Macular Disease Foundation AUSTRALIA

MDFA Research update

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FEATURED ARTICLE

Changes in 12-month outcomes over time for age-related macular degeneration, diabetic macular oedema and retinal vein occlusion.

Eye (London). 2022 May 4.

Bhandari S, Nguyen V, Hunt A, Gabrielle PH, Viola F, Mehta H, Manning, Squirrell D, Arnold J, McAllister IL, Barthelmes D, Gillies M.

Objectives: To identify whether the outcomes of neovascular age-related macular degeneration (nAMD), diabetic macular oedema (DMO) and retinal vein occlusion (RVO) in routine clinical practice have changed over time.
Methods: We analysed 12-month outcomes in treatment-naïve eyes that started aflibercept or ranibizumab for nAMD (3802 eyes), DMO (975 eyes), Branch RVO (BRVO, 357 eyes), Central RVO (CRVO, 371 eyes) and Hemi-RVO (HRVO, 54 eyes) from 2015 and 2019 tracked in the prospectively designed observational Fight Retinal Blindness! Registry.
Results: The mean VA change at 12-month for each year between 2015 and 2019 remained stable or otherwise showed no discernible trends over time in eyes with nAMD (+3.3 to +6 letters), DMO (+3.6 to +6.7 letters) and RVO (+10.3 to +11.7 letters for BRVO, +5.9 to +17.7 letters for CRVO and 10.2 to 20.7 letters for HRVO). The median number of VEGF-inhibitor injections in eyes that completed 12-month follow-up also remained stable at 8-9 for nAMD, 6-7 for DMO, 7-9 for RVO. Fewer eyes (<one-fourth) that started treatment between 2015 and 2018 and more eyes starting in 2019 did not complete 12-month's follow-up visit. The mean VA in non-completers at their last visit was higher than that of their baseline visit.
Conclusions: Treatment patterns and outcomes for nAMD, DMO and RVO in routine clinical practice have stabilised over the past 5 years at levels inferior to those reported by the pivotal phase 3 studies. A conscious effort to treat these conditions more intensively, or with longer lasting agents, would likely improve outcomes further in our patients.

DOI: 10.1038/s41433-022-02075-6

Fluid control in neovascular age-related macular degeneration with brolucizumab: an analysis of the HAWK and HARRIER phase 3 trials.

Ophthalmologica. 2022 Apr 25.

Regillo C, Singh R, Hamilton R, Gedif K, Best C, Koh A, Holz FG.

Introduction: Neovascular age-related macular degeneration (nAMD) is characterised by exudation of fluid from abnormally growing blood vessels in the macula. Anti-vascular endothelial growth factor (VEGF) therapy is standard treatment for nAMD. Fluid resolution is used both as an indicator of disease control and to guide the frequency of treatment because of anti-VEGF therapy effectiveness in reducing neovascularization-related exudation. Herein reports a post-hoc assessment of the HAWK and HARRIER trials comparing efficacy and safety of brolucizumab with aflibercept in patients with nAMD.
Materials And Methods: HAWK randomized 1078 patients with untreated, active choroidal neovascularization due to AMD in the study eye to receive brolucizumab 3mg, 6mg or aflibercept 2mg. In HARRIER, 739 patients received brolucizumab 6mg or aflibercept 2mg. Brolucizumab was injected at weeks 0, 4 and 8, and thereafter q12w unless disease activity was identified (injection interval: q8w). Aflibercept was injected q8w after the loading phase; aligned with approved dosing at study initiation. The objective of this analysis was to assess effects of brolucizumab versus aflibercept on retinal fluid resolution during two phase 3 trials (HAWK and HARRIER) in patients with nAMD. Anatomical assessments for intraretinal fluid (IRF) and subretinal fluid (SRF) were performed every 4 weeks by spectral domain optical coherence tomography. Sustained dryness was defined as a patient being fluid-free (SRF and IRF) on ≥3 consecutive visits. Time to sustained dryness was determined by Kaplan-Meier estimates.
Results: At week 96, fluid resolution (absence of IRF and SRF) was achieved by more brolucizumab- (6mg; 76.1%) versus aflibercept-treated patients (63.1%; p=0.0002, HAWK); 75.4% versus 61.8% (p<0.0001, HARRIER). More patients achieved sustained dryness with brolucizumab versus aflibercept: at 96 weeks, 87.9% (brolucizumab 3mg) and 86.1% (brolucizumab 6mg) versus 82.0% (aflibercept) in HAWK and 91.2% (brolucizumab) versus 78.0% (aflibercept) in HARRIER. Sustained dryness was achieved faster and hence with fewer brolucizumab injections.
Discussion/Conclusion: Brolucizumab dried the macula in patients with nAMD faster and to a greater degree than aflibercept. Achieving sustained dryness faster, and therefore with fewer injections, provides an opportunity for earlier decisions relating to treatment interval extension potentially reducing treatment burden.

DOI: 10.1159/000524096

RISK OF DISEASE

Association between metformin use and the risk of age-related macular degeneration in patients with type 2 diabetes: a retrospective study.

BMJ Open. 2022 Apr 26

Jiang J, Chen Y, Zhang H, Yuan W, Zhao T, Wang N, Fan G, Zheng D, Wang Z.

Objectives: To investigate the effect of metformin on the decreased risk of developing age-related macular degeneration (AMD) in patients with type 2 diabetes mellitus (T2DM) for ≥10 years. DESIGN: A retrospective study.
Participants: Patients aged ≥50 with a diagnosis of T2DM no less than 10 years were included. **Methods**: Variables predisposing to AMD were reviewed; the potential confounders related to T2DM or AMD were selected from literature records; AMD and diabetic retinopathy (DR) were diagnosed by funduscopy, optical coherence tomography and/or fluorescein angiography. The subgroup analysis was performed in early and late AMD. The protective effect of metformin was evaluated in duration-response and dose-response patterns.
Results: A total of 324 patients (115 metformin non-users and 209 users) were included in the final analysis. AMD was observed in 15.8% of metformin users and 45.2% of metformin non-users (p<0.0001). The ORs for any AMD, early AMD and late AMD present in patients with DR were 0.06 (0.02-0.20), 0.03 (0.00-0.20) and 0.17 (0.04-0.75). The serum high-density lipoprotein level was positively associated with the late AMD risk (p=0.0054). When analysed by the tertiles of cumulative duration, a similarly reduced risk was observed for the second (5-9 years) (OR: 0.24, 95% CI: 0.08 to 0.75) and third tertiles (≥10 years) (OR: 0.22, 95% CI: 0.09 to 0.52) compared with the first tertile (≤4 years).
Conclusion: Among patients with T2DM for ≥10 years, metformin users were less likely to develop any AMD and early AMD than non-users; however, the late AMD was not significantly associated with the use of metformin. Also, AMD was less prevalent in patients with DR. The prolonged metformin treatment with a high cumulative dose enhanced the protective effect against AMD. Metformin significantly reduces the AMD risk when the cumulative duration is >5 years.

DOI: 10.1136/bmjopen-2021-054420

Risk of cystoid macular edema following cataract surgery in retinitis pigmentosa: an analysis of United States claims from 2010 to 2018.

Ophthalmology Retina. 2022 May 2.

Antonio-Aguirre B, Swenor B, Canner JK, Singh MS.

Purpose: Cataract surgery is commonly performed to improve vision in patients with retinitis pigmentosa (RP). However, the risk of postoperative cystoid macular edema (CME) in RP remains unclear. Here, we leveraged a large multi-year claims database to estimate the risk of CME after cataract surgery in patients with and without RP.
Design: Retrospective multicenter cohort.
Methods: We identified patients undergoing single-phase cataract surgery between January 1, 2010, and December 31, 2018, using IBM MarketScan® claims database. We evaluated baseline characteristics, outcomes, and estimated the hazard ratio (HR) using multivariable mixed-effects approach. Eyes of patients with RP were categorized as group R1 and those without RP diagnosis by the time of surgery as group R0.
Main Outcome Measure: Incident postoperative CME in the same eye that underwent cataract extraction within 12 months of the procedure.
Results: We included 468,123 patients and 615,645 eyes: 124 eyes with RP (R1) and 615,521 without RP (R0). The mean age was 50.5 ± 9.8 years in R1 and 57.9 ± 6.1 years in R0. Cumulative CME incidence at 12 months was 5.8% (95% CI, 1.2% - 10.3%) in R1 and 1.1% (95% CI, 1.1% - 1.2%), in R0. On average, CME was reported in R1 subjects 3.9 weeks later than R0 subjects (95% CI, 2.04 - 6.5; P<0.001). R1 subjects had 4.83

(95% CI, 2.13 - 10.92, P<0.001) times the risk of CME than those in R0. Stratified analysis showed that epiretinal membrane (ERM) decreased CME risk in R1 (HR, 0.12 [95% CI, 0.48 - 0.97; P = 0.004]) but increased it in R0 (HR, 4.30 [95% CI, 3.12 - 5.93; P<0.001]). **Conclusions**: The cataract surgery-related risk of CME among RP patients may be more than four times that of people without RP. Males and patients aged 18 to 34 and 55 to 65 years may be at greatest risk, whereas ERM may lower the risk. Further study is warranted to stratify risk by RP genotype and phenotype and illuminate the natural history, angiographic features, and functional consequences of postoperative CME.

DOI: 10.1016/j.oret.2022.04.018

PATIENT EXPERIENCE

Analysis of the Long-term visual Outcomes of ForeseeHome Remote Telemonitoring - The ALOFT study.

Ophthalmology Retina. 2022 Apr 25.

Mathai M, Reddy S, Elman MJ, Garfinkel RA, Ladd B, Wagner A, Sanborn GE, Jacobs J, Busquets M, Chew EY; ALOFT study group.

Purpose: To evaluate long-term visual acuity and performance of a monitoring strategy with a self-operated artificial intelligence enabled home monitoring system in conjunction with standard care for early detection of neovascular age related macular degeneration (nAMD).
Design: Retrospective review.
Subjects: Patients with dry AMD from five referral clinics.
Methods: Clinical data of patients monitored with ForeseeHome (FSH) device from August 2010 to July 2020 was reviewed.
Main Outcome Measures: Visual acuity (VA) at baseline, VA at diagnosis of nAMD for eyes that converted while monitored and VA from the final study follow-up, weekly frequency of use, duration of monitoring, modality of conversion diagnosis (system alert vs detection by other standard care means), and duration and number of treatments since conversion to final study follow-up was collected.
Results: 3334 eyes of 2123 patients were reviewed with a mean (SD) age of 74(8) years, monitored for mean (SD) duration of 3.1(2.4) years, with a total of 1,706,433 tests in 10,474 eye-monitoring years. The mean (SD) weekly use per patient was 5.2(3.4) and it was persistent over the usage period. 285 eyes converted while monitored at an annual rate of 2.72%, and were treated with mean (SD) 17.3(16.5) injections over mean (SD) 2.7(2.0) years, with 6.4(3.1) injections per year for eyes treated for greater than one year. The median VA at baseline and final follow-up for eyes that did not convert were 20/27 and 20/34 with a median change of 0.0 letters. The median VA at baseline, conversion and final follow-up for eyes that converted during the monitoring period were 20/30, 20/39 and 20/32 with a median change from baseline to conversion, baseline to recent and conversion to recent of -4, -4 and 0 letters, respectively. 52% of conversions detected had a system alert prior to conversion. 48% of patients were detected by symptoms or routine visit. Patients experienced a non-nAMD alert on average every 4.6 years. At conversion and at final follow-up the proportion (95% CI) of eyes that maintained ≥20/40 was 84%(78%-88%) and 82%(76%-86%), respectively.

Conclusions: Patients in the FSH monitoring program showed excellent long-term VA years after conversion to nAMD.

DOI: 10.1016/j.oret.2022.04.016

Modifiable Determinants of Satisfaction with Intravitreal Treatment in Patients with Neovascular Age-Related Macular Degeneration.

Drugs Aging. 2022 Apr 29.

Calles-Monar PS, Sanabria MR, Alonso-Tarancon AM, Coco-Martin RM, Mayo-Iscar A.

Background: The success of intravitreal treatment for neovascular age-related macular degeneration (nAMD) depends on maximal adherence to treatment, which in turn requires patient satisfaction. **Objective**: The aim of this study was to assess the factors associated with nAMD patient satisfaction to implement actions to improve treatment experiences and increase adherence.
Design: This was a prospective, observational, analytical, cross-sectional study.
Subjects: Our study included 100 consecutive nAMD patients under intravitreal treatment for at least 1 year.
Methods: Patients completed the Macular Disease Treatment Satisfaction Questionnaire (MacTSQ) and the EuroQol Visual Analog Scale (EQ VAS). A logistic regression was estimated to model the low values of the satisfaction score (MacTSQ < 50).
Results: The mean age of patients was 82.1 ± 7.8 years and 62% were female. Males ($p = 0.002$) and patients who improved their visual acuity ($p = 0.004$) were more satisfied, while patients who received a higher number of injections ($p = 0.036$) and treatment in both eyes ($p = 0.001$) were less satisfied. Higher health-related quality of life was related to higher satisfaction. The sensitivity and specificity of the predictive model were 75.8% and 76.1%, respectively. Factors independently associated with low satisfaction were female sex (odds ratio [OR] 6.84), going to the clinic alone (OR 8.51), longer duration of treatment (OR 0.62), receiving treatment in both eyes (OR 3.54), and suffering a decline in visual acuity (OR 3.30). The questionnaire revealed patients' needs for more information and injection points closer to their homes.
Conclusions: Well-defined areas for improvement were identified, i.e. to improve the information offered to each patient, to incorporate new long-acting drugs, and to establish locations for injection services in peripheral areas.

DOI: 10.1007/s40266-022-00937-y

GENETICS

RP1-associated recessive retinitis pigmentosa caused by paternal uniparental disomy.

Ophthalmic Genetics. 2022 Apr 28.

Bedoukian EC, O'Neil EC, Aleman TS.

Background: We report on a patient with a juvenile-onset inherited retinal degeneration (IRD) associated with homozygous RP1 mutations inherited by uniparental disomy (UPD).
Material And Methods: A 6-year-old healthy girl failed school vision screening and was diagnosed with a bull's eye maculopathy. She underwent complete ophthalmic examination, full-field electroretinograms (ERG), kinetic fields, full-field sensitivity testing (FST), and retinal imaging with spectral domain optical coherence tomography (SD-OCT) and near-infrared (NIR) and short wavelength (SW) fundus autofluorescence (FAF).
Results: Visual acuities were relatively preserved (20/30+). There was subtle foveal depigmentation but an otherwise normal fundus examination. SD-OCT revealed a relatively preserved fovea with thinning of the photoreceptor outer nuclear layer with increasing distance from the foveal center coinciding with marked attenuation of the NIR and less marked loss of the SW-FAF signal. ERGs were non-detectable. Kinetic visual fields were generally full to large (V-4e) target but constricted to ~10°of eccentricity to I-4e stimuli. Dark-adapted thresholds by FST were rod-mediated and elevated by ~2 log units. Homozygous pathogenic mutations in RP1 (c.1720_1721del; p.Ser574Asnfs*8) were identified. Family member testing revealed father and siblings to be unaffected carriers; the mother carried wild-type alleles. Further testing suggested UPD of chromosome 8.
Conclusion: This report adds support to UPD as a mechanism of inheritance in IRDs and stresses the importance of familial testing for genetic diagnosis and counseling. Consistent with earlier descriptions of autosomal recessive RP1-IRDs our patient showed an early rod and cone photoreceptor degeneration.

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PATHOPHYSIOLOGY

Differences in long-term progression of atrophy between neovascular and non-neovascular age-related macular degeneration.

Ophthalmology Retina. 2022 Apr 20.

Airaldi M, Corvi F, Cozzi M, Nittala MG, Staurenghi G, Sadda SR.

Purpose: To compare enlargement rates over 5 years of follow-up in geographic atrophy (GA) versus macular atrophy (MA) associated with macular neovascularization (MNV).
Design: Retrospective, longitudinal comparative case series. PARTICIPANTS: Consecutive series of age-related macular degeneration (AMD) patients with GA (dry) or MA with MNV.
Methods: Atrophic regions on serial registered fundus autofluorescence (FAF) images were semiautomatically delineated and area measurements were recorded every 6±3 months for the first 2 years of follow-up and at yearly intervals up to 5 years.
Main Outcome Measures: Annual raw and square root transformed atrophy growth rates. RESULTS: 117 eyes of 95 patients were included (61 in the GA and 56 in the MA cohort); 100% and 38.5% of eyes completed 2 and 5 years of follow-up, respectively. Mean baseline lesion size was similar between the two groups (raw: 1.74 vs. 1.53 mmˆ2, p = 0.56; sqrt transformed: 1.17 vs. 1.02 mm, p = 0.26). Overall enlargement rates were greater for the GA cohort (raw: 1.72 vs. 1.32 mmˆ2/year, p = 0.002; sqrt

transformed: 0.41 vs. 0.33 mm/year; p = 0.03), as well as the area of atrophy growth at 5 years (raw: +8.06 vs. +4.55 mmˆ2, p = 0.001; sqrt transformed: +1.93 vs. +1.38 mm, p = 0.02). Estimated sqrt transformed area was also significantly greater for the GA cohort at 2 years (1.84 vs. 1.67 mm, p = 0.01).
Conclusions: Presence of MNV was associated with a slower rate of expansion resulting in overall smaller areas of atrophy over time. These findings support the hypothesis that MNV may protect against the progression of atrophy.

DOI: 10.1016/j.oret.2022.04.012

COMORBIDITIES

Association of Age-Related Macular Degeneration with Prior Hyperthyroidism and Hypothyroidism: A Case-Control Study.

Journal Personalized Medicine. 2022 Apr 8.

Hung SH, Xirasagar S, Kuang TT, Chang WW, Cheng YF, Kuo NW, Lin HC.

Prior studies suggest a possible association between thyroid disease and the subsequent development of age-related macular degeneration (AMD), although it remains inconclusive. This study aimed to evaluate the association of AMD with prior hyper-/hypothyroidism based on nationwide population-based data. We retrieved records of the study patients from the National Health Insurance Research Database, 7522 patients with a first-time diagnosis of AMD and 7522 propensity score-matched controls. Multiple logistic regression analyses were performed to explore the association of neovascular AMD with previously diagnosed hyperthyroidism or hypothyroidism. The Chi-square test shows that there was a statistically significant difference in the prevalence of prior hyperthyroidism between cases and controls (1.18 vs. 0.13%, p < 0.001). Furthermore, there was a statistically significant difference the prevalence of prior hypothyroidism between cases and controls (0.44 vs. 0.69%, p < 0.001). Multiple logistic regression analysis reveals that AMD was statistically and significantly associated with prior hyperthyroidism after adjusting for age, sex, monthly income, geographical location, urbanization level, hypertension, hyperlipidemia, diabetes, and coronary heart disease (odds ratio (OR) = 9.074, 95% CI = 4.713-17.471). The adjusted OR of prior hypothyroidism in patients with AMD was 3.794 (95% CI: 2.099~6.858) when compared to the controls. We conclude that patients with thyroid dysfunction are at higher risk of developing AMD Results suggest that these patients could benefit from proactive regular eye checkups to detect evolving eye pathology, even while vision remains normal during the initial phases.

DOI: 10.3390/jpm12040602

Examining the Relationship Between Diabetic Macular Edema, and Obstructive Sleep Apnea.

Clinical Ophthalmology. 2022 Apr 21.

Kaba Q, Tai F, Al-Awadi A, Somani S

Purpose: This prospective cohort study examined the relationship between diabetic macular edema (DME), diabetic retinopathy (DR) and obstructive sleep apnea (OSA) in patients after 1 year of treatment with anti-VEGF injection and/or continuous positive airway pressure (CPAP).
Patients And Methods: The study included adults with type 1 or 2 diabetes mellitus with diabetic retinopathy. Polysomnography metrics were measured at baseline. Ophthalmologic metrics were measured at baseline, six-month (6m) and twelve-month (12m) follow-up. All DME+ patients received standard care, and all OSA+ patients were advised continuous positive airway pressure (CPAP). Logistic regression between DR severity and OSA severity was performed. Analysis of variance (ANOVA) was performed between subgroups.
Results: Seventy-four eyes of 49 patients with DR were included. Prevalence of OSA was significantly higher in the DME+ group (70.7%) than DME- group (42.4%, $p < 0.05$). A significantly lower average minimum SaO2 was noted in OSA+DME+ (81.74%) than OSA+DME- eyes (88.23%, $p < 0.05$). Logistic regression analysis of ophthalmological and sleep metrics showed no correlation between DR and OSA severity. CPAP adherence was 20% (6/30) in the OSA+DME+ cohort and 36% (5/14) in the OSA+DME- cohort. At 12m, CPAP-adherent OSA+DME+ showed significantly lower DR severity score (1.00 ± 0.0) than CPAP non-adherent OSA+DME+ (1.36 ± 0.80, $p = 0.042$). No significant patterns were noted for visual acuity and mean central retinal thickness.
Conclusion: DME is associated with the presence of OSA. Minimum SaO2 is a significant OSA clinical variable for DME. DR severity is not associated with OSA severity. CPAP coupled with intravitreal anti-VEGF therapy may be helpful for reducing DR severity in DME+ eyes. Presence of OSA may diminish intravitreal anti-VEGF efficacy on anatomical (mean CRT) and functional (VA) outcomes of DME.

DOI: 10.2147/OPTH.S354087