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Drug treatment

Retina. 2012 Mar 22. [Epub ahead of print]

INTRAVITREAL RANIBIZUMAB FOR EXUDATIVE AGE-RELATED MACULAR DEGENERATION WITH GOOD BASELINE VISUAL ACUITY.

Saito M, Iida T, Kano M.

Department of Ophthalmology, Fukushima Medical University School of Medicine, Fukushima, Japan.

PURPOSE: To clarify the efficacy of ranibizumab for treating age-related macular degeneration in patients with baseline visual acuity exceeding 20/40.

METHODS: We retrospectively reviewed 40 eyes of Japanese patients with age-related macular degeneration (32 men, 8 women) treated with intravitreal injections of ranibizumab (0.5 mg/0.05 mL) (ranibizumab group). We compared the results with observation of 52 eyes (control group). All patients were followed-up for at least 12 months.

RESULTS: In the ranibizumab group, the mean logarithm of the minimum angle of resolution best-corrected visual acuity (Snellen equivalent) with typical age-related macular degeneration (22 eyes) and polypoidal choroidal vasculopathy (18 eyes) statistically significantly ($P < 0.0001$, $P = 0.015$, respectively) improved from 0.17 (20/29) and 0.14 (20/28) at baseline to 0.07 (20/24) and 0.07 (20/24) at Month 12, respectively (mean numbers of treatments, 4.6 and 4.9). The central retinal thickness decreased from 262 ± 105 μm at baseline to 187 ± 62 μm at Month 12 in the ranibizumab group. In the control group, the mean logarithm of the minimum angle of resolution best-corrected visual acuity in eyes with typical age-related macular degeneration (19 eyes) and polypoidal choroidal vasculopathy (33 eyes) statistically significant ($P = 0.017$, $P = 0.023$, respectively) declined from 0.08 (20/24) and 0.10 (20/25) at baseline to 0.18 (20/30) and 0.23 (20/34) at Month 12, respectively.

CONCLUSION: Intravitreal ranibizumab maintained or improved visual acuity and anatomic changes in patients with age-related macular degeneration with better than 20/40 visual acuity.

PMID: 22446886 [PubMed - as supplied by publisher]

Ophthalmology. 2012 Mar 21. [Epub ahead of print]

Verteporfin plus Ranibizumab for Choroidal Neovascularization in Age-Related Macular Degeneration: Twelve-Month Results of the DENALI Study.

Kaiser PK, Boyer DS, Cruess AF, Slakter JS, Pilz S, Weisberger A; DENALI Study Group(□).

Cole Eye Institute, Cleveland Clinic Foundation, Cleveland, Ohio.

PURPOSE: To demonstrate noninferiority of ranibizumab in combination with verteporfin photodynamic therapy (PDT) versus ranibizumab monotherapy in patients with subfoveal choroidal neovascularization secondary to age-related macular degeneration (AMD).

DESIGN: Prospective, multicenter, double-masked, randomized, phase IIIb clinical trial.

PARTICIPANTS: Three hundred twenty-one patients randomized to receive either ranibizumab 0.5 mg monotherapy (n = 112), standard fluence (SF) verteporfin PDT combination therapy (n = 104), or reduced fluence (RF) verteporfin PDT combination therapy (n = 105).

METHODS: Ranibizumab was administered monthly in the monotherapy group. In both combination therapy groups, ranibizumab was initiated with 3 consecutive monthly injections, followed by retreatment as needed (pro re nata) with monthly monitoring. All patients were evaluated monthly for 12 months.

MAIN OUTCOME MEASURES: Mean change in best-corrected visual acuity (BCVA) from baseline at month 12 and proportion of patients randomized to either combination therapy with a ranibizumab treatment -free interval of 3 months or longer.

RESULTS: Two hundred eighty-six patients (89.1%) completed the 12-month study. Mean BCVA change at month 12 was +5.3 and +4.4 letters with verteporfin SF (n = 103) or verteporfin RF (n = 105) plus ranibizumab, respectively, compared with +8.1 letters with ranibizumab monotherapy (n = 110; adjusted 97.5% confidence interval [CI], (-7.90 to infinity); P = 0.0666; and 97.5% CI, (-8.51 to infinity); P = 0.1178; for combination regimens vs. monotherapy, respectively). Noninferiority of either combination regimen to monthly ranibizumab monotherapy was not demonstrated (primary end point). A ranibizumab treatment-free interval of 3 months or longer was achieved in 92.6% and 83.5% of the patients randomized to verteporfin SF or verteporfin RF groups, respectively, with a mean of 5.1 and 5.7 ranibizumab injections, respectively, and patients in the ranibizumab monotherapy arm received 10.5 injections. At month 12, mean central retinal thickness decreased by 151.7 μm and 140.9 μm for the verteporfin SF and RF groups, respectively, and by 172.2 μm with ranibizumab monotherapy. Safety and tolerability of all 3 regimens were similar to and consistent with previous studies in neovascular AMD. The number of ocular serious adverse events was low and occurred largely as single cases.

CONCLUSIONS: Ranibizumab monotherapy or combined with verteporfin PDT improved BCVA at month 12; however, noninferiority (7-letter margin) of combination regimens to ranibizumab monotherapy was not demonstrated. Verteporfin RF did not confer clinical benefits over verteporfin SF. All treatments were well tolerated.

PMID: 22444829 [PubMed - as supplied by publisher]

Nat Rev Drug Discov. 2012 Mar 30;11(4):269-70. doi: 10.1038/nrd3700.

Aflibercept.

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Abstract

In November 2011, aflibercept (Eylea; Regeneron Pharmaceuticals), a recombinant fusion protein that binds to members of the vascular endothelial growth factor family, was approved by the US Food and Drug Administration (FDA) for the treatment of patients with neovascular age-related macular degeneration.

PMID: 22460118 [PubMed - in process]

Curr Opin Ophthalmol. 2012 Mar 23. [Epub ahead of print]

Preferred therapies for neovascular age-related macular degeneration.

Lally DR, Gerstenblith AT, Regillo CD.

Retina Service, Wills Eye Institute, Jefferson Medical College, Philadelphia, Pennsylvania bMid Atlantic Retina, Wyndmoor, Pennsylvania, USA.

PURPOSE OF REVIEW: This report reviews the current treatment strategies and the most recent clinical trials in the treatment of neovascular age-related macular degeneration.

RECENT FINDINGS: The functional and anatomic outcomes achieved in the pivotal ranibizumab trials with monthly injections set the standard for comparison. Since then, various modified dosing regimens with the aim of lessening the treatment burden associated with monthly injections have been investigated. Additionally, level I evidence now exists for the noninferiority of bevacizumab, as compared to ranibizumab, in the treatment of neovascular age-related macular degeneration (AMD) through 1 year of follow-up. Aflibercept has emerged as a new anti- vascular endothelial growth factor (VEGF) therapy showing encouraging treatment results at 1 year. Novel treatments combined with anti-VEGF agents such as localized radiation are currently being investigated.

SUMMARY: Anti-VEGF monotherapy remains the preferred therapy for the management of neovascular AMD at the present time. Aflibercept is a new, FDA-approved, effective, anti-VEGF agent available for clinical use. Ongoing clinical trials will help determine the optimal dosing regimens for all of these agents, as well as the long-term efficacy and safety of combination therapy modalities.

PMID: 22450218 [PubMed - as supplied by publisher]

Curr Opin Ophthalmol. 2012 Mar 23. [Epub ahead of print]

Best practices for treatment of retinal vein occlusion.

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PURPOSE OF REVIEW:

Retinal vein occlusion (RVO) is a sight-threatening retinal vascular disorder associated with macular edema and neovascularization. Until recently, the standard of care for branch RVO-associated macular edema was grid laser photocoagulation and observation for central RVO-associated macular edema. Neovascularization was treated with scatter laser photocoagulation. The purpose of this article is to review recent findings that have changed our treatments of RVO.

RECENT FINDINGS: The recent development of intravitreal pharmacotherapy has demonstrated benefit with anti-vascular endothelial growth factor (VEGF) agents and corticosteroids for the treatment of RVO-associated macular edema. The intravitreal use of FDA-approved ranibizumab (Lucentis) and a sustained release dexamethasone implant (Ozurdex), along with off-label bevacizumab (Avastin) and preservative-free triamcinolone, has significantly expanded our treatment options and replaced standard of care for treatment of RVO-associated macular edema. Whereas anti-VEGF agents can also induce rapid regression of neovascularization, scatter laser photocoagulation remains the standard of care to prevent neovascular complications.

SUMMARY: Intravitreal pharmacotherapy has revolutionized our treatment of retinal vascular diseases, including RVO. Although these intravitreal agents are effective, our understanding of their specific indications and long-term roles is still evolving. Furthermore, until the underlying occlusive pathophysiology of RVO can be addressed, our treatments will be limited to temporizing therapies against a chronic disease.

PMID: 22450223 [PubMed - as supplied by publisher]

J AAPOS. 2012 Mar 28. [Epub ahead of print]

Bilateral response after unilateral subconjunctival bevacizumab injection in a child with Stevens-Johnson syndrome.

Kesarwani S, Sahu SK, Basu S.

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Abstract

Bevacizumab is widely used for several ocular conditions, including age-related macular degeneration, diabetic retinopathy, corneal neovascularization, neovascular glaucoma, and retinopathy of prematurity. We describe a 14-year-old patient with Stevens-Johnson syndrome in whom subconjunctival injection of bevacizumab in one eye caused bilateral regression of corneal neovascularization.

PMID: 22459106 [PubMed - as supplied by publisher]

Doc Ophthalmol. 2012 Mar 29. [Epub ahead of print]

Electroretinographic findings associated with panretinal photocoagulation (PRP) versus PRP plus intravitreal ranibizumab treatment for high-risk proliferative diabetic retinopathy.

Messias A, Filho JA, Messias K, Almeida FP, Costa RA, Scott IU, Gekeler F, Jorge R.

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Abstract

To evaluate changes in electroretinographic (ERG) findings after panretinal photocoagulation (PRP) compared to PRP plus intravitreal injection of ranibizumab (IVR) in eyes with high-risk proliferative diabetic retinopathy (PDR). Patients with high-risk PDR and no prior laser treatment were assigned randomly to receive PRP (PRP group; n = 9) or PRP plus IVR (PRPplus group; n = 11). PRP was administered in two sessions (weeks 0 and 2), and IVR was administered at the end of the first laser session (week 0) in the PRPplus group. Standardized ophthalmic evaluations including (ETDRS) best-corrected visual acuity (BCVA), and fluorescein angiography to measure area of fluorescein leakage (FLA), were performed at baseline and at weeks 16 (±2), 32 (±2) and 48 (±2). ERG was measured according to ISCEV standards at baseline and at week 48 (±2). At 48 weeks, 2,400-3,000 laser spots had been placed in eyes in the PRP group, while only 1,400-1,800 spots had been placed in the PRPplus group. Compared to baseline, there was a statistically significant ($P < 0.05$) FLA reduction observed at all study visits in both groups, with the reduction observed in the PRPplus group significantly larger than that in the PRP group at week 48. ROD b -wave amplitude was significantly reduced to 46 ± 5 % ($P < 0.05$) of baseline in the PRP group and 64 ± 6 % ($P < 0.05$) in the PRPplus group. This reduction was significantly larger in the PRP group than in the PRPplus group ($P = 0.024$; t Test). Similar results were observed for the dark-adapted Combined Response (CR) b-wave amplitude, with a reduction at 48 weeks compared to baseline of 45 ± 4 % in the PRP group and 62 ± 5 % in the PRPplus group; the reduction in CR b-wave amplitude was significantly larger in the PRP group than in the PRPplus group ($P = 0.0094$). CR a-wave, oscillatory potentials, cone single flash, and 30 Hz flicker responses showed statistically significant within-group reductions, but no differences in between-group analyses. These results suggest that treating high-risk PDR with PRP plus IVR is effective for PDR control, and permits the use of less extensive PRP which, in turn, induces less retinal functional loss, in particular for rod-driven post-receptoral responses, than treatment with PRP alone.

PMID: 22457045 [PubMed - as supplied by publisher]

Other treatment & disgnosis

J Psychiatr Ment Health Nurs. 2012 Mar 27. doi: 10.1111/j.1365-2850.2012.01904.x. [Epub ahead of print]

Charles Bonnet syndrome: a literature review into diagnostic criteria, treatment and implications for nursing practice.

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ACCESSIBLE SUMMARY: • While visual hallucinations are often associated with mental illness, they often have an underlying psychical or organic cause. Impaired vision due to cataracts or macular degeneration are such an example. • Antipsychotic medications may provide little or no benefit and add the risk of dangerous side effects. • Mental health nurses are able to identify the condition and provide education and support to the patient which is at present, the most effective treatment.

ABSTRACT: Charles Bonnet syndrome is a disease of vision which may be mistakenly identified as manifestations of psychosis and consequently be treated by psychiatrists and mental health nurses rather than ophthalmologists. This literature review considers current understanding of the syndrome, its treatment and the role of mental health nurses. The two main findings of the review are that despite a long recognition of the syndrome, diagnostic criteria are not established and that there is no recognized evidence-based medical treatment. As well as this, two novel treatments which may offer future benefits are discussed. Current best practice is identified as identifying the condition and providing reassurance and education, a role that mental health nurses that are aware of Charles Bonnet syndrome can fulfil perhaps better than any other discipline.

PMID: 22452327 [PubMed - as supplied by publisher]

Curr Opin Ophthalmol. 2012 Mar 23. [Epub ahead of print]

Stem cell therapy for retinal disease.

Tibbetts MD, Samuel MA, Chang TS, Ho AC.

Wills Eye Institute Retina Service, Mid Atlantic Retina, Philadelphia, Pennsylvania bRetina Institute of California, Pasadena, California, USA.

PURPOSE OF REVIEW: Stem cell therapy holds great promise for the treatment of retinal diseases. This review summarizes recent advances in stem cell biology, outlines ongoing clinical trials and details the obstacles that must be overcome for stem cell therapy to be a viable treatment for retinal disease.

RECENT FINDINGS: Stem cells can now be directed to specific retinal cell fates with high yields and acceptable purity for clinical trials. New stem cell sources have been discovered including induced pluripotent stem cells that can be derived from adult tissues then differentiated into multiple retinal cell types. The initial results of clinical trials of subretinal transplantation of human embryonic stem cell-derived retinal pigment epithelium cells in patients with Stargardt's macular dystrophy and dry age-related macular degeneration showed preliminary safety and possible visual acuity benefits. A phase I trial of intravitreally injected autologous bone marrow-derived mononuclear cells for hereditary retinal dystrophy demonstrated no evidence of toxicity with possible visual acuity benefits but no structural or functional changes. Ongoing trials are examining the trophic effects of undifferentiated umbilical cells for the treatment of geographic atrophy in age-related macular degeneration.

SUMMARY: Stem cell therapy is a promising treatment under active investigation in multiple retinal diseases. Ongoing clinical trials should yield further insights into the potential for stem cell-based retinal

therapies.

PMID: 22450217 [PubMed - as supplied by publisher]

Optom Vis Sci. 2012 Mar 22. [Epub ahead of print]

Panoramic Autofluorescence: Highlighting Retinal Pathology.

Slotnick S, Sherman J.

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PURPOSE: Recent technological advances in fundus autofluorescence (FAF) are providing new opportunities for insight into retinal physiology and pathophysiology. FAF provides distinctly different imaging information than standard photography or color separation. A review of the basis for this imaging technology is included to help the clinician understand how to interpret FAF images. Cases are presented to illustrate image interpretation.

METHODS: Optos, which manufactures equipment for simultaneous panoramic imaging, has recently outfitted several units with AF capabilities. Six cases are presented in which panoramic autofluorescent (PAF) images highlight retinal pathology, using Optos' Ultra-Widefield technology. Supportive imaging technologies, such as Optomap® images and spectral domain optical coherence tomography (SD-OCT), are used to assist in the clinical interpretation of retinal pathology detected on PAF.

RESULTS: Hypofluorescent regions on FAF are identified to occur along with a disruption in the photoreceptors and/or retinal pigment epithelium, as borne out on SD-OCT. Hyperfluorescent regions on FAF occur at the advancing zones of retinal degeneration, indicating impending damage. PAF enables such inferences to be made in retinal areas which lie beyond the reach of SD-OCT imaging. PAF also enhances clinical pattern recognition over a large area and in comparison with the fellow eye. Symmetric retinal degenerations often occur with genetic conditions, such as retinitis pigmentosa, and may impel the clinician to recommend genetic testing.

CONCLUSIONS: Autofluorescent ophthalmoscopy is a non-invasive procedure that can detect changes in metabolic activity at the retinal pigment epithelium before clinical ophthalmoscopy. Already, AF is being used as an adjunct technology to fluorescein angiography in cases of age-related macular degeneration. Both hyper- and hypoautofluorescent changes are indicative of pathology. Peripheral retinal abnormalities may precede central retinal impacts, potentially providing early signs for intervention before impacting visual acuity. The panoramic image enhances clinical pattern recognition over a large area and in comparison between eyes. Optos' Ultra-Widefield technology is capable of capturing high-resolution images of the peripheral retina without requiring dilation.

PMID: 22446719 [PubMed - as supplied by publisher]

Retina. 2012 Feb;32 Suppl 1:416-34.

Retinal angiomatous proliferation in age–related macular degeneration.

Yannuzzi LA, Negrão S, Iida T, Carvalho C, Rodriguez-Coleman H, Slakter J, Freund KB, Sorenson J, Orlock D, Borodoker N.

BACKGROUND: It is known that choroidal neovascularization (CNV) in age-related macular degeneration (ARMD) may erode through the retinal pigment epithelium, infiltrate the neurosensory retina, and communicate with the retinal circulation in what has been referred to as a retinal–choroidal anastomosis (RCA). This is extremely common in the end stage of disciform disease. In recent years, the reverse also

seems to be possible, as angiomatous proliferation originates from the retina and extends posteriorly into the subretinal space, eventually communicating in some cases with choroidal new vessels. This form of neovascular ARMD, termed retinal angiomatous proliferation (RAP) in this article, can be confused with CNV. Purpose: The purpose of this article is 1) to review the clinical and angiographic characteristics of a series of patients with RAP and 2) to propose a theoretical sequence of events that accounts for the neovascularized process.

METHODS: In this retrospective clinical and angiographic analysis, 143 eyes with RAP (108 patients) were reviewed and classified based on their vasogenic nature and course. Clinical biomicroscopic examination, fluorescein angiography, and indocyanine green angiography were used to evaluate patients.

RESULTS: The results of this series suggest that angiomatous proliferation within the retina is the first manifestation of the vasogenic process in this form of neovascular ARMD. Dilated retinal vessels and pre-, intra-, and subretinal hemorrhages and exudate evolve, surrounding the angiomatous proliferation as the process extends into the deep retina and subretinal space. One or more dilated compensatory retinal vessels perfuse and drain the neovascularization, sometimes forming a retinal–retinal anastomosis. Fluorescein angiography in these patients usually revealed indistinct staining simulating occult CNV. Indocyanine green angiography was useful to make an accurate diagnosis in most cases. It revealed a focal area of intense hyperfluorescence corresponding to the neovascularization ("hot spot") and other characteristic findings. Based on understanding of the nature and progression of the neovascularized process, patients with RAP were classified into three vasogenic stages. Stage I involved proliferation of intraretinal capillaries originating from the deep retinal complex (intraretinal neovascularization [IRN]). Stage II was determined by growth of the retinal vessels into the subretinal space (subretinal neovascularization [SRN]). Stage III occurred when CNV could clearly be determined clinically or angiographically. A vascularized pigment epithelial detachment and RCA were inconsistent features of this stage.

CONCLUSIONS: Retinal angiomatous proliferation appears to be a distinct subgroup of neovascular ARMD. It may present in one of three vasogenic stages: IRN, SRN, or CNV. Whereas ICG angiography is helpful in diagnosing RAP and in documenting the stage of the neovascularized process, it is frequently difficult to determine the precise nature and location of the new vessel formation. It is important for clinicians to recognize the vasogenic potential and the associated manifestations of this peculiar form of neovascular ARMD so that a proper diagnosis can be made, and when possible, an appropriate management administered.

PMID: 22451953 [PubMed - in process]

Retina. 2012 Feb;32 Suppl 1:191.

Digital indocyanine green videoangiography and choroidal neovascularization.

Yannuzzi LA, Slakter JS, Sorenson JA, Guyer DR, Orlock DA.

Abstract

This report describes a new system for digital indocyanine green videoangiography (ICGV) that provides enhanced imaging of the choroidal circulation. This newly assembled system was used to study a consecutive series of 129 patients with exudative age-related macular degeneration (AMD), and ill-defined or occult choroidal neovascularization (CNV). Overall, 39% of the patients in this study with occult CNV could be reclassified as having well-delineated or so-called classic CNV by virtue of the additional findings provided by ICGV. In this series, ICGV was particularly useful in identifying occult CNV in eyes with a large, serous pigment epithelial detachment (PED) and in eyes with recurrent CNV after previous laser photocoagulation treatment. Some of these patients were selected for laser photocoagulation of the abnormal choroidal vessels in order to evaluate the feasibility of this form of treatment on the basis of combined clinical, fluorescein angiographic, and ICGV findings. The results of this study suggest that ICGV

is an important adjunct in the evaluation, classification, and laser treatment of patients with occult CNV secondary to AMD.

PMID: 22451951 [PubMed - in process]

Retina. 2012 Feb;32 Suppl 1:1-8.

Idiopathic polypoidal choroidal vasculopathy (IPCV).

Yannuzzi LA, Sorenson J, Spaide RF, Lipson B.

Abstract

Eleven patients, 40 to 71 years old, had a choroidal vasculopathy that led to hemorrhagic and exudative macular degeneration. The patients had peculiar polypoidal, subretinal, vascular lesions associated with serous and hemorrhagic detachments of the retinal pigment epithelium. This macular disorder, which we have named idiopathic polypoidal choroidal vasculopathy (IPCV), appears to represent a distinct entity that differs clinically and demograph-ically from age-related macular degeneration (AMD) and other macular diseases associated with subretinal neovascularization. Recognition of this condition is important because it may have specific risk factors, natural course, and management considerations that differ from those of age -related macular degeneration

PMID: 22451948 [PubMed - in process]

J Ophthalmic Vis Res. 2011 Jul;6(3):166-76.

Oscillatory photodynamic therapy for choroidal neovascularization and central serous retinopathy; a pilot study.

Peyman GA, Tsipursky M, Nassiri N, Conway M.

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PURPOSE: To report the preliminary results of oscillatory photodynamic therapy (OPDT) for choroidal neovascularization (CNV) and central serous retinopathy (CSR).

METHODS: This study included 7 eyes of 6 patients with CSR (2 eyes), idiopathic CNV (2 eyes), CNV due to age-related macular degeneration (AMD) (2 eyes), and peripapillary CNV secondary to presumed ocular histoplasmosis syndrome (1 eye). Intravenous verteporfin (6 mg/m(2) body surface area) was infused over 10 minutes followed by oscillating laser (wavelength 689 nm) covering slightly beyond the entire lesion. An Area Centralis lens was applied and laser was delivered (600 mW/cm(2) fluence rate and 50 J/cm(2) dose). Intravitreal bevacizumab and dexamethasone combination therapy was used with OPDT in 4 eyes with CNV; intravitreal dexamethasone and triamcinolone acetonide were injected in the other eye with CNV. Clinical examination, funduscopy, fluorescein angiography, and optical coherence tomography (OCT) were performed at baseline and after treatment.

RESULTS: After mean follow-up of 7.1±5.1 months, visual acuity improved from 0.87±0.69 logMAR (20/160) to 0.60±0.65 logMAR (20/80) (P = 0.027); central foveal thickness decreased from 322±62.1 to 240.7±34.8 microns as measured by OCT (P = 0.018). Fluorescein angiography and OCT demonstrated cessation of vascular leakage, and resolution of hemorrhage and subretinal fluid in all eyes. No adverse events or recurrence were noted.

CONCLUSION: OPDT was effective in treating CNV lesions and CSR. OPDT may be an improvement on standard PDT due to reduced side effects, thermal damage and scarring.

PMID: 22454731 [PubMed - in process] PMCID: PMC3306098

IEEE Trans Med Imaging. 2012 Mar 19. [Epub ahead of print]

3D Segmentation of Fluid-Associated Abnormalities in Retinal OCT: Probability Constrained Graph-Search¿Graph-Cut.

Chen X, Niemeijer M, Zhang L, Lee K, Abramoff M, Sonka M.

Abstract

An automated method is reported for segmenting 3D fluid and fluid-associated abnormalities in the retina, so-called Symptomatic Exudate-Associated Derangements (SEAD), from 3D OCT retinal images of subjects suffering from exudative age-related macular degeneration. In the first stage of a two-stage approach, retinal layers are segmented, candidate SEAD regions identified, and the retinal OCT image is flattened using a candidate-SEAD aware approach. In the second stage, a probability constrained combined graph search graph cut method refines the candidate SEADs by integrating the candidate volumes into the graph cut cost function as probability constraints. The proposed method was evaluated on 15 spectral domain OCT images from 15 subjects undergoing intravitreal anti-VEGF injection treatment. Leave-one-out evaluation resulted in a true positive volume fraction (TPVF), false positive volume fraction (FPVF) and relative volume difference ratio (RVDR) of 86.5%, 1.7% and 12.8%, respectively. The new graph cut graph search method significantly outperformed both the traditional graph cut and traditional graph search approaches ($p<0.01$, $p<0.04$) and has the potential to improve clinical management of patients with choroidal neovascularization due to exudative age-related macular degeneration.

PMID: 22453610 [PubMed - as supplied by publisher]

Osaka City Med J. 2011 Dec;57(2):49-57.

Progression of cataracts following photodynamic therapy combined with intravitreous triamcinolone injection in cases of age-related macular degeneration.

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BACKGROUND: To present long-term data on the progression of cataracts following photodynamic therapy (PDT) combined with 4 mg intravitreal triamcinolone acetonide (IVTA) for age-related macular degeneration (AMD).

METHODS: Fifty-seven phakic eyes of 56 patients underwent the treatment between October 2004 and November 2006. The follow-up period ranged from 12 to 38 months with 3 months interval of observation and repeated treatment at recurrence.

RESULTS: Cataract progression was noted in 40 eyes 5-21 months after treatment, consisting of 4 eyes between 3 and < 6 months after treatment, 22 eyes between 6 and < 12 months, 8 eyes between 12 and < 18 months, and 6 eyes between 18 and < 24 months. The percentage of the eyes with cataract progression began to decrease 5 months after treatment and, occurred most frequently during the period from 6 months to 12 months after treatment. There was no significant difference in age, follow-up period, or the frequency of the treatment between the cataract progression group and the non progression group. Twenty four eyes underwent surgery 10-31 months after treatment, showing significant improvement in visual acuity.

CONCLUSIONS: This study showed high incidence of cataract during a long-term follow-up after PDT combined with IVTA and significant reduction of visual acuity due to cataract.

PMID: 22443078 [PubMed - in process]

Vestn Oftalmol. 2011 Nov-Dec;127(6):60-4.

[Laser treatment of central retina diseases].

[Article in Russian]

[No authors listed]

Review of literature is devoted to the most up-to-date retinal diseases such as diabetic macular edema and age macular degeneration affecting people of different age and leading to disability. Besides management of central serous retinopathy that affects younger patients is discussed. According to data of domestic and foreign studies common treatment options of central retina diseases along with therapeutic effect have adverse effects leading to damage of neurosensory retina. Thus despite of a great number of studies devoted to this problem a search of effective and safe treatment option of central retina diseases is still important.

PMID: 22443000 [PubMed - in process]

Br J Ophthalmol. 2012 Mar 24. [Epub ahead of print]

Survey of systematic reviews and meta-analyses published in ophthalmology.

Chen H, Jhanji V.

Shantou University & The Chinese University of Hong Kong, Shantou, China.

PURPOSE: To analyse the types of systematic reviews and meta-analyses published in the field of ophthalmology.

METHODS: The systematic reviews and meta-analysis in ophthalmology published in peer-reviewed journals were retrieved. The distribution of systematic reviews and meta-analyses in various ophthalmic subspecialties, type of study and country of origin were determined.

RESULTS: A total of 533 records were identified as systematic reviews and meta-analysis in ophthalmology. Overall, retina and glaucoma were the two major subspecialties accounting for 35% and 21% of the published systematic reviews and meta-analyses, respectively. The major topics published in retina were age-related macular degeneration (37%), tumours (14%), and diabetic retinopathy (12%). More than half (56%) the systematic reviews and meta-analyses were interventional. The author affiliations of these studies were largely from the USA (30%) and the UK (22%). About 60% of the systematic reviews and meta-analyses were published in ophthalmology journals, followed by the Cochrane Library (15.75%) and other non-ophthalmic journals (25.14%), respectively. The number of publications increased from 3 per year in 1994 to almost 100 per year in 2010.

CONCLUSIONS: The number of published systematic reviews and meta-analyses has been increasing progressively over the past few years. Retina and glaucoma are the two most commonly published topics. Non-ophthalmology journals form a sizeable proportion of avenues for ophthalmic publications.

PMID: 22446144 [PubMed - as supplied by publisher]

Pathogenesis

Micron. 2012 Feb 13. [Epub ahead of print]

Ultrastructure of the human retina in aging and various pathological states.

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Abstract

Vision is hampered in aging and diseases, such as age-related macular degeneration, retinitis pigmentosa, diabetic retinopathy and glaucoma. This review collates the fine structural alterations of the human retina in aging and various pathological situations and their links to the disease pathogenesis. It transpires that most changes occur at the level of the retinal pigment epithelium -Bruch's membrane and the photoreceptor layer, causing visual problems to the sufferers. These changes include loss of normal, essential features of these cells and their gradual disappearance. It is important to understand in depth the selective vulnerability of this retinal region to alterations in aging and diseases. Evidence indicates that some of these changes may be mediated by the effects of oxidative stress, inflammation, and chronic light exposure. There are changes also in the inner retinal layers, wherein hypertension, auto-immunity, hypoxia and ischemia could play significant roles in disease pathogenesis. Results of extensive research utilizing animal models have broadened our idea about photoreceptor pathology. However, equivalent knowledge on various changes in aging human retina and in dystrophies that affect the macula is not complete. Since cone photoreceptor and ganglion cell death are a potential problem, it is imperative to know about the basic facts on how they are affected and the mechanisms involved in their death. Thus, prevention of cone and ganglion cell loss should be the target of choice. This review also highlights the significant role played by electron microscopy in understanding such ultrastructural changes and future strategies utilizing it and other techniques to fill some of the existing lacunae and advance our knowledge.

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Secretion of αB-Crystallin via exosomes: New clues to the function of human retinal pigment epithelium.

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Abstract

αB-crystallin (αB) is an archetypical small heat shock protein whose physiological function is not clearly defined. The interest in this protein arises from its well-established but poorly understood association with a myriad of neurodegenerative diseases, cancer and cardiomyopathies. The discovery of the secretion of αB from human adult retinal pigment epithelial cells (ARPE19) via exosomes not only points to the involvement of this protein in lateral transfer of information between cells in the visual system but also to the status of this protein as a potential ligand that may activate or modulate immune and stress responses, normal growth and oncogenic pathways. Retinal pigment epithelium (RPE) is a single layer of polarized cells that supports photoreceptor physiology and function. We have initiated investigations on understanding the origin of the elevated levels of αB in extracellular sub-retinal proteolipid deposits (known as "drusen") associated with the death of photoreceptor neurons in age-related macular degeneration (AMD). Here we discuss the potential implications of the presence and transport of αB in exosomes across cell membranes in RPE.

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Cyclic intensive light exposure induces retinal lesions similar to age-related macular degeneration in APPswe/PS1 bigenic mice.

Dong Z, Li J, Leng Y, Sun X, Hu H, He Y, Tan Z, Ge J.

BACKGROUND: Intensive light exposure and beta-amyloid (Abeta) aggregates have been known as a risk factor for macular degeneration and an important component in the pathologic drusen structure involved in this disorder, respectively. However, it is unknown whether Abeta deposition mediates or exacerbates light exposure-induced pathogenesis of macular degeneration. Several studies including the one from us already showed accumulation of Abeta deposits in the retina in Alzheimer's transgenic mice. Using histopathological analysis combined with electroretinographic functional assessment, we investigated the effects of cyclic intensive light exposure (CILE) on the architecture of retina and related function in the APPswe/PS1bigenic mouse.

RESULTS: Histopathological analysis has found significant loss of outer nuclear layer/photoreceptor outer segment and outer plexiform layer along with abnormal hypo- and hyper-pigmentation in the retinal pigment epithelium (RPE), remarkable choroidal neovascularization (CNV), and exaggerated neuroinflammatory responses in the outer retina of APPswe/PS1 bigenic mice following cyclic intensive light exposure (CILE), whereas controls remained little change contrasted with age-matched non-transgenic littermates. CILE-induced degenerative changes in RPE are further confirmed by transmission electron microcopy and manifest as formation of basal laminar deposits, irregular thickening of Bruch's membrane (BrM), deposition of outer collagenous layer (OCL) in the subretinal space, and vacuolation in the RPE. Immunofluorescence microscopy reveals drusenoid Abeta deposits in RPE as well as neovessels attached which are associated with disruption of RPE integrity and provoked neuroinflammatory response as indicated by markedly increased retinal infiltration of microglia. Moreover, both immunohistochemistry and Western blots detect an induction of vascular endothelial growth factor (VEGF) in RPE, which corroborates increased CNV in the outer retina in the bigenic mice challenged by CILE.

CONCLUSIONS: Our findings demonstrate that degenerative changes in the outer retina in the APPswe/PS1 bigenic mouse induced by CILE are consistent with these in AMD. These results suggest that an Alzheimer's transgenic animal model with accumulation of Abeta deposits might be an alternative animal model for AMD, if combined with other confounding factors such as intensive light exposure for AMD.

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Anti-inflammatory recombinant TSG-6 stabilizes the progression of focal retinal degeneration in a murine model.

Tuo J, Cao X, Shen D, Wang Y, Zhang J, Oh JY, Prockop DJ, Chan CC.

BACKGROUND: Inflammatory responses are detected in the retina of patients with age-related macular degeneration and Ccl2//Cx3cr1/ mice on rd8 background,(Ccl2//Cx3cr1/ mice) a model that develops progressive age-related macular degeneration-like retinal lesions including focal photoreceptor degeneration, abnormal retinal pigment epithelium and A2E accumulation. Tumor necrosis factor-inducible gene 6 protein is an anti-inflammatory protein and has been shown to improve myocardial infarction outcome and chemically injured cornea in mice by suppressing inflammation. In this study, we evaluated the effect of an intravitreous injection of recombinant TSG-6 on the retinal lesions of Ccl2//Cx3cr1/ mice.

METHODS: Recombinant TSG-6 (400 ng) was administered by intravitreous injection into the right eye of six-week-old Ccl2//Cx3cr1/ mice. Their left eye was injected with phosphate-buffered saline as a control. Funduscopic pictures were taken before injection and sequentially once a month after injection. The mice

were killed two months after injection and the ocular histology examined. Retinal A2E, a major component of lipofuscin, was measured by high performance liquid chromatography. The microarray of ocular mRNA of 92 immunological genes was performed. The genes showing differentiated expression in microarray were further compared between the injected right eye and the contralateral (control) eye by [real-time quantitative reverse transcription polymerase chain reaction] qRT-PCR.

RESULTS: The continuous monitoring of the fundus for two months showed a slower progression or alleviation of retinal lesions in the treated right eyes as compared with the untreated left eyes. Among 23 pairs of eyes, the lesion levels improved in 78.3%, stayed the same in 8.7% and progressed in 13.0%. Histology confirmed the clinical observation. Even though there was no difference in the level of A2E between the treated and the untreated eyes, microarray analysis of 92 immune genes showed that IL-17a was substantially decreased after the treatment. Expression of TNF-alpha showed a similar pattern to IL-17a. The results were consistent in duplicated arrays and confirmed by qRT-PCR.

CONCLUSIONS: We concluded that intravitreous administration of recombinant TSG-6 might stabilize retinal lesions in Ccl2//Cx3cr1/ mice on rd8 background. Modulation of ocular immunological gene expressions, especially IL-17a, could be one of the mechanisms.

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Genetics

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Clinical and Genetic Characteristics of Late-onset Stargardt's Disease.

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OBJECTIVE: To describe the genotype and phenotype of patients with a late-onset Stargardt's disease (STGD1).

DESIGN: Retrospective case series.

PARTICIPANTS: Twenty-one unrelated STGD1 patients with an age at onset of ≥45 years and ≥1 rare variant in the ABCA4 gene.

METHODS: Ophthalmologic examination, including best-corrected visual acuity (VA), Amsler grid testing, fundus photography, fluorescein angiography (FA), spectral-domain optical coherence tomography (OCT), fundus autofluorescence (FAF) imaging, full-field electroretinography (ERG), multifocal ERG, and central visual field testing. Analysis of the ABCA4 gene was performed using microarray analysis, sequencing, and multiplex ligation-dependent probe amplification. In addition, the PRPH2 and CFH genes were sequenced.

MAIN OUTCOME MEASURES: Age at onset, VA, fundus appearance, FA, FAF, and OCT findings; ABCA4 mutations; and genotype-phenotype correlation.

RESULTS: The mean age at onset was 55 years (range, 45-72 years). Seven patients were diagnosed without visual symptoms (age range, 45-83 years). The VA was ≥20/40 in 24 eyes of 14 patients (59%) owing to foveal sparing. On ophthalmoscopy, late-onset STGD1 showed flavimaculatus flecks (15 patients), small flecks surrounding mottled foveal changes (3 patients), extensive chorioretinal atrophy (2 patients), or small yellowish spots in the macula (1 patient). The fundus flecks showed increased autofluorescence on FAF. The choroidal background fluorescence on FA was obscured in 16 patients (80%). We found a single heterozygous ABCA4 variant in 11 patients (52%), 2 compound heterozygous variants in 8 patients (38%), and a homozygous variant in 2 patients (10%). No PRPH2 or CFH mutations were detected.

CONCLUSIONS: Late-onset STGD1 is at the mild end of the spectrum of retinal dystrophies caused by ABCA4 mutations. The VA is frequently preserved in late-onset STGD1 patients owing to foveal sparing. This phenotype may be caused by 1 or 2 ABCA4 variants. The differential diagnosis between late-onset STGD1 and age-related macular degeneration may be challenging. A thorough clinical and genetic analysis makes a distinction possible, which is important for clinical and genetic counseling.

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Diet

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Changes in blood oxidative and antioxidant parameters in a group of chinese patients with age-related macular degeneration.

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Objective: To measure the oxidative and antioxidant biochemical parameters in the serum of Chinese patients with age-related macular degeneration (AMD) and in a similar age control group from the same area.

Design: A case-control study.

Participants: 56 AMD patients (21 early dry, 13 geographic atrophy and 22 wet form) and 34 normal subjects, similar for age and sex were studied. Measurements: Both groups completed a questionnaire about demographic characters and dieatry habit, and the levels of serum lipid peroxidation (malondialdehyde, MDA) and antioxidants parameters (vitamin C and E, the activities of superoxide dismutase-SOD, total antioxidant capacity -TAC) were determined.

Results: There was a significantly higher frequency of daily intake of fruit and legumes in controls than in AMD patients. There was a significantly increased serum MDA levels and SOD activities, and significantly decreased serum vitamin C and total antioxidant capacity in AMD patients as compared to controls. The intensity of lipid peroxidation was higher with the progression of AMD. There was not difference in serum vitamin E levels between AMD patients and controls.

Conclusion: Oxido-reduction disturbance may be involved in the pathogenesis of AMD. There is a significantly decreased antioxidant capacity in AMD patients.

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