Deep Learning Detection of Sea Fan Neovascularization from Ultra-Widefield Fundus Images of Sickle Cell Hemoglobinopathy

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OBJECTIVE To develop and test a deep learning system for detecting sea fan neovascularization with ultra-widefield fundus images from patients with sickle cell hemoglobinopathy.

PURPOSE To train and evaluate the performance of a deep learning system for detecting sea fan neovascularization from ultra-widefield fundus images, with the goal of developing an automated screening aid for proliferative sickle cell retinopathy.

METHODS 1131 deidentified ultra-widefield color fundus images were retrospectively collected from 181 adult nondiabetic patients with sickle cell hemoglobinopathy, no prior treatment for sickle cell retinopathy, and no other retinal vascular disease. Two independent masked retinal specialists graded images for presence or absence of sea fans; a third masked grader adjudicated discrepancies. The Inception-v4 convolutional neural network was used to train a model to classify images by presence or absence of sea fans, using the retinal specialist grades as the reference standard. Diagnostic performance was assessed by sensitivity, specificity, and area under the receiver operating characteristic curve.

RESULTS Characteristics of included patients were as follows: 93% African descent, 47% male, 64% Hemoglobin SS, 25% Hemoglobin SC, 8% Hemoglobin S/beta-thalassemia, 2% sickle cell trait. The mean age of patients at time of first included images was 36.3±12.4 years. 202 (18%) of images from 57 (31%) of patients had sea fan neovascularization. The two-way mixed-effects interclass correlation coefficient between the two primary retinal specialist graders was 0.771 (95% CI, 0.746-0.794), allowing for indeterminate grades subsequently adjudicated by the third retinal specialist grader. The model's area under the receiving operating characteristic curve for detection of sea fan neovascularization was 0.952, with sensitivity 94.9% (95% CI, 82.7%-99.4%) and specificity 94.6% (95% CI, 90.3%-97.4%).

CONCLUSION We report the first deep learning system with high sensitivity and specificity for detection of sea fan neovascularization. To our knowledge, this is the largest existing database of ultra-widefield fundus images of sickle cell hemoglobinopathy. With further prospective and external validation, this system may enhance automated screening for vision-threatening sickle cell retinopathy.

HUMAN RESEARCH Yes: Approved by institutional review board

Real-world Treatment Patterns in Patients With Macular Edema due to Retinal Vein Occlusion

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OBJECTIVE To describe real-world treatment patterns for macular edema due to retinal vein occlusion in the United States based on data from a medical claims database and a direct survey of retina specialists.

PURPOSE A variety of management options are available for macular edema (ME) due to branch or central retinal vein occlusion (BRVO or CRVO). This analysis investigated the treatment patterns in patients with ME due to RVO based on data from a US medical claims database and from a survey of retina specialists in the United States.

METHODS Treatment patterns in patients with ME due to RVO across a diverse health care provider population were investigated using US claims data from the Truven MarketScan database. Adults with a first diagnosis of ME due to BRVO (H34.83X0) or CRVO (H34.81X0) between January and June 2017 and continuous enrollment for ≥ 180 days before and ≥ 365 days after diagnosis were included. Patients with diabetic ME or neovascular age-related macular degeneration or who received prior treatment for RVO were excluded. In addition, 35 retina specialty sites (randomly selected from across the United States) were surveyed between June and August 2019 regarding their treatment patterns for ME due to RVO.

RESULTS MarketScan claims data indicate that over half of patients with ME due to RVO diagnosis were managed with observation, while approximately one quarter were treated with anti-vascular endothelial growth factor (VEGF) monotherapy during the first year after

diagnosis (Figure 1). Retina specialists, in contrast, reported treating all of their patients with anti-VEGF therapy (Figure 1), and most initiated treatment either immediately or within 1—2 weeks of the first visit (Figure 2). Among retina specialists, the most commonly reported anti-VEGF regimen (for BRVO and CRVO, respectively) was monthly injections (24/35 and 22/35 respondents), with pro re nata (4/35 and 4/35 respondents) and treat-and-extend (7/35 and 9/35 respondents) regimens used less often. The most commonly reported duration of treatment among retina specialists (for BRVO and CRVO, respectively) was > 2 years (18/32 and 23/32 respondents), with several reporting that they treated for 1—2 years (6/32 and 6/32 respondents).

CONCLUSION In the MarketScan claims analyses, the most common treatment strategy during the first year after diagnosis of ME due to RVO was observation, with < 40% of patients receiving any treatment. In contrast, all retina specialists surveyed reported treating all patients with ME due to RVO with anti-VEGF injections, and approximately 80% initiated treatment within 2 weeks of their first visit.

HUMAN RESEARCH No: Study does not involve human research

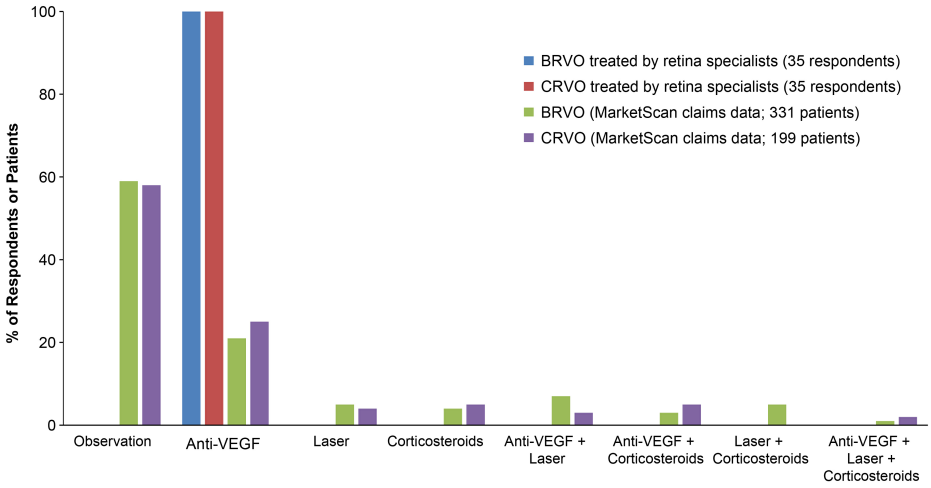

Figure 1. Most common approaches to treatment for ME due to RVO.

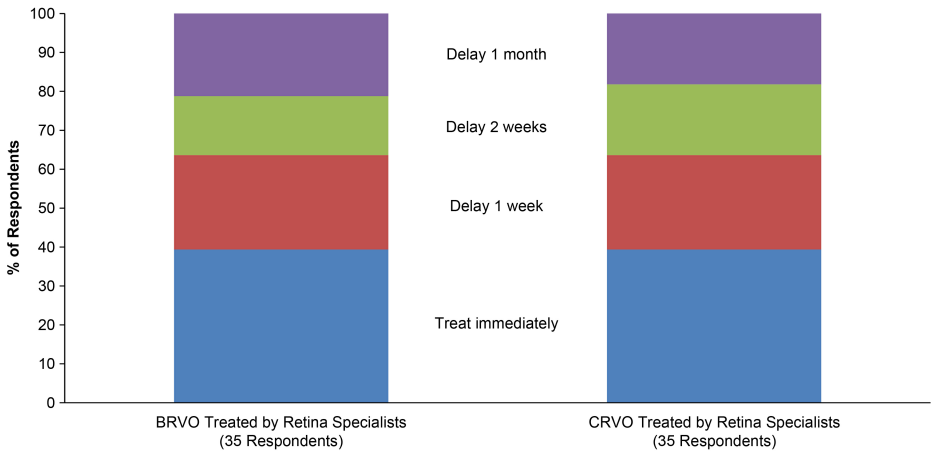

Figure 2. Time to treatment for ME due to RVO among retina specialists.

Intravitreal Triamcinolone Acetonide in Advanced Coats' Disease Revisited: The Results of the King Khaled Eye Specialist Hospital

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OBJECTIVE To assess the efficacy and long-term outcomes of intravitreal triamcinolone acetonide injection (IVTA) in individuals diagnosed with advanced Coats' disease.

PURPOSE To assess if intravitreal triamcinolone acetonide injection can be considered as an alternative to surgical drainage of subretinal fluid in advanced Coats disease prior to ablative therapy of telangiectatic retinal blood vessels, and hence the avoidance of complications of the surgical management.

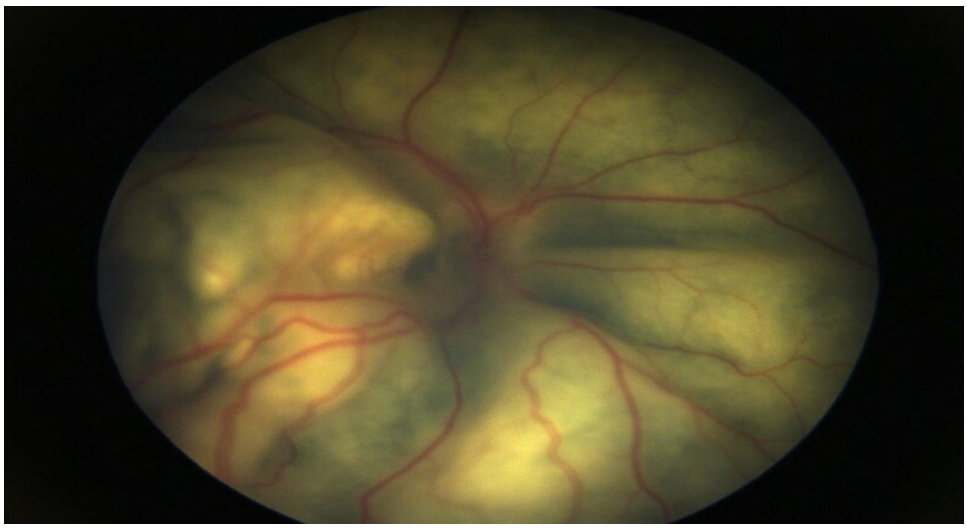
METHODS A retrospective chart review of clinical data of Coats' disease patients who received IVTA to hasten subretinal fluid (SRF) resolution prior to definite ablative therapy. Eyes that had primary surgical drainage of SRF or a follow up less than 12 months after injection were excluded.

RESULTS A total of 17 eyes of 17 patients (mean age 3.9 ± 3.4 years) were identified. The ERD configuration was bullous in 7 and shallow in 10 eyes. Thirteen eyes (76.5%) showed complete SRF resolution after treatment without the need for surgical drainage at last follow up (mean 45.05 ± 22.69 months). Four eyes showed persistent SRF, all of which had bullous ERD at presentation (P=0.015). The mean interval between the primary IVTA and ablative therapy was 2.1 (±3.0) weeks. In eyes with complete resolution, visual acuity (VA) ranged from 20/100 to no light perception. Cataract developed in 11 eyes (64.70%) at the

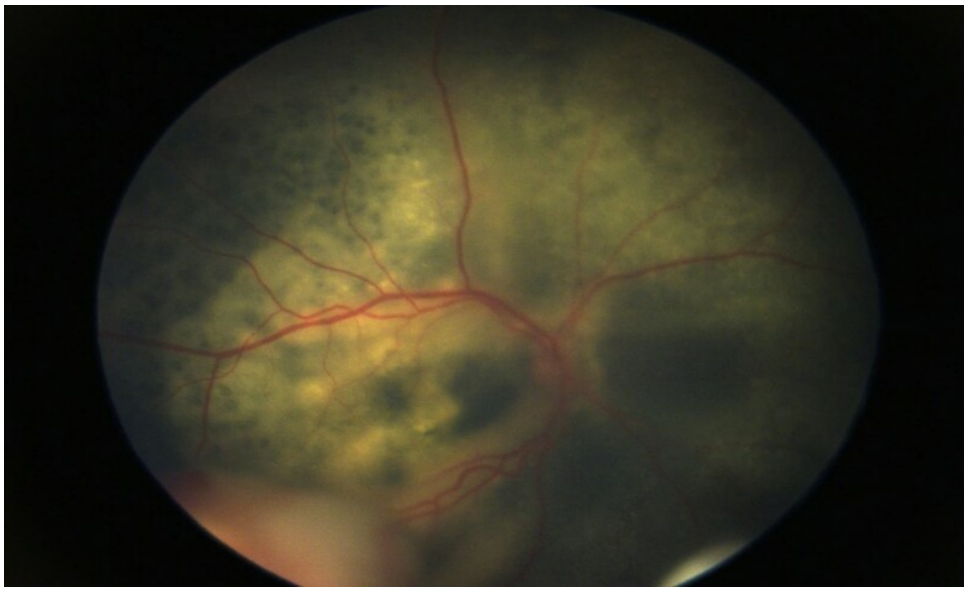
end of follow up. None of the patients developed rise in intraocular pressure.

CONCLUSION IVTA for advanced Coats' disease could be considered as an alternative management modality to primary surgical drainage to address SRF prior to definitive ablative therapy. Resolution of SRF can be expected in 2 to 5 weeks at which time IVTA can be reinjected or ablative therapy performed.

HUMAN RESEARCH Yes: Approved by institutional review board



Fundus photograph of the right eye at presentation showing bullous exudative retinal detachment with extensive subretinal exudations.



Fundus photograph six months following treatment showing total resolution of subretinal fluid and marked reduction in the amount of posterior pole exudates. Laser scars can be noted adjacent to blood vessels.

Intravitreal Anti-VEGF Injections for Exudative Retinal Arterial Macroaneurysms: Results of an International Multicenter Study

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OBJECTIVE To demonstrate that intravitreal vascular endothelial growth factor antagonists improve visual acuity and decrease macular edema via their vasoconstrictive effect and their stabilizing effect on the blood retinal barrier while retinal macroaneurysms are undergoing progressive fibrosis and closure.

PURPOSE There is no established therapy for exudative-hemorrhagic complications in primary retinal arteriolar macroaneurysm (RAM).

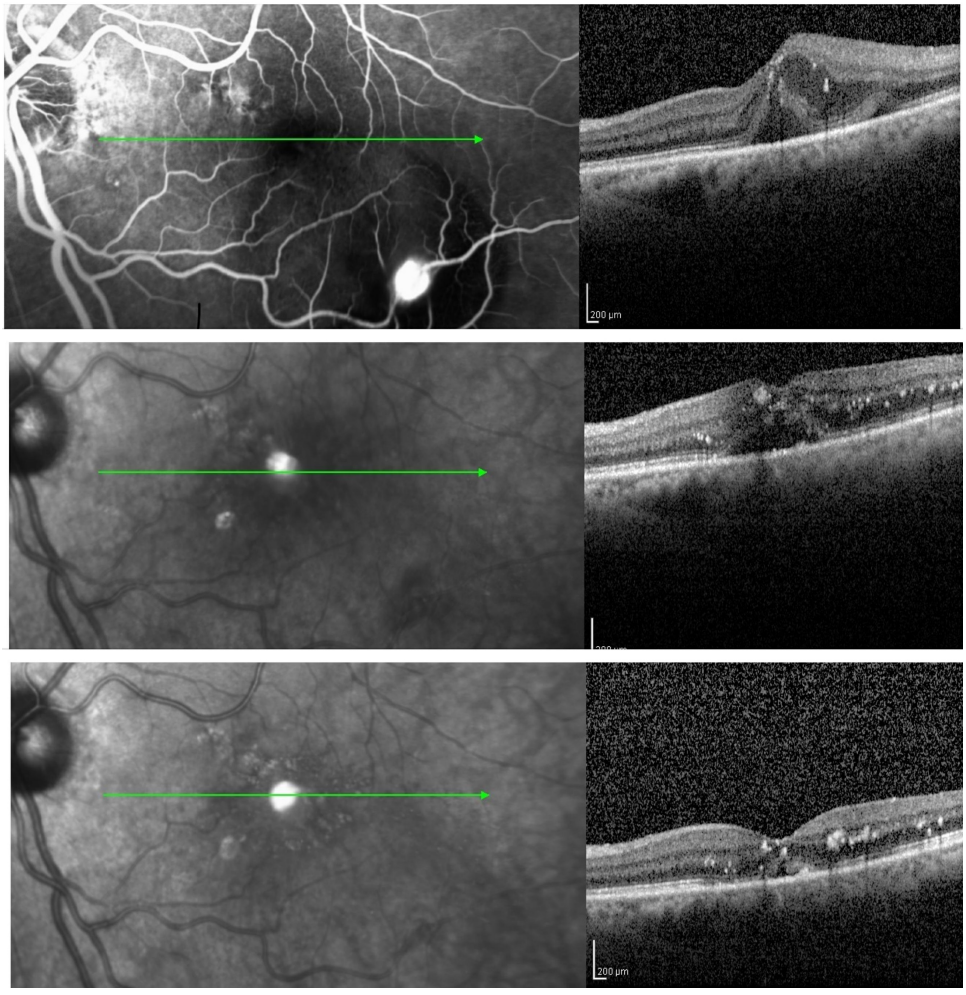
METHODS Retrospective multicenter interventional study of anti-vascular endothelial growth factor (anti-VEGF) in symptomatic RAM. Central macular thickness (CMT) in microns and best corrected visual acuity (BCVA) in logMar were correlated with RAM size and distance to the macula. Statistical analyses were performed using paired comparisons

and Pearson correlation.

RESULTS 32 eyes (32 patients) were treated with a mean of 2.7 injections over mean follow-up of 16.6 months. Initial BCVA correlated with RAM size and distance to the macula (p=0.02). CMT decreased by 131,180, 211 at 1, 2, 3 months after the first injection (p<0.001). BCVA improved by 0.47 and 0.38 at 2 and 3 months (p=0.005). Anti-VEGF response correlated with RAM size (p=0.04) and distance to the macula (p=0.009).

CONCLUSION Symptomatic RAM can be treated successfully with anti-VEGF injections leading to decrease in macular edema.

HUMAN RESEARCH Yes: Approved by institutional review board



This 78-year-old Caucasian woman received a single ranibizumab injection with baseline BCVA 0.4 and CMT of 554 micron (1a) with gradual closure of RAM noted 2 months later (1b) and obliteration at the 3 month follow-up with BCVA of 0.15 and CMT of 237 microns (1c). There was no further change at the 9-month follow-up.

Etiologic Profiling and Visual Outcomes of Dense Vitreous Hemorrhage among Non-Diabetics Treated with Pars Plana Vitrectomy

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OBJECTIVE Determination of the visual outcomes and demographic characteristices of non-diabetic causes of vitreous hemorrhage treated with surgery.

PURPOSE The aim of this study is to determine the visual outcomes and demographic characteristics of the non-diabetic causes of dense vitreous hemorrhage (VH) treated with pars plana vitrectomy.

METHODS A retrospective chart review was done on 120 eyes with non-diabetic, dense vitreous hemorrhage treated with either elective or emergency pars plana vitrectomy (PPV), performed by a single surgeon in Cardinal Santos Medical Center and Legazpi Eye Center from January 2013 to January 2018. The primary outcome of this study was improvement of visual acuity (VA) after 1 year post-operatively, defined as equal or more than 2 lines of improvement in VA. The secondary outcomes are obtained, which included sex, age, and phakic status. The diagnoses are based on codes based on the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM).

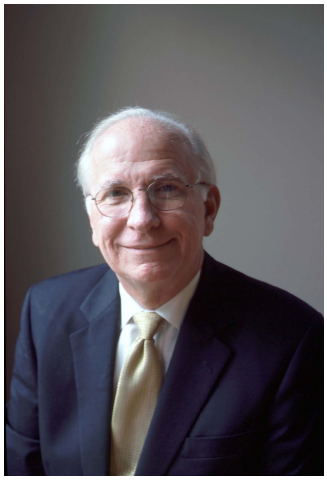
RESULTS A total of 171 patients records were initially gathered, 120 patients were included after determining the exclusion and inclusion criteria. 70% had 2 lines of improvement of VA (n=84) and 30% had no improvement or worsened within 1 year of follow up (n=36). Vitreous hemorrhage secondary to vascular diseases had an overall improvement in VA of 86% after PPV (n=73). Vascular etiologies that had 2 lines of VA improvement include choroidal neovascularization (CNV) from neovascular age-related

macular degeneration (NAMD) or polypoidal choroidal vasculopathy (PCV) (n=30) at 35.7%, central retinal vein occlusion (CRVO) (n=5) at 5.9%, branched retinal vein occlusion (BRVO) (n=36) at 42.8%, tractional retinal detachment (n=1) at 1.1%, and retinal macroanuerysm (n=1) at 1.1%. Other etiologies are as follows: posterior vitreous separation (n=3), Eales Disease (n=1), and retinal angioma (n=1), and toxocariasis (n=1).

CONCLUSION There is significant improvement of visual acuity 1 year post-operatively in non-diabetic causes of dense vitreous hemorrhage when treated with PPV. Branched retinal vein occlusion (BRVO) was the most common cause of non-diabetic dense vitreous hemorrhage. It was also demonstrated that visual acuity significantly improved after pars plans vitrectomy in BRVO at 42.8%, followed by CNV from PCV or NAMD at 35.7% and CRVO at 5.9%.

HUMAN RESEARCH No: Study does not involve human research

VEGF blockage prevents healthy retinal regeneration Noregen promotes VEGF modulation and healthy insitu retinal regeneration in vascular disease



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- Antonio Capone, MD
- Kimberly A. Drenser, MD

OBJECTIVE to understand how VEGF blockage prevents healthy retinal regeneration and how can we promote in situ retinal regeneration in retinal vascular diseases

PURPOSE It has been shown in many USA and French clinical trials by wide field Flourescien Angiography and OCT A that eyes treated with VEGF blockage do not regenerate capillary and neuronal tissue even though the disease staging improves. This study will demonstrate why that happens and how it might be altered to yeild healthy in situ regenerated retina

METHODS Summarizing human data from five French and USA clinical trials of Dibetic retinopathy and retinal vein occlusion which clearly demonstrate that VEGF blockage does not promote retinal regeneration. That areas of retinal vessel loss are the same at the begining of treatmnet and the end of treatment\ In vivo animal syudies which will demonstrate that VEGF blockage not only suppresses pathologic angiogenasis but also blocks the development of healthy angiogenasis which can lead to in situ retinal regeneration. These studies also show that Noregen driven Wnt signalling promotes this in situ retinal regeneration even in adult retinal endothelial cells.

RESULTS We will show that VEGF blockage in human trials does nothing to encourage retinal regeneration of damaged retina by retinal vascular disease. It does allow the damaged retina to become anoxic and no longer stimulate the production of VEGF leading to improvment in clinical staging. We will also show how Noregen repairs and regenerates

retinal tissue using Noregen to stimulate Norrin driven Wnt signalling to activate retinal progenetor cells which is how thr retina was initially formed.

CONCLUSION VEGF blockage suppresses healthy insitu retinal regeneration in human and animal studies. Noregen driven activation of the Norrin wnt signalling system to allow us to regenerate a healthy retina after the injury of retinal vasclar disease as we did as infants.

HUMAN RESEARCH Yes: Exempt from approval