

# Deep Capillary Macular Flow Index and Degree of Vessel Density Obtained With OCT Angiography Strongly Correlate With Severity of Diabetic Retinopathy



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**OBJECTIVE** To evaluate the integrity of retinal vascular complex in non- proliferative diabetic retinopathy (NPDR) with noninvasive SSADA assisted OCTA and correlate perfusion indices with severity of NPDR.

**PURPOSE** We evaluated the integrity of retinal vascular complex in non- proliferative diabetic retinopathy (NPDR) with noninvasive OCTA and correlated perfusion indices with degree of NPDR. Split-spectrum amplitude decorrelation angiography (SSADA) algorithm based optical coherence angiography (OCTA) was used for objective metric evaluation of both superficial and deep retinal capillary plexus.

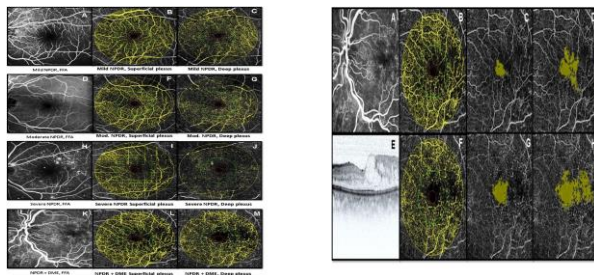
**METHODS** In this prospective study, Optical Coherence Tomography Angiography (RTVue, Optovue Inc) was performed in 102 eyes of newly diagnosed NPDR cases with or without DME with varying severity.(mild-NPDR=36; moderate NPDR=21, severe NPDR= 13;and NPDR+DME=32). 60 normal eyes served as controls. Automated software processed the image-information generating sets of perfusion indexes for four en-face section (superficial plexus, deep plexus, outer retina and chorio-capillaries). Software acquired perfusion indices separately in parafoveal areas and perifoveal area.

Values for FAZ area (mm<sup>2</sup>) were also obtained. The perfusion index of superficial and deep retinal plexus were included.

**RESULTS** Mean parafoveal vessel density (VD) of superficial and deep plexus in normal was  $46.82\% \pm 8.96$  and  $36.93\% \pm 8.1$ . VD in superficial plexus was  $35.9\% \pm 7.6$  in mild,  $29.8\% \pm 7.12$  in moderate,  $20.3\% \pm 6.81$  in severe and  $38.87\% \pm 7.9$  in NPDR+DME; deep plexus was  $25.23\% \pm 6.1$ ,  $20.16 \pm 6.16$ ,  $11.16 \pm 4.81$  and  $17.91 \pm 4.42$  respectively. Mean perifoveal VD decreased with the increase in severity of DR (mild  $42.81\% \pm 8.64$ , moderate  $35.2\% \pm 8.65$ , severe  $26.1\% \pm 7.91$  and NPDR+ DME  $35.97\% \pm 9.36$ ) in superficial plexus. The decline was more pronounced (mild  $31.95\% \pm 9.1$ , moderate  $24.94 \pm 9.14$ , severe  $16.11 \pm 6.11$ ) in deep plexus. Flow index also decreased with increase in severity both in superficial (normal 0.38, severe 0.16) and deep plexus (normal 0.32, severe 0.10) in parafoveal and perifoveal regions. Deep capillary flow was more severely compromised with increase in severity of NPDR (4X;  $r=0.98$ ) than superficial plexus (2X;  $r=0.72$ ) when compared to normal ( $p<0.001$ ).

**CONCLUSION** OCT-angiography visualize the retinal microcirculation clearly, and enables quantification of superficial and deep capillary plexus perfusion separately in diabetic retinopathy. As diabetic retinopathy progresses, a decrease in flow index and vessel density becomes more profound in deep retinal plexus and facilitate early detection of diabetic retinopathy before they become evident on FA.

**TAKE HOME MESSAGE** This study demonstrates the potential of perfusion indices in objectively grading and linearly assessing microvascular compromise in diabetic retinopathy.



# Baseline Characteristics Associated With Changes in Diabetic Retinopathy Severity Scale (DRSS) Score: Analyses From the VISTA and VIVID Studies

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**OBJECTIVE** To identify baseline characteristics that influence changes in Diabetic Retinopathy Severity Scale (DRSS) Score following anti-vascular endothelial growth factor therapy.

**PURPOSE** To evaluate the influence of baseline characteristics on improvement of DRSS scores at week 100 compared with baseline.

**METHODS** VISTA and VIVID were phase 3 trials randomizing 466 and 406 DME patients, respectively, to receive intravitreal aflibercept injection (IAI) 2 mg every 4 weeks (2q4), IAI 2 mg every 8 weeks following 5 monthly doses (2q8), or laser. Change in DRSS score was an exploratory endpoint at week 100. The aim of this ad hoc analysis was to determine, using observed data, what factors influenced  $\geq 2$ -step improvement in DRSS scores at week 100. Factors considered were baseline age, gender, race, HbA1c level, duration of diabetes, best-corrected visual acuity (BCVA), central retinal thickness (CRT), and baseline DRSS score. Regression analysis was used to determine the impact of these factors.

**RESULTS** In the integrated VIVID and VISTA studies, 10.2%, 34.7% ( $p = .0018$ ), and 38.5% ( $p < .001$ ) of laser, 2q4, and 2q8 patients, respectively, experienced a  $\geq 2$ -step improvement in DRSS score at week 100 compared with baseline. Baseline DRSS score was the only factor significantly associated with  $\geq 2$ -step DRSS score improvement ( $p < .0001$ ). Age, gender, race, HbA1c level, duration of diabetes, BCVA and CRT did not have an impact on the ability to gain  $\geq 2$ -step improvement in DRSS score. The most

frequent ocular serious adverse event from baseline to week 100 was cataract (2.4%, 1.0%, and 0.3% for the 2q4, 2q8, and laser groups, respectively) in a pooled analysis of VISTA and VIVID.

**CONCLUSION** Overall, a significant proportion of patients in the VIVID and VISTA trials experienced at least a 2-step improvement in DRSS score at week 100. Baseline DRSS score was the most significant identified factor associated with  $\geq 2$ -step improvement in DRSS score at week 100.

**TAKE HOME MESSAGE** In VIVID and VISTA, baseline Diabetic Retinopathy Severity Scale score and IAI treatment assignment were the most significant predictors of 2-step DRSS score improvement at 100 weeks vs. baseline.

**HUMAN RESEARCH** This study involves human research.  
IRB Approval Status: Approved by institutional review board

# Effect of Vitreomacular Adhesion on Treatment Outcomes in the Ranibizumab for Edema of the Macula in Diabetes (READ-3) Study



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**OBJECTIVE** To assess the role of vitreomacular adhesion (VMA) in visual and anatomic outcomes in patients with diabetic macular edema (DME).

**PURPOSE** To assess the role of vitreomacular adhesion (VMA) in visual and anatomic outcomes in patients with diabetic macular edema (DME).

**METHODS** In the READ-3 study, patients with DME received monthly intravitreal injections of either 0.5 or 2.0 mg ranibizumab. Optical coherence tomography images from patients who completed the month 6 visit of the study were analyzed at the baseline visit to identify the presence (VMA+) or absence (VMA-) of VMA. Patients with any degree of vitreomacular traction were excluded from the analysis. Two independent graders graded all images. Vitreomacular adhesion was classified by size of adhesion into either focal ( $<1500\ \mu\text{m}$ ) or broad ( $\geq 1500\ \mu\text{m}$ ).

**RESULTS** One hundred fifty-two eyes (152 patients) were randomized in the READ-3 study. One hundred twenty-four eyes (124 patients) were eligible for the study based on study criteria. Twenty-eight eyes did not meet study criteria and were excluded from the

study. At baseline, 26 patients were classified as VMA+ and 98 patients were classified as VMA-. The distribution of the 2 doses of ranibizumab (0.5 and 2.0 mg) in the 2 groups was similar. At month 6, the mean improvement in BCVA was  $11.31 \pm 6.67$  and  $6.86 \pm 7.58$  letters in the VMA+ and VMA- groups, respectively ( $P = 0.007$ ). Mean improvement in CRT was  $-173.81 \pm 132.31$  and  $-161.84 \pm 131.34$   $\mu\text{m}$  in the VMA+ and VMA- groups, respectively ( $P = 0.681$ ). At month 6, among the 26 VMA+ eyes (at baseline), 7 eyes demonstrated PVD, 17 eyes showed no change in VMA status, and 2 eyes were not gradable and were excluded.

**CONCLUSION** Diabetic macular edema patients with VMA have a greater potential for improvement in visual outcomes with anti-vascular endothelial growth factor therapy. Therefore, the presence of VMA should not preclude patients with DME from receiving treatment.

**TAKE HOME MESSAGE** Diabetic macular edema patients with VMA have a greater potential for improvement in visual outcomes with anti-vascular endothelial growth factor therapy. Therefore, the presence of VMA should not preclude patients with DME from receiving treatment.

**HUMAN RESEARCH** This study involves human research.

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