PCV, the use of en face optical coherence tomography (OCT) and OCT angiography are useful tools in the diagnosis of PCV. Studies demonstrate superior treatment outcomes with combination photodynamic therapy (PDT) and anti-vascular endothelial growth factor (VEGF) therapy.

**SUMMARY:** PCV is a disease most commonly in Asians and African-Americans and presents with an orange-red nodule in the macula or the peripapillary region. While ICGA remains the most accurate method to diagnose PCV, newer non-invasive imaging modalities (eg. OCT-A and en face OCT) can be used to identify PCV lesions. The combination of PDT and anti-VEGF therapy is superior to either monotherapy. Future studies of OCT modalities and other anti-VEGF agents will be important in guiding PCV diagnosis and management, respectively.

PMID: 29276655 PMCID: PMC5736141 [Available on 2018-06-01]


**The national and subnational prevalence and burden of age-related macular degeneration in China.**

Song P, Du Y, Chan KY, Theodoratou E, Rudan I.

**BACKGROUND:** Age-related macular degeneration (AMD) is the third most common cause of blindness, and the fourth leading cause of visual impairment worldwide, but little is known about the burden of this disease in the most populous country-China. This study provides the first comprehensive estimates of the prevalence and burden of AMD in China from 1990 to 2015, with projections till 2050.

**METHODS:** In this study, a systematic review and meta-analysis was conducted to estimate the prevalence of AMD in China. China National Knowledge Infrastructure (CNKI), Wanfang, Chinese Biomedicine Literature Database (CBM-SinoMed), PubMed, Embase and Medline were searched before September 2016. Multilevel mixed-effect meta-regression was performed to define the prevalence rates of AMD and its subtypes. UN population data were used to estimate and project the number of people affected from 1990 to 2050. Based on different demographic and geographic features, the national burden of AMD in 2000 and 2010 was distributed to different regions in China.

**RESULTS:** Our search returned 2016 citations, of which 25 met the inclusion criteria. The prevalence of any AMD ranged from 2.44% (95% CI = 1.85-3.22) in people aged 45-49 years to 18.98% (95% CI = 15.05-23.66) in people aged 85-89 years. Prevalence of early AMD ranged from 1.79% (95% CI = 1.05-3.02) to 10.05% (95% CI = 6.17-15.97), and, in the case of late AMD, from 0.38% (95% CI = 0.16-0.97) to 3.88% (95% CI = 1.68-9.13). In late AMD, the prevalence of geographic atrophy (GA) was 0.15% (95% CI = 0.05-
0.47) in people aged 45-49 years and 1.09% (95% CI = 0.35-3.36) in those aged 85-89 years, and the prevalence of neovascular AMD (NVAMD) ranged between 0.24% (95% CI = 0.11-0.50) and 2.79% (95% CI = 1.33-5.77). The number of people with any AMD was 12.01 million (95% CI = 9.29-15.46) in 1990 and 26.65 million (95% CI = 20.62-34.27) in 2015. Within the same period, the number of people with early AMD increased from 9.44 million (95% CI = 7.74-11.15) to 20.91 million (95% CI = 17.16-24.68), and those with late AMD rose from 2.58 million (95% CI = 1.56-4.30) to 5.74 million (95% CI = 3.46-9.59). In late AMD, the number of people living with GA ranged from 0.87 million (95% CI = 0.40-1.83) in 1990 to 1.93 million (95% CI = 0.89-4.08) in 2015, and NVAMD from 1.71 million (95% CI = 1.16-2.47) to 3.81 million (95% CI = 2.57-5.51). The projected number of people with any AMD in 2020 is 31.23 million (95% CI = 24.18-40.14), increasing to 55.19 million (95% CI = 43.04-70.30) in 2050. Between different regions, the South Central owed the most AMD cases (5.50 million in 2000 and 7.52 million in 2010), whereas the North-West China the least (0.66 million in 2000 and 0.95 million in 2010).

CONCLUSIONS: The estimates in this study suggest a substantial burden of AMD in China, with the ageing process in Chinese society, this burden will be increasing in the foreseen future. Primary and secondary prevention and treatment and effective government response are urgently needed. Improved epidemiological studies are also required to better develop eye-care strategies and health services.

PMID: 29302323 PMCID: PMC5735777

Sebag J, Binder S.
PMID: 29268875

Erratum: Genetic and environmental factors strongly influence risk, severity and progression of age-related macular degeneration.
Abstract
[This corrects the article DOI: 10.1038/sigtrans.2016.16.].
Erratum for
Genetic and environmental factors strongly influence risk, severity and progression of age-related macular degeneration. [Signal Transduct Target Ther. 2016]
PMID: 29266102 PMCID: PMC5657419

Seddon JM.
PMID: 29288272 PMCID: PMC5749242
Genetics & gene therapy


The Association Between Variants of Receptor for Advanced Glycation End Products (RAGE) Gene Polymorphisms and Age-Related Macular Degeneration.

Banevicius M, Vilkeviciute A, Kriauciuniene L, Liutkeviciene R, Deltuva VP.

BACKGROUND: Age-related macular degeneration (AMD) is the leading cause of blindness in people aged 65 years and older in developed countries. The pathogenesis of AMD has been linked to mechanisms involving inflammation, oxidative stress, and basal laminar deposit formation between retinal pigment epithelium (RPE) cells and the basal membrane, caused by advanced glycation end products (AGEs). AGEs are implicated in the pathogenesis of AMD through the AGE-and receptor for AGE (RAGE) interaction, which can be altered by polymorphisms of the RAGE gene. We examined RAGE rs1800624 and rs1800625 gene polymorphisms contributing to AMD development.

MATERIAL AND METHODS: The study enrolled 300 patients with early AMD, 300 patients with exudative AMD, and 800 healthy controls. The genotyping was carried out using the RT-PCR method.

RESULTS: The analysis of two single nucleotide polymorphisms (SNPs) in the RAGE gene showed that rs1800624 was associated with a 1.6-fold decreased risk for exudative AMD under the dominant model after adjustment for age (OR=0.616; 95% CI: 0.394-0.963; p=0.034) and each copy of allele T at rs1800624 was associated with a 1.4-fold decreased risk for exudative AMD development under the additive model after adjustment for age (OR=0.701; 95% CI: 0.510-0.962; p=0.028). Analysis revealed that the rs1800625 allele G at rs1800625 was associated with a 1.5-fold increased risk for exudative AMD after adjustment for age (OR=1.545; 95% CI: 1.003-2.379; p=0.048). These results suggested that the allele G at rs1800625 was a risk-allele for exudative AMD development. In haplotype analysis, A-G haplotype was significantly more frequently observed in exudative AMD patients compared to healthy controls (3.3% versus 1.4%, p=0.035).

CONCLUSIONS: We revealed a significant association between RAGE gene rs1800624 and rs1800625 polymorphisms and AMD risk. We considered T allele at rs1800624 to be protective against AMD development, while allele G at rs1800625 was considered to be a marker of poor prognosis in AMD development.

PMID: 29317590

Angiogenesis. 2018 Jan 9. [Epub ahead of print]

AAV-mediated gene delivery of the calreticulin anti-angiogenic domain inhibits ocular neovascularization.


Abstract: Ocular neovascularization is a common pathological feature in diabetic retinopathy and neovascular age-related macular degeneration that can lead to severe vision loss. We evaluated the therapeutic efficacy of a novel endogenous inhibitor of angiogenesis, the calreticulin anti-angiogenic domain (CAD180), and its functional 112-residue fragment, CAD-like peptide 112 (CAD112), delivered using a self-complementary adeno-associated virus serotype 2 (scAAV2) in rodent models of oxygen-induced retinopathy and laser-induced choroidal neovascularization. The expression of CAD180 and CAD112 was elevated in human umbilical vein endothelial cells transduced with scAAV2-CAD180 or scAAV2-CAD112, respectively, and both inhibited angiogenic activity in vitro. Intravitreal gene delivery of scAAV2-CAD180 or scAAV2-CAD112 significantly inhibited ischemia-induced retinal neovascularization in...
rat eyes (CAD180: 52.7% reduction; CAD112: 49.2% reduction) compared to scAAV2-mCherry, as measured in retinal flatmounts stained with isolectin B4. Moreover, the retinal structure and function were unaffected by scAAV2-CAD180 or scAAV2-CAD112, as measured by optical coherence tomography and electroretinography. Moreover, subretinal delivery of scAAV2-CAD180 or scAAV2-CAD112 significantly attenuated laser-induced choroidal neovascularization in mouse eyes compared to scAAV2-mCherry, as measured by fundus fluorescein angiography (CAD180: 62.4% reduction; CAD112: 57.5% reduction) and choroidal flatmounts (CAD180: 40.21% reduction; CAD112: 43.03% reduction). Gene delivery using scAAV2-CAD180 or scAAV2-CAD112 has significant potential as a therapeutic option for the management of ocular neovascularization.

PMID: 29318471


Mutations in MERTK are not associated with age-related macular degeneration.
Al-Khersan H, Kwong A, Grassi MA.

PURPOSE: To assess whether mutations in Mer tyrosine kinase (MERTK) are associated with age-related macular degeneration (AMD).

METHODS: An association study using whole-genome sequencing was performed to determine whether rare variants in MERTK are associated with AMD. The data set included 4787 propensity score-matched case-control samples: 2394 AMD cases and 2393 controls. Whole-genome sequencing was performed and variants in MERTK were identified. Combined annotation-dependent depletion (CADD) scores and allele frequencies were calculated for each variant identified in MERTK. Student's t-test was used to assess the mean number of MERTK variants per subject between case and control cohorts (Bonferroni adjusted α = 0.0125). The number of subjects carrying at least one high CADD score loss-of-function or nonsynonymous mutation in each cohort was compared using Fisher's exact test (p < 0.05).

RESULTS: No significant difference was found in the mean number of MERTK variants in AMD versus control subjects (p = 0.0502). Additionally, there was no significant difference between cohorts in the number of subjects with at least one high CADD score loss-of-function or nonsynonymous variant (p = 0.15 at CADD > 10 and p = 0.91 at CADD > 20).

CONCLUSIONS:
The present study provides a meaningfully negative result demonstrating that rare variants in MERTK are not associated with AMD. The study also demonstrates the role of large sample size genetic studies utilizing whole-genome sequencing as a powerful tool that can resolve clinically relevant questions regarding the genetic basis of ophthalmic disease.

PMID: 29299721


Elovl4 5-bp deletion does not accelerate cone photoreceptor degeneration in an all-cone mouse.
Schori C, Agbaga MP, Brush RS, Ayyagari R, Grimm C, Samardzija M.

Abstract: Mutations in the elongation of very long chain fatty acid 4 (ELOVL4) gene cause Stargardt macular dystrophy 3 (STGD3), a rare, juvenile-onset, autosomal dominant form of macular degeneration. Although several mouse models have already been generated to investigate the link between the three identified disease-causing mutations in the ELOVL4 gene, none of these models recapitulates the early-onset cone photoreceptor cell death observed in the macula of STGD3 patients. To address this
specifically, we investigated the effect of mutant ELOVL4 in a mouse model with an all-cone retina. Hence, we bred mice carrying the heterozygously mutated Elovl4 gene on the R91W;Nrl-/--; all-cone background and analyzed the retinal lipid composition, morphology, and function over the course of 1 year. We observed a reduction of total phosphatidylcholine-containing very long chain-polysaturated fatty acids (PC-VLC-PUFAs) by 39% in the R91W;Nrl-/--;Elovl4 mice already at 6 weeks of age with a pronounced decline of the longest forms of PC-VLC-PUFAs. Total levels of shorter-chain fatty acids (< C26) remained unaffected. However, this reduction in PC-VLC-PUFA content in the all-cone retina had no impact on morphology or function and did not accelerate retinal degeneration in the R91W;Nrl-/--;Elovl4 mice. Taken together, mutations in the ELOVL4 gene lead to cone degeneration in humans, whereas mouse models expressing the mutant Elovl4 show predominant rod degeneration. The lack of a phenotype in the all-cone retina expressing the mutant form of the protein supports the view that aberrant function of ELOVL4 is especially detrimental for rods in mice and suggests a more subtle role of VLC-PUFAs for cone maintenance and survival.

PMID: 29293603

Mol Ther. 2017 Dec 8. [Epub ahead of print]

AAV8-antiVEGF Fab Ocular Gene Transfer for Neovascular Age-Related Macular Degeneration.


Abstract: Sustained suppression of VEGF is needed in many patients with neovascular age-related macular degeneration (NVAMD), and gene transfer of a VEGF-neutralizing protein is a promising approach to achieve it. Initial clinical trials testing this approach have shown encouraging signals, but evidence of robust transgene expression and consistent antiangiogenic and antipermeability activity has been lacking. In this study, we demonstrate expression of an anti-human VEGF antibody fragment (antiVEGF Fab) after subretinal injection of AAV8-antiVEGF Fab. In transgenic mice expressing human VEGF in retina (rho/VEGF mice), a model of type 3 choroidal neovascularization (NV), eyes injected with ≥1 × 10^7 gene copies (GC) of AAV8-antiVEGF Fab had significantly less mean area of NV than null vector-injected eyes. A dose-dependent response was observed with modest reduction of NV with ≤3 × 10^7, >50% reduction with ≥1 × 10^8 GC and almost complete elimination of NV with 3 × 10^9 or 1 × 10^10 GC. In Tet/opsin/VEGF mice, in which doxycycline-induced high expression of VEGF leads to severe vascular leakage and exudative retinal detachment (RD), reduction of total RD by 70%-80% occurred with 3 × 10^9 or 1 × 10^10 GC of AAV8-antiVEGF Fab, an effect that was sustained for at least a month. These data strongly support initiating clinical trials testing subretinal injection of AAV8-antiVEGF Fab in patients with NVAMD.

PMID: 29292162


Epigenetic Treatment of Neurodegenerative Ophthalmic Disorders: An Eye Toward the Future.


Abstract: Eye disease is one of the primary medical conditions that requires attention and therapeutic intervention in ageing populations worldwide. Further, the global burden of diabetes and obesity, along with heart disease, all lead to secondary manifestations of ophthalmic distress. Therefore, there is increased interest in developing innovative new approaches that target various mechanisms and sequelae driving conditions that result in adverse vision. The research challenge is even greater given that the terrain of eye diseases is difficult to landscape into a single therapeutic theme. This report addresses the burden of eye disease...
disease due to mitochondrial dysfunction, including antioxidant, autophagic, epigenetic, mitophagic, and other cellular processes that modulate the biomedical end result. In this light, we single out lipoic acid as a potent known natural activator of these pathways, along with alternative and potentially more effective conjugates, which together harness the necessary potency, specificity, and biodistribution parameters required for improved therapeutic outcomes.

PMID: 29291141 PMCID: PMC5747116


[The research advances of microRNA-184 and related ocular diseases]. [Article in Chinese]
Zong RR, Zhou YP, Liu ZG.

Abstract: microRNA-184 (miR-184) is a small, non-coding, endogenic RNA molecule of 22 nucleotides in length. It is a highly conserved sequence throughout many different species. Multiple studies have demonstrated that miR-184 is an important factor in regulating gene expression at the post-transcriptional level. miR-184 plays vital roles in many biological processes, including development and differentiation in many tissues and organs. Meanwhile, the research on the physiological and pathological role of miR-184 in eyes draws more and more attention lately. Recent research indicates that miR-184 is highly expressed in the cornea and lens of mice. miR-184 plays crucial regulatory roles in several ocular diseases, such as neovascularization, keratoconus, endothelial dystrophy-iris hypoplasia-congenital cataract-stromal thinning syndrome, corneal squamous cell carcinoma, age-related macular degeneration and cataract. Here we summarize and discuss the recent findings of miR-184 in its gene structure, gene expression and regulation, biological function and its relevance with ocular diseases. (Chin J Ophthalmol, 2017, 53: 950-955).

PMID: 29325388

J Gene Med. 2018 Jan 11. [Epub ahead of print]

Association of IGFN1 Variant with Polypoidal Choroidal Vasculopathy.

BACKGROUND: Polypoidal choroidal vasculopathy (PCV) and neovascular age-related macular degeneration (nAMD) share similar phenotype but are different in clinical manifestations, responses to treatment, and prognosis. Whether PCV is a subtype of AMD or a distinct entity from nAMD remains elusive. Therefore, we performed a whole-exome sequencing (WES) based association analysis to compare the genetic architecture of PCV and nAMD in Han Chinese.

METHODS: Whole-exome sequencing analysis was performed on 21 nAMD cases, 20 PCV cases and 20 healthy controls. As a follow-up validation, 145 nAMD cases, 160 PCV cases and 193 controls were genotyped using Sequenom MassARRAY.

RESULTS: A novel variant, c.6196A>G in IGFN1 gene, was significantly associated with only PCV (combined P = 7.1 × 10-11, OR = 9.44), but not with nAMD (combined P = 0.683, OR = 1.30). The minor allele G conferred an increased risk of PCV.

CONCLUSIONS: Our findings indicate that although some of the susceptibility loci are shared between PCV and nAMD, a unique genetic signature may decide the pathogenesis of PCV.

PMID: 29323771

Issues with the Specificity of Immunological Reagents for NLRP3: Implications for Age-related Macular Degeneration.


Abstract: Contradictory data have been presented regarding the implication of the NACHT, LRR and PYD domains-containing protein 3 (NLRP3) inflammasome in age-related macular degeneration (AMD), the leading cause of vision loss in the Western world. Recognizing that antibody specificity may explain this discrepancy and in line with recent National Institutes of Health (NIH) guidelines requiring authentication of key biological resources, the specificity of anti-NLRP3 antibodies was assessed to elucidate whether non-immune RPE cells express NLRP3. Using validated resources, NLRP3 was not detected in human primary or human established RPE cell lines under multiple inflammasome-priming conditions, including purported NLRP3 stimuli in RPE such as DICER1 deletion and Alu RNA transfection. Furthermore, NLRP3 was below detection limits in ex vivo macular RPE from AMD patients, as well as in human induced pluripotent stem cell (hiPSC)-derived RPE from patients with overactive NLRP3 syndrome (Chronic infantile neurologic cutaneous and articulate, CINCA syndrome). Evidence presented in this study provides new data regarding the interpretation of published results reporting NLRP3 expression and upregulation in RPE and addresses the role that this inflammasome plays in AMD pathogenesis.

PMID: 29323137

Stem cells


Human induced pluripotent stem cells illuminate pathways and novel treatment targets for age-related macular degeneration.

Farrer LA, DeAngelis MM.

Comment on:

Nicotinamide Ameliorates Disease Phenotypes in a Human iPSC Model of Age-Related Macular Degeneration. [Cell Stem Cell. 2017]  
PMID: 29270418 PMCID: PMC5723744


Organoid technology for retinal repair.

Llonch S, Carido M, Ader M.

Abstract: A major cause for vision impairment and blindness in industrialized countries is the loss of the light-sensing retinal tissue in the eye. Photoreceptor damage is one of the main characteristics found in retinal degeneration diseases, such as Retinitis Pigmentosa or age-related macular degeneration. The lack of effective therapies to stop photoreceptor loss together with the absence of significant intrinsic regeneration in the human retina converts such degenerative diseases into permanent conditions that are currently irreversible. Cell replacement by means of photoreceptor transplantation has been proposed as a potential approach to tackle cell loss in the retina. Since the first attempt of photoreceptor transplantation in humans, about twenty years ago, several research groups have focused in the development and improvement of technologies necessary to bring cell transplantation for retinal degeneration diseases to
reality. Progress in recent years in the generation of human tissue derived from pluripotent stem cells (PSCs) has significantly improved our tools to study human development and disease in the dish. Particularly the availability of 3D culture systems for the generation of PSC-derived organoids, including the human retina, has dramatically increased access to human material for basic and medical research. In this review, we focus on important milestones towards the generation of transplantable photoreceptor precursors from PSC-derived retinal organoids and discuss recent pre-clinical transplantation studies using organoid-derived photoreceptors in context to related in vivo work using primary photoreceptors as donor material. Additionally, we summarize remaining challenges for developing photoreceptor transplantation towards clinical application.

PMID: 29291970

Diet, lifestyle & low vision


Simulation of a central scotoma using contact lenses with an opaque centre.

Almutleb ES, Bradley A, Jedlicka J, Hassan SE.

PURPOSE: This study evaluated the feasibility of using soft contact lenses (CLs) with an opaque centre to induce absolute central scotomas that move with the eye. We examined the geometrical optics prediction that scotoma size will vary with the size of the CL’s opaque centre and with ocular pupil size. We also tested the hypothesis that high environmental light levels will ensure that the ocular pupil will remain small enough, even with opaque centre CLs, to generate absolute scotomas representative of those experienced by patients with age-related macular disease.

METHODS: Using an Octopus 900 Perimeter (www.Haag-Streit.com), kinetic visual fields (VFs) were measured in five normally-sighted subjects using a V4e Goldmann target with CLs that had central opaque areas with diameters of 2.8, 3.0, and 3.2 mm. To control pupil size, VFs were measured with background perimeter bowl luminances of 10, 585, and 1155 cd m\(^{-2}\). Subjects attempted to (i) fixate the bowl centre; and (ii) place the scotoma edge at the bowl fixation target (eccentric viewing).

RESULTS: As predicted, there was a direct relationship between scotoma size and both luminance level and diameter of the opacity. Mean scotoma diameters were 0°, 17.6° and 22°, for the low, medium and high bowl luminances, respectively. Scotoma size was determined primarily by the difference between the diameters of CL opacity and the entrance pupil of the eye and the axial separation between them, and between-subject differences in pupil diameters contributed most to the between-subject variability in scotoma diameter at each light level (SD: 6.01°). Scotoma displacement during eccentric fixation confirmed the gaze-contingent characteristics of this experimental model.

CONCLUSION: It is possible to induce a gaze-contingent absolute scotoma and hence mimic central vision loss using centrally-opaque CLs provided that the CL opacity is larger than the entrance pupil of the eye. This simulation tool will, therefore, be ineffective at low environmental light levels (as shown previously) if the entrance pupil of the eye is larger than the CL opacity.

PMID: 29265475 PMCID: PMC5744893 [Available on 2019-01-01]


The reading accessibility index and quality of reading grid of patients with central vision loss.

Tarita-Nistor L, González EG, Mandelcorn MS, Brent MH, Markowitz SN, Steinbach MJ.
PURPOSE: In this study we evaluated the reading accessibility index (ACC) and a quality of reading grid as assessment tools for reading and as outcome measures for reading rehabilitation of patients with central vision loss.

METHODS: Reading performances on the MNRead chart (www.precision-vision.com) were reviewed from our research database. Participants were 24 controls with normal vision [mean age: 34 (SD, 14) years] and 61 patients with bilateral central vision loss [mean age: 81 (SD, 9) years] among which a subgroup of 18 patients [mean age, 76 (SD, 13) years] had undergone perceptual learning training for reading rehabilitation. The outcome measures were maximum reading speed, reading acuity, critical print size, ACC, and the reading quality. A reading quality grid that classified reading speed as spot, slow, functional, or fluent and print size as small, regular, medium, or large was used. All reading speed values were normalised (i.e., divided by 200, the average reading speed in young adults with normal vision measured with the MNRead).

RESULTS: The ACC was associated perfectly with the maximum reading speed in the control group (r2 = 0.99, P < 0.001) and strongly with all parameters of reading in the patient group (smallest r value: r59 = -0.66, P < 0.001). For patients with central vision loss, reading was functional for large print, but slow for medium print and spot for regular print. For some patients with the same ACC values, the quality of reading grid revealed important performance differences. For the subgroup (n = 18) of patients who were trained, the ACC revealed a greater effect of training than the other three parameters of reading, and although there were statistically significant improvements across all print size categories, a qualitative improvement in reading was noticed only for the medium print sizes.

CONCLUSIONS: The ACC is a good measure of reading performance in patients with central vision loss. Examining reading quality for different print size categories can provide a more detailed picture of reading impairment and should be considered as an outcome for rehabilitation in addition to the ACC.

PMID: 29265468


Age-Related Eye Disease and Participation in Cognitive Activities.


Abstract: Studies have found a benefit to living a cognitively active life in older age. Our goal was to quantify participation in cognitively stimulating activities in adults with and without age-related eye disease. We conducted a cross-sectional hospital-based study in Montreal, Canada of older adults (n = 303) having either age-related macular degeneration (AMD) (n = 96), glaucoma (n = 93), or normal vision (n = 114). To be eligible, the AMD group had to have bilateral late stage AMD with a better eye visual acuity of 20/30 or worse. The glaucoma group had to have a diagnosis of bilateral primary open-angle glaucoma with visual field mean deviation < -4 dB in their better eye. Further inclusion criteria included age ≥ 65 and a Mini-Mental State Exam Blind score ≥ 10. Cognitive activities were measured using the Victoria Longitudinal Study Activity Questionnaire. Linear regression was used. Patients with AMD (β = -4.2, 95% confidence interval (CI) -6.0, -2.4) and glaucoma (β = -1.8, 95% CI -3.3, -0.3) participated in fewer cognitive activities per month compared to those with normal vision after adjusting for age, sex, education, diabetes, number of comorbidities, cognition, and cataract. People with AMD and glaucoma participated in fewer cognitive activities, which could put them at risk for future cognitive impairment.

PMID: 29269882


Smartphones, tele-ophthalmology, and VISION 2020.
Mohammadpour M, Heidari Z, Mirghorbani M, Hashemi H.

Abstract: Telemedicine is an emerging field in recent medical achievements with rapid development. The "smartphone" availability has increased in both developed and developing countries even among people in rural and remote areas. Tele-based services can be used for screening ophthalmic diseases and also monitoring patients with known diseases. Electronic ophthalmologic records of the patients including captured images by smartphones from anterior and posterior segments of the eye will be evaluated by ophthalmologists, and if patients require further evaluations, they will be referred to experts in the relevant field. Eye diseases such as cataract, glaucoma, age-related macular degeneration, diabetic retinopathy, and retinopathy of prematurity are the most common causes of blindness in many countries and beneficial use of teleophthalmology with smartphones will be a good way to achieve the aim of VISION 2020 all over the world. Numerous studies have shown that teleophthalmology is similar to the conventional eye care system in clinical outcomes and even provides more patient satisfaction as it saves time and cost. This review explains how teleophthalmology helps to improve patient outcomes through smartphones.

PMID: 29259912 PMCID: PMC5733521


Suh YW, Lee JS, Heo H, Park SH, Kim SH, Lim KH, Moon NJ, Lee SJ, Park SH, Baek SH.

PURPOSE: To investigate the association between vision improvement with refractive correction in the visually impaired eyes and the prevalence of ocular comorbidities in the South Korean population.

MATERIALS AND METHODS: The data of 24,620 individuals in the Korea National Health and Nutrition Examination Survey (KNHANES 2009-2011) were reviewed. Visual impairment was defined as a presenting visual acuity < 20/60. The participants with visual impairment in at least one eye were divided into 3 groups according to the best-corrected visual acuity (group 1: <20/30, group 2: ≥20/30 but <20/25, and group 3: ≥20/25). The prevalence of ocular comorbidities was estimated and compared between the three groups.

RESULTS: Visual impairment in at least one eye was found in 3031 individuals. Groups 1, 2, and 3 comprised 23.5%, 22.2%, and 54.3% of these visually impaired eyes, respectively. The prevalence of cataract, diabetic retinopathy, age-related macular degeneration, corneal opacity, blepharoptosis, and pterygium was similar to or even higher in group 2 compared to group 1. The prevalence of glaucoma and age-related macular degeneration was 5.40% and 11.39%, respectively, in group 2 and 3.31% and 3.76%, respectively, in group 3.

CONCLUSIONS: Appropriate ophthalmologic examination is necessary even if people exhibit vision improvement after optical correction.

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[Evaluation of the medical treatment situation of the visually impaired : Significant differences between young and old]. [Article in German]


BACKGROUND AND OBJECTIVE: Patients with irreversible visual impairment need individual visual
rehabilitation to regain or improve reading ability and mobility. To analyze the prescription of low vision aids (LVA) and their relation to age, we performed a retrospective chart analysis of our specialized low vision outpatient clinic.

METHODS: Patient charts of all patients who attended our low vision outpatient clinic from 2014-2016 were analyzed with respect to the diagnosis, visual acuity, magnification needs, age and prescribed or used LVA.

RESULTS: The evaluation comprised data from 1548 patients (age 0-97 years). Most patients (72%) were underage (<18 years). Retinoblastoma (11%), congenital cataract (10%) and age-related macular degeneration (AMD, 6%) were the most frequent diagnoses. Mean magnification need of the 568 patients with LVAs was 9.9 ± 7. Desktop video magnifiers (22%), cut-off filter spectacles (15%) and electronic magnifiers (13%) were most commonly prescribed. Children and juveniles used smart phones and tablets (smart devices) as a LVA significantly more often (8% vs. 0.6%, p < 0.01) compared to older visually impaired patients (>60 years). Electronic magnifying devices were more often prescribed to these older patients (30% vs. 3%, p < 0.01).

CONCLUSION: The visual rehabilitation showed significant differences between underage and older visually impaired patients. Children and juveniles needed electronic magnifiers less often because they used smart devices as a mobile LVA. This significant difference might be due to much lower social stigmatization of smart devices and the higher affinity to technology of this age group. Based on the positive experiences of younger visually impaired patients, such smart devices should also be introduced to older patients.

PMID: 29318381