Quantification of Nonperfusion And Neovascularization on Ultrawide-field Fluorescein Angiography in Patients with Diabetes and Association with Vitreous Hemorrhage, Macular Edema, and Vitrectomy

Gina Yu[1], Michael Aaberg[1], Tapan Patel[1], Rahul Iyengar[1], Corey Powell[2], Annie Tran[1], Caitlin Miranda[1], Emma Young[1], Katarina Demetriou[1], Laxmi Devisetty[1], Yannis Paulus[1]
[1]Department of Ophthalmology and Visual Sciences, Kellogg Eye Center, University of Michigan, Ann Arbor, MI, USA
[2]Department of Statistics, University of Michigan, Ann Arbor, MI, USA

University of Michigan Kellogg Eye Center

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Purpose

- To identify risk factors associated w/ increased areas of foveal avascular zone (FAZ), neovascularization (NV) and nonperfusion (NP) in diabetic patients
- To calculate a threshold total NP associated with an increased risk of proliferative diabetic retinopathy (PDR)

Methods

Patient Enrollment

- IRB-approved retrospective chart review (HUM00120509) b/w Jan 2009 and May 2018
- **Inclusion:** 18 years or older, diagnosed w/ type 1 or 2 diabetes mellitus (DM)

Statistical Analysis

- All analysis conducted in R (Core Team, 2019)
- **For associations analysis,** linear multivariate regression performed w/ *geelm* and *geepack*.[1] Demographic (eye laterality, sex, race, age, type of DM) and advanced DR features (vitreous hemorrhage [VH], macular edema [DME], requirement of PPV) were independent. FAZ, NP and NV areas were dependent. $P<.05$ was significant
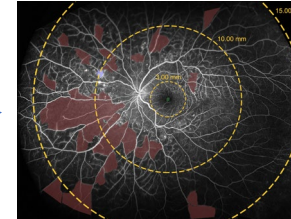- **For threshold analysis,** Youden index calculated for total NP w/ best sensitivity and specificity in predicting PDR[2]

Segmentation
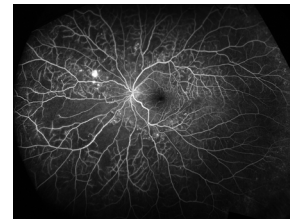
Stereographic Projection: Pixels were projected onto 3D globe (d=24 mm)
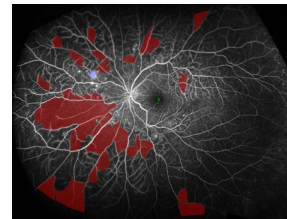
Grading: Trained, masked segmentation of NP (red), NV (blue), and FAZ (green) in mm^2
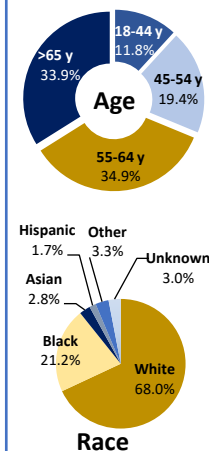
Posterior pole (r≤3.00), mid-periphery (3.00<r ≤10.00), far-periphery (10.00<r ≤15.00)

Results

- 651 eyes from 363 patients (42.4% female)
- 76 (11.7%) no DR, 92 (41.1%) mild non-proliferative DR (NPDR), 144 (22.1%) moderate NPDR, 101 (15.5%) severe NPDR, 220 (33.8%) PDR, 18 (2.8%) unknown

Demographics

Age
- >65 y 33.9%
- 18-44 y 11.8%
- 45-54 y 19.4%
- 55-64 y 34.9%

Race
- Hispanic 1.7%
- Other 3.3%
- Asian 2.8%
- Unknown 3.0%
- Black 21.2%
- White 68.0%

Nonperfusion and Neovascularization Analysis

Significant associations: male w/ total NP (P=.005), black race (Figure 1) w/ total NV (P=.04), VH (Figure 2) w/ total NP (P=.02)

Total Area of Neovascularization

Figure 1

*Indicates significance

Total Area of Non-Perfusion

Figure 2
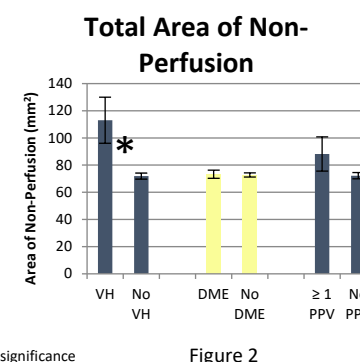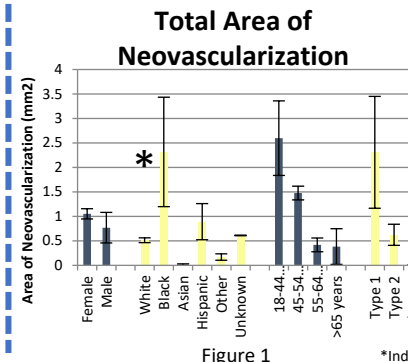
Further Analysis

Total NP threshold of 77.48 mm^2 (95% CI: 54.24-92.66) for increased risk of PDR (sensitivity 59.5%, specificity 73.6%)
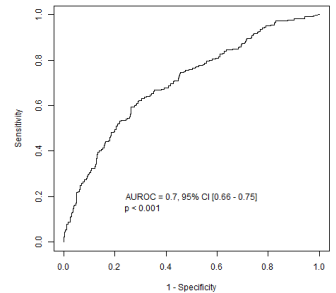
Conclusion

These findings suggest eyes with at least 77.48 mm^2 of NP are at risk for PDR. Male sex, black race, and presence of VH are associated with greatest areas of NP and NV.

Acknowledgements

References

[1]Højsgaard S, Halekoh U, Yan J. The R package geepack for generalized estimating equations. Journal of Statistical Software. 2006;15(2):1–11. [p181]
[2] Nicholson L, Ramu J, Chan EW, et al. Retinal Nonperfusion Characteristics on Ultra-Widefield Angiography in Eyes with Severe Nonproliferative Diabetic Retinopathy and Proliferative Diabetic Retinopathy. JAMA Ophthalmology; 2019 Apr 11. [Epub ahead of print]. doi: 10.1001/jamaophthalmol.2019.0440