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Loss to Follow-Up in Patients with Proliferative Diabetic Retinopathy after Panretinal Photocoagulation or Intravitreal Anti-VEGF Injections

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Purpose: Loss to follow-up (LTFU) may contribute to vision loss in patients with active proliferative diabetic retinopathy (PDR). The aim of this study is to determine and compare the rates of LTFU in patients with PDR receiving panretinal photocoagulation (PRP) or intravitreal injections (IVIs) with anti-vascular endothelial growth factor (VEGF) over approximately 4 years. Moreover, this study evaluates various risk factors for LTFU.

Design: Retrospective cohort study.

Participants: A total of 2302 patients with PDR receiving IVIs with anti-VEGF or PRP between January 1, 2012, and April 20, 2016.

Methods: Intervals between each procedure and the subsequent follow-up visit were measured. Loss to follow-up was defined as at least 1 interval exceeding 12 months duration.

Main Outcome Measures: The LTFU rates and associated risk factors.

Results: A total of 1718 patients (74.6%) followed up postprocedure and 584 patients (25.4%) were LTFU over approximately 4 years. Of the patients receiving PRP, 28.0% were LTFU compared with 22.1% of patients receiving IVI with anti-VEGF ($P = 0.001$). The LTFU rates decreased as age increased, with rates of 28.1% for patients aged ≤55 years, 27.0% for patients aged 56 to 65 years, and 20.9% for patients aged >65 years ($P = 0.002$). Loss to follow-up also differed by race, with rates of 19.4% for whites, 30.2% for African Americans, 19.7% for Asians, 38.0% for Hispanics, Native Americans, and Pacific Islanders, and 34.9% for patients of unreported race ($P < 0.001$). The LTFU rates also increased as regional average adjusted gross incomes (AGIs) decreased, with rates of 33.9% for patients with regional average AGI of ≤$40 000, 24.0% for patients with regional average AGI from $41 000 to $80 000, and 19.7% for patients with regional average AGI >$80 000 ($P < 0.001$). Procedure type, age, race, and regional average AGI were all significant ($P < 0.05$) independent risk factors of LTFU in the multivariate regression.

Conclusions: A large proportion of patients with PDR were LTFU after receiving PRP or an anti-VEGF injection over approximately 4 years. Key risk factors included age, race, and regional average AGI. *Ophthalmology 2018;■:1–7 © 2018 by the American Academy of Ophthalmology*

Proliferative diabetic retinopathy (PDR) is a major contributor to vision loss in patients with diabetes mellitus.[1] Panretinal photocoagulation (PRP) has been shown to decrease the risk of severe vision loss by approximately 50% in high-risk patients with PDR.[2] Although effective, PRP has potential side effects, including night vision loss, exacerbation of macular edema, and decreases in both peripheral vision and contrast sensitivity.[3-5] Recent studies have demonstrated that intravitreal injections (IVIs) with ranibizumab or aflibercept provide comparable and potentially even superior outcomes to PRP.[6,7] However, both PRP and IVI with anti-vascular endothelial growth factor (VEGF) require close follow-up to reassess response to therapy, disease progression, and need for additional treatment to optimize outcomes. To date, there is limited understanding on loss to follow-up (LTFU) rates after these procedures for patients with PDR. Moreover, there has yet to be an assessment of potential risk factors that might contribute to LTFU in these patients. This study aims to determine and compare patient LTFU after PRP or IVI with anti-VEGF and to identify potential risk factors of LTFU after these treatments.

Methods

Study Population

The approval of the Wills Eye Hospital Institutional Review Board was obtained before conducting this study, which was performed in accordance with the Health Insurance Portability and Accountability Act of 1996 and adhered to the tenets of the Declaration of Helsinki. The study was conducted as a retrospective analysis

https://doi.org/10.1016/j.ophtha.2018.02.034
ISSN 0161-6420/18

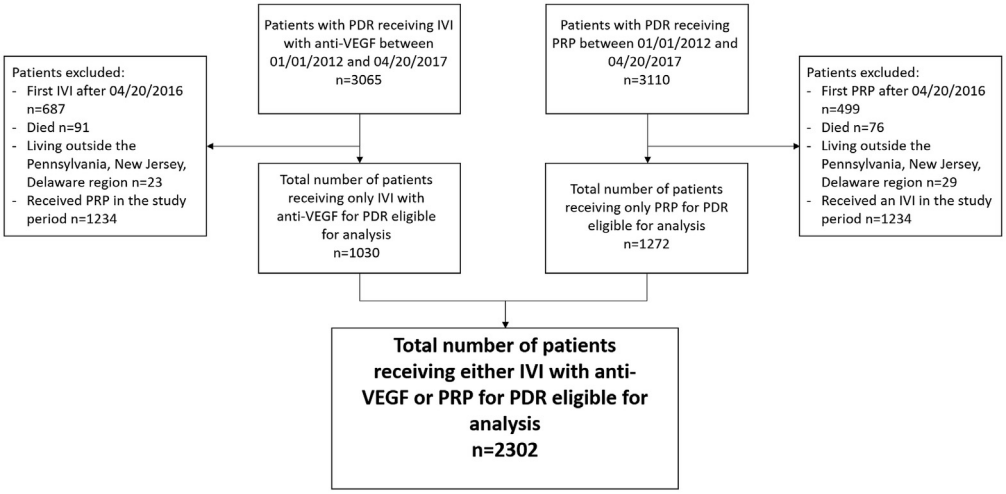

Figure 1. Flowchart of patients with proliferative diabetic retinopathy (PDR) included in the final analysis. Flowchart showing the total number of patients receiving panretinal photocoagulation (PRP) or intravitreal injection (IVI) with anti-vascular endothelial growth factor (VEGF) for PDR included in the final analysis.

using diagnostic and procedural billing codes. Patients with PDR receiving PRP or IVI with anti-VEGF at Wills Eye Hospital and the offices of Mid Atlantic Retina between January 1, 2012, and April 20, 2016, were identified using International Classification of Diseases 9th and 10th Revisions, and Current Procedural Terminology billing codes. Mid Atlantic Retina is a large retina practice with multiple clinics in Pennsylvania, Delaware, and New Jersey. Exclusion criteria included (1) patients with their first procedure occurring after April 20, 2016; (2) patients living outside of the states of Pennsylvania, New Jersey, and Delaware; (3) patients receiving both PRP and IVI during the study period; and (4) patients who died during the study period. Death was ascertained via 2 close emergency contacts designated at the time of clinical registration.

Patient Characteristics

Baseline patient characteristics collected included age, gender, race, and regional average adjusted gross income (AGI). Race and gender were self-reported by patients at the time of clinical registration. Regional average AGI was determined by cross referencing the patient's current residential ZIP code with the average AGI per ZIP code supplied by the Internal Revenue Service.[8] To determine the spherical distance to the clinic, the patient's home address along with all the clinics of the practice were converted to a coordinate format using the Bing maps application program interface (Microsoft Corp., Redmond, WA). The spherical distance from the patient's address to the clinic visited was then calculated using a Haversine formula.[9]

Visual Acuity

Only a subgroup of our patient cohort had recorded visual acuities (VAs) that could be used in the final analysis. During the study period, the patient charts were transitioned to an electronic health record system. As a result, the majority of patient history and clinical data before this implementation were no longer accessible. Best available Snellen VA measurements based on corrected or pinhole vision were obtained on the first and the final procedure. For patients with bilateral disease, the eye with the better VA was used. The VA measurement was converted to the logarithm of the minimum angle of resolution (logMAR) for analysis. Change of logMAR VA was calculated only for patients with 2 or more procedures by subtracting the logMAR VA obtained at the first procedure from the logMAR VA at the final procedure.

Definition of Loss to Follow-up

To assess for LTFU, the interval between each procedure and the subsequent follow-up visit was determined. Loss to follow-up was defined as at least 1 interval exceeding 12 months without a subsequent visit. Thus, patients with multiple IVIs or PRP sessions required only 1 interval exceeding 12 months to be considered as LTFU. A window period of observation was used between April 20, 2016, and April 20, 2017, to ensure that patients who had procedures between April 20, 2015, and April 20, 2016, had at least 12 months to return for follow-up or be considered LTFU. Therefore, patients were required to have initiated therapy at least 12 months before the end date of the observation period (April 20, 2017) to have sufficient time for follow-up. Thus, any procedure taking place after April 20, 2016, was not used in the analysis.

Statistical Analysis

All statistical tests were performed using SPSS, Version 24 (SPSS, Inc., Chicago, IL). Continuous variables were categorized on the basis of distribution or clinical relevance. Differences in LTFU rates between categoric risk factors were assessed using a chi-square test. Univariate logistic regression was used to determine the odds of LTFU based on age, gender, race, regional average AGI, distance to clinic, and procedure performed. Factors with a P value <0.2 were then used in a stepwise backward likelihood multivariate regression model to determine the adjusted odds ratio for each risk factor. Statistical significance was considered as a P value of <0.05.

Results

There were 2302 patients eligible for the final analysis (Fig 1). Of these, 1272 (55.3%) received only PRP and 1030 (44.7%) received only IVI with anti-VEGF. Patients receiving PRP had a mean ($\pm$ standard deviation) of 2.0 ($\pm$1.3) sessions, whereas patients