Progression to Proliferative Diabetic Retinopathy in Nonproliferative Diabetic Retinopathy Eyes without Diabetic Macular Edema in the United States

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Purpose:
To evaluate the natural history of disease progression from nonproliferative diabetic retinopathy (NPDR) to PDR in routine clinical practice in the United States in patients with NPDR without diabetic macular edema (DME).

Methods:
This retrospective analysis evaluated electronic medical records (Vestrum Health Retina Research Dataset; Naperville, IL) during January 2013 through June 2019 from adult eyes diagnosed with NPDR without DME and prior intravitreal anti-vascular endothelial growth factor treatment. Eyes were excluded if they converted to PDR or DME within 1 week of index NPDR diagnosis or showed evidence of age-related macular degeneration or retinal vein occlusion during the study period. Time to PDR conversion was analyzed by Kaplan–Meier estimation. Cox multivariable regression was used for adjusted analyses. Data were censored from the time of DME development.

Results:
Of 135,324 eyes included in the study, 52% had mild NPDR, 29% had moderate NPDR, 8% had severe NPDR, and 11% had unspecified NPDR. Median baseline visual acuity (VA) was the same across NPDR severity groups, 76 letters (20/32 Snellen equivalent). Patients with severe NPDR were slightly younger (median age: 60 years vs 64–67 across mild, moderate, and unspecified severities), and less likely to have been diagnosed with hypertension (60% vs 64–79% across mild, moderate, and unspecified severities). The 4-year risk (95% CI) of progression to PDR was 14.9% (14.5%, 15.4%) in overall patient population. This risk increased with higher NPDR severity (mild: 7.9% [7.4, 8.3], moderate: 20.9% [20.0, 21.7], severe: 46.8% [44.4, 49.2], unspecified: 13.5% [12.7, 14.4]). This relationship persisted when adjusting for baseline characteristics. Additional baseline factors associated with increased risk of progression to PDR included younger age, type 1 diabetes, and worse VA.

Conclusions:
Baseline NPDR severity was a strong predictor of progression to PDR. When left untreated, nearly half of eyes with severe NPDR progressed to PDR within 4 years in routine clinical practice in the United States.