Drug treatment


**Evaluation of the effect of combined intravitreal ranibizumab injection and sub-tenon steroid injection in the treatment of resistant diabetic macular edema.**


**Purpose:** To compare sub-tenon steroid plus anti-VEGF injection with anti-VEGF injection solely in the treatment of resistant diabetic macular edema (DME).

**Method:** Patients who exhibited insufficient anatomic [over 350 μm central macular thickness (CMT)] and less than 3 lines of visual gain at least six anti-VEGF injections, were randomly divided into two groups. In group I, the anti-VEGF injection was performed 10 days after the sub-tenon steroid injection [Triamcinolone acetonide (Sinakort-A®)]. And anti-VEGF was performed when needed during the follow-up period. In group II, treatment was continued with anti-VEGF only. All patients’ visual acuity and CMT were followed up for 6 months.

**Results:** The baseline BCVA in group I and group II was 0.51 ± 0.667 logMAR and 0.47 ± 0.60 logMAR, respectively (p = 0.52). In group I and II, at the end of 6-month follow-up, BCVA improved to 0.38 ± 0.60 logMAR (p < 0.001) and 0.43 ± 0.60 logMAR (p = 0.20), respectively. The baseline CMT in group I and group II was 494 ± 118.32 and 438.20 ± 90.99 μm, respectively (p = 0.029). In group I and II, at the end of 6 months, CMT decreased to 302.57 ± 69.89 μm (p < 0.001) and 439.20 ± 107.6 μm (p = 0.96), respectively.

**Conclusion:** Adding steroid to routine anti-VEGF treatment is an effective way of treatment method for resistant DME.

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**J Manag Care Spec Pharm. 2018 Jul;24(7):608-616.**

**Intravitreal aflibercept versus ranibizumab for wet age-related macular degeneration: a cost-effectiveness analysis.**


**Background:** Age-related macular degeneration (AMD) is the leading cause of vision loss in the United States. The most severe vision loss occurs in patients with neovascular AMD, known as wet AMD (wAMD).
The most commonly used antivascular endothelial growth factor (VEGF) therapies approved by the FDA to treat patients with wAMD are ranibizumab, 0.5 mg administered by intravitreal injection once a month (approximately every 28 days), and intravitreal aflibercept injection (IAI), 2 mg every 4 weeks (monthly) for the first 12 weeks (3 months), followed by IAI 2 mg once every 8 weeks (2 months). Given the similar efficacy and safety profiles between IAI and ranibizumab, their associated costs and comparative cost-effectiveness are key factors in determining which one represents a more rational investment of scarce health care resources to help address the increasing cost of prescription drugs in the United States, a source of concern for patients, prescribers, payers, and policymakers.

Objective: To assess the cost-effectiveness of intravitreal aflibercept injection 2 mg every 8 weeks after 3 initial monthly doses (IAI 2q8) versus ranibizumab 0.5 mg monthly (Rq4) and pro re nata (PRN) in the treatment of patients with wAMD from a U.S. payer perspective.

Methods: A Markov cohort model was developed to estimate the lifetime quality-adjusted life-years (QALYs) and costs of treating patients with wAMD with IAI 2q8, Rq4, and ranibizumab PRN. The model considered changes in best-corrected visual acuity in the affected and fellow eyes over time, and the effect of blindness on mortality. Efficacy for IAI 2q8 and Rq4 was from VIEW 1 and VIEW 2 studies and from the Comparison of AMD Treatments Trials for ranibizumab PRN. Utilities and costs (in 2016 U.S. dollars) were from published literature. Health outcomes and costs were discounted at an annual rate of 3%.

Results: Over a lifetime, IAI 2q8 provided equal health benefits with Rq4 (5.44 QALYs) at a lower total cost ($33,745 vs. $48,031) as a result of fewer injections. IAI 2q8 yielded slightly greater QALYs versus ranibizumab PRN (5.44 vs. 5.40) at a slightly higher cost ($33,745 vs. $33,652), with an incremental cost per QALY gained of $2,583. Results were sensitive to variations in drug acquisition costs and number of injections of both drugs and the baseline age of the cohort.

Conclusions: IAI 2q8 can be cost saving and cost-effective compared with Rq4 and ranibizumab PRN for the treatment of wAMD in the United States.

Disclosures: This study was funded by Regeneron Pharmaceuticals, the manufacturer of aflibercept. Hernandez, Lanitis, Cele, and Toro-Diaz are employed by Evidera, which received funding from Regeneron Pharmaceuticals to conduct this study. Gibson and Kuznik are employed by and own stock in Regeneron Pharmaceuticals.

PMID: 29952707 DOI: 10.18553/jmcp.2018.24.7.608


Real-life clinical effectiveness of Razumab® (the world’s first biosimilar of ranibizumab) in retinal vein occlusion: a subgroup analysis of the pooled retrospective RE-ENACT study.

Sharma S, Khan MA, Chaturvedi A; RE-ENACT Study Investigators Group.

Background: This subgroup analysis of the RE-ENACT study evaluates the effectiveness of Razumab® (the world’s first biosimilar of ranibizumab by Intas Pharmaceuticals Ltd.) in Indian patients with retinal vein occlusion (RVO).

Methods: The data on patients with RVO who had received ≥3 injections of Razumab® between January and August 2016 were analyzed. Endpoints were: improvement in best corrected visual acuity (BCVA), and a decrease in central macular thickness (CMT), intraretinal fluid (IRF), and subretinal fluid (SRF) from baseline at weeks 4, 8, and 12.

Results: Of 160 patients, the majority (61.87%) were men. The mean (±SE) BCVA improved from baseline (0.76 ± 0.04) to week 4 (0.73 ± 0.03; p = 0.0656), which attained significance at week 8 (0.55 ± 0.02; p < 0.0001) and week 12 (0.47 ± 0.02; p < 0.0001). The mean (±SE) CMT significantly decreased from baseline (447.60 ± 10.91 μm) to week 4 (431.84 ± 10.92 μm; p = 0.0028), week 8 (339.28 ± 8.12 μm; p < 0.0001), and week 12 (298.23 ± 6.68 μm; p < 0.0001). The proportion of patients with IRF and SRF significantly (p
< 0.0001) decreased from baseline to weeks 4, 8, and 12 (IRF: from 70.63 to 45.63, 39.38, and 30.00%, respectively; SRF: from 65.63 to 37.50, 28.13, and 24.38%, respectively). A subgroup analysis of branch RVO and central RVO showed similar results. No new safety concerns were observed.

**Conclusion:** Razumab® (biosimilar of ranibizumab) effectively improved visual acuity and disease outcomes in patients with RVO in a real-world setting with no new safety concerns.

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### Other treatment and diagnosis


**Polypoidal choroidal vasculopathy: pearls in diagnosis and management.**


**Abstract:** Polypoidal choroidal vasculopathy (PCV) is increasingly recognized as an important cause of exudative maculopathy in Asians as against Wet age-related macular degeneration in Caucasians. A panel of retinal experts methodically evaluated pertinent updated literature on PCV with thorough PubMed/MEDLINE search. Based on this, the panel agreed upon and proposed the current consensus recommendations in the diagnosis (clinical and imaging), management and follow-up schedule of PCV. Diagnosis of PCV should be based on the gold standard indocyanine green angiography which demonstrates early nodular hyperfluorescence signifying the polyp with additional features such as abnormal vascular network (AVN). Optical coherence tomography is an excellent adjuvant for diagnosing PCV, monitoring disease activity, and decision-making regarding the treatment. Current treatment modalities for PCV include photodynamic therapy, anti-vascular endothelial growth factor agents, and thermal laser. Choice of specific treatment modality and prognosis depends on multiple factors such as the location and size of PCV lesion, presence or absence of polyp with residual AVN, amount of submacular hemorrhage, presence or absence of leakage on fundus fluorescein angiography, visual acuity, and so on. Current recommendations would be invaluable for the treating physician in diagnosing PCV and in formulating the best possible individualized treatment strategy for optimal outcomes in PCV management.

PMID: 29941728 DOI: 10.4103/ijo.IJO_1136_17

### Pathogenesis

**Front Immunol. 2018 Jun 7;9:1302. eCollection 2018.**

**The clinical significance and potential role of C-reactive protein in chronic inflammatory and neurodegenerative diseases.**

Luan YY, Yao YM.

**Abstract:** C-reactive protein (CRP) is an acute-phase protein synthesized by hepatocytes in response to pro-inflammatory cytokines during inflammatory/infectious processes. CRP exists in conformationally distinct forms such as the native pentameric CRP and monomeric CRP (mCRP) and may bind to distinct receptors and lipid rafts and exhibit different functional properties. It is known as a biomarker of acute inflammation, but many large-scale prospective studies demonstrate that CRP is also known to be associated with chronic inflammation. This review is focused on discussing the clinical significance of CRP in chronic inflammatory and neurodegenerative diseases, such as cardiovascular disease, type 2 diabetes mellitus, age-related macular degeneration, hemorrhagic stroke, Alzheimer's disease, and Parkinson's disease, including recent advances on the implication of CRP and its forms specifically on the pathogenesis of these
Overall, we highlight the advances in these areas that may be translated into promising measures for the diagnosis and treatment of inflammatory diseases.

PMID: 29951057 PMCID: PMC6008573 DOI: 10.3389/fimmu.2018.01302


**C3a triggers formation of sub-retinal pigment epithelium deposits via the ubiquitin proteasome pathway.**

Fernandez-Godino R, Pierce EA.

Abstract: The mechanisms that connect complement system activation and basal deposit formation in early stages of age-related macular degeneration (AMD) are insufficiently understood, which complicates the design of efficient therapies to prevent disease progression. Using human fetal (hf) retinal pigment epithelial (RPE) cells, we have established an in vitro model to investigate the effect of complement C3a on RPE cells and its role in the formation of sub-RPE deposits. The results of these studies revealed that C3a produced after C3 activation is sufficient to induce the formation of sub-RPE deposits via complement-driven proteasome inhibition. C3a binds the C3a receptor (C3aR), stimulates deposition of collagens IV and VI underneath the RPE, and impairs the extracellular matrix (ECM) turnover by increased MMP-2 activity, all mediated by downregulation of the ubiquitin proteasome pathway (UPP). The formation of basal deposits can be prevented by the addition of a C3aR antagonist, which restores the UPP activity and ECM turnover. These findings indicate that the cell-based model can be used to test potential therapeutic agents in vitro. The data suggest that modulation of C3aR-mediated events could be a therapeutic approach for treatment of early AMD.

PMID: 29946065 DOI: 10.1038/s41598-018-28143-0

Brain Struct Funct. 2018 Jun 27. [Epub ahead of print]

Age-related macular degeneration affects the optic radiation white matter projecting to locations of retinal damage.


Abstract: We investigated the impact of age-related macular degeneration (AMD) on visual acuity and the visual white matter. We combined an adaptive cortical atlas and diffusion-weighted magnetic resonance imaging (dMRI) and tractography to separate optic radiation (OR) projections to different retinal eccentricities in human primary visual cortex. We exploited the known anatomical organization of the OR and clinically relevant data to segment the OR into three primary components projecting to fovea, mid- and far-periphery. We measured white matter tissue properties-fractional anisotropy, linearity, planarity, sphericity-along the aforementioned three components of the optic radiation to compare AMD patients and controls. We found differences in white matter properties specific to OR white matter fascicles projecting to primary visual cortex locations corresponding to the location of retinal damage (fovea). Additionally, we show that the magnitude of white matter properties in AMD patients’ correlates with visual acuity. In sum, we demonstrate a specific relation between visual loss, anatomical location of retinal damage and white matter damage in AMD patients. Importantly, we demonstrate that these changes are so profound that can be detected using magnetic resonance imaging data with clinical resolution. The conserved mapping between retinal and white matter damage suggests that retinal neurodegeneration might be a primary cause of white matter degeneration in AMD patients. The results highlight the impact of eye disease on brain tissue, a process that may become an important target to monitor during the course of treatment.

PMID: 29951918 DOI: 10.1007/s00429-018-1702-5
Complete blood cell count-derived inflammation biomarkers in men with age-related macular degeneration.

Pinna A MD, Porcu T MD, D'Amico-Ricci G MD, Dore S MD, Boscia F MD, Paliogiannis P PhD, Carru C PhD, Zinellu A PhD.

Purpose: To investigate the role of some blood count-derived inflammation biomarkers in age-related macular degeneration (AMD).

Methods: Seventy-nine men with late-stage AMD and 79 male age-matched cataract controls without AMD were recruited in March-December, 2016. A blood sample was taken. The following blood cell count-derived indexes were evaluated: neutrophil/lymphocyte ratio (NLR), derived NLR [dNLR = neutrophils/(white blood cells – neutrophils)], platelet/lymphocyte ratio (PLR), monocyte/lymphocyte ratio (MLR), (neutrophils × monocytes)/lymphocyte ratio (SIRI), and (neutrophils × monocytes × platelets)/lymphocyte ratio (AISI).

Results: AMD patients had significantly lower median values of white blood cells, monocytes, neutrophils, platelets, and mean platelet volume (MPV). Regarding the combined indexes, only AISI was significantly lower in AMD patients than in controls. Receiver operating characteristics curve analysis revealed that the ability of AISI and MPV to predict AMD is poor.

Conclusion: Results suggests that NLR, dNLR, PLR, MLR, SIRI, and AISI are unreliable disease biomarkers in men with AMD. Larger scale studies are necessary to confirm these findings.

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Epidemiology

Ophthalmologe. 2018 Jun 15. [Epub ahead of print]

Analysis of real-life data on treatment quality in patients with exudative age-related macular degeneration (AMD) and vein occlusion at a German university eye hospital.

[Article in German]

Treder M, Gaber A, Rudloff B, Eter N.

Purpose: Real-life data provide an insight into the reality of patient care under everyday conditions. Digitization in ophthalmology has led to a structured documentation of patient data. This makes it possible to automate the retrieval of a huge amount of real-life data by developing suitable query algorithms.

Methods: Using an automated query from fully electronic patient documentation, real-life therapy data were obtained in patients with intravitreal operative drug delivery (IVOM) in age-related macular degeneration (AMD) and vein occlusion (VO). Among other things, injection frequency, frequency of visits and best-corrected visual acuity over a total of 4 years of treatment were recorded. The influence of factors, such as patient age, distance to the clinic and type of insurance on the quality of care were also investigated. Treatment-naïve and pretreated patients were analyzed.

Results: In the first year AMD patients received an average of 4.59 ± 2.00 injections with 10.29 ± 4.47 visits, in the second year 3.83 ± 2.23 injections with 7.72 ± 5.78 visits, in the third year 3.40 ± 2.18 injections with 7.19 ± 5.44 visits and in the fourth year 3.11 ± 2.29 injections with 6.46 ± 6.20 visits. The VO patients received an average of 4.17 ± 2.15 injections with 9.60 ± 4.88 visits in the first year, 3.31 ± 2.03 injections with 7.75 ± 4.88 visits in the second year, 2.94 ± 2.00 injections with 6.55 ± 4.77 visits in the third year and 3.03 ± 1.94 injections with 7.18 ± 5.26 visits in the fourth year. The course of the visual acuity was relatively stable over 4 years. With respect to the quality of care, a younger patient age and a closer distance to the clinic were associated with a better treatment result.
clinic seemed to have a positive influence.

Conclusion: The study results show a positive trend towards an improved quality of care in intravitreal injection therapy in patients with AMD and VO. The age of the patient and the place of residence are factors influencing the therapy.

PMID: 29948152 DOI: 10.1007/s00347-018-0746-5

**Ophthalmol Retina. 2018 Jun;2(6):525-530.**

**Baseline predictors for five-year visual acuity outcomes in the comparison of AMD treatment trials.**

Ying GS, Maguire MG, Pan W, Grunwald JE, Daniel E, Jaffe GJ, Toth CA, Hagstrom SA, Martin DF; CATT Research Group.

**Purpose:** To determine baseline predictors of visual acuity (VA) outcomes at 5 years after initiating treatment with ranibizumab or bevacizumab for neovascular age-related macular degeneration (AMD).

**Design:** Secondary analysis of data from a cohort study.

**Participants:** Patients enrolled in the Comparison of AMD Treatments Trials (CATT) who completed a 5-year follow-up visit.

**Methods:** Participants were randomly assigned to ranibizumab or bevacizumab and to 1 of 3 dosing regimens. After two years, patients were released from the clinical trial protocol, and were recalled for examination at 5 years. Trained readers evaluated baseline lesion features, fluid and thickness. Baseline predictors were determined using univariate and multivariate regression analysis.

**Main Outcome Measures:** VA score and change from baseline, ≥3-line gain, and VA 20/200 or worse at 5 years.

**Results:** Among 647 patients with VA measured at 5 years, mean VA score in the study eye was 58.9 letters (=20/63), mean decrease from baseline was 3.3 letters, 17.6% eyes gained ≥3 lines, and 19.9% had VA of 20/200 or worse. In multivariate analysis, worse baseline VA was associated with worse VA, more VA gain, higher percentage with ≥3-line gain, and higher percentage with 20/200 or worse at 5 years (all p<0.001). Larger baseline CNV lesion area was associated with worse VA, greater VA loss, and higher percentage with 20/200 or worse at 5 years (all p<0.05). Absence of baseline subretinal fluid was associated with worse VA (p=0.03) and more VA loss (p=0.03). Female gender, bevacizumab treatment in the first 2 years, and absence of RPE elevation were associated with higher percentage with ≥3-line gain. Cigarette smoking was associated with a higher percentage with 20/200 or worse. None of the 21 SNPs evaluated were associated with VA outcomes.

**Conclusions:** Five years after initiating treatment with ranibizumab or bevacizumab in CATT participants, worse baseline VA, larger baseline CNV lesion area, and presence of baseline RPE elevation remained independently associated with worse VA at 5 years. In addition, male gender, cigarette smoking, absence of subretinal fluid and treatment with ranibizumab in the first 2 years were independently associated with worse vision outcomes at 5 years.


**JAMA Neurol. 2018 Jun 25. [Epub ahead of print]**

**Association of retinal neurodegeneration on optical coherence tomography with dementia: a population-based study.**

CCW, Ikram MK.

Importance: Retinal structures may serve as a biomarker for dementia, but longitudinal studies examining this link are lacking.

Objective: To investigate the association of inner retinal layer thickness with prevalent and incident dementia in a general population of Dutch adults.

Design, Setting, and Participants: From September 2007 to June 2012, participants from the prospective population-based Rotterdam Study who were 45 years and older and had gradable retinal optical coherence tomography images and at baseline were free from stroke, Parkinson disease, multiple sclerosis, glaucoma, macular degeneration, retinopathy, myopia, hyperopia, and optic disc pathology were included. They were followed up until January 1, 2015, for the onset of dementia.

Exposures: Inner retinal layer thicknesses (ie, retinal nerve fiber layer [RNFL]) and ganglion cell-inner plexiform layer (GC-IPL) thicknesses measured on optical coherence tomography images.

Main Outcomes and Measures: Odds ratios and hazard ratios for incident dementia per SD decrease in retinal layer thickness adjusted for age, sex, education, and cardiovascular risk factors.

Results: Of 5065 individuals eligible for optical coherence tomography scanning, 3289 (64.9%) (mean [SD] age 68.9 [9.9] years, 1879 [57%] women) were included in the analysis. Of these 3289 individuals, 41 (1.2%) already had dementia. Thinner GC-IPL was associated with prevalent dementia (odds ratio per SD decrease in GC-IPL, 1.37 [95% CI, 0.99-1.90]). No association was found of RNFL with prevalent dementia.

During 14,674 person-years of follow-up (mean [SD], 4.5 [1.6] years), 86 individuals (2.6%) developed dementia of whom 68 (2.1%) had Alzheimer disease. Thinner RNFL at baseline was associated with an increased risk of developing dementia (hazard ratio per SD decrease in RNFL, 1.44 [95% CI, 1.19-1.75]), which was similar for Alzheimer disease (hazard ratio, 1.43 [95% CI, 1.15-1.78]). No association was found between GC-IPL thickness and incident dementia (hazard ratio, 1.13 [95% CI, 0.90-1.43]).

Conclusions and Relevance: Thinner RNFL is associated with an increased risk of dementia, including Alzheimer disease, suggesting that retinal neurodegeneration may serve as a preclinical biomarker for dementia.

PMID: 29946702 DOI: 10.1001/jamaneurol.2018.1563

Genetics and gene therapy


Identification and characterization of the VAX2 p.Leu139Arg variant: possible involvement of VAX2 in cone dystrophy.

Alfano G, Waseem NH, Webster AR, Bhattacharya SS.

Objective: This study was undertaken with the objective to investigate the potential involvement of VAX2 in retinal degeneration.

Methods: A cohort of macular and cone dystrophy patients (n = 70) was screened for variant identification. Polymerase chain reaction (PCR) products were purified using ExoSAP-IT. Direct sequencing of PCR products was performed using BigDye 3.1 on the ABI 3730 DNA Analyzer and analyzed using DNASTAR software tool. Search for known variant was performed using the following platforms: 1000 Genomes Project, Ensembl, UCSC, ExAc, and dbSNP. The VAX2 mutants were generated using the GeneArt® Site-Directed Mutagenesis kit. In vitro analysis was performed in hTERTRPE-1 (RPE-1) cell line. Cells were photographed using a Zeiss AXIOVERT S100 microscope. Images were analyzed using Photoshop CS4 software.
Results: Here, we report the identification of a heterozygous non-synonymous variant (c.416T>G; p.Leu139Arg) in one cone dystrophy proband. Functional characterization of this variant in vitro revealed an aberrant phenotype seen as protein mislocalization to cytoplasm/nucleus and aggregates undergoing degradation or forming aggresomes. The cellular phenotype suggests protein loss-of-function. Analysis of the VAX2 p.Leu139Met, a variant present in the normal population, showed a phenotype similar to the wild-type, further supporting the hypothesis for the Leucine 139 to Arginine change to be damaging.

Conclusions: This study raises the interesting possibility for evaluating VAX2 as a candidate gene for cone dystrophy.

PMID: 29947570 DOI: 10.1080/13816810.2018.1484927

The association of matrix metalloproteinases polymorphisms and interleukins in advanced age-related macular degeneration.

Purpose: To assess the impact of matrix metalloproteinase (MMP)1-1607 1G/2G (rs1799750), MMP7-181 A/G (rs11568818) single-nucleotide polymorphism and systemic cytokins interleukin-1 beta (IL-1β), IL-6 levels on the development of exudative age-related macular degeneration (eAMD) Methodology: The study group comprised 282 patients with eAMD, and the control group enrolled 379 randomly selected persons. The genotyping of MMP1-1607 (rs1799750) and MMP7-181 (rs11568818) was performed by using the polymerase chain reaction-based restriction fragment length polymorphism method. To determine IL-1β and IL-6 serum levels, the immunoenzymatic method with monoclonal antibodies coated plates was performed.

Results: MMP1 rs1799750 1G/2G genotype was more frequently found in the development of eAMD. It was associated with a 4.3-fold increased risk for eAMD under the codominant model and a 4.9-fold increased risk for eAMD under the overdominant model. The effect was more pronounced at the age of less than 65 years. IL-1β concentration was significantly higher for MMP1 rs1799750 1G/1G genotype and MMP7 rs11568818 A/G genotype in eAMD patients compared with control group subjects.

Conclusions: MMP1 rs1799750 1G/2G genotype was found to play a significant role in the development of eAMD at the age of less than 65 years. IL-1β concentration was significantly higher in eAMD patients for MMP1 rs1799750 1G/1G genotype and MMP7 rs11568818 A/G genotype compared with control group subjects.

PMID: 29947568 DOI: 10.1080/13816810.2018.1484928

Severe retinal degeneration at an early age in Usher syndrome type 1B associated with homozygous splice site mutations in MYO7A gene.
Abdelkader E, Enani L, Schatz P, Safieh L.

Purpose: Usher syndrome is the most common cause of deafness associated with visual loss of a genetic origin. The purpose of this paper is to report very severe phenotypic features of type 1B Usher syndrome in a Saudi family affected by positive homozygous splice site mutation in MYO7A gene.

Methods: Affected siblings went through detailed history. Complete ophthalmic examination was done. Imaging with colour fundus photography, fundus autofluorescence (AF), and optical coherence tomography
(OCT) scans was performed. Full field electroretinogram (ffERG) was recorded. Molecular genetic testing was done using next-generation sequencing.

Results: Visual acuity was more reduced (range 20/300-20/40) in older siblings (age>30 years), than in younger (age <30 years) siblings (range 20/70-20/25). OCT scans showed macular atrophy in all but one case that has cystoid macular edema (CME). AF demonstrated atrophy outside a small foveal area showing high signal. FfERG was flat in all cases. The homozygous splice site mutation c.470+1G>A in intron 5 of the MYO7A gene was detected in all affected siblings.

Conclusions: This mutation manifested with advanced retinal degeneration at a young age. This may have implications regarding future gene therapy in Usher syndrome cases with this genotype.

PMID: 29942180 PMCID: PMC6010603 DOI: 10.1016/j.sjopt.2017.10.004

Diet, lifestyle and low vision


Association of obesity and age-related macular degeneration in Indian population.

Jaisankar D, Swaminathan G, Roy R, Kulothungan V, Sharma T, Raman R.

Purpose: The aim of this study was to establish the prevalence and association of age-related macular degeneration (AMD) and obesity which was not studied extensively in Indian population over 60 years of age.

Methods: This was a cross-sectional, population-based study. A total of 4791 patients with gradable fundus photography were included. All patients underwent detailed ophthalmic examination and AMD was graded with retinal photographs. Grading of AMD was done according to the International ARM Epidemiological Study Group and staged based on grading in worse eye. The association of AMD severity and obesity (based on body mass index, waist-hip ratio, waist circumference, isolated abdominal obesity, isolated generalized obesity, and combined obesity) was assessed. The main outcome variable was an association between the presence and severity of AMD with different grades of obesity.

Results: No direct significant association was noted between the presence and severity of AMD and any obesity indices. Subgroup analyses based on lifestyle patterns and common systemic pathologies in AMD population were done. Late AMD was significantly associated with tobacco consumption in population with combined obesity (P = 0.033 and odds ratio = 2.998).

Conclusion: No direct association was noted between the presence or severity of AMD and obesity in South Indian population. However, indirect associations between the severity of AMD and combined obesity were found.

PMID: 29941743 DOI: 10.4103/ijo.IJO_1265_17

Case Reports


Long-term intravitreal ranibizumab as a potential additional risk factor for neurodegeneration in parkinson's disease: a case report.

Trifirò G, Marcianò I, Cutroneo PM, Spina E, Mirabelli E, Trombetta CJ, Morgante F.

Abstract: In November 2012, a 72-year old patient was diagnosed with left eye wet age-related macular
degeneration. The patient received three monthly intravitreal injections of ranibizumab, with complete resolution of retinal hemorrhage and edema and reinstatement of visual acuity. In May 2015, symptomatic relapse was detected. The patient was again treated with intravitreal ranibizumab, with overall six injections till the end of February 2016. In May 2016, the patient complained of left hand resting tremor, bradykinesia, and postural rigidity of head and trunk. A diagnosis of clinically established PD was made based on new criteria of the Movement Disorders Society. Single Photon Emission Computerized Tomography of the Dopamine Transporter with (123I) ioflupane documented a low Dopamine Transporter (DAT) uptake mostly in the right striatum. Due to the documented protective role of vascular endothelial growth factor (VEGF) on the dopaminergic neurons, intensive intravitreal injections of the anti-VEGF agent ranibizumab may have played as an additional risk factor accelerating the neurodegeneration process related to PD and the onset of the related clinical signs and symptoms.

PMID: 29937731 PMCID: PMC6003275 DOI: 10.3389/fphar.2018.00608