Causes and clinical impact of loss to follow-up in patients with proliferative diabetic retinopathy

MATERIALS AND METHODS

This study was reviewed and approved by the Medical Research and Ethics Committee of the Faculty of Medicine at Assiut University (Assiut, Egypt). Written informed consent was obtained from all patients after the nature/purpose of the study and risks/benefits of study participation were explained. All study conduct adhered to the tenets of the declaration of Helsinki.

Study population

This prospective cohort study was conducted between May 25, 2013 and June 5, 2018 and included treatment-naïve patients who had developed PDR in one eye with a best corrected visual acuity (BCVA) ranging from 20/22 to 20/69, as determined by the Snellen equivalent. Patients were allocated to receive PRP, IVIs of anti-VEGF, or a combination of both procedures. Treatment decisions for each patient was guided by careful consideration of relative advantages of each treatment and the anticipated compliance with follow up and treatment recommendations. A single retina specialist (M.S.) performed all laser and injection procedures at the Retina outpatient clinic in Assiut University Hospital (Assiut, Egypt). No new patients were recruited in the last 6 months of the observation period. Exclusion criteria were outlined as follows: 1) patients receiving follow-up ophthalmic care for their PDR with or without interventions at any other medical care provider during the observation period, as declared by the patients at any follow up visit; 2) patients LTFU who did not resume follow-up until the end of the observation period; 3) patients needing PPV

at first presentation or having additional retinal pathology; and 4) patients receiving their treatment procedure during December 2017 or having vitreous hemorrhage that failed to clear up by June 2018 but still ineligible candidates for PPV. LTFU was defined as missing any follow-up visit for any interval exceeding 6 months provided that patients eventually resumed care before the end of the study period (time zero was defined as the date of the missed follow-up visit).

Patient characteristics and clinical assessment

Patient characteristics, including age and sex, were collected. Each patient received detailed complete ophthalmic examinations, including BCVA measurements, which were converted to a logarithm of the minimum angle resolution (Log MAR); intraocular pressure (IOP); slit lamp biomicroscopy; and indirect ophthalmoscopy, at the initial visit and at each follow-up visit. Fundus photography and fluorescein angiography were also performed at enrollment and when indicated during the follow-up period. The number of PRP sessions and IVIs of anti-VEGF and the need for PPV were also recorded. For LTFU subjects, a convenient treatment plan was established when care had resumed.

Subject questionnaire

Subjects in the LTFU group were asked to complete an 8 item questionnaire regarding the reason(s) for missing their follow-up appointment. The questionnaire items were carefully chosen based on pilot discussions with subjects that had been in similar situations before conducting the study. Subjects were reminded that their answers would remain confidential and would not influence their future medical care. For patients with reading difficulties, the questionnaire was vocally administered. The questionnaire asked about the following potential causes for LTFU: (1) lack of information provided by medical care providers on follow-up need and/or date, (2) lack of concern and/or compliance (self-reported by

subject), (3) lack of trust in and/or satisfaction with treatment, (4) lack of treatment affordability, (5) difficulty with transportation, (6) other disabling conditions (comorbidity) that hindered appointment attendance, (7) lack of a social support system, and (8) employment obligations. Because discussing treatment affordability and the potential lack of a support system may have upset some subjects, these questions were placed at the end of the survey to establish subject trust and to prevent emotional distress from confounding responses to the other questions. Subjects rated the impact of each item using a 5-point scale: 1 = "not significant at all" and 5 = "strongly significant cause." Only completed surveys were used for analyses.

Statistical analysis

Statistical tests were performed using SPSS, version 24 (SPSS, Inc., Chicago, IL, USA). Continuous variables are presented as mean ± standard deviation, and the frequency distributions of categorical variables were recorded. Age, sex, and type of intervention were used as categorical risk factors, and the differences in the rates of these factors for LTFU were assessed using chi- square tests. Univariate logistic regression was used to determine the odds of LTFU based on age, sex, and the type of intervention used. Factors with a *P* value < 0.1 were then used in a multivariate logistic regression model to determine the adjusted odds ratios for each risk factor. A *t*-test was used to compare the mean log MAR BCVA between compliant patients group and LTFU group. Need for PPV was assessed in patients who followed-up and those who were LTFU; this information was analyzed in relation to risk factors (age, sex and interventions) using a chi-square test. Spearman's rank correlation coefficients were used to assess correlations between the answer scale given for each question and the scales given for other questions as well as age and intervention used.

Statistical significance was set at $P < 0.05$. Questionnaire responses were analyzed by mode of answers and frequencies.