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Validity of Self Report in Type 1 Diabetic Subjects for Laser Treatment of Retinopathy

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Abstract

Purpose—This study sought to determine the validity of self report of prior pan-retinal photocoagulation (PRP) and focal photocoagulation (FP) compared to fundus photography.

Design—Prospective cohort study.

Participants—1363 type 1 diabetic subjects from the Epidemiology of Diabetes Interventions and Complications (EDIC) Study, a subset of the 1441 subjects originally enrolled in the multi-center Diabetes Control and Complications Trial.

Methods—At each annual visit, subjects were asked by EDIC staff whether they had PRP and/or FP since the last completed annual clinic visit. Fundus photographs were collected in one quarter of the cohort each year and in the whole cohort at EDIC years 4 and 10. Photographs were graded for the presence and extent of PRP and FP. Seventeen years of subject reporting and photograph grading of PRP and FP were compared in EDIC subjects.

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Main Outcome Measures—Kappa, sensitivity, specificity, and positive and negative predictive values were calculated for subject-reported PRP and FP. Factors influencing subject misreporting were investigated.

Results—For subject reporting, 1244 (96%) of 1296 subjects with gradable photographs accurately reported whether they had a history of PRP in one or both eyes, and 1259 (97.5%) of 1291 with valid photographs correctly reported their history of FP. Sensitivities for PRP and FP were 90.4 and 74.0%; specificities, 96.0 and 98.8%; positive predictive values, 75.9 and 80.3%; negative predictive values, 98.9 and 98.4%; and kappa 0.80 and 0.76. Risk factors associated with misreporting include prior laser for diabetic retinopathy and prior ocular surgery (each $p < 0.04$).

Conclusions—For subjects with type 1 diabetes, in the absence of a clinical exam or fundus photographs, subject self report could be a reliable tool in a well-monitored study for assessing laser treatment type in diabetic retinopathy.

Diabetic retinopathy is the number one cause of vision loss in working age adults in the developed world.¹ Over 300,000 people in the United States are estimated to have vision-threatening complications from diabetic retinopathy.² These complications include clinically significant macular edema, a pathological increase in retinal thickness in the macula related to increased intraretinal fluid from abnormal vascular permeability, and proliferative diabetic retinopathy, the result of pathological neovascularization related to retinal hypoxia. Focal laser photocoagulation (FP) treatment in clinically significant macular edema lessens retinal thickening and decreases the rate of vision loss.^{3, 4} Proliferative diabetic retinopathy is treated by pan-retinal laser photocoagulation (PRP) that results in a reduction of hypoxic retinal tissue.^{3, 5} Clinically significant macular edema may be also treated with the intravitreal injection of steroids^{6, 7} or anti-vascular endothelial growth factor^{8, 9} compounds. However, these are relatively recent additions to the therapeutic armamentarium for clinically significant macular edema.

The Diabetes Control and Complications Trial^{10, 11} (DCCT, 1983–93) was a multi-center randomized clinical trial that demonstrated the benefit of intensive insulin treatment in reducing the incidence of microvascular complications in patients with type 1 diabetes. Follow-up of the DCCT cohort has been carried out in the Epidemiology of Diabetes Interventions and Complications observational study (EDIC, 1994–present).¹² EDIC is unique in that all subjects have had standardized fundus photography for diabetic retinopathy staging and were queried about history of treatment with PRP or FP. This is in contrast to the DCCT and other studies, in which subjects were asked about treatment with any laser photocoagulation without distinguishing between PRP and FP. The combination of self report data and standardized fundus photography for each of the EDIC subjects enabled us in the present study to assess the reliability and accuracy of subject self report for specific laser type in diabetic retinopathy. Hence, the EDIC cohort provides an opportunity to address the following questions: 1) Can subjects accurately report prior PRP or FP? 2) Can they reliably distinguish between these two interventions?

A subject-reported history of prior laser photocoagulation can be a useful surrogate for a clinical exam to indicate the presence of severe diabetic retinopathy with the sight-threatening complications of proliferative diabetic retinopathy or clinically significant macular edema. A previous single-center clinical study of 100 diabetic subjects found that 96% of subjects were accurate in reporting whether they had received previous laser treatment for diabetic eye disease.¹³ A retrospective review of the Wisconsin Epidemiologic Study of Diabetic Retinopathy (n=2348) showed that 99% of subjects were accurate in reporting whether they had prior laser treatment for diabetic eye disease. Similarly, Patty et al demonstrated a very high specificity for self-reported prior laser or ophthalmic surgery in their subjects with diabetic retinopathy from the Los Angeles Latino Eye Study.¹⁴ It would

be advantageous if self report offered more specific information given its widespread use in the acquisition of medical data. However, none of these studies addressed whether subjects were able to differentiate between the two different types of laser photocoagulation used to treat diabetic retinopathy. Anecdotal opinion among retina specialists suggests that it is difficult for patients to reliably distinguish between the two types of laser photocoagulation treatment. In the present paper, we sought to explore this issue. Herein, we report the findings from subjects in the EDIC cohort who were asked specifically whether they had previous PRP or FP.

Methods

Study Design and Interview Data

Annually during EDIC, a structured interview was conducted by the study coordinators, which included the following questions for PRP and FP, respectively: “Have you had scatter treatment (given for retinopathy) since the last completed annual clinic visit?” and “Have you had focal treatment (given for macular edema) since the last completed annual clinic visit?” When the subjects answered “yes” to having had laser, there was often an exchange between the coordinator and the subject verifying the type of laser. The research was approved by the Institutional Review Board at the consenting institutions and adhered to the tenets of the Declaration of Helsinki.

Fundus Photography Grading of PRP and FP

Standardized seven-field stereoscopic color fundus photographs were collected in about one quarter of the EDIC cohort each year, and in the whole cohort during the 4th and 10th years of the study. The fundus photography grading protocol has been described in detail previously.¹⁰ All photos were double-graded by certified graders (masked to DCCT treatment group) at the Central Fundus Photograph Reading Center (University of Wisconsin), and discrepancies reviewed by a senior grader. Prior to 2008, grading (Number, N=13,522 photos, 90.4%) indicated a history of laser treatment but without distinction between FP and PRP. After 2008, grading (N=1435 photos, 9.6%) distinguished between a history of PRP and FP. In 2011, all photographs from prior to 2008 with any amount of laser (N=805 photos from 210 subjects) were reassessed retrospectively by a single senior grader and classified as PRP, FP, or PRP and FP.

Comparison of Self Reporting and Fundus Photography Grading of PRP and FP

For each subject, 17 years of self report were summarized into the presence or absence of self-reported PRP or FP based on any report of laser during that period. Likewise, 17 years of fundus photography grading were summarized into one final grading for each laser based on any grading of laser during the same interval. Analyses of concordance between subject report and fundus photography grade were conducted.

As the fundus photography grade was the standard by which we determined the accuracy of self report, and fundus photography grading itself can be susceptible to error, we took an additional quality control measure. When there was a discrepancy between subject self report and fundus photography grade (53 subjects for PRP and 41 subjects for FP), the fundus photos were re-evaluated by an ophthalmologist. In the event of a disagreement (N=10), the ophthalmologist’s grade was used for the analysis.

Subjects

Figure 1 (available at <http://aaojournal.org>) depicts PRP evaluation during the DCCT and EDIC. Among the original 1441 DCCT subjects, 36 had PRP during the DCCT. Because subject reporting during DCCT did not distinguish between PRP and FP, these 36 subjects

were excluded from this analysis. Among the 1405 (97.5%) subjects free of PRP at the beginning of EDIC, 1357 had at least one fundus photographic visit graded in EDIC, and 48 (23 died and 25 became inactive) had no fundus photographs collected during EDIC. Of the 1357, 54 reported PRP at their last annual EDIC visit. However, fundus photographs have yet to be collected to verify these reports. Therefore, these 54 subjects were also excluded from the analysis in this paper. A total of 1303 EDIC subjects who were free of PRP during the DCCT, who had at least one fundus photograph graded during EDIC, and who did not report PRP at the last EDIC visit, were included in the PRP analysis. Likewise, the flow chart of FP evaluation in the DCCT and EDIC (Figure 2, available at <http://aaojournal.org>) shows that 1322 subjects were included in the final FP analysis. Combining PRP and FP, a total of 1363 EDIC subjects were included in the current analyses (1262 in the PRP plus FP, 41 in the PRP only, and 60 in the FP only analyses).

Statistical Methods

The proportions reported to have PRP and FP by self report and photography were compared using McNemar's test.¹⁵ Agreement between subject reporting and fundus photography grading of photocoagulation for both PRP and FP was assessed. Cohen's kappa statistic,¹⁵ the difference between the observed % agreement and that expected by chance alone, was calculated to assess agreement of the two measurements. Landis and Koch's guidelines were used for interpretation: 0.0–0.2 indicates slight; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, substantial; and 0.81–1.00, almost perfect agreement.¹⁶ Sensitivity, specificity, false positive and negative rates, and positive and negative predicted probabilities were computed. Logistic regression was employed to assess the effect of risk factors on misreporting of PRP or FP.

Results

The demographic characteristics for the 1363 EDIC subjects included in the PRP and/or FP analyses at DCCT baseline (1983–1989) and EDIC baseline (or equivalently, DCCT closeout, 1992–1993) are shown in Table 1 (available at <http://aaojournal.org>). At EDIC baseline, these subjects were on average 33 years old, 47.7% were female, 96.3% were Caucasian, 86.3% had a college or higher-level education, 62.3% were employed as professionals, and 77.7% had medical insurance coverage. Duration of type 1 diabetes was on average 12 years. 50.7% of subjects were from the primary cohort, 49.8% were from the DCCT intensive therapy group, 53.1% were overweight (body mass index >25 kg/m²), and 4.8% had hypertension. Average fasting serum total cholesterol was 181.8 mg/dL. The mean hemoglobin A1c level in the total cohort dropped from an average of 9.0% at DCCT baseline to 8.1% at EDIC baseline due to glycemic control in the intensive group during the DCCT (7.2% in the intensive and 9.1% in the conventional groups at DCCT end).

Self Report of PRP

Table 2 presents the cross-tabulation of self report versus fundus photography for PRP, and Table 3 reports the agreement statistics. The 12.5% reported positive by self report was significantly more than the 10.5% reported positive by photography ($p=0.0003$). Fundus photographs from four subjects were ungradable and photographs from three subjects were questionable or had probable PRP. Among the four subjects with ungradable photographs, two reported having a history of PRP and two reported no history of PRP. Among the three subjects with questionable/probable PRP, one reported having PRP and two reported no history of PRP. Excluding these seven subjects with questionable or probable PRP or ungradable photographs, 1244 (96%) subjects accurately reported a history of PRP with high sensitivity (90.4%), specificity (96.6%), negative predictive value (98.9%), and a fair positive predictive value (75.9%). The incidence rate of PRP based on fundus photographs

was 10.5% as compared to 12.5% based on subject reporting. The overall kappa statistics showed a substantial agreement (0.80) between subject report and grading of photos for PRP.

Table 4 separates misreporting of photocoagulation by fundus photography laser status. Fundus photographs from subjects with misreported PRP were reviewed. As shown in Table 4, among the 39 subjects with false-positive PRP (photos graded negative, but reported positive), 3 had high risk characteristics (Early Treatment Diabetic Retinopathy Study, ETDRS, score >71) and may have had PRP shortly after the photographs were obtained, 22 had definite (19) or questionable/probable (3) focal lasers and may have confused the FP for PRP, and 4 had no laser spots but had a history of other ocular surgeries (3 had cataract extraction and 1 had vitrectomy) and may have confused these procedures with PRP. For the remaining 10 subjects, no laser spots were seen in their photographs, which could be due to the laser spots being peripheral and hence not captured on the fundus photographs of the seven standard fields. Among the 13 with false-negative PRP (photos graded positive, but reported negative), 10 had definite PRP laser spots and 3 had laser spots of both PRP and FP in their photographs. Of the latter 3, 2 subjects reported FP and 1 reported neither PRP nor FP. Compared to the other subjects in the cohort, the 13 subjects with false-negative reports were not significantly older ($p=0.11$) and did not have any underlying dementia or other significant comorbidities other than end-stage renal disease in one person.

Table 5 reports the risk factors for mis-reporting PRP or FP. Multivariate logistic regression revealed that those with a history of FP but no PRP had a 34.92-fold higher risk (95% confidence interval (CI): 15.75, 77.50, $p<0.0001$) of over-reporting PRP. Those subjects with a history of any ocular surgery (including cataract extraction, vitrectomy, etc.) had a 3.84-fold higher risk (95% CI: 1.60, 9.23, $p=0.003$) of over-reporting PRP compared to those free of ocular surgeries. Under-reporting of PRP was found in subjects who were treated with both PRP and FP (odds ratio (OR): 7.76, 95% CI: 1.78, 33.82, $p<0.006$). Age, gender, education, and medical insurance coverage were not associated with PRP misreporting.

Self Report of FP

Table 2 presents the cross-tabulation of self report versus fundus photography for FP. In contrast to PRP, the proportion with FP positive by self report was slightly less than that with photography but did not reach statistical significance (5.3% versus 6.0%, $p=0.16$). Among the 1322 subjects, photos from 26 subjects had questionable or probable FP and 5 subjects had ungradable photographs. Among the 26 subjects with questionable FP in photographs, 17 reported having no history of FP, and 9 reported a history of FP. The five subjects with ungradable photographs reported having no history of FP.

In Table 3, after removing these 31 subjects with questionable or probable FP or ungradable photographs, 1259 (97.5%) of the remaining 1291 subjects accurately reported a history of FP with a high specificity (99.0%) and negative predictive value (98.4%). However, the sensitivity (74.0%) and positive predictive value (82.6%) were lower. The overall kappa of reliability was 0.78, representing a substantial level of agreement between self report and photo grading for laser treatment of clinically significant macular edema.

Fundus photographs of the misreported FP were reviewed (Table 4). Among the 12 subjects with false-positive FP, 7 had PRP laser spots in their photographs, 1 had ETDRS high risk characteristics for proliferative diabetic retinopathy (Level >71) and clinically significant macular edema but no visible PRP or FP laser spots on photographs, and 4 had no evidence of PRP or FP laser spots observed. Of the 20 subjects with false negative FP, 9 had definite

FP laser spots and 11 had both PRP and FP laser spots in their photographs. Of these 11, 9 reported PRP and 2 did not report either PRP or FP.

In Table 5, multivariate logistic regression revealed that those with a history of PRP but no FP had a 43.33 fold higher risk of over-reporting FP (95% CI: 9.02, 208.23, $p < 0.0001$) than the others. Those with a history of PRP and FP had a 64.27 fold higher risk of under-reporting FP (95% CI: 21.81, 189.42, $p < 0.0001$). As with PRP, age, gender, education, and insurance were not associated with FP misreporting.

Combined Self Report of PRP and FP

Tables 2 and 3 also present the cross-tabulation and agreement statistics of each assessment for any photocoagulation (PRP and/or FP). As anticipated, subject reporting of any laser treatment for diabetic retinopathy (combining rather than trying to distinguish between PRP and FP) revealed an improved kappa of 0.87 (compared to 0.80 for PRP alone and 0.78 for FP alone) and better positive predictive value (92.2% combined vs. 75.9% for PRP alone and 82.6% for FP alone). These findings are consistent with our prior observations.¹³

Discussion

In this study, we found that subjects with type 1 diabetes participating in a long-term study of diabetic complications were reasonably accurate in reporting prior PRP or FP. The overall kappa statistics showed a substantial agreement for PRP (0.80) and for FP (0.78) between subject self report and fundus photograph assessment. From a practical perspective, the results from this study support the accuracy of self report of PRP or FP in Caucasian individuals with type 1 diabetes. Self report of previous PRP or FP may be a reliable surrogate when data from fundus photographs or clinical exams are not available. These data may have important implications for the ascertainment of diabetic retinopathy treatment type in the modern era as care evolves toward increasing use of intravitreal biologics over laser treatment. Since subjects have high reliability in distinguishing between the two different kinds of laser treatment, it is possible that they will be even more accurate in reporting a more invasive intraocular injection. As intravitreal injections do not leave any sign on fundus photographs, clinical history gathering will be of significant value in this regard.

The fundamental question this study attempted to address is whether self report is a reliable mechanism by which to identify individuals who have specifically had PRP or FP for diabetic retinopathy. The present study is the first to examine the validity of subject-reported interview data specifically for PRP and FP. Many large cohorts have been developed to investigate diabetes and its attendant complications. Unfortunately, not all of these studies included clinical assessment and/or standardized grading of retinopathy in the subjects. Given the wealth of clinical and genetic data available for many of these cohorts, if meaningful retinopathy severity can be determined or inferred, these cohorts can be incorporated into large-scale meta-analyses of diabetic retinopathy.¹⁷

The present findings may also have implications for providers who are not eye-care specialists and who treat diabetic patients. These results support the potential reliability of patient report regarding prior PRP for diabetic eye disease, thus providing the practitioner with an immediate barometer for the severity of the diabetes. This is especially important given the high concordance between retinopathy and other diabetic co-morbidities like nephropathy.^{18, 19}

There are a number of limitations to this study. The EDIC cohort is composed of primarily Caucasian individuals (96.3%) with type 1 diabetes who have been involved in a research study of microvascular complications for approximately 25 years. DCCT recruited patients

diagnosed with type 1 diabetes within the past 5 years in the primary cohort and within the past 15 years in the secondary cohort. Therefore, the average age of the EDIC cohort may be older than that in an average clinical type 1 diabetic population. However, as revealed by the multivariate regressions in Table 5, age is not a risk factor for over- or under-reporting of PRP or FP (OR: 1.01–1.04 per year, each $p>0.40$). Therefore, age should not be a major limitation for the external validity of these results in subjects with type 1 diabetes. Although education and medical insurance coverage were also not associated with misreporting of laser therapy, the different racial composition between EDIC and the United States population (63.7% white in 2010²⁰), limits generalizing these results to non-research populations of patients with type 1 or type 2 diabetes. Further, the reliability of subject report from EDIC subjects could have been influenced by the detailed questioning by EDIC coordinators, who may have been more knowledgeable about laser than usual providers, and may have had access to additional medical records to verify the subject report. Nevertheless, clinical data gathering in clinical trials and epidemiological studies will become increasingly dependent upon subject reporting of treatment given the proliferation of treatments that leave no identifiable fundus changes, like intravitreal injections. This report suggests that subjects could be considered reliable for reporting treatment of this nature.

We investigated the possible reasons for subject over-reporting. As shown in Table 5, faulty subject recall is the most likely explanation for over-reporting as the majority of these subjects appear to have confused the two laser treatment types. Those with a history of FP but no PRP had a 34.92-fold higher risk of over-reporting PRP and those with a history of PRP but no FP had a 43.33 fold higher risk of over-reporting FP. In most ophthalmology offices, the two treatments would be easy to confuse as they are often delivered in the same room with the same laser. A few of these subjects had both clinically significant macular edema and high-risk characteristics for proliferative diabetic retinopathy. These individuals likely had subsequent laser of a different respective type soon after fundus photographs were obtained. For the remaining subjects who over-reported laser treatment type but who had no laser spots in their retinal photographs, we suspect these individuals may have had laser surgery to their eyes for other reasons, including Yag capsulotomy or slit-lamp trabeculoplasty. Multivariate analysis is consistent with these observations, revealing other ocular surgery as another risk factor for over-reporting PRP (OR: 3.84, $p=0.003$).

The reasons for under-reporting are less clear. Several of these subjects had both PRP and FP, and appear to simply have reported only one laser treatment type, (OR for under-reporting PRP: 7.76, $p=0.006$; OR for under-reporting FP: 64.27, $p<0.0001$). Not surprisingly, additional analyses revealed that subject reporting of any laser treatment for diabetic retinopathy combining PRP and FP had a higher validity ($\kappa=0.87$) than PRP (0.80) or FP alone (0.78). The other subjects who under-reported appear to simply not have remembered the event, which is surprising as one can envision ocular laser treatment being a seminal event for an individual. The relative brevity and mildness of FP could have contributed to this lack of subject recall but it is surprising for PRP, which tends to require a longer, more intense treatment. In the Los Angeles Latino Eye Study a multivariate analysis did not identify any factors significantly associated with inaccurate subject reporting although the sensitivity decreased the longer the interval from the last reported eye examination.¹⁴

In summary, in the EDIC type 1 diabetes cohort, we found subject reporting of prior PRP or FP to be relatively accurate, compared with fundus photograph grading. It will be important to determine if these results are similar for more generalized subject cohorts, since such a finding may have implications for the future use of subject report data for phenotypic stratification of type 1 diabetes subjects with diabetic retinopathy or for the clinical assessment of diabetic patients by non-ophthalmic health care providers.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 2
Cross-tabulation of Self-Report vs. Photography Grading of Pan-retinal, Focal and Any Photocoagulation in EDIC

Pan-retinal Photocoagulation (PRP) N=1303 [*] -7 ^{**} =1296	Photography Grading		
	No	Yes	Total
Subject reporting			
No	1121 (86.5%)	13 (1.0%)	1134 (87.5%)
Yes	39 (3.0%)	123 (9.5%)	162 (12.5%)
Total	1160 (89.5%)	136 (10.5%)	1296 (100%)
Focal Photocoagulation (FP) N=1322 [†] -31 ^{††} =1291			
	Photography Grading		
	No	Yes	Total
Subject reporting			
No	1202 (93.1%)	20 (1.6%)	1222 (94.7%)
Yes	12 (0.9%)	57 (4.4%)	69 (5.3%)
Total	1214 (94.0%)	77 (6.0%)	1291 (100%)
Any Photocoagulation (PRP and/or FP) N=1363 [‡] -5 ^{‡‡} =1358			
	Photography Grading		
	No	Yes	Total
Subject reporting			
No	1151 (84.8%)	14 (1.0%)	1165 (85.8%)
Yes	28 (2.1%)	165 (12.2%)	193 (14.2%)
Total	1179 (86.8%)	179 (13.2%)	1358 (100%)

Epidemiology of Diabetes Interventions and Complications Study (EDIC). Diabetes Control and Complications Trial (DCCT). Number (N)

^{*} 1303 subjects were based on Figure 1, obtained as the original 1441 DCCT participants less 36 subjects who underwent PRP during the DCCT (10 in intensive and 26 in conventional group), 49 subjects with no photo collection in EDIC, and 54 who reported PRP at the last visit without subsequent photos.

^{**} 7 subjects had ungradable (n=4) photos or questionable PRP (n=3)

[†] 1322 subjects were based on Figure 2, obtained as the original 1441 DCCT participants less 51 subjects who underwent focal photocoagulation during the DCCT, 48 subjects with no photo collection in EDIC, and 20 who reported focal photocoagulation at the last visit without subsequent photos.

^{††} 31 subjects had ungradable photos (n=5) or questionable FP (n=26).

*1363 subjects had pan-retinal and/or focal photocoagulation.

**5 subjects had ungradable or questionable PRP or FP.

Table 3

Comparison of Subject Self-Report versus the Fundus Photography Assessment of Pan-retinal or Focal Photocoagulation in EDIC

	Type of Photocoagulation		Any Photocoagulation (Pan-retinal or Focal)
	Pan-retinal Photocoagulation (PRP)	Focal Photocoagulation (FP)	
N	1296	1291	1358
Proportion of PRP or FP based on fundus photo grading	10.5%	6.0%	14.2%
Proportion of PRP or FP based on subject reporting	12.5%	5.3%	13.2%
Overall Agreement %	96.0%	97.5%	96.9%
Kappa *	0.80	0.78	0.87
Sensitivity (reported +/graded +)	90.4%	74.0%	85.5%
Specificity (reported -/graded -)	96.6%	99.0%	98.8%
False Positive Rate (reported +/graded -)	3.4%	1.0%	1.2%
False Negative Rate (reported -/graded +)	9.6%	26.0%	14.5%
Positive Predictive Value (graded +/reported +)	75.9%	82.6%	92.2%
Negative Predictive Value (graded -/reported -)	98.9%	98.4%	97.6%

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* Cohen's kappa is calculated as the ratio of the difference between the overall agreement and the percent agreement expected by chance alone to 1 minus the latter.

Table 4
Summary of Subject Misreporting versus Pan-retinal Photocoagulation (PRP) or Focal Photocoagulation (FP)

	Pan-retinal Photocoagulation	Total N N=52 (100%)	Focal Photocoagulation	Total N N=32 (100%)
Misreported Photocoagulation		52		32
	1. Subject False Positive	39(75%)	1. Subject False Positive	12(38%)
	a. High risk characteristics (ETDRS>71) possibly had laser after (self reported yes, no PRP scar)	3	a. High risk characteristics for PDR (ETDRS>71) and clinically significant macular edema, no PRP or FP scar	1
	b. Focal scar, no PRP scar	19	b. PRP Scar	7
	c. Questionable focal scars, no PRP scar.	3	c. No scar, no other ocular surgeries.	4
	d. No scar but with other ocular surgeries	4		
	e. No scar, no other ocular surgeries	10		
	2. Subject False Negative	13(25%)	2. Subject False Negative	20(62%)
	a. PRP scar	10	a. Focal scar	9
	b. PRP and focal scars ***	3	b. Focal and PRP scars †	11

*** Among the 3 subjects with PRP false negative, 2 reported FP and 1 did not report FP.

† Among the 11 with FP false negative, 9 reported PRP and 2 did not report PRP. Early Treatment Diabetic Retinopathy Study (ETDRS). Proliferative Diabetic Retinopathy (PDR).

Table 5

Multivariate Logistic Model of Risk Factors for Subject Over- and Under-reporting of Pan-retinal Photocoagulation (PRP) or Focal Photocoagulation (FP)

Risk Factors	Over-reporting of PRP (Event N=39)		Under-reporting of PRP (Event N=13)		Over-reporting of FP (Event N=12)		Under-reporting of FP (Event N=20)	
	Odds Ratio	P value	Odds Ratio	P value	Odds Ratio	P value	Odds Ratio	P value
Age at EDIC baseline	1.01 (0.96, 1.07)	0.74	1.02 (0.93, 1.11)	0.73	1.04 (0.94, 1.15)	0.42	1.01 (0.93, 1.09)	0.89
Male vs. Female	0.89 (0.42, 1.90)	0.77	2.09 (0.61, 7.24)	0.24	0.90 (0.27, 3.06)	0.87	1.19 (0.43, 3.30)	0.74
Intensive vs. Conventional Control	0.88 (0.42, 1.88)	0.75	1.21 (0.37, 4.01)	0.75	2.55 (0.72, 8.94)	0.87	0.56 (0.19, 1.61)	0.28
Secondary vs. Primary Cohort	0.67 (0.31, 1.41)	0.29	4.50 (0.95, 21.45)	0.06	0.75 (0.17, 3.25)	0.70	1.20 (0.43, 3.35)	0.73
Secondary or lower Education vs. College	1.05 (0.48, 2.29)	0.91	2.98 (0.85, 10.43)	0.09	0.80 (0.21, 3.08)	0.75	0.89 (0.29, 2.75)	0.83
Insured years in EDIC	0.98 (0.89, 1.08)	0.67	1.02 (0.88, 1.18)	0.80	0.91 (0.80, 1.04)	0.17	1.00 (0.89, 1.12)	0.99
History of FP with no PRP	34.94 (15.75, 77.50)	<.0001	n/a	n/a	n/a	n/a	37.8 (11.8, 118.8)*	<.0001
History of PRP with no FP	n/a	n/a	41.0 (9.0, 185.5)**	<.0001	43.33 (9.02, 208.23)	<.0001	n/a	n/a
History of PRP and FP	n/a	n/a	7.76 (1.78, 33.82)**	0.006	n/a	n/a	64.27 (21.81, 189.42)*	<.0001
Any Ocular Surgery	3.84 (1.60, 9.23)	0.003	1.09 (0.22, 5.33)	0.92	0.98 (0.22, 4.45)	0.98	1.10 (0.31, 3.84)	0.88

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* Odds ratio for History of FP with no PRP and for History of PRP and FP were from two separate models adjusting for other factors. The two covariates cannot be included in the same model simultaneously because those with a history of PRP and FP cannot have a history of FP with no PRP.

** Odds ratio for History of PRP with no FP and for History of PRP and FP were from two separate models adjusting for other factors. The two covariates cannot be included in the same model simultaneously because those with a history of PRP and FP cannot have a history of PRP with no FP.