Retina Roundup
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Spectral Domain Optical Coherence Tomography Predictors of Visual Acuity in the Study of COmparative Treatments for REtinal Vein Occlusion 2 (SCORE2)

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ABSTRACT

Objective: To evaluate the association between baseline demographic and SD-OCT features with visual acuity (VA) in the Study of Comparative Treatments for Retinal Vein Occlusion 2 (SCORE2) over 2 years.

Design: Post-hoc analysis of prospective clinical trial data.

Participants: 362 SCORE2 participants with macular edema secondary to central retinal (CRVO) or hemi-retinal vein occlusion (HRVO).

Methods: SD-OCT volume scans were assessed at the SCORE2 reading center at baseline, month 01 (M01), month 06 (M06), month 12 (M12), and month 24 (M24) for central subfield thickness (CST), subretinal fluid, intraretinal fluid, vitreoretinal interface abnormalities, disorganization of retinal inner layers (DRIL), and ellipsoid zone (EZ) within the central subfield (CSF).

Main outcome measures: VA at M06, M12, and M24 RESULTS: Mean baseline age was 68.9 years. Mean VA at M01 was 63.2 letters and central subfield thickness was 299.7 microns. At M01, subretinal fluid was seen in 28.5% intraretinal fluid in 67.2%, DRIL was seen in 73.8%, mostly within CSF and EZ was absent in 9.8 and patchy in 31.7%. In multivariate analysis including all M01 demographics and SDOCT parameters and their association with VA at M06,

M12 and M24, VA at M01 remained significant across all time points up to M24 ($p<0.001$).

Conclusions: In this 2 year follow up of eyes that were treated with both per protocol and off protocol for RVO, visual acuity at M01 was an important predictor of long-term vision and change in vision. Establishing predictors of visual recovery helps identify causes for poor responders to treatment in patients with RVO.

Autologous full-thickness retinal transplant for refractory large macular holes

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ABSTRACT

Background: Despite the constant refinement of techniques and surgical aids, extremely large and refractory macular holes continue to have poor surgical outcomes with the current standard of care. The objective of the present study is to assess the anatomical and functional outcomes, as well as the structural change through time, of the optical coherence tomography of patients with refractory macular holes treated with a full-thickness autologous retinal transplant.

Methods: Prospective, case series. We include patients with a clinical diagnosis of refractory macular holes with a minimum diameter of at least 500 µm. All the patients had a comprehensive ophthalmological examination, which included a best-corrected visual acuity assessment, fundus examination, and optical coherence analysis. All the patients underwent a 23-gauge pars plana vitrectomy with a full-thickness retinal transplant and silicone oil tamponade (5000 cs<). Follow-up was done at 1, 3, 6, and 12 months. Statistical analysis was done with a test for repeated measurements and Bonferroni correction, with an alpha value of 0.05 for statistical significance and a Mann-Whitney U test for nonparametric continuous variables.

Results: We enrolled 13 eyes from 13 patients (mean age: 67.15 years) with refractory macular holes, with a mean base diameter of 1615.38 ± 689.19 µm and a minimum diameter of 964.08 ± 709.77 µm. The closure rate after 12 months of follow-up was 76.92%. Six patients with a closed macular hole at the end of the follow-up had complete recovery of the myoid/ellipsoid layer. The remaining showed a 44.9% reduction of the initial gap. Most patients formed a pseudofovea and normalization of the internal retinal layers. Despite a positive

trend toward visual recovery (p = 0.034), after the correction of the alpha value, the change lost its statistical significance. During follow-up, one patient developed mild proliferative vitreoretinopathy and epiretinal membrane without anatomical or functional consequences.

Conclusions: An autologous full-thickness retinal transplant may improve the anatomical and structural outcome of patients with refractory macular holes. The full safety profile of this new technique is still unknown. More studies are needed in order to assess functional changes through time.

Lyophilized amniotic membrane patch (LAMPatch) as a replacement of tamponades in the treatment of primary rhegmatogenous retinal detachment

Saravia M, Zeman L, Berra A

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ABSTRACT

Background: The basis of retinal detachment repair is sealing the retinal breaks. In order to seal the retinal breaks, chorioretinal adhesion around these lesions has to be achieved. Laser retinopexy is not immediate thus necessitates the use of a temporal endotamponade to maintain both tissues in apposition. We propose the use of a patch of lyophilized human amniotic membrane (LAMPatch) in order to occlude the retinal tear effectively until the chorioretinal adhesion is settled, overcoming the risks and limitations of the current tamponades.

Methods: 23-gauge vitrectomy was performed on eyes with primary retinal detachment with single retinal breaks of less than one-hour extension. A LAMPatch was deployed over the retinal breaks after retina was repositioned with perfluorocarbon. Neither gas nor silicon oil were injected.

Results: Six eyes of six patients with total or partial retinal detachment were included. Retinas remained reattached in all cases until the end on follow-up (3, 5 months). Best-corrected visual acuity at 1-week postop was between 20/30 and 20/100. Neither elevations of intraocular pressure, cataracts nor signs of inflammation were registered during follow-up. No second surgeries were needed.

Conclusion: This technique has proven to be safe and effective in this small case series. No intraocular pressure rise, inflammation or cataracts were registered until last follow-up visit.

HAWK and HARRIER: Ninety-Six-Week Outcomes from the Phase 3 Trials of Brolucizumab for Neovascular Age-Related Macular Degeneration

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ABSTRACT

Purpose: To report the 96-week outcomes from HAWK and HARRIER.

Design: Phase 3, prospective, randomized, double-masked, multicenter studies comparing efficacy and safety of brolucizumab 3 mg (HAWK only) and 6 mg with aflibercept 2 mg in eyes with neovascular age-related macular degeneration (nAMD).

Participants: Treatment-naïve eyes with nAMD were randomized 1:1:1 to brolucizumab 3 mg (n = 358), brolucizumab 6 mg (n = 360), aflibercept 2 mg (n = 360; HAWK) or 1:1 to brolucizumab 6 mg (n = 370), aflibercept 2 mg (n = 369; HARRIER).

Methods: After 3 monthly loading doses, brolucizumab patients received every (q)-12-week (w) dosing, possibly adjusting to q8w dosing if disease activity was present at predefined disease activity assessment (DAA) visits. Aflibercept was dosed in a fixed q8w regimen. Visual and anatomic parameters were assessed throughout. Primary end point was at week 48 (48w), confirmed at 96w.

Main outcome measures: Mean best-corrected visual acuity (BCVA) change from baseline, proportion of patients on an q12w regimen, retinal thickness, retinal fluid changes, and safety, all to 96w.

Results: Mean change (least squares [LS] mean ± standard error) in BCVA from baseline to 96w in HAWK was 5.6±0.79 Early Treatment Diabetic Retinopathy

Study (ETDRS) letters for brolucizumab 3 mg, 5.90±0.78 letters for brolucizumab 6 mg, and 5.3±0.78 letters for aflibercept and in HARRIER was 6.1±0.73 letters for brolucizumab 6 mg and 6.6 ± 0.73 letters for aflibercept. Greater central subfield thickness reductions were observed with brolucizumab 6 mg versus aflibercept in HAWK (LS mean, -174.8 µm vs. -148.7 µm; 95% confidence interval for treatment difference, -46.2 to -5.9 µm; P = 0.0115) and HARRIER (LS mean, -197.7 µm vs. -155.1 µm; 95% confidence interval for treatment difference, -62.0 to -23.3 µm; P < 0.0001). The proportions of eyes with intraretinal fluid and/or subretinal fluid (IRF/SRF) at 96w in HAWK were 31% (P = 0.0688) and 24% (P = 0.0002) for brolucizumab 3 mg and 6 mg and 37% for aflibercept, whereas in HARRIER, they were 24% for brolucizumab 6 mg (P < 0.0001) and 39% for aflibercept. At 92w (last DAA), a 45.4% and 38.6% probability was observed for brolucizumab 6 mg patients of maintaining an q12w treatment regimen in HAWK and HARRIER, respectively. Brolucizumab exhibited an overall well-tolerated safety profile.

Conclusions: Visual outcomes from 48w to 96w confirm the efficacy achieved at 48w. Brolucizumab demonstrated greater fluid resolution compared with aflibercept. The q12w potential for brolucizumab observed at 48w was maintained to 96w.

Optical coherence tomography angiography measured area of retinal neovascularization is predictive of treatment response and progression of disease in patients with proliferative diabetic retinopathy

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ABSTRACT

Background: The purpose of this study was to evaluate the area of retinal neovascularization in patients with treatment-naïve proliferative diabetic retinopathy (PDR) as measured by optical coherence tomography angiography (OCT-A) as a marker of subsequent treatment response after panretinal photocoagulation (PRP), and to examine if this area correlated with area of retinal neovascularization as measured by fluorescein angiography (FA).

Methods: En face OCT-A scans (4.5 × 4.5 mm) of neovascularizations were obtained at baseline (BL) before PRP and at month (M) 3 and M6 after treatment. Progression of PDR were defined as lesion growth (assessed by ophthalmoscopy and wide-field fundus photo) or increasing leakage by Optos ultra-widefield FA, and patients were divided into two groups; progression or non-progression. Mann-Whitney U test and Wilcoxon signed-rank test were used to analyse differences between groups and between time points. Areas of retinal neovascularizations (OCT-A and FA) were calculated by algorithms developed in Python (version 3.6.8, The Python Software Foundation, USA).

Results: Of 21 eyes included, 14 had progression of disease. Median OCT-A area did not differ between the two groups (progression vs. non-progression) at BL (76.40 ± 162.03 vs. 72.62 ± 94.15, p = 0.43) but were statistically significantly larger in the progression group at M6 (276.69 ± 168.78 vs. 61.30 ± 70.90, p = 0.025). Median FA area did not differ in the progression vs. the non-progression

group at BL (111.42 ± 143.08 vs. 60.80 ± 54.83, p = 0.05) or at M6 (200.12 ± 91.81 vs. 123.86 ± 162.16, p = 0.62). Intraclass correlation between area by OCT-A and FA was -5.99 (95% CI: -35.28-0.993), p = 0.71.

Conclusions: In this study of patients with treatment-naïve PDR, we showed that increasing area of retinal neovascularizations measured by OCT-A at M6 indicated progression of disease after PRP treatment. Our results suggest that area by OCT-A reflects disease activity and that it can be used as an indicator to monitor the progression of PDR over time, and to evaluate treatment response six months after PRP.

Drusen and pachydrusen: the definition, pathogenesis, and clinical significance

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ABSTRACT

The pachychoroid disease spectrum encompasses seven major retinal conditions including central serous chorioretinopathy (CSC), polypoidal choroidal vasculopathy (PCV), and pachychoroid neovasculopathy or type I macular neovascularisation (MNV) secondary to chronic persistent thickening and dysfunction of the choroidal vasculature. Drusen are focal yellow-white deposits of extracellular debris, which consist of complement proteins, esterified and nonesterified cholesterol, apolipoproteins, carbohydrates, and trace elements, above the retinal pigment epithelium (RPE) or between the RPE and Bruch's membrane. Although drusen are an essential disease precursor of advanced age-related macular degeneration (AMD), a new entity "pachydrusen" has been identified to be associated with some of the enitites that constitute the pachychoroid spectrum. It remains to be determined what the exact differences are between soft drusen, pseudodrusen, and pachydrusen in terms of phenotype, genotype, and pathogenesis. Improving our knowledge in these areas will inevitably improve our understanding of their clinical significance especially as in disease prediction in AMD and the pachychroid spectrum disorders. It remains controversial whether PCV is a subtype of AMD. Understanding the pathogenesis of different types of drusen may also help in addressing if phenotype and/or genotype of type 1 MNV associated with pachychoroid are similar to type 1 MNV related to AMD. Furthermore, because pachydrusen links two pachychoroid diseases, CSC and PCV, it is also of great interest to investigate if CSC is an early stage or a predictor of PCV in future research. In this review, we share our experience in clinical practice and the latest published evidence-based literature to emphasize the differences and similarities in morphology, pathogenesis, and clinical significance of drusen and pachydrusen, a new member of the pachychoroid spectrum disorders.

Fluorescence lifetime imaging ophthalmoscopy: autofluorescence imaging and beyond

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ABSTRACT

Fluorescence lifetime imaging ophthalmoscopy, FLIO, has gained large interest in the scientific community in the recent years. It is a noninvasive imaging modality that has been shown to provide additional information to conventional imaging modalities. The FLIO device is based on a Heidelberg Engineering Spectralis system. Autofluorescence lifetimes are excited at 473 nm and recorded in two spectral wavelength channels, a short spectral channel (SSC, 498-560 nm) and a long spectral channel (LSC, 560-720 nm). Typically, mean autofluorescence lifetimes in a 30° retinal field are investigated. FLIO shows a clear benefit for imaging different retinal diseases. For example, in age-related macular degeneration (AMD), ring patterns of prolonged FLIO lifetimes 1.5-3.0 mm from the fovea can be appreciated. Macular telangiectasia type 2 (MacTel) shows a different pattern, with prolonged FLIO lifetimes within the typical MacTel zone. In Stargardt disease, retinal flecks can be appreciated even before they are visible with other imaging modalities. Early hydroxychloroquine toxicity appears to be detectable with FLIO. This technique has more potential that has yet to be discovered. This review article focuses on current knowledge as well as pitfalls of this technology. It highlights clinical benefits of FLIO imaging in different ophthalmic and systemic diseases, and provides an outlook with perspectives from the authors.