7/16/2022 08:00 am

Retinal Vascular Disease Symposium

Subclinical Retinal Ischemia in Individuals With Atrial Fibrillation

- Mathieu Bakhoum, MD, PhD
- Christine Bakhoum, MD, MAS
- Samantha Madala
- David Sarraf, MD
- Christopher Long
- Leonardo Lando
- Adeleh Yarmohammadi
- Michael Goldbaum
- Alison Chan

Objective:
To determine whether atrial fibrillation (AF) is associated with retinal ischemic perivascular lesions (RIPLs), which are anatomical biomarkers of subclinical retinal ischemia.

Purpose:
We previously demonstrated that RIPLs, which are anatomical biomarkers of subclinical microvascular ischemia in the middle retina (inner nuclear layer or INL), are present in eyes of individuals with ischemic heart disease. Here we sought to determine whether AF, a common source of cardiac emboli, is also associated with RIPLs. Given that AF is often associated with other cardiovascular diseases, we examined the relationship between RIPLs and atrial fibrillation, independent of any underlying ischemic heart disease.

Methods:
This is a case-control study that adhered to the tenets of the Declaration of Helsinki and was conducted in accordance with the regulations of the Health Insurance Portability and Accountability Act. We identified individuals who were between 50 and 90 years of age and had a macular optical coherence tomography (OCT) scan between January 1, 2018 and December 31, 2020 for various clinical indications. Exclusion criteria were presence of retinal vascular occlusions, history of retinal laser, intravitreal injections, or a surgical history of pars plana vitrectomy. Of those meeting criteria, we then identified subjects as cases if they had a diagnosis of AF by the ICD-10 diagnostic code I48 and who also had a heart monitor recorded. An equal number of subjects that was age and sex matched, but without a diagnosis of AF was selected. All subjects in this study had a SD-OCT macular scan that was acquired on a Spectralis SD-OCT machine (Heidelberg Engineering, Heidelberg, Germany). RIPLs were identified using the previously published criteria (Long et al. EClinical Medicine, 2021). Briefly, individual b-scans were reviewed by three independent and masked observers, and a RIPL was defined by the focal atrophy of the INL with a compensatory expansion of the outer nuclear layer. A consensus between all three observers was required to identify a RIPL. All statistical analyses were performed using R. When comparing variables between two groups, we utilized Student's *t*-test and Pearson-Chi Square tests for continuous and categorical variables, respectively. Multivariable logistic regression models were used to analyze the relationship between presence of RIPLs and a diagnosis of AF, using odds ratios with 95% confidence intervals.

Results:
We identified 106 subjects with AF, and 91 age and sex-matched controls. The percentage of subjects with RIPLs was higher in the AF group compared to the control group (57.5% vs 37.4%, p = 0.005). After adjusting for covariates including age, sex, hypertension, diabetes mellitus, smoking status and ischemic heart disease, presence of RIPLs was associated with an odds ratio of 2.0 (95% confidence interval, 1.1 – 3.7) of having AF.

Conclusion:
The presence of RIPLs, which are anatomical markers of prior subclinical retinal infarcts, may be indicative of coexisting AF. RIPLs detection, obtained from OCT scans, may thus serve as an additional biomarker to identify patients with AF.

IRB APPROVAL Yes

7/16/2022 08:06 am

Retinal Vascular Disease Symposium

Point of Care Diagnosis of CRAO With OCT at the Stroke Center: Lessons Learned in Our First Year

- Gareth Lema, MD, PhD

Objective:
Can point of care OCT improve management of CRAO?

Purpose:
Central retinal artery occlusion is a visually debilitating affliction of the retina without a universally accepted treatment. Fibrinolysis has been shown to improve visual outcomes, but timing is critical. Treatment must be administered within hours of symptom onset, and timeis retina. Delays in diagnosis reduce the likelihood that treatment can be accomplished in time to improve vision. Point of care diagnosis streamlines throughput to treatment by eliminating the need for an onsight ophthalmologist and preserves precious minutes or hours to improve visual outcomes.

Methods:
OCT machines have been installed at three stroke centers within our health system in New York City. Any patient who reports to the emergency department with painless monocular vision loss that is suspicious for a CRAO or stroke activates the stroke protocol. Simultaneously, the retina service is alerted that a possible CRAO has arrived. The patient is evaluated by the stroke team, who collectsa pertinent history, visual acuity data, pupil exam, and OCT scan of the macula. The clinical data and images are transmitted to members of the retina service who assist inmaking the diagnosis. If a diagnosis of CRAO can be confirmed and the patient can be treated with 12 hours of last known well, the patient is taken directly for treatment with intra-arterial recombinant tisue plasminogen activator (tPA). If another diagnosis is considered at any time, a full ophthalmology consult is performed before treatment is considered. Patients who are not eligible for treatment are still evaluated with a full stroke work up. Upon admission, the patient is followed by the ophthalmology service to document visual outcomes and safety.

Results:
The service went live in May of 2021. At the annual meeting, our experince through the first year will be presented. To date, we have evaluated 31 patients, 16 of which (52%) were diagnosed with a retinal artery occlusion (CRAO, BRAO, or ophtalmic artery occlusion). Of those, 6 (38%) were eligible for treatment and 5 received tPA. The average time to treatment was 8.6 hours (range: 6.5 - 11.75 hours). All patients showed improvement in visual acuity: HM --> 20/200, LP --> 20/200, 20/800 --> 20/20, HM --> 20/40, and HM --> 20/30. Visual gains were measured witin 24 hours of treatment. Interstingy, two patients lost vision again within 2 days of treatment, presumably from secondary emboli or thrombosis. In one, instituting antiplatelt therapy reversed the vision loss. There were no sigificant adverse events related to tPA administration.

Conclusion:
Point of care OCT in stroke centers can improve throughput to treatment of CRAO, increase eligibility for patients to receive treatment, and thereby maximize visual improvement.

IRB APPROVAL Yes

7/16/2022 08:12 am

Retinal Vascular Disease Symposium

Effects of Time Since Diagnosis to Intravitreal Aflibercept Injection and Baseline BCVA on Outcomes in CRVO: Post Hoc Analysis of the COPERNICUS and GALILEO Trials

- Dilsher Dhoot, MD

Objective:
To examine impacts of time since diagnosis of macular edema due to central retinal vein occlusion (MEfCRVO) to first intravitreal aflibercept injection (IAI) and baseline best-corrected visual acuity (BCVA) on visual and anatomic outcomes.

Purpose:
Understanding the factors that may affect visual and anatomic outcomes can inform treatment decisions and the management of physician and patient expectations.

Methods:
This *post hoc* analysis included patients from COPERNICUS and GALILEO with MEfCRVO treated with IAI 2 mg q4 weeks followed by dosing as needed from Week 24 to Week 100 (COPERNICUS) or Week 76 (GALILEO). Patients were grouped by time from initial MEfCRVO diagnosis to first IAI in both COPERNICUS and GALILEO: <1, 1-3, or >3 months. Impact of baseline BCVA was evaluated by tertiles: ≤44 (T1), >44-≤58 (T2), or >58 letters (T3) in COPERNICUS, and ≤47 (T1), >47-≤65 (T2), or >65 letters (T3) in GALILEO. Visual and anatomic outcomes were analyzed using mixed-effect model repeat measurement.

Results:
In COPERNICUS, 113 patients initiated IAI at <1 (n=44), 1-3 (n=33), or >3 months (n=36) post-MEfCRVO diagnosis. Mean BCVA gains from baseline at Week 24 were 19.8, 15.6, and 11.9 letters in the <1-, 1-3-, and >3-month groups, respectively. Mean (95% CI) difference in BCVA letter gains between <1-month versus >3-month groups was +7.9 (1.7, 14.1; *P*=0.01). Central retinal thickness (CRT) decreased substantially and to a similar extent from baseline at Week 24 across all time-since-diagnosis subgroups (-466.6, -456.4, and -479.2 µm, respectively). Mean BCVA gains from baseline at Week 100 were greater for baseline BCVA T1 versus T2/T3 (16.0 vs 8.3 and 5.6 letters) but final BCVAs were lower (49.8 vs 60.9 and 71.2 letters, respectively). Final CRT at Week 100 was similar across all baseline BCVA tertiles (243.8, 276.7, and 291.5 µm, respectively). Similar outcomes were observed in GALILEO.

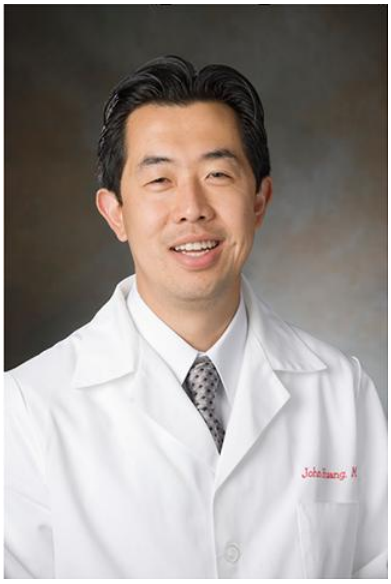
Conclusion:
Longer time to IAI treatment (>3 months) resulted in less visual improvement versus <1 month. Patients with poorer baseline BCVA showed greater visual improvement but worse mean final BCVA versus patients with better baseline BCVA.

IRB APPROVAL Yes

7/16/2022 08:16 am

Retinal Vascular Disease Symposium

Impact of COVID-19 and Delay on Macular Edema After Retinal Vein Occlusion (MEfRVO) Comparing Ozurdex vs Anti-VEGF Therapy



- John Huang, MD

Objective:
Ths retrospective study evaluated the impact of the delay on Ozurdex and Anti-VEGF therapeis in patients with MEfRVO.

Purpose:
The leading cuase of vision loss after RVO is macula edema MEfRVO. During the COVID-19 pandemic in 2020, there were significant delay in treating patients with MEfRVO. This study analyzes the impact of the delays on MEfRVO patients on anti-VEGF and Ozurdex treatments. This study analyze the differences between the patients utilizing 3 different anti-VEGFand Ozurdex treatment.

Methods:
This study is a 12 months retrospective chart review of New England Retina Associates patients with the diagnosis of MEfRVO schedueld for anti-VEGF or Ozurdex treatment. Inclusion criteria included patients who have received a minimum of 1 anti-VEGF or Ozurdex injection before and after March, 2020. All patients in the Ozurdex group were preiously treated with anti-VEGF prior to being switched to Ozurdex treatment. Data collected included demographics, visual acuity, central macular thickness on OCT, and length of delay due to COVID-19 pandemic. This study included 121 patients: 74 treated with Eylea, 53 patients treated with Avastin, 11 patients treated with Lucentis, and 10 patients treated with Ozurdex, with 27 patients on a combination of the different anti-VEGF agents.

Results:

- Patients had an average age of 74.22 years. 60 (49.6%) were female, 61 (50.4%) were male. 59 (48.76%) of eyes were left eyes, 62 (51.24%) of eyes were right.
- On average, all anti-VEGF patient's eyes saw an increase of 0.0232 on the logMar scale per week of delay while Ozurdex patients saw an average increase of 0.0158 on the logMar scale per week of delay.
- Eylea patients saw an average increase of 0.0153 on the logMar scale per week of delay, Avastin patients saw an average increase of 0.0284 on the logMar scale per week of delay, and Ozurdex patients saw an average increase of 0.0158 on the logMar scale per week of delay.
- During the study period of 12 months, Ozurdex patients received significantly fewer injections at 2.4 injections, with 6.85 injection for Avastin and 7.32 for Eylea patients.
- Ozurdex patients also sustained lower levels of increased macular thickness on OCT scan following the delay. When treated after the delay, all patients groups were able to improved their OCT to at least pre-COVID levels.

Conclusion:

- As expected, there was a correlation between the length of the dela and the amount of visions loss due ot the pandemic.
- Ozurdex patients outperformed anti-VEGF patients as a whole in terms of per week of delay and decrease visual acuity.
- Ourdex patients was equivalent ot Eylea patients per week of delay in term of decrease visual acuity.

- Ozurdex patients during the same period of 12 months required significantly fewer injections when compare to anti-VEGF patients.
- Ozurdex patients with MEfRVO required fewer injections maintained visual acuity level similar to Eylea and better than Avastin per week of delay due to the COVID pandemic.
- Ozurdex can be safely used to minimize treatment burden while also decrease the potential of vision loss due to the COVID-19 pandemic.

IRB APPROVAL Yes

7/16/2022 08:30 am

Retinal Vascular Disease Symposium
Longitudinal Macular Thickness and Microvascular Changes in Children with Sickle Cell Disease

- Adrienne Scott, MD, FASRS
- Sally Ong, MD
- Grace Reilly, MS3

Objective:

To assess macular vascular density and retinal thickness changes in children with sickle cell disease over time.

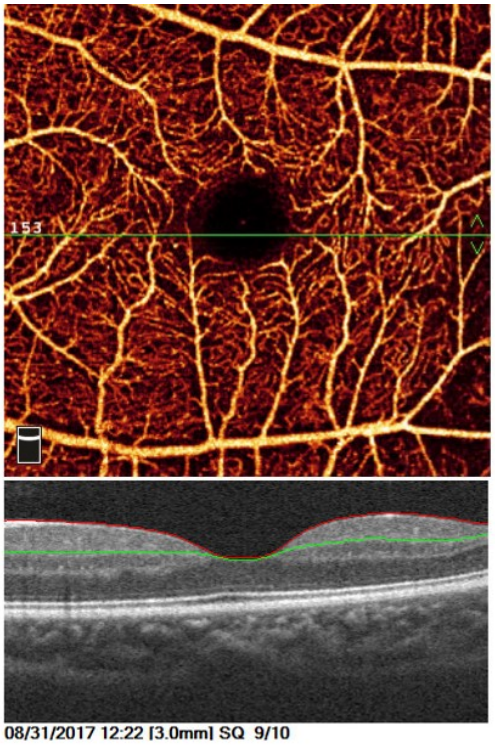
Purpose:
Sickle cell disease (SCD) is the most common inherited hematologic disorder in which deoxygenated erythrocytes form a rigid sickle shape disrupting blood flow in small vessels, causing repetitive vaso-occlusions, endothelial damage and cellular adhesions, resulting in microvascular ischemia. These vascular insults occur from birth, and cumulatively lead to loss of macular vascular density and progressive macular thinning. Our previous study showed children with SCD have decreased macular vascular density but similar retinal thickness compared to unaffected controls. In the present study, we evaluate OCTA images in children with sickle cell disease in a longitudinal fashion to compare measures of retinal thickness, vessel density, and foveal avascular zone area changes over time.

Methods:
In this prospective study, children, ages 5 to 18, with HbSS and HbS variant (HbSC and HbS thalassemia) genotypes were recruited between January 2017 and May 2019. All subjects underwent baseline macular OCT and OCTA scans, and were included for analysis if they had at least 1 year of follow up comparator imaging. Retinal thickness, superficial capillary plexus (SCP) and deep capillary plexus (DCP) vessel density, and foveal avascular zone size were measured at the baseline visit and at least one annual follow-up visit. Imaging was compared to that of age- and race-matched control subjects. The baseline and follow-up visit measurements were compared. Visual acuity, sickle cell retinopathy staging, as well as systemic health information characteristics including disease modifying therapies were collected at the time of clinic visit and used for analysis among genotypes.

Results:
56 eyes of 28 patients are included for analysis to date (26 HbSS, 30 HbS variant (HbSC or other)). All eyes have Goldberg peripheral sickle cell retinopathy stages 1-3. Pathologic areas of retinal thinning on OCT, and associated areas of decreased vascular density in the SCP and DCP on OCTA were common in the cohort across genotypes. Preliminary data suggest that macular vascular flow deficits are common and progressive in children with SCD across genotypes. All patients in the cohort maintained good vision with no appreciable distance visual acuity loss. Therapeutics such as hydroxyurea and chronic red cell exchange transfusions appear to be protective against retinal vascular changes.

Conclusion:
Children with SCD demonstrate progressive decreases in macular vascular density on OCTA and thinning on OCT. Distance visual acuity is typically preserved, but impact of these changes on macular visual function remains unclear. Systemic disease severity and therapeutics may also impact changes in the macular microvasculature.

IRB APPROVAL Yes



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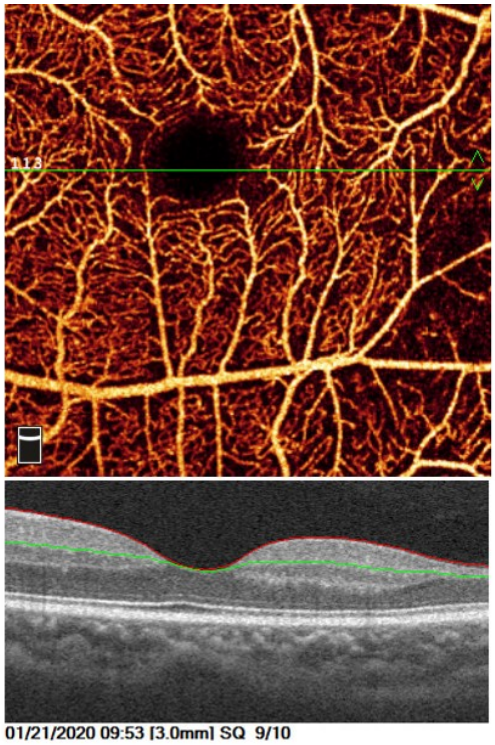

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Progressive loss of vascular density in pediatric patient with HbSS.

7/16/2022 08:36 am

Retinal Vascular Disease Symposium
Spatial Correlation Between Retinal Ischemia and Reactive Choroidal Changes in Retinal Vein Occlusion

- Junyeop Lee, MD, PhD
- Solah Han, MD
- Sang Uk Choi, MD
- Young Hee Yoon, MD, PhD

Objective:
To assess the impact of retinal ischemia on the choroid in patients with retinal vein occlusion (RVO)

Purpose:
The choroid supplies nutrients and oxygen to the retina: However, it has not been fully understood whether the impairment of retinal circulation affects the choroid. Preclinical studies demonstrated that retinal hypoxia induces choroidal vasculopathy spatially corresponding with the avascular retinal area. This study explored patients with RVO whether retinal ischemia induces choroidal changes using multimodal imaging and evaluated associated factors affecting choroidal changes and visual prognosis.

Methods:
Retrospective, single-center, case-control study of 29 RVO unilateral RVO patients, the unaffected eyes were included as the control group. All patients underwent wide-field indocyanine green angiography (wICGA), wide-field fluorescein angiography (wFA), wide-field optical coherence tomography (wOCT), and optical coherence tomography angiography (OCTA). The primary outcome measures included choroidal vascular density (CVD) and choroidal vascular fractal dimension (CFD) in each quadrant from wICGA; non-perfusion area (NPA) from wFA; mean choroidal thickness (MCT) and choroidal vascular index (CVI) from wOCT; vascular densities, foveal avascular zone (FAZ) area, and FAZ perimeter from OCTA.

Results:
Out of 29 RVO patients, 19 (65.5%) were women and the mean age was 61.2 ± 11.9 years. Fifteen patients (51.7%) had hypertension, and six (20.7%) had diabetes. RVO eyes showed increased MCT, CVI, and CVD but reduced CFD compared to the unaffected eyes ($P < 0.05$). The choroidal vascular changes in wICGA were only significant at the corresponding quadrant where the RVO was affected. The choroid of the other quadrants in RVO eyes were not different from fellow eyes. Deep capillary plexus (DCP) density, FAZ area, FAZ perimeter in OCTA, and NPA in wFA showed a significant correlation with CVD in wICGA ($P < 0.05$). These OCTA and wICGA parameters correlated with visual outcomes.

Conclusion:
Enlarged choroidal vessels with less complexity are locally observed at the correspondent quadrant where the RVO is affected. The degree of retinal ischemia is associated with these choroidal vascular changes. This study provides essential evidence showing the bidirectional crosstalk between retina and choroid. Loss of compensatory mechanism from the choroid in the retinal vascular insufficiency may be one of the important causes of the photoreceptor loss in RVO.

IRB APPROVAL Yes

7/16/2022 08:40 am

Retinal Vascular Disease Symposium

Predicting Outcomes and Treatment Frequency After Monthly Aflibercept for Macular Edema Secondary to Central Retinal Vein Occlusion: A Machine-Learning Model Approach

- Yasha Modi, MD
- Nitish Mehta, MD
- Weiming Du, MS
- Fabiana Silva, MD
- Hadi Moini, PhD
- Rishi Singh, MD

Objective:
To develop machine learning (ML) algorithms to predict visual and anatomic outcomes and treatment frequency in patients with macular edema secondary to central retinal vein occlusion (ME-CRVO) at 52 weeks after undergoing treatment with aflibercept.

Purpose:
Using ML models to predict visual and anatomic outcomes following initial treatment with aflibercept may help manage physicians` and patients` expectations with regards to the management of ME-CRVO.

Methods:
A dataset of 198 patients with ME-CRVO treated with monthly IAI 2 mg for 24 weeks in the COPERNICUS (n=107) and GALILEO (n=91) trials was used to develop ML algorithms. In both trials, patients were switched after 6 monthly intravitreal aflibercept injection (IAI) at week 24 to pro-re-nata (PRN) dosing through Week 52. The ML algorithm was used to predict the absolute and change from baseline in best-corrected visual acuity (BCVA) at Week 52, gain of ≥15-letter at Week 52, the absolute and change from baseline in central subfield thickness (CST) at Week 52, and IAI frequency during Weeks 24−52. Random decision forests were used to develop the ML algorithms. Algorithm performance was assessed using correlation coefficient (r) and area under the curve (AUC) for continuous and categorical variables, respectively. Predictive factors identified with ML algorithms were confirmed using univariate analyses.

Results:
The ML algorithm predicted the actual observed values at Week 52 with strong correlation (r) for absolute BCVA (r=0.87), change in BCVA from baseline (r=0.76), gain of ≥15 letters (AUC=0.81), and change in CST from baseline (r=0.76). While change in CST was predicted, there was no correlation (r=0.07) between predicted and observed absolute CST at Week 52. BCVA at weeks 16, 20, and 24 were predictors of absolute BCVA; BCVA at baseline, week 20 and week 24 were predictors of change in BCVA; BCVA at baseline and at Week 20 were predictors of ≥15-letter gain; and CST and BCVA at baseline were predictors of change in CST. ML algorithm predicted PRN injection frequency from Week 24 through Week 52 with high accuracy (AUC=0.83). Key factors predicting >2 injections between Weeks 24-52 were thicker CST at baseline and at Week 4. Univariate analyses confirmed all predictive factors described herein.

Conclusion:
ML algorithms successfully predicted visual and anatomic outcomes as well as dosing frequency with high accuracy, except for absolute CST. ML may help inform patients' and clinicians' expectations during management of ME-CRVO.

IRB APPROVAL No - exempt

7/16/2022 08:46 am

Retinal Vascular Disease Symposium

Prospective Randomized Trial of Treat-and-Extend Intravitreal Aflibercept for Radiation Retinopathy: One-Year Outcomes

- Amy Schefler, MD FACS FASRS
- Chelsey Moore
- Cecilia Villanueva Boone
- Alex Brown, BS
- Thomas Aaberg, MD
- Stephanie Trejo Corona

Objective:
This is a prospective study examining the role of aflibercept in preventing vision loss and improving vision in patients with radiation retinopathy.

Purpose:
Radiation retinopathy (RR) commonly causes poor, long-term visual acuity outcomes in patients previously treated with radiation plaque, proton beam, or orbital radiation therapy. Current treatments are not FDA-approved and prior studies have had variable outcomes with small sample sizes. We performed a multi-center, prospective randomized clinical trial to assess the safety and efficacy of 2 mg intravitreal aflibercept injections (IAI) given in a treat-and-extend regimen for radiation retinopathy and optic neuropathy.

Methods:
Thirty-nine eyes in 39 patients with RR were assigned randomly to cohorts (1:1 ratio) in which patients either did or did not receive a loading dose of 3 IAI followed by a treat-and-extend regimen. The primary outcome measure was the mean Early Treatment Diabetic Retinopathy Study (ETDRS) best-corrected visual acuity (BCVA) change from baseline. Statistical analyses were performed in RStudio (Version 4.0.5, RStudio Inc., Boston, MA) using Student's t-tests for comparison of groups.

Results:
Mean ETDRS BCVA letters were 64.4 and 52.8 at baseline for Cohorts 1 and 2, respectively (Snellen equivalent, 20/51 and 20/88). Mean ETDRS BCVA gains over the first 52 weeks were 2.7 and 6.2 letters for Cohorts 1 and 2, respectively. Student's t-test demonstrated no significant differences between baseline and year 1 mean BCVA values overall and within cohorts. However, there was a significant difference between cohorts in the mean BCVA change from baseline over the 1-year period. ($P = 0.0025$). There was also a significant difference between baseline and year 1 mean CRT values overall ($P = 0.00001$) and within cohorts 1 ($P = 0.00030$) and 2 ($P = 0.00087$). ETDRS BCVA scores were converted into Snellen equivalents to compare these data with historical controls. Accounting for all subjects, at week 52, 97.2% of patients had vision of 20/200 or better; 50.0% of patients had vision of 20/40 or better; and 30.6% had improved 10 ETDRS letters or more from baseline. Only 2.8% of patients had 20/200 or worse vision at week 52.

Conclusion:
In this cohort, aflibercept improved vision and CRT in patients with radiation retinopathy compared to historical controls using a treat-and-extend regimen. Given that the natural history of vision in patients who have undergone radiation is relentless vision loss, larger studies are needed to confirm the findings of this study as they may have a major impact on the approach to long-term management of vision in these patients.

IRB APPROVAL Yes

7/16/2022 09:01 am

Retinal Vascular Disease Symposium

Characterization of Vascular Abnormalities in X-Linked Retinoschisis Using Widefield Digital Fluorescein Angiography

- Audina Berrocal, MD FASRS
- Hasenin Al-khersan, MD
- Nimesh Patel, MD
- kenneth Fan, md
- Julia hudson, md
- diana laura, md
- Ashley Lopez, MD
- Piero Carletti

Objective:
To characterize fluorescein angiography findings in X-linked retinoschisis

Purpose:
While schisis is the predominant finding in X-linked retinoschisis (XLRS), these patients may also have significant vascular abnormalities resulting in sight-threatening complications including vitreous hemorrhage. We sought to characterize vascular abnormalities in patients with XLRS using fluorescein angiography (FA).

Methods:
IRB approved retrospective chart review of patients with a genetically confirmed diagnosis of XLRS and baseline FA. Information collected from the medical record included demographic data, baseline clinical examination findings, OCT findings, and FA findings. Fluorescein angiography images were reviewed for findings including peripheral ischemia, neovascularization, and vascular abnormalities.

Results:
Seven patients with a genetically confirmed diagnosis of XLRS were included. All patients were male and had mutations in the *RS1* gene. The average age was 50 months (range: 3-142 months). 4 patients were black (57%) while 3 (43%) were white. Three (43%) were of Hispanic ethnicity. Baseline fundus examination findings included retinal schisis in all patients, intraretinal hemorrhage (2/7, 29%), vitreous hemorrhage (1/7, 14%), macular folds (1/7, 14%). Three of 7 patients (43%) had retinal detachments (one of which was bilateral) requiring surgical repair.

On FA, all patients demonstrated vascular leakage, peripheral ischemia, and vascular abnormalities. Vascular abnormalities included aberrant circumferential vessels (6/7, 86%), terminal bulbing of vessels (4/7, 57%), straightening of vessels (3/7, 43%), vessel arborization (3/7, 43%), and abnormal vascular loops (3/7, 43%). Two patients (29%) demonstrated neovascularization while one patient (14%) had a vasoproliferative lesion.

Conclusion:
Fluorescein angiography can be a useful clinical tool in XLRS by revealing vascular abnormalities which can guide the management and treatment of these difficult cases.

IRB APPROVAL Yes

7/16/2022 09:07 am

Retinal Vascular Disease Symposium

National vs International Outcomes and Practice Patterns of Intravitreal Anti-VEGF Injections for Retinopathy of Prematurity

- Nimesh Patel, MD
- Luis Acaba-Berrocal, MD
- Sandra Hoyek, MD
- Kenneth Fan, MD, MBA
- Caroline Baumal, MD
- Clio Harper, MD
- Audina Berrocal, MD FASRS

Objective:
What are the global variations in practice patterns and outcomes in relation to the use of the anti-VEGF therapy for Retinopathy of Prematurity?

Purpose:
There is a paucity of large-scale, real-world, comparative, international data regarding intravitreal anti-vascular endothelial growth factor (VEGF) therapy for retinopathy of prematurity (ROP). Reporting of variations in outcomes based on region and resources is required to guide management on the local level.

Methods:
Subgroup analysis was performed from the ROP Injection Consortium (ROPIC) data from 23 sites (16 national from the USA and 7 international from Canada, Chile, Dominican Republic, Japan, Mexico, Taiwan and Turkey) from 2007 to 2021. Primary outcomes included rates and types of retreatment as well as complications. Secondary outcomes included specifics of the injection protocol practice pattens.

Results:
1677 eyes (873 national and 804 international) of 918 patients were included. Mean birth weight and gestational age were lower in the national (665.6 g and 24.5 weeks respectively) compared with the international group (912.7 g and 26.9 weeks respectively) ($p<0.0001$). The percentage of APROP and plus disease were higher in the national group (26.2% and 88.7%, respectively) compared with the international group (8.7% and 81.9% respectively) ($p=0.0001$). Ranibizumab was used more frequently in the national group (30.9% versus 17.4%; $p<0.0001$) versus Aflibercept in the international group (5.3% versus 0.8%; $p<0.0001$). Ranibizumab dosage was lower in the national (0.15 mg in 75.2%) compared to the international group (0.25 mg in 65.7%). Intravitreal injection was administered with a 32-gauge short needle in 48.2% of national cases versus 5.5% of international cases ($p<0.0001$) where a 30-gauge needle was primarily used (68.2%). Rates of retreatment with anti-VEGF reinjection or laser post-injection were higher in the national compared to the international group (8.5% vs 4.7% [$p=0.0016$] and 55% vs 7.2% [$p<0.001$] respectively). Average time to retreatment with laser was longer nationally (134.2 days vs. 36.4 days, $p<0.0001$). However, retreatment time with injection was similar between both groups (62.2 vs. 48.7; $p=0.082$). There was no difference in the incidence of complications including endophthalmitis between the two geographical subgroups.

Conclusion:
Related to global variations in neonatal care, those with ROP receiving anti-VEGF injections nationally tended to be younger, smaller, treated earlier, and require more anti-VEGF retreatments when compared to international neonates with ROP.

IRB APPROVAL Yes

7/16/2022 09:11 am

Retinal Vascular Disease Symposium

Long-Term Follow-up of Patients Treated With Laser for Retinopathy of Prematurity

- Rita Ehrlich, MD
- Dolev Dolberg
- Karny Shouchane-Blum
- Amir Sternfeld
- Ruth Axer- Siegel
- Orly Gal-Or, MD

Objective:

Long-term follow up on patients treated with laser for retinopathy of prematurity

Purpose:

To evaluate the long-term functional and structural findings in eyes treated with laser photocoagulation for ROP.

Methods:

Observational cross-sectional study on patients with ROP that were treated with laser photocoagulation between 1997 and 2004. All patients underwent best corrected visual acuity (BCVA) assessment, autorefraction, biometry evaluation (OA-2000, Tomy GmbH, Nagoya, Japan) for axial length (AXL), anterior chamber depth, corneal thickness (pachymetry) . We also retrieved from the patients' neonatal medical records disease characteristics including disease severity and the extent of laser treatment.

Results:

Included 63 eyes of 33 patients with a mean follow up of 19 years. The mean BCVA was 0.133 (± 0.18) logMAR, and the BCVA was 6/12 or better in 92% of eyes. The refraction of the patients was between -19D to +3.5D with mean spheric equivalent of -5.04 (±5.13) D, the mean AXL was 22.97 (± 1.99) mm, mean ACD of 2.96 (± 0.41) mm and a mean corneal thickness of 533 (±32.14) µ. Mean keratometry values were 45.62 (± 1.96) D for flat K, 47.1 (± 2.28) D for steep K and 46.34(± 2.04) D for average K. The amount of laser energy delivered at baseline was negatively correlated with corneal thickness (r=-0.391, p=0.013). No correlation was found between amount of laser energy delivered and BCVA, refraction or keratometry readings at follow up.

Conclusion:

Two decades after ROP treatment our patients demonstrated excellent long term visual acuity outcome and were moderately myopic on average. There may be a dose dependent relation between laser energy and corneal thinning.

IRB APPROVAL Yes

7/16/2022 09:15 am

Retinal Vascular Disease Symposium

Modeling Zone as a Proxy for Absolute Avascular Retina Area and Retinopathy of Prematurity Risk

- Darius Moshfeghi, MD, FASRS
- Sean Wang, MD
- Moosa Zaidi
- Edward Korot, MD
- Jochen Kumm, PhD
- Marco Ji
- Ahmad Al Moujahed
- Natalia Callaway, MD

Objective:
We set out to create an objective baseline assessment of avascular retina that can be tested for suitability in risk stratification for clinical trials of retinopathy of prematurity (ROP), as opposed to traditional descriptors which do not correlate with outcomes as much as avascular retina does.

Purpose:
Absolute amount of avascular retina is known to drive development of retinal neovascularization and vascular endothelial growth factor (VEGF) production in experimental models of retinopathy of prematurity (ROP), treatment response followingretinopexy as a function of untreated avascular retina, and dosing with VEGF-inhibitors.We have developed a model to predict the amount of avascular retina at baseline by normalizing the zone subtended by 30 degree arc to the axial length (or predicted axial length based on gestational age) and propose to use this normalization of avascular retina as a treatment risk stratifier as opposed to zone which only incorporates vascularized retina.

Methods:
In this study, we estimated the area of Zone I in relation to different ocular parameters to determine how variability in the size and refractive power of the eye may affect zoning. Using Gaussian optics, a model was constructed to calculate the absolute area of Zone I as a function of corneal power, anterior chamber depth, lens power, lenst hickness, and axial length (AL), with Zone I defined as a circle with radius set by a 30-degree visual angle.

Position of posterior nodal point:

Xnodal=1.4000/(Plens/1000+1.3375/(1.3375/(Pcornea/1000)−
(ACD+LT/2)))+ACD+LT/2−√((1/(−Pcornea/1000+1.3375/(1.3375/((−Plens/1000))+ACD+LT/2))+100)
((1.4000/(Plens/1000+1.3375/(1.3375/(Pcornea/1000−1/100)−(ACD+LT/2)))+ACD+LT/2−1.4000/(Plens/1000+1.3375/(1.3375/(Pcornea/1000−(ACD+LT/2))))−
(ACD+LT/2)))/1.3375)

Area of Zone I:

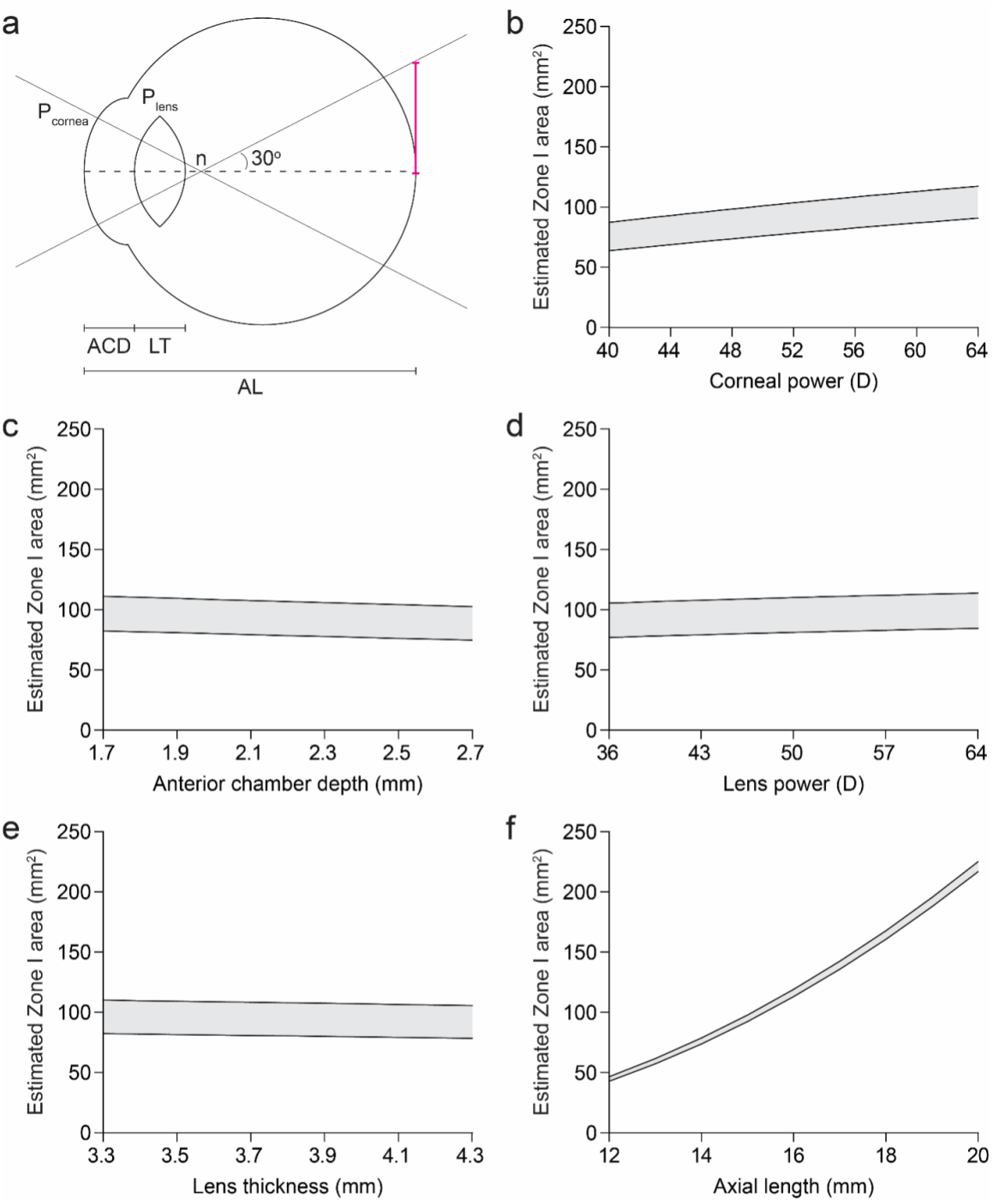
A=π∗〖((AL−Xnodal)∗tan30^o)〗^2

Total Retinal Area (TRA) was calculated based on normative values for every given axial length. Absolute Avascular Area (AAA) was then calculated by subtracting Area of Zone I from the Total Retinal Area.

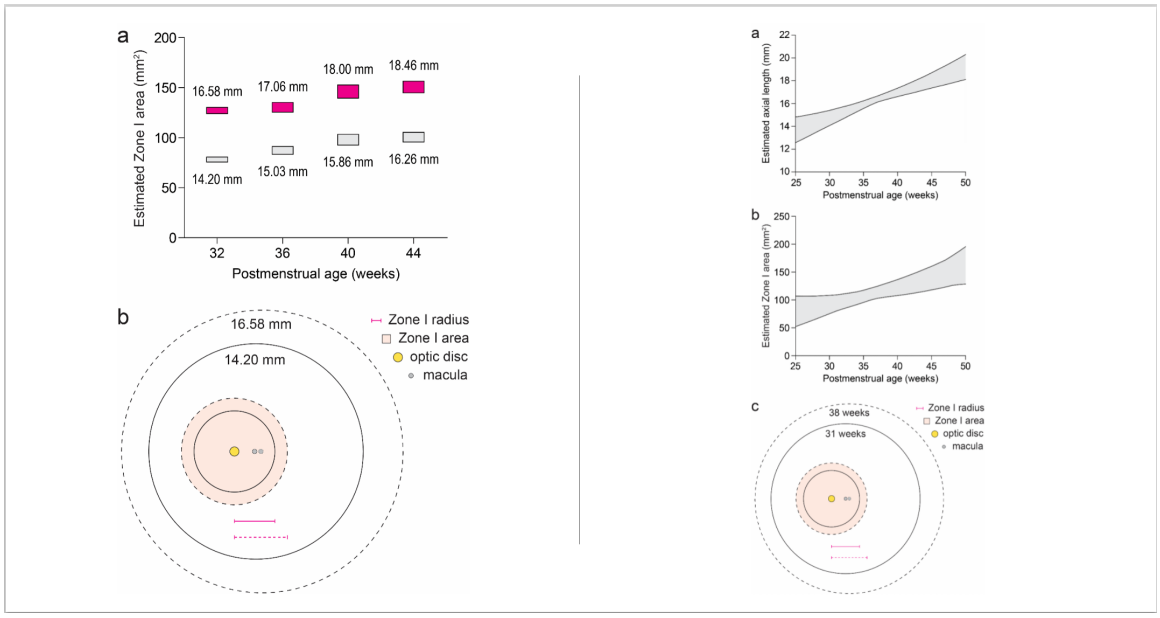
Results:
At PMA 32 weeks, Zone I in the longest eye (AL = 16.58 mm) was predicted to be up to 72% larger than in the shortest eye (AL = 14.20 mm). Analyses using AL values from other ages revealed predicted area differences of up to 62%, 65%, and 64% at PMA 36, 40, and 44 weeks, respectively. Vascularized Zone I ranged from 52-196 mm^2, a nearly four-fold change. From PMA 31 to 38 weeks, our model predicted that the absolute area of ICROP Zone I could expand by up to 60%. Our model thus predicts that absolute area of retina vascularization grows considerably during ROP screening due to increasing AL, and hence the absolute area of retina avascularity would shrink, representing different risk profiles for retinal neovascularization.

Conclusion:
Absolute avascular retina area (a known risk factor for poor outcomes) at baseline screening can be calculated by knowing the axial length. These findings motivate several hypotheses which upon future testing may help optimize treatment decisions for ROP.

IRB APPROVAL



Zone I area is most sensitive to changes in axial length



Zone I Area by axial length (left) and post menstrual age (right)

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Retinal Vascular Disease Symposium

Rate of and Time for Complete Retinal Vascularization in Premature Infants and Its Associated Factors

- Tso-Ting Lai, MD
- Chung-May Yang, MD
- Ching-Wen Huang, MD
- Chia-Ying Tsai, MD

Objective:
What is the proportion of premature infants that had reach complete vascularization and when did vascularization complete?

Purpose:
Incomplete vascularization (or persistent avascular retina, PAR) in premature infants has been linked to late complications in preterms with treated or untreated retinopathy of prematurities. Understanding the rate of and time for complete vascularization, as well as its associating factors, might help planning prophylatic treatments for PAR in preterms.

Methods:
A retrospective cohort study including all premature infants who underwent screening for retinopathy of prematurity (ROP) at a tertiary referral center. All infants received regular dilated fundus examination with indirect ophthalmoscopy until complete vascularization was achieved. Perinatal and postnatal factors, ROP outcomes, and time to complete vascularization were recorded.

Results:
Among the 541 infants included, 490 eyes of 490 infants (90.57%) had a known retinal vascularization outcome, of which 439 (89.59%) eyes had complete vascularization. The average postmenstrual age (PMA) at completion was 45.39 ± 11.04 weeks, and 95.22% of the infants with full vascularization completed before 64 weeks of PMA. ROP developed in 118 (22.56%) infants, of which 33 (6.10%) received anti-vascular endothelial growth factor (VEGF) treatment. Factors predicting delayed complete vascularization includes smaller birth weight (BW), presence of ROP, and VEGF therapy. In subgroup analysis, BW was associated with the time for complete vascularization in infants with ROP; while the presence of preplus or plus disease, female gender, smaller GA, and anti-VEGF treatment showed a trend toward delayed vascularization with borderline significance.

Conclusion:
Almost 90% of the infants screened for ROP had complete vascularization, with the majority accomplished before 64 weeks of PMA. Smaller BW predicts delayed complete vascularization. Anti-VEGF therapy and presence of ROP, including the severity of ROP, might also affect the time for complete vascularization. These findings might help improve our understanding and the management of persistent avascular retina in preterms.

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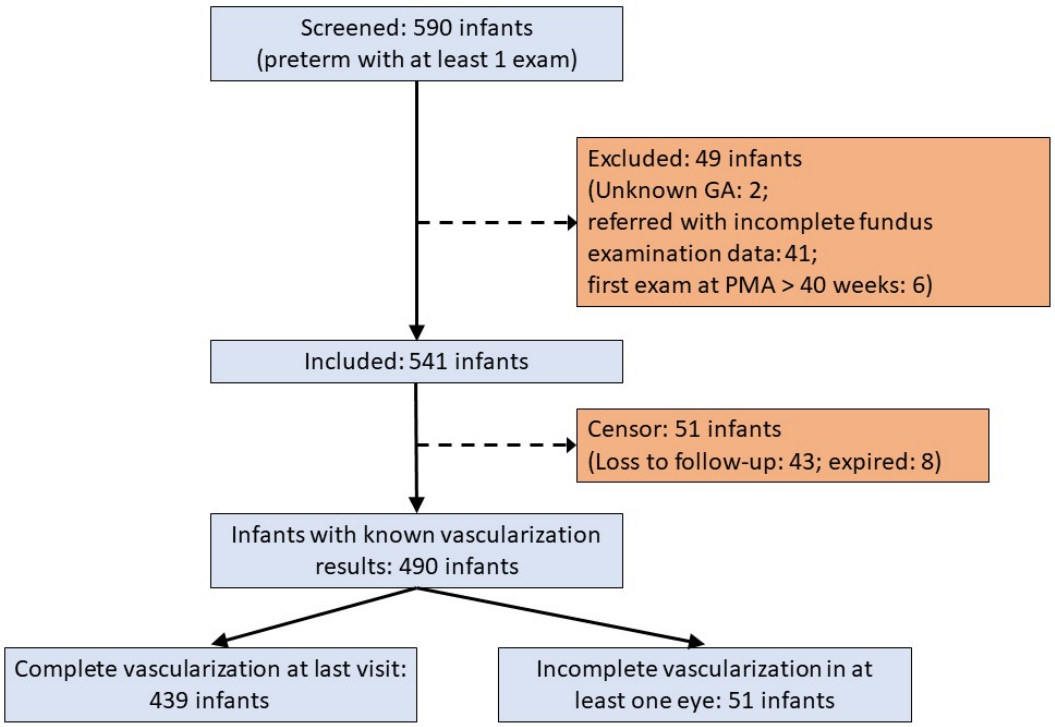
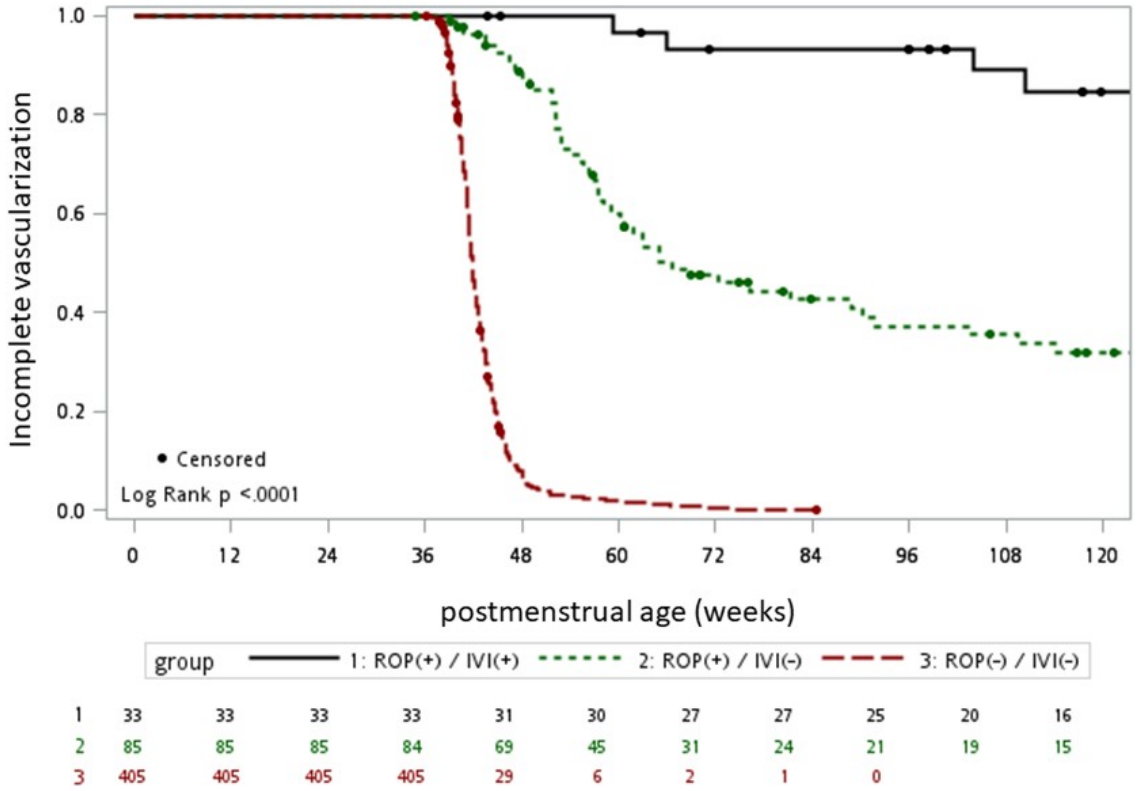


Flow diagram showing patient selection for inclusion in this cohort study



Kaplan-Meier curve for the time for complete vascularization in 3 subgroups