Double-masked, randomized, phase 2 evaluation of Abicipar Pegol (an anti-VEGF DARPin therapeutic) in neovascular age-related macular degeneration.

Callanan D, Kunimoto D, Maturi RK, et al.

PURPOSE: To evaluate safety and efficacy of the vascular endothelial growth factor binding protein abicipar pegol (abicipar) versus ranibizumab for neovascular age-related macular degeneration.

METHODS: Phase 2, multicenter, randomized, double-masked comparison (REACH study, stage 3). Patients (n = 64) received intravitreal injections of abicipar 1 mg or 2 mg at baseline, week 4, and week 8 (3 injections) or ranibizumab 0.5 mg at baseline and monthly (5 injections).

RESULTS: In the abicipar 1 mg (n = 25), abicipar 2 mg (n = 23), and ranibizumab (n = 16) arms, respectively, least-squares mean best-corrected visual acuity (BCVA) change from baseline was +6.2, +8.3, and +5.6 letters at week 16 (primary endpoint) and +8.2, +10.0, and +5.3 letters at week 20. Least-squares mean central retinal thickness (CRT) reduction from baseline was 134, 113, and 131 μm at week 16 and 116, 103, and 138 μm at week 20. Intraocular inflammation adverse events (AEs), reported in 5/48 (10.4%) abicipar-treated patients, resolved without sustained vision loss or other sequelae.

CONCLUSIONS: Abicipar demonstrated durability of effect: BCVA and CRT improvements were similar between abicipar and ranibizumab at weeks 16 and 20 (8 and 12 weeks after the last abicipar injection and 4 weeks after the last ranibizumab injection). No serious AEs were reported.

PMID: 30412448 DOI: 10.1089/jop.2018.0062
Comparative effectiveness and harms of intravitreal antivascular endothelial growth factor agents for three retinal conditions: a systematic review and meta-analysis.

Low A, Faridi A, Bhavsar KV, et al.

ABSTRACT: Intravitreal antivascular endothelial growth factor (VEGF) agents are widely used to treat ocular conditions but the benefits and harms of these treatments are uncertain. We conducted a systematic review to compare the effects of aflibercept, bevacizumab and ranibizumab on best-corrected visual acuity (BCVA) changes, quality of life and ocular or systemic adverse events in patients with neovascular age-related macular degeneration (NVAMD), diabetic macular oedema (DME) and central or branch retinal vein occlusion (RVO). We searched published and unpublished literature sources to February 2017 for randomised controlled trials and cohort or modelling studies reporting comparative costs in the USA. Two reviewers extracted data and graded the strength of the evidence using established methods. Of 17 included trials, none reported a clinically important difference (≥ 5 letters) in visual acuity gains between agents. Nine trials provide high-strength evidence of no difference between bevacizumab and ranibizumab for NVAMD. Three trials provide moderate-strength evidence of no difference between bevacizumab and ranibizumab for DME. There was low-strength evidence of similar effects between aflibercept and ranibizumab for NVAMD, aflibercept and bevacizumab for RVO and all three agents for DME. There was insufficient evidence to compare bevacizumab and ranibizumab for RVO. Rates of ocular adverse events were low, and systemic harms were generally similar between groups, although 1 DME trial reported more arterial thrombotic events with ranibizumab versus aflibercept. Overall, no agent had a clear advantage over another for effectiveness or safety. Aflibercept and ranibizumab were significantly less cost-effective than repackaged bevacizumab in two trials. Systematic review registration number: CRD42016034076. 

PMID: 30409915 DOI: 10.1136/bjophthalmol-2018-312691

The efficacy and safety of aflibercept and conbercept in diabetic macular edema.

Cai S, Yang Q, Li X, Zhang Y.

ABSTRACT: Diabetic macular edema (DME) has shown an increasing prevalence during the past years and is the leading cause of diabetic retinopathy blindness. Traditional treatment modalities include laser and corticosteroid therapy, which, however, either act through unclear mechanisms or cause cataracts and elevated intraocular pressure. In recent years, as the pathogenic role of VEGF in DME has been well-recognized, the intravitreal injection of anti-VEGF drugs has become the first-line treatment of DME due to their great efficacy in improving visual acuity and mitigating macular edema. Advantages have been shown for aflibercept and conbercept, the two recombinant decoy receptors that can bind VEGF with high specificity and affinity, in DME treatment in clinical trials conducted both worldwide and in People's Republic of China. This review introduces the structural characteristics and molecular mechanisms of action of these two anti-VEGF drugs, and summarizes the clinical trials evaluating their efficacy and safety, with the hope to provide clues for designing optimal and personalized therapeutic regimens for DME patients.

PMID: 30410308 PMCID: PMC6197825

Efficacy and safety of an aflibercept Treat-and-Extend regimen in treatment-naïve patients with macular oedema secondary to central retinal vein occlusion (CRVO): a prospective 12 -Month, single-arm, multicentre trial.


OBJECTIVES: To evaluate efficacy and safety of an aflibercept treat-and-extend (TAE) regimen in patients with macular oedema (MO) secondary to central retinal vein occlusion (CRVO).
**DESIGN SETTING AND PATIENTS:** Phase IV, prospective, open-label, single-arm trial in 11 Spanish hospitals. Treatment-naïve patients with <6 month diagnosis of MO secondary to CRVO and best-corrected visual acuity (BCVA) of 73-24 ETDRS letters were included between 23 January 2015 and 17 March 2016.

**INTERVENTION:** Intravitreal aflibercept 2 mg monthly (3 months) followed by proactive individualized dosing.

**MAIN OUTCOMES:** Mean change in BCVA after 12 months.

**RESULTS:** 24 eyes (24 patients) were included; mean (SD) age: 62.8 (15.0) years; 54.2% male; median (IQR) time since diagnosis: 7.6 (3.0, 15.2) days. Mean BCVA scores significantly improved between baseline (56.0 (16.5)) and Month 12 (74.1 (17.6)); mean (95% CI) change: 14.8 (8.2, 21.4); P=0.0001. Twelve (50.0%) patients gained ≥15 ETDRS letters. Foveal thickness improved between baseline (mean: 569.4 (216.8) µm) and Month 12 (mean 257.4 (48.4) µm); P < 0.0001. At Month 12, 8.3% patients had MO.

**CONCLUSIONS:** An aflibercept TAE regimen improves visual acuity in patients with MO secondary to CRVO over 12 months with good tolerability.

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**Ranibizumab 0.5 mg treatment in adolescents with choroidal neovascularization: subgroup analysis data from the MINERVA study.**


**PURPOSE:** To evaluate the efficacy and safety of ranibizumab 0.5 mg in adolescent patients with any choroidal neovascularization etiology enrolled in the 12-month MINERVA study.

**METHODS:** In the open-label, non-randomized study arm, ranibizumab 0.5 mg was administered to five adolescents (aged 13-17 years). The findings were assessed descriptively as individual case reports at Month 12. Best-corrected visual acuity changes, central subfield thickness, treatment exposure, and safety were described over 12 months.

**RESULTS:** Baseline choroidal neovascularization etiologies of the study eye included choroidal neovascularization secondary to Best disease (n = 2), idiopathic chorioretinopathy (n = 2), and optic disk drusen (n = 1). At Months 2, 6, and 12, the observed mean best-corrected visual acuity changes in the study eye from baseline were +9.2, +16.6, and +16.6 letters, respectively, and the observed mean central subfield thickness change from baseline was -31.4, -87.6, and -116.4 µm, respectively. Adolescent patients received a mean of three (range, 2-5) ranibizumab injections in the study eye. No adverse events or serious adverse events related to ranibizumab were reported.

**CONCLUSION:** Ranibizumab 0.5 mg treatment was beneficial in improving visual acuity and stabilizing or reducing central subfield thickness in five adolescents with differing choroidal neovascularization etiologies requiring infrequent injection. No new safety findings were observed over 12 months. This is an open access article distributed under the Creative Commons Attribution License 4.0 (CCBY), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

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**Diagnosis**


**Validated prediction models for macular degeneration progression and predictors of visual acuity loss identify high risk individuals.**
Seddon JM, Rosner B.

**Purpose:** To determine predictive factors and risk scores for conversion to overall advanced age-related macular degeneration (AMD), geographic atrophy (GA), neovascular disease (NV), and loss of vision, and to validate the model for AMD in an external cohort.

**Methods:** Progression to advanced AMD was evaluated using stepwise survival analysis. Risk scores including genetic, demographic, behavioral, and ocular factors were derived for three AMD endpoints and were validated and calibrated in a large independent cohort. Vision loss of 15 or more letters was evaluated as a new endpoint in genetic analyses.

**Results:** Eight common and rare variants in genes CFH, C3, ARMS2, COL8A1, and HSPH1/B3GALTL conferred a significantly higher risk of transition to advanced AMD. Three loci (C2, CFB, RAD51B) were associated with lower rate of progression. A protective effect was suggested for CTRB1 and PELI3. The age-adjusted area under the curve (AUC) for the composite model including 13 loci model was 0.900 over 12 years (0.896 in the validation cohort). Progressors had a higher risk category when genetic factors were considered and there was heterogeneity between models for GA and NV. The model was calibrated in the validation cohort. Determinants of visual loss included age, education, BMI, smoking, and several common and rare genetic variants.

**Conclusion:** Eyes with the same macular grade had higher or lower risk of subsequent progression and visual loss based on the validated risk score. Identifying high risk individuals at an earlier stage using predictive modeling could lead to improved preventive and therapeutic strategies in the era of precision medicine.

PMID: 30389371 DOI: 10.1016/j.ajo.2018.10.022

**Morphological difference of choroidal vasculature between polypoidal choroidal vasculopathy and neovascular age-related macular degeneration on OCT: from the perspective of pachychoroid.**


**Background and Objective:** To investigate the morphological difference of choroidal vasculature between polypoidal choroidal vasculopathy (PCV) and neovascular age-related macular degeneration (nAMD) on optical coherence tomography (OCT).

**Patients and Methods:** One hundred eighty-nine patients with macula-involved PCV (n = 107) or nAMD (n = 82) were retrospectively reviewed. The subfoveal choroidal thickness (SFCT) and thickness of the Haller's layer were determined on enhanced depth imaging optical coherence tomography (EDI-OCT). The mean diameters of subfoveal large choroidal vessels were also calculated.

**Results:** Both the SFCT (257.31 μm ± 100.50 μm vs. 209.95 μm ± 97.51 μm) (P < .01) and the thickness of the Haller's layer (213.68 μm ± 82.65 μm vs. 159.67 μm ± 79.86 μm) (P < .01) were greater in PCV patients than nAMD patients. The ratio of thickness of the Haller's layer to the SFCT was higher in the PCV group (0.83 ± 0.07) than the nAMD group (0.75 ± 0.11) (P < .01). The mean diameter of subfoveal large choroidal vessels was greater in PCV patients (163.55 μm ± 62.23 μm vs. 112.81 ± 58.87 μm) (P < .01).

**Conclusion:** Choroidal thickening and dilation of large choroidal vessels were commonly seen in PCV patients, supporting that PCV belongs to the pachychoroid spectrum disorders and might be a different entity from nAMD.

PMID: 30395671 DOI: 10.3928/23258160-20181002-13

**Prognostic tomographic classification of myopic choroidal neovascularization.**
Pascual-Camps I, Andreu-Fenoll M, Ruiz-Moreno JM, et al.

**BACKGROUND AND OBJECTIVES:** To investigate the prognostic value of the development of a hyperreflective envelopment of the neovascular tissue in myopic choroidal neovascularization (mCNV) after the first intravitreal ranibizumab injection and to establish a tomographic classification of mCNV depending on this healing process.

**PATIENTS AND METHODS:** Twenty-five eyes of 25 patients with mCNV were retrospectively studied. Patients were classified into type A (presence of a hyperreflective coating of the neovascular tissue 1 month after first intravitreal ranibizumab) and type B (absence of or partial coating). Visual acuity (VA) and number of injections were recorded. Differences between both types were assessed at 6 and 12 months of follow-up.

**RESULTS:** Fifteen patients (60%) were classified as type A and 10 as type B (40%). Type A showed better VA than type B. VA improvement was only significant for type A. No differences in the number of injections were observed; however, a trend to a larger amount in type B was observed.

**CONCLUSIONS:** The proposed classification may have prognostic value, with type A mCNV showing better visual outcomes. Further studies are needed to confirm these findings.

PMID: 30395663 DOI: 10.3928/23258160-20181002-05


**Radial shape discrimination testing for new-onset neovascular age-related macular degeneration in at-risk eyes.**

Pitrelli Vazquez N, Harding SP, Heimann H, et al.

**ABSTRACT:** We investigated the performance of the handheld radial shape discrimination (hRSD) test in detecting the development of neovascular AMD (nAMD) in a prospective, longitudinal, observational study. Patients diagnosed with unilateral nAMD, with no nAMD in the other eye (the study eye, SE), completed the hRSD test on consecutive, routine clinic visits up to a maximum of 12, or until they were diagnosed with nAMD in the SE based on slit-lamp biomicroscopy and spectral-domain OCT assessment, with fluorescein angiography confirmation. Masked grading was carried out to confirm the diagnosis of nAMD, and to ensure no cases of nAMD were missed. Receiver operating characteristics (ROC) analysis was used to explore the diagnostic performance of the hRSD test relative to clinical diagnosis. Data were available from 179 patients of whom 19 (10.6%; “converters”) developed nAMD in the SE. The mean hRSD threshold at conversion was -0.47 (95% CI -0.38 to -0.55) logMAR compared to -0.53 (-0.50 to -0.57) logMAR in 160 non-converters. hRSD threshold in the converters began to decline 190 days before diagnosis of nAMD. The ROC curve demonstrated that at an hRSD cut-off of -0.60 logMAR, sensitivity was 0.79 (0.54-0.94) with a specificity of 0.54 (0.46-0.62); positive and negative predictive values were 0.16 and 0.96 respectively. We conclude that the hRSD test has moderate sensitivity for detecting the earliest stages of nAMD in the at-risk fellow eyes of patients with unilateral nAMD, compared to clinical diagnosis. Given its relative inexpensiveness, ease of use and the inherent connectivity of the platforms it can be presented on, it may have a role in early detection of nAMD in the population at large.

PMID: 30408127 DOI: 10.1371/journal.pone.0207342

**Sci Transl Med. 2018 Nov 7;10(466). pii: eaa4544.**

**Calcified nodules in retinal drusen are associated with disease progression in age-related macular degeneration.**

Tan ACS, Pilgrim MG, Fearn S, et al.

**ABSTRACT:** Drusen are lipid-, mineral-, and protein-containing extracellular deposits that accumulate between the basal lamina of the retinal pigment epithelium (RPE) and Bruch's membrane (BrM) of the human eye. They are a defining feature of age-related macular degeneration (AMD), a common sight-threatening disease of older adults. The appearance of heterogeneous internal reflectivity within drusen
(HIRD) on optical coherence tomography (OCT) images has been suggested to indicate an increased risk of progression to advanced AMD. Here, in a cohort of patients with AMD and drusen, we show that HIRD indicated an increased risk of developing advanced AMD within 1 year. Using multimodal imaging in an independent cohort, we demonstrate that progression to AMD was associated with increasing degeneration of the RPE overlying HIRD. Morphological analysis of clinically imaged cadaveric human eye samples revealed that HIRD was formed by multilobular nodules. Nanoanalytical methods showed that nodules were composed of hydroxyapatite and that they differed from spherules and BrM plaques, other refractile features also found in the retinas of patients with AMD. These findings suggest that hydroxyapatite nodules may be indicators of progression to advanced AMD and that using multimodal clinical imaging to determine the composition of macular calcifications may help to direct therapeutic strategies and outcome measures in AMD.

PMID: 30404862 DOI: 10.1126/scitranslmed.aat4544

Pathogenesis


Quantitative proteomic analysis of aqueous humor from patients with drusen and reticular pseudodrusen in age-related macular degeneration.

Baek JH, Lim D, Park KH, et al.

**BACKGROUND:** To identify novel biomarkers related to the pathogenesis of dry age-related macular degeneration (AMD), we adopted a human retinal pigment epithelial (RPE) cell culture model that mimics some features of dry AMD including the accumulation of intra- and sub-RPE deposits. Then, we investigated the aqueous humor (AH) proteome using a data-independent acquisition method (sequential window acquisition of all theoretical fragment ion mass spectrometry) for dry AMD patients and controls.

**METHODS:** After uniformly pigmented polarized monolayers of human fetal primary RPE (hfRPE) cells were established, the cells were exposed to 4-hydroxy-2-nonenal (4-HNE), followed by Western blotting, immunofluorescence analysis and ELISA of cells or conditioned media for several proteins of interest. Data-dependent acquisition for identification of the AH proteome and SWATH-based mass spectrometry were performed for 11 dry AMD patients according to their phenotypes (including soft drusen and reticular pseudodrusen [RPD]) and 2 controls (3 groups).

**RESULTS:** Increased intra- and sub-RPE deposits were observed in 4-HNE-treated hfRPE cells compared with control cultures based on APOA1, cathepsin D, and clusterin immunoreactivity. Additionally, the differential abundance of proteins in apical and basal chambers with or without 4-HNE treatment confirmed the polarized secretion of proteins from hfRPE cells. A total of 119 proteins were quantified in dry AMD patients and controls by SWATH-MS. Sixty-five proteins exhibited significantly altered abundance among the three groups. A two-dimensional principal component analysis plot was generated to identify typical proteins related to the pathogenesis of dry AMD. Among the identified proteins, eight proteins, including APOA1, CFHR2, and CLUS, were previously considered major components or regulators of drusen. Three proteins (SERPINA4, LUM, and KERA proteins) have not been previously described as components of drusen or as being related to dry AMD. Interestingly, the LUM and KERA proteins, which are related to extracellular matrix organization, were upregulated in both RPD and soft drusen.

**CONCLUSIONS:** Differential protein expression in the AH between patients with drusen and RPD was quantified using SWATH-MS in the present study. Detailed proteomic analyses of dry AMD patients might provide insights into the in vivo biology of drusen and RPD.

PMID: 30404605 DOI: 10.1186/s12886-018-0941-9
Stem cells


Possibilities for using pluripotent stem cells for restoring damaged eye retinal pigment epithelium.

Kharitonov AE, Surdina AV, Lebedeva OS, et al.

**ABSTRACT:** The retinal pigment epithelium is a monolayer of pigmented, hexagonal cells connected by tight junctions. These cells compose part of the outer blood-retina barrier, protect the eye from excessive light, have important secretory functions, and support the function of photoreceptors, ensuring the coordination of a variety of regulatory mechanisms. It is the degeneration of the pigment epithelium that is the root cause of many retinal degenerative diseases. The search for reliable cell sources for the transplantation of retinal pigment epithelium is of extreme urgency. Pluripotent stem cells (embryonic stem or induced pluripotent) can be differentiated with high efficiency into the pigment epithelium of the retina, which opens up possibilities for cellular therapy in macular degeneration and can slow down the development of pathology and, perhaps, restore a patient's vision. Pioneering clinical trials on transplantation of retinal pigment epithelial cells differentiated from pluripotent stem cells in the United States and Japan confirmed the need for developing and optimizing such approaches to cell therapy. For effective use, pigment epithelial cells differentiated from pluripotent stem cells should have a set of functional properties characteristic of such cells in vivo. This review summarizes the current state of preclinical and clinical studies in the field of retinal pigment epithelial transplantation therapy. We also discuss different differentiation protocols based on data in the literature and our own data, and the problems holding back the widespread therapeutic application of retinal pigment epithelium differentiated from pluripotent stem cells.

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Genetics

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SIRT1 rs12778366, FGFR2 rs2981582, STAT3 rs744166, LIPC rs10468017, rs493258 and LPL rs12678919 genotypes and haplotype evaluation in patients with age-related macular degeneration.

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

**OBJECTIVE:** Age-related macular degeneration (AMD) is the leading cause of blindness in elderly individuals in the developed countries. The etiology of AMD is thought to be multifactorial, including environmental and genetic factors. Our purpose was to determine the genotype frequencies of six different SNPs in genes that encode proteins involved in AMD-related molecular changes (SIRT1 rs12778366, FGFR2 rs2981582, STAT3 rs744166, LIPC rs10468017, rs493258 and LPL rs12678919) for evaluation of haplotype risk in patients with AMD.

**METHODS:** The study cohort consisted of 652 AMD patients and 829 healthy controls. The genotyping was carried out using the RT-PCR.

**RESULTS:** TT genotype of the LIPC rs493258 polymorphism was associated with decreased odds of early AMD development under the codominant and recessive models (OR = 0.446; 95% CI: 0.258-0.772; p = 0.004 and OR = 0.455; 95% CI: 0.274-0.756; p = 0.002, respectively) after Bonferroni correction, (p > 0.05/6, since we analyzed 6 different SNPs). The haplotype containing the two minor alleles T-T in rs10468017-rs493258 were significantly (p = 0.034) associated with early AMD development decreasing. There were no associations found with atrophic AMD development.

**CONCLUSION:** The study showed that LIPC rs493258 gene and haplotype containing the two minor alleles
T-T in rs10468017-rs493258 may decrease AMD development.

PMID: 30399423 DOI: 10.1016/j.gene.2018.11.004

Expression of ABCA4 in the retinal pigment epithelium and its implications for Stargardt macular degeneration.

Lenis TL, Hu J, Ng SY, et al.

Abstract: Recessive Stargardt disease (STGD1) is an inherited blinding disorder caused by mutations in the Abca4 gene. ABCA4 is a flipase in photoreceptor outer segments (OS) that translocates retinaldehyde conjugated to phosphatidylethanolamine across OS disc membranes. Loss of ABCA4 in Abca4 -/- mice and STGD1 patients causes buildup of lipofuscin in the retinal pigment epithelium (RPE) and degeneration of photoreceptors, leading to blindness. No effective treatment currently exists for STGD1. Here we show by several approaches that ABCA4 is additionally expressed in RPE cells. (i) By in situ hybridization analysis and by RNA-sequencing analysis, we show the Abca4 mRNA is expressed in human and mouse RPE cells. (ii) By quantitative immunoblotting, we show that the level of ABCA4 protein in homogenates of wild-type mouse RPE is about 1% of the level in neural retina homogenates. (iii) ABCA4 immunofluorescence is present in RPE cells of wild-type and Mertk -/- but not Abca4 -/- mouse retina sections, where it colocalizes with endolysosomal proteins. To elucidate the role of ABCA4 in RPE cells, we generated a line of genetically modified mice that express ABCA4 in RPE cells but not in photoreceptors. Mice from this line on the Abca4 -/- background showed partial rescue of photoreceptor degeneration and decreased lipofuscin accumulation compared with nontransgenic Abca4 -/- mice. We propose that ABCA4 functions to recycle retinaldehyde released during proteolysis of rhodopsin in RPE endolysosomes following daily phagocytosis of distal photoreceptor OS. ABCA4 deficiency in the RPE may play a role in the pathogenesis of STGD1.

PMID: 30397118 DOI: 10.1073/pnas.1802519115

Low vision


Charles Bonnet Syndrome: cortical hyperexcitability and visual hallucination.

Coltheart M.

ABSTRACT: Loss of foveal vision with sparing of peripheral vision, as in macular degeneration, is often associated with visual hallucinations: it has been suggested that these occur because deafferentation of neurons in regions of visual cortex results in local neuronal hyperexcitability, and new evidence supports this hypothesis.

PMID: 30399348 DOI: 10.1016/j.cub.2018.09.007

Diet


The role of diet, micronutrients and the gut microbiota in age-related macular degeneration: new perspectives from the gut-retina axis.


ABSTRACT: Age-related macular degeneration (AMD) is a complex multifactorial disease and the primary cause of legal and irreversible blindness among individuals aged ≥65 years in developed countries.
Globally, it affects 30-50 million individuals, with an estimated increase of approximately 200 million by 2020 and approximately 300 million by 2040. Currently, the neovascular form may be able to be treated with the use of anti-VEGF drugs, while no effective treatments are available for the dry form. Many studies, such as the randomized controlled trials (RCTs) Age-Related Eye Disease Study (AREDS) and AREDS 2, have shown a potential role of micronutrient supplementation in lowering the risk of progression of the early stages of AMD. Recently, low-grade inflammation, sustained by dysbiosis and a leaky gut, has been shown to contribute to the development of AMD. Given the ascertained influence of the gut microbiota in systemic low-grade inflammation and its potential modulation by macro- and micro-nutrients, a potential role of diet in AMD has been proposed. This review discusses the role of the gut microbiota in the development of AMD. Using PubMed, Web of Science and Scopus, we searched for recent scientific evidence discussing the impact of dietary habits (high-fat and high-glucose or -fructose diets), micronutrients (vitamins C, E, and D, zinc, beta-carotene, lutein and zeaxanthin) and omega-3 fatty acids on the modulation of the gut microbiota and their relationship with AMD risk and progression.

PMID: 30400586 DOI: 10.3390/nu10111677

Case Reports


Complete regression of branching vascular network in polypoidal choroidal vasculopathy by ranibizumab and photodynamic therapy, two case reports.


**Background:** Polypoidal choroidal vasculopathy (PCV) consists of polyps that potentially cause massive subretinal hemorrhage and their branching vascular network (BVN) of feeder vessels. Although conventional indocyanine green angiography (IA) has shown anti-vascular endothelial growth factor (VEGF) agents and/or photodynamic therapy (PDT) to successfully induce polyp closure, the BVN appears resistant to these therapies and serves as the origin of recurrent active polyps. Recently introduced optical coherence tomography angiography (OCT-A) enables more frequent angiographic evaluation of polyps and the BVN than does conventional IA since it does not require intravenous fluorescent dye injection and is thus considered non-invasive.

**Case Presentation:** Case 1. A 70-year-old male with PCV in his left eye suffered from vision deterioration (20/40) due to persistent subretinal fluid despite 42 intravitreal injections of ranibizumab (IVRs) over 5 years and 7 months. PDT was performed as an adjunct therapy 3 days after the 43rd IVR. IA at 3 months after PDT showed successful polyp closure but persisting BVN. However, more frequent evaluation with OCT-A starting at 1 week after PDT demonstrated complete regression of both the BVN and polyp. OCT-A at every subsequent outpatient visit depicted gradual re-perfusion of the BVN and the restoration of most of its original network at 3 months, which was compatible with IA findings. Neither OCTA nor IA revealed polyp recurrence at 3 months. Case 2. A 65-year-old female suffering from left vision deterioration due to PCV underwent 5 intravitreal injections of aflibercept. Since her subretinal fluid persisted, the treatment was switched to a combination of IVR and PDT. OCT-A revealed marked regression of the BVN and polyp at 2 weeks, but the BVN had regained its original shape at 2 months without any sign of polyp recurrence.

**Conclusions:** Differently from previous observations obtained by IA alone, more frequent non-invasive OCT-A examination revealed complete but transient regression of the BVN just after combination therapy with IVR and PDT.

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