Predictors of treatment response to intravitreal anti-vascular endothelial growth factor (anti-VEGF) therapy for choroidal neovascularisation secondary to chronic central serous chorioretinopathy.

Romdhane K, Zola M, Matet A, Daruich A, Elalouf M, Behar-Cohen F, Mantel I.

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ABSTRACT

PURPOSE:

The aim of this study was to evaluate the effect of anti-vascular endothelial growth factor (VEGF) therapy on choroidal neovascularisation (CNV) complicating central serous chorioretinopathy (CSC) using multimodal imaging, and to identify possible predictive factors of the treatment response.

DESIGN:

Retrospective study.

METHODS:

Data of 27 eyes with CNV complicating CSC treated with anti-VEGF therapy (either ranibizumab or aflibercept) were reviewed. Response to anti-VEGF treatment was evaluated by change in visual acuity, intra/subretinal fluid modifications and CNV changes on optical coherence tomography angiography (OCTA). Univariate and multivariate analyses were performed to identify predictive factors for central retinal thickness (CRT) change and for the relative degree of treatment response (complete, incomplete or absent fluid reduction).

RESULTS:

CRT was significantly reduced at 32±15 days after 2.8±1.3 injections (p=0.0004) as was the subretinal fluid (p=0002). Complete fluid resorption was observed in 45% of cases. Best corrected visual acuity did not significantly improve (p=0.18). CNV area (p=0.09) and CNV flow area (p=0.07) did not significantly decrease. No changes in CNV pattern were noted. Univariate analysis identified greater CRT at baseline (p<0.0001), greater amount of subretinal fluid (p<0.0001), a shorter period of retinal fluid (p=0.04) and female gender

(p=0.04) as predictors for CRT reduction. After multivariate analysis the factor of greater CRT at baseline (p<0.0001) proved independent. The degree of treatment response was dependent on the size of CNV surface (p=0.05) and flow area (p=0.05) on OCTA in the univariate analysis, and the latter independent after multivariate analysis. In addition, a shorter time period of retinal fluid appeared to play a role (p=0.01 multivariate, p=0.19 univariate).

CONCLUSION:

The anti-VEGF response was highly variable and often incomplete, suggesting that CNV was not solely responsible for the fluid accumulation. Predictive factors may guide indication for anti-VEGF in CNV associated with CSC.

KEYWORDS:

choroid; neovascularisation; retina; treatment other

The use of optical coherence tomography angiography and optical coherence tomography to predict visual acuity in diabetic retinopathy.

DaCosta J, Bhatia D, Talks J.

Eye (Lond). 2019 Oct 7. doi: 10.1038/s41433-019-0606-9. [Epub ahead of print]

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ABSTRACT

INTRODUCTION:

Diabetic macular ischaemia (DMI) is associated with reduced visual acuity. Limitations exist in assessing the ischaemic component of diabetic retinopathy. Optical coherence tomography angiography (OCTA) is a non-invasive imaging technique to distinguish retinal capillary layers and allow microvascular assessment. Evaluation of DMI is of prognostic significance when planning treatment regimens for diabetic maculopathy. The aims of this study were to evaluate OCTA to assess DMI and correlate findings with structural optical coherence tomography (OCT) features to predict visual acuity.

METHODS:

Cross sectional study of fifty-seven eyes ($n = 57$) of thirty-seven subjects with diabetic retinopathy. 26/57 (46%) eyes had diabetic macular cysts. OCT and OCTA data from a single visit were analysed. Central retinal thickness, the presence of intraretinal cysts, ellipsoid zone (EZ) disruption, disorganisation of the retinal inner layers (DRIL), foveal avascular zone (FAZ) area, FAZ acircularity, and level of DMI in the superficial capillary plexus were graded according to ETDRS protocols. The deep vascular plexus was also graded for ischaemia. Correlations between measures and visual acuity were explored using regression models.

RESULTS:

Median age was 55 years. Multiple regression analysis showed EZ disruption ($p < 0.05$), horizontal DRIL length ($p < 0.01$), DMI grade, and FAZ area ($p < 0.1$) correlated with visual acuity. Central retinal thickness and the presence of intraretinal cysts did not predict visual acuity in this study.

DISCUSSION:

FAZ area, DMI grade, EZ disruption, and DRIL length correlate with visual acuity and could be incorporated into longitudinal clinical assessment of individual patients with diabetic retinopathy.

Imaging of Hydroxychloroquine Toxicity with Fluorescence Lifetime Imaging Ophthalmoscopy.

Sauer L, Calvo CM, Vitale AS, Henrie N, Milliken CM, Bernstein PS.

Ophthalmol Retina. 2019 Oct;3(10):814-825. doi: 10.1016/j.oret.2019.04.025. Epub 2019 May 2.

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ABSTRACT

PURPOSE:

To investigate the impact of retinal toxicity from hydroxychloroquine (HCQ) on fundus autofluorescence lifetimes using fluorescence lifetime imaging ophthalmoscopy (FLIO).

DESIGN:

Cross-sectional study.

PARTICIPANTS:

Twenty-four eyes of 12 patients with definite HCQ toxicity, 31 eyes of 16 clinically normal patients at high risk of developing HCQ toxicity (taking HCQ longer than 5 years), and 16 eyes of 8 clinically normal patients at low risk of developing HCQ toxicity (taking HCQ fewer than 5 years), as well as 22 age-matched healthy subjects.

METHODS:

Fluorescence lifetime images of a 30° retinal field centered at the fovea were collected at the Moran Eye Center, Salt Lake City, Utah. A prototype Heidelberg Engineering Spectralis-based FLIO was used to detect autofluorescence lifetimes in short (SSC; 498-560 nm) and long (LSC; 560-720 nm) spectral channels. Mean fluorescence lifetimes were calculated. OCT scans and macular pigment measures were also recorded. Additionally, the autofluorescence lifetimes of HCQ were measured in a cuvette.

MAIN OUTCOME MEASURES:

Mean autofluorescence lifetimes (τ_m).

RESULTS:

All patients with HCQ toxicity showed significantly prolonged FLIO lifetimes in regions of damage, typically in a bulls-eye distribution corresponding to toxic lesions in the retina (SSC: lesion, 400 ps; unremarkable retina, 294 ps; $P < 0.001$; LSC: lesion, 404 ps; unremarkable retina, 316 ps; $P < 0.001$).

Some clinically normal patients at high risk (9 of 16) and at low risk (2 of 8) of developing HCQ toxicity also showed prolonged FLIO lifetimes in the parafoveal region, whereas age-matched healthy subjects did not. HCQ at a concentration of 46 mM exhibited long autofluorescence lifetimes of around 1100 ps in either spectral channel.

CONCLUSIONS:

Fluorescence lifetime imaging ophthalmoscopy seems to detect retinal toxicity from HCQ at very early stages and could be a novel method to detect retinal toxicity before irreversible damage is manifest.

Classification and Guidelines for Widefield Imaging: Recommendations from the International Widefield Imaging Study Group.

Choudhry N, Duker JS, Freund KB, Kiss S, Querques G, Rosen R, Sarraf D, Souied EH, Stanga PE, Staurenghi G, Sadda SR.

Ophthalmol Retina. 2019 Oct;3(10):843-849. doi: 10.1016/j.oret.2019.05.007. Epub 2019 May 13.

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ABSTRACT

PURPOSE:

To summarize the results of a consensus meeting aimed at defining terminology for widefield imaging across all retinal imaging methods and to provide recommendations for the nomenclature used to describe related images.

DESIGN:

An international panel with expertise in retinal imaging was assembled to define consensus terminology for widefield imaging and associated terminology.

PARTICIPANTS:

A panel of retina specialists with expertise in retinal imaging.

METHODS:

Before the consensus meeting, a set of 7 images acquired with a range of imaging methods and representing both healthy and diseased eyes was circulated to the expert panel for independent assignment of nomenclature for each example. The outputs were assembled and used as the starting point for discussions occurring at a subsequent roundtable meeting. The anatomic location, field of view, and perspective provided by each image example was reviewed. A process of open discussion and negotiation was undertaken until unanimous terminology for widefield imaging was achieved.

MAIN OUTCOME MEASURES:

Definitions of widefield imaging applicable to multiple imaging methods.

RESULTS:

Across a range of different imaging methods, the expert panel identified a lack of uniform terminology being used in recent literature to describe widefield images. The panel

recommended the term widefield be limited to images depicting retinal anatomic features beyond the posterior pole, but posterior to the vortex vein ampulla, in all 4 quadrants. The term ultra widefield was recommended to describe images showing retinal anatomic features anterior to the vortex vein ampullae in all 4 quadrants. The definitions were recommended over other device-specific terminology.

CONCLUSIONS:

A consistent nomenclature for widefield imaging based on normal anatomic landmarks that is applicable to multiple retinal imaging methods has been proposed by the International Widefield Imaging Study Group. The panel recommends this standardized nomenclature for use in future publications.

Evaluation of Transplanted Autologous Induced Pluripotent Stem Cell-Derived Retinal Pigment Epithelium in Exudative Age-Related Macular Degeneration.

Takagi S, Mandai M, Gocho K, Hirami Y, Yamamoto M, Fujihara M, Sugita S, Kurimoto Y, Takahashi M.

Ophthalmol Retina. 2019 Oct;3(10):850-859. doi: 10.1016/j.oret.2019.04.021. Epub 2019 Apr 26.

PMID:31248784

ABSTRACT

PURPOSE:

To report the results after 4 years of follow-up in a previously presented first case of induced pluripotent stem cell (iPSC)-derived retinal pigment epithelium (RPE) sheet autologous transplantation using multimodal imaging.

DESIGN:

Follow-up of a single case.

PARTICIPANT:

A patient with exudative age-related macular degeneration and polypoidal choroidal vasculopathy.

METHODS:

Transplantation of an autologous iPSC-derived RPE cell sheet after removal of choroidal neovascularization (CNV) in September 2014.

MAIN OUTCOME MEASURES:

The function of the graft was assessed 4 years after surgery by color fundus photography, spectral-domain (SD) OCT, fluorescein angiography, indocyanine green angiography, and an adaptive optics (AO) retinal camera.

RESULTS:

At the 4-year follow-up, the transplanted autologous iPSC-derived RPE sheet had survived beneath the retina with slight expansion of the pigmented area and no adverse events. The outer

nuclear layer above and adjacent to the graft showed acceptable thickness and an organized structure. Fluorescein angiography and SD OCT suggested the presence of vessel-like structures confined to the grafted area associated with the remaining trunk vessel of preoperative polypoidal choroidal vasculopathy but with no exudative changes.

Visual acuity has been stable with no additional injections of anti-vascular endothelial growth factor agent. The choroidal volume at the graft site is relatively preserved when compared with the volume outside this site without RPE after removal of the CNV. Indocyanine green angiography revealed a preserved choriocapillaris around the iPSC-derived RPE sheet. Dark cell-like structures with a predominantly hexagonal arrangement were observed by AO imaging in an area located near the margin of the graft sheet. The average intercell distance was found to be stable over time.

CONCLUSIONS:

Thus far, the grafted iPSC-derived RPE sheet has survived for 4 years and seems to support photoreceptors and choroidal vessels. The morphologic characteristics of the RPE are observed at the transplant site.

Autologous Retinal Transplant for Refractory Macular Holes: Multicenter International Collaborative Study Group.

Grewal DS, Charles S, Parolini B, Kadonosono K, Mahmoud TH.

Ophthalmology. 2019 Oct;126(10):1399-1408. doi: 10.1016/j.ophtha.2019.01.027. Epub 2019 Jan 31.

PMID:30711606

ABSTRACT

PURPOSE:

To report the structural and functional outcomes of autologous neurosensory retinal transplant for closure of refractory large macular holes (MHs).

DESIGN:

Multicenter, retrospective, consecutive case series.

PARTICIPANTS:

A total of 41 eyes of 41 patients with a full-thickness MH refractory to prior vitrectomy with internal limiting membrane (ILM) peel and tamponade.

METHODS:

All patients underwent pars plana vitrectomy, autologous neurosensory retinal transplant with gas, silicone oil tamponade, or short-term perfluoro-n-octane heavy-liquid tamponade. All patients had at least 6 months' follow-up.

MAIN OUTCOME MEASURES:

Anatomic closure of MH, change in ellipsoid zone (EZ) and external limiting membrane (ELM) defect on OCT, visual acuity (VA) recovery, and surgical complications were analyzed.

RESULTS:

Mean number of prior surgeries was 1.5±0.94 (range, 1-3), and patients were followed for a mean of 11.1±7.7 months (range, 6-36 months). Complete anatomic closure of MH by OCT was achieved in 36 of 41 eyes (87.8%). Mean corrected VA (logarithm of the minimum angle of resolution [logMAR]) improved (P = 0.03) from 1.11±0.66 (range, 0.48-3) to 1.03±0.51 (range, 0.1-2) at the last postoperative visit. The VA improved (≥0.3 logMAR units) in 15 eyes (36.6%), was stable in 17 eyes (41.5%), and worsened in 9 eyes (21.9%). Among eyes with

anatomic closure, VA improved in 52.3% and worsened in 13.8%, whereas in those without closure, VA worsened in 40% and improved in none.

Mean preoperative largest basal diameter was 1468.1±656.4 µm (range, 621-2600 µm), and mean inner-opening diameter was 825±422.5 µm (range, 336-1649 µm). Mean preoperative EZ defect was 1777.3±513.8 µm (range, 963-2808 µm), which decreased to 1370±556.9 µm (range, 288-2000 µm) at final follow-up (P = 0.007). Mean preoperative ELM was 1681.5±429 µm (range, 1172-2606 µm), which decreased to 1408.5±571.2 µm (range, 200-2000 µm) at final follow-up (P = 0.017). Major postoperative complications were retinal detachment (n = 1) and vitreous hemorrhage (n = 1). There were no cases of proliferative vitreoretinopathy, endophthalmitis, suprachoroidal hemorrhage, or choroidal neovascularization.

CONCLUSIONS:

The autologous retinal transplant technique offers a high degree of anatomic success and proved safe in this initial experience for closure of refractory MHs.

Foveal microstructure and visual outcomes of myopic macular hole surgery with or without the inverted internal limiting membrane flap technique.

Hu XT, Pan QT, Zheng JW, Zhang ZD.

Br J Ophthalmol. 2019 Oct;103(10):1495-1502. doi: 10.1136/bjophthalmol-2018-313311. Epub 2018 Nov 23.

PMID:30470714

ABSTRACT

PURPOSE:

The aim of this study was to determine the effect of the inverted internal limiting membrane (ILM) flap technique on the macular hole (MH) closure and foveal microstructure recovery of patients with highly myopic MH.

METHODS:

Pars plana vitrectomy and gas tamponade with the inverted ILM flap technique (19 eyes) or with the ILM peeling technique (21 eyes) were performed in patients with highly myopic MH with or without retinal detachment. The rate of MH closure and retinal reattachment, the reconstructive anatomical change of the foveal microstructure and the best-corrected visual acuities (BCVA) of the two groups were compared.

RESULTS:

The anatomic closure rate was statistically significantly higher in the inverted group (100%) than in the peeling group (66.7%; p=0.009). All eyes with MH retinal detachment had successful retinal reattachment in these two groups. However, the rate of the external limiting membrane (ELM) and ellipsoid zone (EZ) (p=0.020), as well as gliosis (p=0.049) in macular area, detected by OCT, was significantly greater in the inverted group than in the peeling group. The postoperative BCVA was significantly better in the eyes with ELM, EZ (p=0.031) and gliosis (p=0.008), but without hyperreflective foci (p=0.001).

CONCLUSIONS:

These findings demonstrate that the inverted ILM flap technique has better efficacy than the ILM peeling technique for patients with myopic MH in closure rate, foveal microstructure and postoperative BCVA.

KEYWORDS:

inverted internal limiting membrane flap technique; macular hole retinal detachment; myopic macular hole; optical coherence tomography

October 2019 segment compiled by: Dr. Chitaranjan Mishra, Aravind Eye Hospital Madurai