

Relationship Between Neovascularization of the Optic Disc and Diabetic Macular Edema

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Introduction

Neovascularization in proliferative diabetic retinopathy (PDR) is associated with tractional retinal detachment and vitreous hemorrhage, which cause severe visual impairment. Neovascularization of the disc (NVD) has already been studied with regard to occurrence and morphology.^{1,2} However, the effects of NVD on the macula are unexplored. In this retrospective study, we examined the effects of NVD on the macula in PDR.

Materials and Methods

The study follows the Declaration of Helsinki's tenets and has been approved by the Institutional Review Board of Gunma University Graduate School of Medicine (HS2021-242). We obtained informed consent from all participants. Forty eyes of 31 PDR patients who presented to Gunma University from February 2013 to November 2018 were included. Half of the eyes (n=20) had developed NVD and the other half (n=20) had not. NVD was defined as neovascularization within the diameter of one disc from the optic nerve. All patients received an ophthalmologic examination upon their first visit, including best-corrected visual acuity (BCVA), intraocular pressure (IOP), slit-lamp biomicroscopy, color fundus photography, and swept-source or spectral domain optical coherence tomography (OCT). Central macular thickness (CMT) was defined as the distance between the internal limiting membrane and surface of the retinal pigment epithelium at the fovea. Patients with a history of vitrectomy and other retinal disorders, including severe vitreous hemorrhage, severe cataracts, neovascular glaucoma, and vitreomacular traction, and those who had previously received intravitreal injections of anti-vascular endothelial growth factor (VEGF) drugs were excluded. All data are expressed as mean \pm SD. The Mann–Whitney *U*-test was used for comparison of unpaired groups and Fisher's exact test was used for categorical variables. $P < 0.05$ was considered statistically significant. GraphPad Prism version 6 (GraphPad Software Inc., La Jolla, CA, USA) was used for statistical analysis.

Results

Table 1 shows the characteristics of the PDR patients with and without NVD. There were no significant differences between PDR with and without NVD when considering age, sex, BCVA, IOP, laser treatment history, and presence of posterior vitreous detachment (PVD). The CMT was $322.2 \pm 133.7 \mu\text{m}$ in cases of PDR with NVD and $449.3 \pm 148.9 \mu\text{m}$ in cases without NVD. The CMT of PDR patients with NVD was significantly lower than that of patients without NVD ($P = 0.0057$) (Figure 1A). Figure 1B shows a representative case. To further examine CMT due to differences in NVD cite, the PDR group with NVD was classified into the (1) temporal NVD group, (2) nasal NVD group, or (3) unclassifiable group according to NVD cite. The CMT was $256.4 \pm 62.6 \mu\text{m}$, $368.8 \pm 136.7 \mu\text{m}$, and $382.0 \pm 162.1 \mu\text{m}$ for the temporal, nasal, and unclassifiable groups, respectively, with no significant difference among the three groups.

Table 1 Characteristics of 40 Eyes of 31 Patients with Proliferative Diabetic Retinopathy

	NVD (+) (n=20)	NVD (-) (n = 20)	P value
Age, y	43.6 ± 13.3	51.7 ± 12.1	0.06
Sex, n (%)			1
Male	16 (80)	15 (75)	
Female	4 (20)	5 (25)	
BCVA, logMAR	0.15 ± 0.25	0.25 ± 0.29	0.24
IOP, mmHg	16.6 ± 4.1	15.7 ± 2.9	0.35
Laser treatment, n (%)			1
PRP	10 (50)	9 (45)	
None	10 (50)	11 (55)	
Presence of PVD, n (%)	2 (10)	3 (15)	1

Abbreviations: NVD, neovascularization of the disc; BCVA, best-corrected visual acuity; logMAR, logarithm of the minimum angle of resolution; IOP, intraocular pressure; PRP, pan-retinal photocoagulation; PVD, posterior vitreous detachment.

Discussion

A previous report showed high oxygen tension at the posterior pole of the retina in PDR, which is caused by an abundant supply of oxygen from neovascularization occurring in the same area of the eye.³ Another report indicated that PDR eyes have numerous neovascular vessels and abundant blood flow, whereas oxygen consumption is low, thus, excess oxygen diffuses into the eye.⁴ Thus, neovascularization in PDR contributes to improving retinal ischemia, resulting in a decrease in intraocular VEGF concentration. The ischemic retina produces VEGF, and vitreous VEGF concentration correlates with CMT measured on OCT in diabetic macular edema (DME).⁵ The presence of NVD near the macula increases

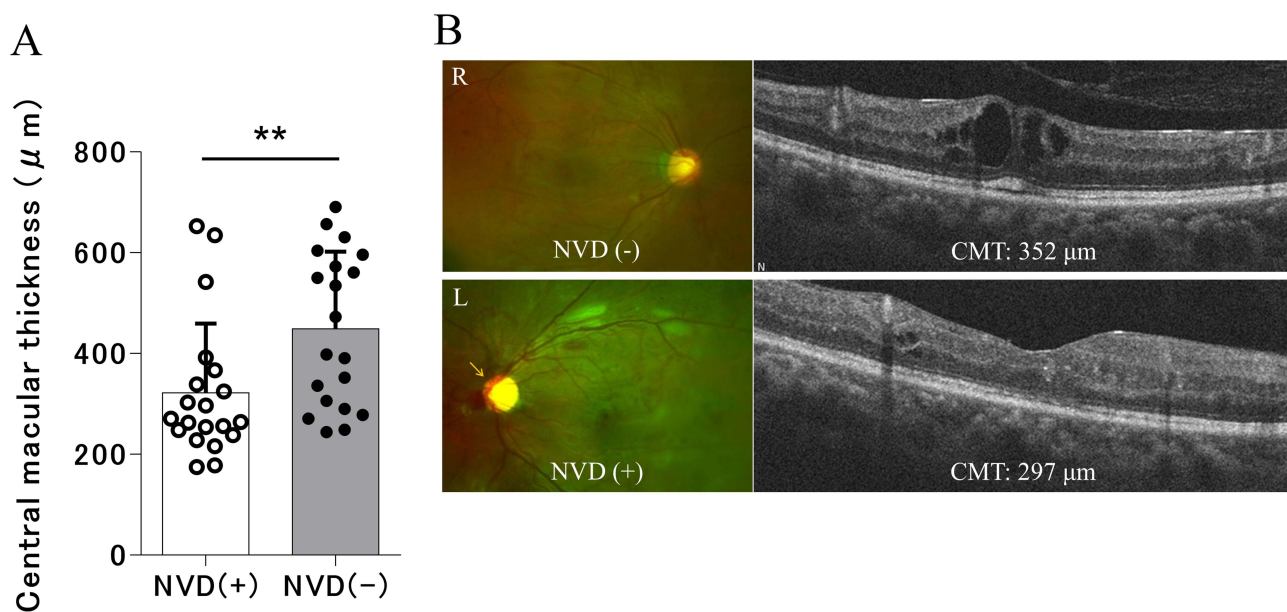


Figure 1 Comparison of central macular thickness (CMT) between proliferative diabetic retinopathy (PDR) patients with and without neovascularization of the optic disc (NVD). **(A)** Mean CMT in eyes with NVD was significantly lower than that in eyes without NVD (** $P < 0.01$). **(B)** This representative case shows a 29-year-old man with PDR in both eyes. His right eye has PDR without NVD and his left eye has PDR with NVD. The yellow arrow indicates NVD. On his initial visit, the CMT was 352 μm in his right eye and 297 μm in his left.

oxygen saturation and decreases VEGF concentrations at the macula, which may prevent the formation of DME. NVDs can cause vitreous hemorrhage and tractional retinal detachment, resulting in severe visual impairment. They may also improve intraocular ischemia and protect the macula. According to previous reports, the NVD associated with PDR grows along the posterior wall of the vitreous and the absence of PVD in the optic nerve is essential for NVD growth.¹ In addition, NVDs are fragile and lead to leakage of plasma components. This leakage has been reported to affect changes in vitreous components, including PVD,⁶ and may be associated with DME formation. Limitations of the current study include its retrospective design and the inclusion of only a few cases. Further investigation is needed to confirm the present findings.

In conclusion, our results suggest that NVDs in PDR may improve intraocular ischemia and reduce DME.

Disclosure

The authors report no conflicts of interest in this work.

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