This free weekly bulletin lists the latest published research articles on macular degeneration (MD) as indexed in the NCBI, PubMed (Medline) and Entrez (GenBank) databases. These articles were identified by a search using the key term "macular degeneration".

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Drug treatment

Ophthalmology. 2012 Aug 28. [Epub ahead of print]
Optical Coherence Tomography Grading Reproducibility during the Comparison of Age-Related Macular Degeneration Treatments Trials.

Decroos FC, Toth CA, Stinnett SS, Heydary CS, Burns R, Jaffe GJ; CATT Research Group.
Wills Eye Institute (Mid Atlantic Retina), Philadelphia, Pennsylvania; Duke University Eye Center, Durham, North Carolina.

OBJECTIVE: To report reading center reproducibility during grading of Stratus optical coherence tomography (OCT) (Carl Zeiss Meditec, Dublin, CA) images obtained during the Comparison of Age-Related Macular Degeneration Treatments Trials (CATT).

DESIGN: Prospective, clinical trial.

PARTICIPANTS: Independent reading teams reevaluated 270 OCT scans randomly sampled from the first 2 years of CATT enrollment. To assess temporal drift, a cohort of 23 scans submitted during the initial portion of the CATT study was longitudinally followed with serial reproducibility analysis.

INTERVENTION: The CATT readers performed standardized grading of OCT images. A reader team, composed of 2 independent readers and a senior reader, evaluated each scan. Grading included the CATT OCT end points of total thickness at the foveal center point and intraretinal fluid (IRF), subretinal fluid (SRF), and subretinal pigment epithelium (RPE) fluid. Independent reading teams masked to the results of initial grading reevaluated scans to determine the reproducibility of qualitative grading and measurements.

MAIN OUTCOME MEASURES: Categorical grading agreement was reported using percent agreement and kappa statistic, and measurement agreement was reported using intraclass correlations and paired differences.

RESULTS: Reading center teams reproducibly graded IRF (percent agreement = 73%, kappa = 0.48; 95% confidence interval [CI], 0.38-0.58), SRF (percent agreement = 90%; kappa = 0.80; 95% CI, 0.73-0.87), and sub-RPE fluid (percent agreement 88%; kappa = 0.75; 95% CI, 0.67-0.83). For independent reading center team measurements of total thickness at the foveal center point, the intraclass correlation was 0.99 (95% CI, 0.99-0.99), and the mean paired difference between reading center teams was 4 μm (95% limits of agreement, -55 to 47 μm). There was no qualitative or quantitative grading drift.

CONCLUSIONS: The standardized protocols used to evaluate OCT scans from the CATT study were reproducible. The methods used are suitable to monitor OCT imaging data from a large, neovascular age-related macular degeneration, interventional, multicenter study.

PMID: 22939114 [PubMed - as supplied by publisher]

Case Report Ophthalmol. 2012 May;3(2):251-7. Epub 2012 Aug 15.
Rapid regression of exudative maculopathy in idiopathic retinitis, vasculitis, aneurysms and neuroretinitis syndrome after intravitreal ranibizumab.

Marín-Lambíes C, Gallego-Pinazo R, Salom D, Navarrete J, Díaz-Llopis M.
Department of Ophthalmology, University and Polytechnic Hospital La Fe, Alzira, Spain.

Abstract
The idiopathic retinitis, vasculitis, aneurysms and neuroretinitis syndrome is a rare retinal vascular disorder characterized by multiple leaking aneurysmal dilations, retinal vasculitis, neuroretinitis and peripheral vascular ischemia. Visual loss mainly occurs due to the development of retinal neovascularization and/or exudative maculopathy. Although the treatment of choice has not yet been established, retinal photocoagulation seems to be the best option to control the disease and to prevent its progression. Herein, we report a case of idiopathic retinitis, vasculitis, aneurysms and neuroretinitis syndrome with both retinal neovascularization and macular exudation successfully managed with intravitreal ranibizumab (Lucentis(®)) as adjunctive therapy to retinal photocoagulation.

PMID: 22949913 [PubMed - in process] PMCID: PMC3433025

Ophthalmic Surg Lasers Imaging. 2012 Aug 30:1-4. doi: 10.3928/15428877-20120823-03. [Epub ahead of print]
Acute Anterior Uveitis Following Intravitreal Injection of Bevacizumab.

Mozayan A, Farah S.

BACKGROUND AND OBJECTIVE: To report five cases of iritis after intravitreal injection of bevacizumab.

PATIENTS AND METHODS: The clinical charts of patients who received intravitreal injections of bevacizumab or ranibizumab from January 2009 to September 2011 by one physician were retrospectively reviewed.

RESULTS: A total of 1,097 injections of bevacizumab and 571 of ranibizumab were administered. Five patients developed acute anterior uveitis and presented with severe pain, photophobia, conjunctival injection, and anterior chamber reaction 2 to 24 hours after intravitreal injection of bevacizumab. All five patients were treated with topical corticosteroids with rapid resolution of the inflammation.

CONCLUSION: Although uncommon, acute iritis is a complication of intravitreal injection of bevacizumab.

PMID: 22938633 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Graefes Arch Clin Exp Ophthalmol. 2012 Sep 5. [Epub ahead of print]
Overestimation of subfoveal choroidal thickness by measurement based on horizontally compressed optical coherence tomography images.

Kim JH, Kang SW, Ha HS, Kim SJ, Kim JR.

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PURPOSE: To measure the difference in subfoveal choroidal thickness between 1:1 pixel (horizontally compressed) images and 1:1 micron images in age-related macular degeneration.

METHODS: This study included 122 eyes from 122 patients diagnosed with age-related macular degeneration. Choroidal thickness was measured using enhanced-depth imaging optical coherence tomography. The measurement line was drawn as a perpendicular line between Bruch's membrane and the chorio-scleral interface. The thickness was compared between measurements based on a 1:1 pixel image and a 1:1 micron image. Eyes with a straight vertical measurement line and oblique measurement line were classified into vertical measurement group and oblique measurement group, respectively. Intra-group comparisons of subfoveal choroidal thickness measurements based on the 1:1 pixel images and the 1:1 micron images were performed for the two groups.

RESULTS: The mean subfoveal choroidal thicknesses measured on the 1:1 pixel images and the 1:1 micron images were 232.3 ± 106.4 μm and 228.9 ± 108.1 μm, respectively ($p = 0.003$). In the vertical measurement group (86 eyes), the mean subfoveal choroidal thickness was 226.3 ± 109.9 μm and 225.4 ± 112.0 μm, respectively ($p = 0.423$). In the oblique measurement group (36 eyes), the thickness was 246.5 ± 97.3 μm and 237.5 ± 98.9 μm, respectively ($p < 0.001$).

CONCLUSIONS: Significant overestimation of the subfoveal choroidal thickness was noted when it was measured on a 1:1 pixel image. This finding suggests that the measurement of choroidal thickness should be performed based on a 1:1 micron image, especially if the measurement line is not vertical.

PMID: 22948949 [PubMed - as supplied by publisher]

Retina. 2012 Sep;32 Suppl 2:S216-20.
Vitreomacular adhesion and neovascular age-related macular degeneration.

Thompson JT.

Retina Specialists, Towson, Maryland.

PMID: 22929324 [PubMed - in process]

Pathogenesis

BMJ Case Rep. 2012 Sep 3;2012. pii: bcr2012006619. doi: 10.1136/bcr-2012-006619.
Intravitreal dobesilate in the treatment of choroidal neovascularisation associated with age-related macular degeneration: report of two cases.

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Departamento de Investigación, IRYCIS, Hospital Universitario Ramón y Cajal, Madrid, Spain.

Abstract
This case report presents the effectiveness of intravitreal administration of dobesilate, a synthetic fibroblast growth factor inhibitor, in two patients showing neovascular age-related macular degeneration of the classic, and of the occult choroidal neovascularisation types, respectively. Our study demonstrates that the treatment induces the regression of both forms of this pathology, as assessed by spectral optical coherence tomography. Improvement of the lesions was accompanied of visual acuity improvement.

PMID: 22948997 [PubMed - in process]

Zhonghua Yan Ke Za Zhi. 2012 Jul;48(7):649-52.
[The latest advance of the relationship between autophagy and diabetic retinopathy]. [Article in Chinese]

Lu Y, Xu X.

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Abstract
As a serious complication of diabetes mellitus, diabetic retinopathy (DR) is one of the major causes of blindness, and its prevalence has been increasing worldwide. Therefore, there is an urgent need to figure out the mechanism of DR and identify an effective therapeutic target to prevent it. Autophagy is a major catabolic pathway involved in degrading and recycling damaged organelles and macromolecules to maintain intracellular homeostasis. The study of autophagy in mammalian systems is advancing rapidly and has revealed that it is involved in the pathogenesis of various metabolic and age-related diseases. The role of autophagy in such diseases as tumors, diabetic nephropathy (DN), age-related macular degeneration (AMD), etc, is currently under intense investigation. And there's a close relationship between autophagy and DR related factors as well including nutrient stress, oxidative stress, hypoxia, endoplasmic reticulum stress, and so on.

PMID: 22943871 [PubMed - in process]

Genetics

Age (Dordr). 2012 Sep 7. [Epub ahead of print]
Regulatory regions of the paraoxonase 1 (PON1) gene are associated with neovascular age-related macular degeneration (AMD).

Oczos J, Grimm C, Barthelmes D, Sutter F, Menghini M, Kloeckener-Gruissem B, Berger W.

Institute of Medical Molecular Genetics, University of Zurich, Schwerzenbach, Switzerland.

Abstract
Physiological stress response and oxidative damage are factors for aging processes and, as such, are thought to contribute to neovascular age-related macular degeneration (AMD). Paraoxonase 1 (PON1) is an enzyme that plays an important role in oxidative stress and aging. We investigated association of DNA sequence variants (SNP) within the upstream regulatory region of the PON1 gene with neovascular AMD in 305 patients and 288 controls. Four of the seven tested SNPs (rs705379, rs705381, rs854573, and rs757158) were more frequently found in AMD patients compared to controls (P = 0.0099, 0.0295, 0.0121, and 0.0256, respectively), and all but one (SNP rs757158) are in linkage disequilibrium. Furthermore, haplotype TGGCCTC conferred protection (odds ratio (OR) = 0.76, (CI) = 0.60-0.97) as it was more frequently found in control individuals, while haplotype CGATGCT increased the risk (OR = 1.55, CI = 1.09-2.21) for AMD. These results were also reflected when haplotypes for the untranscribed and the 5'untranslated regions (5'UTR) were analyzed separately. To assess haplotype correlation with levels of gene expression, the three SNPs within the 5'UTR were tested in a luciferase reporter assay. In retinal pigment epithelium-derived ARPE19 cells, we were able to measure significant differences in reporter levels, while this was not observed in kidney-derived HEK293 cells. The presence of the risk allele A (SNP rs705381) caused an increase in luciferase activity of approximately twofold. Our data support the view that inflammatory reactions mediated through anti-oxidative activity may be relevant to neovascular age-related macular degeneration.

PMID: 22956172 [PubMed - as supplied by publisher]

Mol Med Report. 2012 Sep 4. doi: 10.3892/mmr.2012.1063. [Epub ahead of print]
Evaluation of the ELOVL4, PRPH2 and ABCA4 genes in patients with Stargardt macular degeneration.

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Department of Ophthalmology, The Third Xiangya Hospital, Central-South University, Changsha, Hunan 410013, P.R. China.

Abstract
Mutations in the ATP-binding cassette, subfamily A, member 4 (ABCA4), elongation of very long chain fatty acids 4 (ELOVL4) and peripherin-2 (PRPH2) genes have been identified in patients with Stargardt macular degeneration (STGD). The aim of this study was to investigate which of these genes is responsible for susceptibility in Chinese patients. A total of 41 probands with STGD or suspected STGD were enrolled in the study. The coding regions and adjacent intronic sequences of the ELOVL4 and PRPH2 genes and 3 coding exons of the ABCA4 gene were amplified by polymerase chain reaction (PCR). The nucleotide sequences of the amplicons were determined by Sanger sequencing. Three novel heterozygous missense mutations in the ABCA4 gene were identified: c:2633C>A (p:Ser878X), c:5646G>A (p:Met1882Ile) and c:6389T>A (p:Met2130Lys). These mutations were not present in 176 normal individuals and were predicted to be pathogenic. Two benign variations were found: a reported variation, c:5682G>C in ABCA4 and a novel variation, c:699G>A in ELOVL4. In addition, 5 single nucleotide polymorphisms (SNPs: rs3812153, rs7764439, rs390659, rs434102 and c:929G>A) were detected in ELOVL4 and PRPH2. The c:929G>A variation has not been previously reported. We conclude that no pathogenic variations in ELOVL4 and PRPH2 were detected in the Chinese STGD patients. Our results imply that ABCA4 is more likely to be significant in Chinese STGD patients.

PMID: 22948568 [PubMed - as supplied by publisher]

Diet

J Pharm Biomed Anal. 2012 Aug 4. [Epub ahead of print]
Structural and spectroscopic features of lutein/butanoyl-β-cyclodextrin nanoassemblies.

Stancanelli R, Løjkner LD, Larsen KL, Guardo M, Cannavà C, Tommasini S, Ventura CA, Calabrò ML, Micali N, Villari V, Mazzaglia A.

Dipartimento Farmaco-Chimico, Università di Messina, V.le Annunziata, 98168 Messina, Italy.

Abstract
Lutein, the primary carotenoid present in the central area of the retina of eye appears to be associated with the protection against age-related macular degeneration (the leading cause of blindness in older adults). Its lipophilicity and consequently its scarce water solubility (1.3×10(-9)M) represent a drawback for bioavailability. To circumvent these unfavorable characteristics, in this work lutein (Lut) have been encapsulated in amphiphilic cyclodextrin (ACyD) by following the well-established strategy of entrapping a lipophilic drug in CyD carriers. Primary face butyrate modified β-cyclodextrins (C(4:7)) form in water nanoaggregates with a average size of 250nm and a ζ-potential of about -6mV. They are able to entrap lutein at 1:6 Lut/ACyD molar ratio by yielding nanoassemblies of vesicular aspect (320nm and -8mV) such as observed by static, dynamic and electrophoretic light-scattering. UV-vis measurements revealed that electronic properties of lutein were maintained when interact with ACyD nanoaggregate. The monitoring of the entapped carotenoid leaking from ACyD nanostructures was investigated suggesting the potential of Lut/ACyD nanoassemblies in drug delivery.

PMID: 22938801 [PubMed - as supplied by publisher]