FEATURED ARTICLE

Understanding patient preferences in anti-VEGF treatment options for age-related macular degeneration.

PLoS One. 2022 Aug 11

Ozdemir S, Finkelstein E, Lee JJ, Too IHK, Teo KYC, Tan ACS, Wong TY, Cheung GCM.

Purpose: (1) To investigate the relative importance of convenience (consultation frequency and injection frequency) against treatment outcomes (visual and anatomical outcomes) and out-of-pocket medical costs via a discrete choice experiment (DCE), and (2) to investigate how patient characteristics affect patient treatment preferences.

Methods: Eligibility criteria were: (1) receiving a neovascular age-related macular degeneration (nAMD) diagnosis; (2) receiving anti-VEGF treatment; (3) being ≥21 years old, and (4) being able to speak and understand English/Mandarin. Patients were presented with eight choice tasks and asked to choose between their current treatment and two hypothetical treatments that varied by six attributes: number of clinic visits in a year, number of injections in a year, vision quality, control of swelling in retina, drug labelling and out-of-pocket cost.

Results: This analysis involved 180 patients. Based on latent class logistic regressions, vision quality was the most important attribute (34%) followed by cost (24%). The frequency of total clinic visits (15%) was the third most-important attribute, closely followed by labelling (12%) and control of retina swelling (11%). Injection frequency was the least important attribute (4%).

Conclusions: Vision quality was the most important attribute followed by the out-of-pocket costs. Given the same outcomes, patients preferred treatment regimens which require fewer total clinic visits. In comparison, injection frequency alone did not influence patient preferences. With increasing treatment options for nAMD, understanding patients' preferences can help clinicians in selecting agents and treatment regimen most preferred for each patient, which may lead to improved long-term adherence and outcomes.

DOI: 10.1371/journal.pone.0272301

DIAGNOSIS AND IMAGING

Relationship of Retinal Vessel Caliber with Age-Related Macular Degeneration.

Journal of Ophthalmology. 2022 Jul 31.

Toulouie S, Chang S, Pan J, Snyder K, Yiu G.

Purpose: Evaluate the relationship between retinal vascular caliber and age-related macular degeneration (AMD) severity or progression.

Methods: A retrospective secondary analysis of 1172 fundus photographs and clinical data from the prospective Age-Related Eye Disease Study (AREDS). Central retinal artery equivalent (CRAE), central retinal vein equivalent (CRVE), and arteriole-to-venule ratio (AVR) were measured using the Parr-Hubbard-Knudtson formula. Univariate and multivariate regressions were used to determine the

association of CRAE, CRVE, and AVR with age, sex, smoking status, presence of cilioretinal artery, and AMD severity at baseline and 5 years using the 9-step AMD severity score.

Results: Only CRAE and CRVE were higher in men (P < 0.001), current smokers (P < 0.001), and the eyes with a cilioretinal artery (P=0.009 - 0.043). AMD severity was greater in older patients (P=0.001), current smokers (P=0.012), the eyes without a cilioretinal artery (P=0.001), and lower AVR (P=0.034) on multivariate regression but was not influenced by CRAE or CRVE (P=0.240 - 0.500). Choroidal neovascularization (CNV) presence was associated with older age (P=0.003) and absence of a cilioretinal artery (P=0.009), while central geographic atrophy (CGA) was associated with narrower CRAE (P=0.002) and possibly AVR (P=0.046). None of the retinal vessel parameters were predictive of AMD severity score or new onset of CNV or CGA at 5 years.

Conclusion: A lower arteriole-to-venule ratio may be associated with AMD severity, with narrower arterioles seen in the eyes with geographic atrophy, suggesting a role of the retinal vasculature in AMD pathophysiology. This trial is registered with ClinicalTrials.gov Identifier: NCT00000145.

DOI: 10.1155/2022/8210599

Association of Ultra-Widefield Fluorescein Angiography-Identified Retinal Nonperfusion and the Risk of Diabetic Retinopathy Worsening Over Time.

JAMA Ophthalmology. 2022 Aug 18

Silva PS, Marcus DM, Liu D, Aiello LP, Antoszyk A, Elman M, Friedman S, Glassman AR, Googe JM, Jampol LM, Martin DF, Melia M, Preston CM, Wykoff CC, Sun JK; DRCR Retina Network.

Importance: Presence of predominantly peripheral diabetic retinopathy (DR) lesions on ultra-widefield fluorescein angiography (UWF-FA) was associated with greater risk of DR worsening or treatment over 4 years. Whether baseline retinal nonperfusion assessment is additionally predictive of DR disease worsening is unclear.

Objective: To assess whether the extent and location of retinal nonperfusion identified on UWF-FA are associated with worsening in Diabetic Retinopathy Severity Scale (DRSS) score or DR treatment over time.

Design, Setting, and Participants: This cohort study was a prospective, multicenter, longitudinal observational study with data for 508 eyes with nonproliferative DR and gradable nonperfusion on UWF-FA at baseline. All images were graded at a centralized reading center; 200° ultra-widefield (UWF) color images were graded for DR at baseline and annually for 4 years. Baseline 200° UWF-FA images were graded for nonperfused area, nonperfusion index (NPI), and presence of predominantly peripheral lesions on UWF-FA (FA PPL).

Interventions: Treatment of DR or diabetic macular edema was at investigator discretion.

Main Outcomes and Measures: Association of baseline UWF-FA nonperfusion extent with disease worsening, defined as either 2 or more steps of DRSS worsening within Early Treatment Diabetic Retinopathy Study fields on UWF-color images or receipt of DR treatment.

Results: After adjusting for baseline DRSS, the risk of disease worsening over 4 years was higher in eyes with greater overall NPI (hazard ratio [HR] for 0.1-unit increase, 1.11; 95% CI, 1.02-1.21; P = .02) and NPI within the posterior pole (HR for 0.1-unit increase, 1.35; 95% CI, 1.17-1.56; P < .001) and midperiphery (HR for 0.1-unit increase, 1.08; 95% CI, 1.00-1.16; P = .04). In a multivariable analysis

adjusting for baseline DRSS score and baseline systemic risk factors, greater NPI (HR, 1.11; 95% CI, 1.02-1.22; P = .02) and presence of FA PPL (HR, 1.89; 95% CI, 1.35-2.65; P < .001) remained associated with disease worsening.

Conclusions and Relevance: This 4-year longitudinal study has demonstrated that both greater baseline retinal nonperfusion and FA PPL on UWF-FA are associated with higher risk of disease worsening, even after adjusting for baseline DRSS score and known systemic risk. These associations between disease worsening and retinal nonperfusion and FA PPL support the increased use of UWF-FA to complement color fundus photography in future efforts for DR prognosis, clinical care, and research.

DOI: 10.1001/jamaophthalmol.2022.3130

DRUG TREATMENT

The impact of the vitreomacular interface on functional and anatomical outcomes in diabetic macular edema treated with three different anti-VEGF agents: post hoc analysis of the Protocol T study.

Retina. 2022 Aug 12

Mylonas G, Najeeb BH, Goldbach F, Deak GG, Michl M, Brugger J, Schmidt-Erfurth U, Gerendas BS.

Purpose: To investigate the impact of baseline vitreomacular interface (VMI) status on treatment outcomes in patients treated with three different anti-vascular endothelial growth factors (anti-VEGF) for diabetic macular edema (DME).

Methods: Post-hoc analysis from patients enrolled in the DRCR.net Protocol T study. Optical coherence tomography images were analyzed at baseline and at the end of follow-up to identify the presence of complete vitreomacular adhesion (VMA), partial vitreomacular adhesion, vitreomacular traction syndrome and complete posterior vitreous detachment (PVD).

Results: Six hundred twenty-nine eyes were eligible for the study based on the study criteria. Complete adhesion eyes gained on average +3.7 more ETDRS letters compared to the complete PVD group at the end of the 12 months follow-up (p < 0.001). Baseline VMI status had no significant influence on CST at 12 months (p=0.144). There was no difference between the treatment arms based on effect of baseline VMI status on BCVA gain.

Conclusions: This study provides evidence that VMI status affects functional outcomes in DME patients treated with anti-VEGF injections. The presence of complete or partial VMA at baseline might be associated with a larger treatment benefit than those with complete PVD.

DOI: 10.1097/IAE.0000000000003594

RISK OF DISEASE

Predicting the incidence of age-related diseases based on biological age: The 11-year national health examination data follow-up.

Archive of Gerontology & Geriatrics. 2022 Aug 8

Bae CY, Kim IH, Kim BS, Kim JH, Kim JH.

Purpose: As the population ages rapidly, the incidence of age-related diseases (ARDs) is also increasing fast. Predicting the incidence of ARDs is a challenge since the rates of individual aging vary, and objective assessments of the stages of aging based on chronological age (CA) may be inaccurate. Thus, in this study, we developed a biological age (BA) model based on the National Health Examination (NHE) data and analyzed the model prediction results for the incidence of 16 ARDs.

Methods: This study was based on the 2002-2019 National Health Information Databases of the National Health Insurance Service (NHIS-NHID). The data from a total of 10,002,494 subjects were selected between 2009 and 2010, and the principal component analysis (PCA) was performed to develop the BA model. The Cox-proportional hazard model was used to perform predictive analysis of the ARD incidence.

Results: For the unit increase in the difference between corrected biological age (cBA) and chronological age (CA), the hazard ratios (HRs) of ARDs increased significantly for both sexes ($p < 0.001$). In descending order, the corresponding ARDs' HRs were obesity (1.655), chronic renal failure (1.362), hypertension (1.301), hyperlipidemia (1.264), diabetes mellitus (1.261), fracture (1.119), dementia (1.163), cataract (1.116), myocardial infarction (1.097), stroke (1.169), macular degeneration (1.075), osteoarthritis (1.059), osteoporosis (1.124), Parkinson's disease (1.048), and chronic obstructive pulmonary disease (1.026).

Conclusions: In this study, the incidence of 16 ARDs were analyzed based on BA. Therefore, conducting the NHIS health examination can facilitate the prevention of ARDs by estimating HRs for at least 16 diseases.

DOI: 10.1016/j.archger.2022.104788

Polypoidal Choroidal Vasculopathy Based on Non-ICGA Criteria In White Patients With Neovascular Age-Related Macular Degeneration.

American Journal of Ophthalmology. 2022 Aug 8

Chaikitmongkol V, Ozimek M, Srisomboon T, Patikulsila D, Fraser-Bell S, Chhablani J, Choovuthayakorn J, Watanachai N, Kunavisarut P, Rodríguez-Valdés PJ, Lozano-Rechy D, Lupidi M, Al-Sheikh M, Fung AT, Busch C, Mehta H, Gabrielle PH, Zur D, Ramon D, Sangkaew A, Ingviya T, Amphornprut A, Cebeci Z, Couturier A, Mendes TS, Giancipoli E, Iglicki M, Invernizzi A, Lains I, Rehak M, Sala-Puigdollers A, Okada M, Loewenstein A, Bressler NM.

Purpose: To determine prevalence of probable polypoidal choroidal vasculopathy (PCV) among White patients with neovascular age-related macular degeneration (nAMD) using non-ICGA criteria

Design: : Multicenter, multinational retrospective cross-sectional study

Methods: : 208 treatment naïve eyes from Hispanic and non-Hispanic White individuals diagnosed with nAMD were included. All underwent color fundus photography (CFP), optical coherence tomography (OCT), and fluorescein angiography (FFA). De-identified images of study eyes were sent to 2 groups of graders. Group 1 reviewed CFP, OCT, and FFA to confirm nAMD diagnosis. Group 2 reviewed CFP and OCT to determine highly suggestive features for PCV. Probable PCV diagnosis defined as the presence of ≥2 of 4 highly suggestive features for PCV: notched or fibrovascular

pigment epithelial detachment (PED) on CFP; sharply-peaked PED, notched PED, and hyperreflective ring on OCT.

Results: Eleven eyes were excluded: poor image quality (6), non-nAMD diagnosis (5). Of 197 eligible eyes (197 patients), mean age (SD) was 78.8 years (8.9), 44.2% were men, 26.4% were Hispanic and 73.6% were non-Hispanic white individuals; 41.1%, 23.4%, 9.1%, and 2.5% had ≥1, ≥2, ≥3, and 4 highly suggestive features. Results showed 23.4% (95%CI, 17.6% to 29.9%) had probable PCV diagnosis. Predominantly occult CNV was more frequently found in probable PCV than nAMD subgroup (84.8% vs. 64.9%, P=.01). Hispanic white individuals had a lower prevalence of probable PCV than non-Hispanic white individuals (9.6% vs. 28.2%, P=.006)

Conclusions: : These findings suggest probable PCV occurs between 17.6% to 29.9% among nAMD in White individuals, and more commonly in non-Hispanic than Hispanic White individuals.

DOI: 10.1016/j.ajo.2022.07.024

FUTURE TREATMENTS

Investigational drugs in clinical trials for macular degeneration.

Expert Opinion on Investigational Drugs. 2022 Aug 12

Tolentino MJ, Tolentino AJ.

Introduction: Intravitreal anti-vascular endothelial growth factor (VEGF) injections for exudative age-related macular degeneration (eAMD) are effective and safe but require frequent injections and have nonresponding patients. Geographic atrophy/dry AMD (gaAMD) remains an unmet medical need . New therapies are needed to address this leading cause of blindness in the increasing aged population.

Areas Covered: This paper reviews the pathogenesis of macular degeneration, current and failed therapeutics, therapies undergoing clinical trials and a rationale for why certain AMD therapies may succeed or fail .

Expert Opinion: VEGF- inhibitors reduce both vascular leakage and neovascularization. Experimental therapies that only address neovascularization or leakage will unlikely supplant anti-VEGF therapies. The most promising future therapies for eAMD, are those that target, more potently inhibit and have a more sustained effect on the VEGF pathway such as KSI-301, RGX-314, CLS-AX, EYEP-1901, OTX-TKI. GaAMD is a phenotype of phagocytic retinal cell loss. Inhibiting phagocytic activity of retinal microglial/macrophages at the border of GA and reducing complement derived activators of microglial/macrophage is the most promising strategy. Complement inhibitors (Pegcetacoplan and Avacincaptad pegol) will likely obtain FDA approval but will serve to pave the way for combined complement and direct phagocytic inhibitors such as AVD-104.
DOI: 10.1080/13543784.2022.2113375

IMPACT OF DISEASE

Cognitive Performance and Diabetic Retinopathy: What Your Eyes Can Reveal About Your Brain.

Current Diabetes Review. 2022 Aug 5

de Almeida Faria ACR, Dall'Agnol JF, Gouveia AM, De Paiva CI, Segalla VC.

Background Diabetic retinopathy (DR) is a chronic diabetes complication. People with Type 2 Diabetes Mellitus (T2DM) have two times the risk for dementia, suggesting it is a new chronic diabetes complication.

Objective: Evaluate the association of DR with cognitive performance in a T2DM population.
Methods: Cross-sectional study with 251 T2DM adults from whom socio-demographic, clinical, laboratory data, a screening test for depression symptoms [Patient Health Questionaire-9 (PHQ-9)], Mini-Mental State Examination (MMSE), Semantic Verbal Fluency Test, Trail Making Test A and B, Word Memory test were collected and performed. All cognitive test scores were converted into Global Cognition z-Score [GCS(z)]. The association between GCS(z) < 0 with DR was performed using a multivariate binary logistic regression model adjusted for age ≥ 65 years, school years ≤ 6 years, DM duration ≥ 10 years, depression symptoms score > 9 at PHQ-9, arterial hypertension, physical activity, diabetic retinopathy, macular edema, and cardiovascular disease.

Results: After exclusions, the 251 eligible patients were 56.6% female, with a mean age of 61.1(±9.8) years, DM duration of 12.6(±8.9) years, and 7.6(±4.2) years of school education. DR prevalence was 46.5%. Multivariate Logistic Regression Model showed an association between DR and GCS(z) < 0, with odds ratio (CI95%) of 2.50 (1.18-5.34), adjusted for age, low education level, arterial hypertension and depression symptoms [OD and CI95% respectively: 5.46(2.42-12.34); 12.19(5.62-26.46); 2.55(0.88-7.39); 3.53(1.55-8.07)].

Conclusion: In this T2DM population, having DR increased the chance for worse cognitive performance even when adjusted for age, low education level, presence of arterial hypertension, and depression symptoms.

DOI: 10.2174/1573399819666220805154638

Large socioeconomic gap in period life expectancy and life years spent with complications of diabetes in the Scottish population with type 1 diabetes, 2013-2018.

PLoS One. 2022 Aug 11

Höhn A, McGurnaghan SJ, Caparrotta TM, Jeyam A, O'Reilly JE, Blackbourn LAK, Hatam S, Dudel C, Seaman RJ, Mellor J, Sattar N, McCrimmon RJ, Kennon B, Petrie JR, Wild S, McKeigue PM, Colhoun HM; SDRN-Epi Group.

Background: We report the first study to estimate the socioeconomic gap in period life expectancy (LE) and life years spent with and without complications in a national cohort of individuals with type 1 diabetes.

Methods: This retrospective cohort study used linked healthcare records from SCI-Diabetes, the population-based diabetes register of Scotland. We studied all individuals aged 50 and older with a diagnosis of type 1 diabetes who were alive and residing in Scotland on 1 January 2013 (N = 8591). We used the Scottish Index of Multiple Deprivation (SIMD) 2016 as an area-based measure of socioeconomic deprivation. For each individual, we constructed a history of transitions by capturing whether individuals developed retinopathy/maculopathy, cardiovascular disease, chronic kidney disease, and diabetic foot, or died throughout the study period, which lasted until 31 December 2018. Using parametric multistate survival models, we estimated total and state-specific LE at an attained age of 50.

Results: At age 50, remaining LE was 22.2 years (95% confidence interval (95% CI): 21.6 - 22.8) for males and 25.1 years (95% CI: 24.4 - 25.9) for females. Remaining LE at age 50 was around 8 years lower among the most deprived SIMD quintile when compared with the least deprived SIMD quintile: 18.7 years (95% CI: 17.5 - 19.9) vs. 26.3 years (95% CI: 24.5 - 28.1) among males, and 21.2 years (95% CI: 19.7 - 22.7) vs. 29.3 years (95% CI: 27.5 - 31.1) among females. The gap in life years spent without complications was around 5 years between the most and the least deprived SIMD quintile: 4.9 years (95% CI: 3.6 - 6.1) vs. 9.3 years (95% CI: 7.5 - 11.1) among males, and 5.3 years (95% CI: 3.7 - 6.9) vs. 10.3 years (95% CI: 8.3 - 12.3) among females. SIMD differences in transition rates decreased marginally when controlling for time-updated information on risk factors such as HbA1c, blood pressure, BMI, or smoking.

Conclusions: In addition to societal interventions, tailored support to reduce the impact of diabetes is needed for individuals from low socioeconomic backgrounds, including access to innovations in management of diabetes and the prevention of complications.

DOI: 10.1371/journal.pone.0271110

PATIENT EXPERIENCE

The intraocular implant and visual rehabilitation improve the quality of life of elderly patients with geographic atrophy secondary to age-related macular degeneration.

Graefes Archive of Clinical & Experimental Ophthalmology. 2022 Aug 19

Nekolova J, Kremlacek J, Lukavsky J, Sikl R, Sin M, Langrova J, Szanyi J, Jiraskova N.

Introduction: The objective of this prospective study was to evaluate the effects of intraocular macular lens implantation and visual rehabilitation on the quality of life of patients with geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

Methods: Patients with bilaterally decreased near vision (not better than 0.3 logMAR with the best correction), pseudophakia, were included in the project. The Scharioth macula lens (SML) was implanted into the patients' better-seeing eye. Intensive visual rehabilitation of the ability to perform nearby activities was performed for 20 consecutive postoperative days. All subjects were examined before and after SML implantation ophthalmologically. The National Eye Institute 25-Item Visual Function Questionnaire (NEI VFQ-25) was administered before and 6 months after surgery.

Results: Twenty eligible patients with mean age 81 years (63 to 92 years) were included in the project: 7 males and 13 females. Nineteen of them completed the 6-month follow-up. Near uncorrected visual acuity was 1.321 ± 0.208 logMAR before SML implantation and improved to 0.547 ± 0.210 logMAR after 6 months ($dz = -2.846$, $p < 0.001$, $BF10 = 3.29E+07$). In the composite score of the NEI VFQ-25, there was an improvement in the general score and the specific domains related to the implantation. Participants reported fewer difficulties in performing near activities ($dz = 0.91$, $p = 0.001$, $BF10 = 39.718$) and upturns in mental health symptoms related to vision ($dz = 0.62$, $p = .014$, $BF10 = 3.937$).

Conclusion: SML implantation, followed by appropriate rehabilitation, improved near vision and increased the quality of life of visually handicapped patients with AMD in our project.

DOI: 10.1007/s00417-022-05803-6

CASE REPORT

Severe Macular Edema after Traumatic Head Injury: A Case of Whiplash Maculopathy.

Retina Cases Brief Rep. 2022 Jul 29

Ballios BG.

Purpose: Whiplash or "traumatic" maculopathy is associated with retinal concussion, typically following the rapid acceleration/deceleration experienced in motor vehicle collisions. It has rarely been discussed in the literature, likely given the spontaneous and relatively rapid nature with which the acute macular edema resolves. A focused clinical history around the trauma, as well as characteristics signs and structural features on retinal imaging, help to distinguish this condition from other sequelae of concussive retinal injury. We report a case of whiplash maculopathy following a blunt injury to the head, which presented with unilateral and substantial macular edema in the left eye.

Methods: Case report.

Results: A 38 year old male presented with complaint of a central scotoma in his left eye following a blunt trauma to his head. Comprehensive ophthalmological evaluation and retinal imaging with optical coherence tomography (OCT) confirmed whiplash maculopathy, with acute macular edema in his left eye. Management with observation and close follow-up showed rapid improvement in his visual symptoms over the course of days, and improvements in the severity of macular edema. One month following his injury, macular edema had resolved with only mild irregularities, the patient's vision had improved and he was asymptomatic.

Conclusions: When observing patients with significant macular edema following concussive head injury, whiplash maculopathy should be considered, regardless of the history of motor vehicle collision. The condition can present with significant asymmetry of disease. The diagnosis generally carries a good prognosis for vision; however, there are cases of persistent central visual disturbances.

DOI: 10.1097/ICB.0000000000001305