FEATURED ARTICLE

Mental health and visual acuity in patients with age-related macular degeneration.

BMC Ophthalmology 2022 Oct 2022

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Background: Visual acuity (VA) loss has been associated with depression in patients with age-related macular degeneration (AMD). However, previous studies did not incorporate subgroups of AMD when correlating VA and mental health. The goal of this study was to describe the relationship between VA and mental health questions in patients with different classifications of AMD, and to identify associations of mental health subscale scores.

Methods: AMD patients classified by multi-modal imaging were recruited into an AMD registry. Habitual VA was obtained by ophthalmic technicians using the Snellen VA at distance. At enrollment, patients completed the NEI-VFQ-25, which includes 25 questions regarding the patient's visual functionality. Median with interquartile-range (IQR) scores on the mental health subscale of the VFQ were calculated by AMD classification and VA groups. Univariate and multivariable general linear models were used to estimate associations between mental health scores and variables of interest.

Results: Eight hundred seventy-five patients were included in the study. Patients with bilateral geographic atrophy (GA) or bilateral GA and neovascular (NV) AMD scored lowest on the mental health subscales with a median (IQR) of 58.2 (38-88) and 59.3 (38-88). When stratified by VA, patients with a habitual VA of 20/200 or worse scored the lowest on mental health subscales scores: median of 43.8 (IQR: 31-62). Patients with a VA of 20/20 scored the highest: 87.5 (IQR: 81-94). Habitual VA of the better- and worse-seeing eye and AMD classification were significantly associated with mental health subscale scores (all $p < 0.0001$ in both the univariate and multivariable analysis, except the VA of the worse-seeing eye in multivariable model $p = 0.027$). Patients enrolled during the COVID pandemic had mental health scores that were 2.7 points lower than prior to the pandemic, but this difference was not significant in univariate ($p = 0.300$) or multivariable analysis ($p = 0.202$).

Conclusion: There is a significant association between mental health questionnaire scores and AMD classification, as well as VA in both the better and worse-seeing eyes in patients with AMD. It is important for clinicians to recognize feelings of worry/ frustration in these patients, so they can be appropriately referred, screened, and treated for mental health problems.

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BIOMARKERS

Optical Coherence Tomography Risk Factors for Development of Atrophy in Eyes with Intermediate Age-related Macular Degeneration.

Ophthalmology, Retina 2022 Oct 5

Hirabayashi K, Yu HJ, Wakatsuki Y, Marion KM, Wykoff CC, Sadda SR.

Purpose: To determine the frequency of multiple optical coherence tomography (OCT) biomarkers of intermediate age-related macular degeneration (iAMD) and their relationship with the development of complete retinal pigment epithelium and outer retinal atrophy (cRORA) after 2 years. DESIGN: Retrospective cohort study.

Participants: This retrospective analysis included 330 eyes of 330 consecutive patients with iAMD in at least one eye who had 24 months of follow-up data.

Methods: Spectralis OCT volumes scans (49 B-scans over 6x6mm, ART = 6, fovea-centered) at baseline were evaluated for previously described iAMD biomarkers including a high central drusen volume (DV; ≥0.03 mm3), intraretinal hyperreflective foci (IHRF), subretinal drusenoid deposits (SDD), hypo-reflective drusen cores (hDC), and a thin or thick (multi-layered) double layer sign (DLS). The AMD status in the fellow eye was also assessed and classified as normal or early AMD, iAMD, exudative macular neovascularization (MNV), or cRORA.

Main outcome measures: Incidence of cRORA, Odds ratio (OR) for demographics and OCT features. RESULTS: At month 24, 16.36% (54/330) of the iAMD eyes developed cRORA. Several baseline features, including high central DV, IHRF, SDD, hDC, thin DLS, and cRORA on fellow eye were associated with a significantly greater risk for development of cRORA at 2 years. Odds ratio, 95% confidence interval, p-value, and baseline frequencies of these biomarkers were: DV (6.510, 2.467-17.176, p<0.001, 49.1%), IHRF (12.763, 4.763-34.202, p<0.001, 38.8%), SDD (2.307, 1.003-5.304, p=0.049, 34.2%), hDC (3.012, 1.152-7.873, p=0.024, 13.0%), thin DLS (4.517, 1.555-13.126, p=0.006, 11.8%), and cRORA in the fellow eye (7.184, 1.938-26.623, p=0.003, 8.2%).

Conclusion: In addition to the four previously reported factors that are present in a significant proportion of iAMD (DV, IHRF, hDC, SDD), a thin DLS, and cRORA in the fellow eye were associated with an increased risk of progression to cRORA over 2 years. These biomarkers may aid in prognostication, risk stratification, and selection of patients for clinical trials.

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A Cross-Sectional Study of Various Imaging and Biochemical Biomarkers in Patients with Diabetic Macular Edema in Different Stages of Diabetic Retinopathy.

Clinical Ophthalmology. 2022 Sep 23

Naveen P, Sahu V, Pathak M.

Purpose: To compare which imaging and biochemical biomarkers are associated with different stages of diabetic retinopathy (DR) in type 2 diabetes mellitus patients with diabetic macular edema (DME).

Patients and Methods: It was a cross-sectional, observational study that included 100 patients of DME with different stages of DR. Patients were divided into two groups: Group A - DME with non-proliferative diabetic retinopathy (NPDR) and Group B - DME with proliferative diabetic retinopathy (PDR). Group A was further subdivided into three subgroups: A (1) - DME with mild NPDR, A (2) - DME with moderate NPDR, and A (3) - DME with severe NPDR. The primary outcome measure was

the association of imaging and biochemical biomarkers with different stages of DR in patients with DME.

Results: Out of 100 patients, Group A (1) had 1, Group A (2) 44, Group A (3) 29, and group: B had 29 patients. As Group A (1) had only one patient, we did not include it in the calculation. The overall mean age of the study population was 54.84+9.87 years, with a male preponderance (76%). The HbA1c levels, serum triglyceride level, serum cholesterol level, and microalbuminuria level showed no significant association with different stages of DR (P>0.05). Still, we found high serum urea levels (p=0.027) in Group B patients. The optical coherence tomography (OCT)-based imaging biomarkers - central subfield thickness (CST), cystoid macular edema (CME), subretinal fluid (SRF), and hyperreflective foci (HRF) - showed no significant association with various stages of DR. The presence of diffuse retinal thickness (DRT) (p=0.04) and the epiretinal membrane (ERM) (p=0.04) showed significant association with Group B patients.

Conclusion: The essential biochemical biomarkers such as serum urea levels and DRT and ERM may be considered an important imaging biomarker for the advanced stage of DR.

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DRUG TREATMENTS

Risk factors for myopic choroidal neovascularization-related macular atrophy after anti-VEGF treatment.

PLoS One 2022 Sep 22

Bae KW, Kim DI, Kim BH, Oh BL, Lee EK, Yoon CK, Park UC.

Purpose: The study aimed to evaluate risk factors for macular atrophy (MA) associated with myopic choroidal neovascularization (mCNV) during long-term follow-up after intravitreal anti-vascular endothelial growth factor (VEGF) treatment in highly myopic eyes.

Methods: The medical records of patients who received intravitreal injection of anti-VEGF agents as mCNV treatment and were followed-up for more than 36 months were retrospectively reviewed. The risk factors for the development of mCNV-MA, which is the fovea-involving patchy atrophy lesion adjacent to mCNV, were investigated using the Cox proportional hazard model.

Results: A total of 82 eyes (74 patients) were included in the study. The mean age at anti-VEGF treatment was 56.3 ± 12.5 years (range, 26-77), and the mean follow-up period was 76.3 ± 33.5 months (range, 36-154). During follow-up, mCNV-MA developed in 27 eyes (32.9%), and its occurrence was estimated to be 24.5% at 3 years and 37.3% at 5 years after the first anti-VEGF treatment. Old age (hazard ratio [HR] = 1.054, 95% confidence interval [CI]: 1.018-1.091; P = 0.003) and greater CNV size at baseline (HR = 2.396, CI: 1.043-5.504; P = 0.040) were significant factors for mCNV-MA development. Eyes with a thinner subfoveal choroid were more likely to show faster enlargement of the mCNV-MA during follow-up.

Conclusions: In mCNV eyes treated with intravitreal anti-VEGF agents, older age and greater mCNV size at baseline were risk factors for the development of MA during long-term follow-up, which was associated with a poor visual prognosis.

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Incidence of metformin use in patients with age-related macular degeneration versus normal controls: A population-based study in Olmsted County, Minnesota.

Eye (London). 2022 Sep 23

Starr MR, Dalvin LA, AbouChehade JE, Damento GM, Garcia M, Shah SM, Hodge DO, Iezzi R, Bakri SJ.

Purpose: The purpose of this study is to compare the use of metformin in patients with both exudative and non-exudative age-related macular degeneration (AMD) versus control populations.

Design: Retrospective review of three age- and sex-matched cohorts from 1/1/2004 to 12/31/2013: patients with exudative AMD, a cohort of dry AMD patients, and a cohort of patients without AMD. The primary endpoint was the incidence of metformin use in all of the cohorts.

Results: There were 1512 patients, with 504 in each of the three cohorts. There was no difference in the prevalence of diabetes between cohorts. Compared to patients with dry AMD, patients with no AMD had increased likelihood of metformin use (p = 0.0168, OR 1.66 (1.09-2.51). There was no difference in the likelihood of metformin use between exudative AMD patients and non-AMD controls.

Conclusions: There appears to be an increased incidence of metformin use in patients without AMD compared to patients with dry AMD. Metformin's current role in the treatment of anti-aging diseases makes it a plausible target for use in the treatment of AMD, particularly dry AMD.

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Practical implementation of a q4-q16 aflibercept treat-and-extend pathway for the treatment of neovascular age-related macular degeneration: Updated guidance from a UK expert panel.

Eye (London, England) 2022 Oct 7

Bailey C, Cackett P, Kotagiri A, Mahmood S, Minos E, Narendran N, Patwardhan A, Sim DA, Morgan-Warren P, O'Neil C, Straw K.

Objectives: This report, based on guidance from a panel of UK retina specialists, introduces a revised intravitreal aflibercept (IVT-AFL) treat-and-extend (T&E) pathway for the treatment of neovascular age-related macular degeneration (nAMD). The T&E pathway incorporates the updated IVT-AFL label (April 2021) allowing flexible treatment intervals of 4 weeks to 16 weeks, after three initiation doses and a further dose after 8 weeks. Practical guidance is provided on the clinical implementation of the revised pathway, with the aim of supporting clinical decision-making to benefit patients and addressing capacity issues in nAMD services.

Methods: Three structured round-table meetings of UK retina specialists were held online on 19 May, 16 June and 13 October 2021. These meetings were organised and funded by Bayer.

Results: The authors revised the previously published consensus pathway to reflect the changes to the IVT-AFL label and developed guidelines for the implementation of the pathway in UK clinical

practice. The guidelines include topics such as recommendations for extending patients with 2- or 4-week adjustments, extending patients to 16-week treatment intervals, managing fellow eye involvement, and reducing treatment intervals for patients with particularly active disease.

Conclusions: The revised IVT-AFL T&E nAMD pathway offers guidance to clinicians seeking to increase the dosing flexibility of IVT-AFL, with 4- to 16-week treatment intervals, in line with the updated IVT-AFL label, to meet the continually evolving demands of nAMD service provision.

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GENETICS

High-resolution genome topology of human retina uncovers super enhancer-promoter interactions at tissue-specific and multifactorial disease loci.

Nature Communications 2022 Oct 7

Marchal C, Singh N, Batz Z, Advani J, Jaeger C, Corso-Díaz X, Swaroop A.

Chromatin organization and enhancer-promoter contacts establish unique spatiotemporal gene expression patterns in distinct cell types. Non-coding genetic variants can influence cellular phenotypes by modifying higher-order transcriptional hubs and consequently gene expression. To elucidate genomic regulation in human retina, we mapped chromatin contacts at high resolution and integrated with super-enhancers (SEs), histone marks, binding of CTCF and select transcription factors. We show that topologically associated domains (TADs) with central SEs exhibit stronger insulation and augmented contact with retinal genes relative to TADs with edge SEs. Merging genome-wide expression quantitative trait loci (eQTLs) with topology map reveals physical links between 100 eQTLs and corresponding eGenes associated with retinal neurodegeneration. Additionally, we uncover candidate genes for susceptibility variants linked to age-related macular degeneration and glaucoma. Our study of high-resolution genomic architecture of human retina provides insights into genetic control of tissue-specific functions, suggests paradigms for missing heritability, and enables the dissection of common blinding disease phenotypes.

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DIAGNOSIS AND IMAGING

Central posterior hyaloidal fibrosis - A novel optical coherence tomography feature associated with choroidal neovascular membrane.

American Journal of Ophthalmology Case Rep. 2022 Sep 20

Khan H, Amjad R, Keane PA, Denniston AK, Lujan BJ.

Purpose: To describe a novel optical coherence tomography (OCT) finding at the vitreomacular interface (VMI), and report its association with advanced choroidal neovascularisation (CNV).

Observations: Optical coherence tomography (OCT) scans performed at three retinal imaging centres at Amanat Eye Hospital, Pakistan from May 2016 till May 2021 were reviewed. A specific change at the vitreomacular interface was noted consisting of abnormal hyper reflectivity at the point of attachment of the posterior hyaloid membrane to the foveal center which appears to 'fill in' the foveolar depression.Eight eyes of eight patients were identified. All affected eyes had advanced CNV and persistent vitreofoveolar adhesion. In all eyes, the foveal contour (concavity) was maintained and there was no inner retinal surface wrinkling which differentiates this OCT feature from vitreomacular traction or epiretinal membranes. The authors propose the term Central Posterior Hyaloidal Fibrosis (CPHF) for this specific OCT finding.

Conclusions and Importance: Central Posterior Hyaloidal Fibrosis (CPHF) is a newly reported OCT finding associated with advanced CNV, which may represent a possible profibrotic influence of a choroidal neovascular membrane to the overlying posterior hyaloid adhesion.

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The Fovea-Protective Impact of Double-Layer Sign in Eyes With Foveal-Sparing Geographic Atrophy and Age-Related Macular Degeneration.

Investigative Ophthalmology & Visual Science 2022 Oct 3

Fukuyama H, Huang BB, BouGhanem G, Fawzi AA.

Purpose: The purpose of this study was to investigate the impact of double-layer sign (DLS) on geographic atrophy (GA) progression in eyes with foveal-sparing GA and age-related macular degeneration (AMD).

Methods: This is a retrospective, consecutive case series of eyes with foveal-sparing GA secondary to AMD with more than 6 months of follow-up. The size of the foveal-sparing area was measured on the fundus autofluorescence images at the first and last visits. Each eye was evaluated for the presence or absence of DLS inside the foveal-sparing area. We graded eyes based on the presence of DLS within the foveal-sparing area and compared the progression of GA between two groups (DLS (+) versus DLS (-)).

Results: We identified 25 eyes with foveal-sparing GA with at least 2 follow-up visits (average interval = 22.7 ± 11.8 months between visits). The mean foveal sparing area was 1.74 ± 0.87 mm2 (range = 0.42-4.14 mm2) at baseline and 1.26 ± 0.75 mm2 (range = 0.25-2.92 mm2) at the last visit. Seventeen eyes (65.3%) were graded as DLS (+) within the foveal-sparing area. Square root progression of GA toward the fovea was significantly faster in the DLS (-) eyes (0.149 ± 0.078 mm/year) compared to the DLS (+) group (0.088 ± 0.052 mm/year; P = 0.04).

Conclusions: The DLS (-) group showed significantly faster centripetal GA progression than the DLS (+) group. Our data suggest that the presence of DLS in the spared foveal area could be a protective factor against foveal progression of GA in eyes with AMD.

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