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Retinopathy During the First 5 Years of Type 1 Diabetes and Subsequent Risk of Advanced Retinopathy

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INDIVIDUALS WITH ANY SIGN OF RETINOPATHY WITHIN THE FIRST 5 YEARS OF TYPE 1 DIABETES ONSET MAY BE AT HIGHER RISK OF LONG-TERM DEVELOPMENT OF ADVANCED DIABETIC RETINOPATHY

- **Current eye examination guidelines recommend an initial comprehensive dilated eye examination or validated retinal imaging evaluation within the first 5 years of type 1 diabetes (T1D).**
- **We investigated whether individuals with T1D who develop any retinopathy prior to 5 years' duration have an increased subsequent risk of advanced retinopathy.**
- **Diabetic retinopathy (DR) was assessed longitudinally using standardized stereoscopic seven-field fundus photography at time intervals of 6 months to 4 years.**
- **Early-onset DR (EDR) was defined as onset prior to 5 years of T1D duration. Cox proportional hazards models assessed the associations of EDR with subsequent risk of outcomes.**
- **In unadjusted models, EDR was associated with an increased risk of proliferative DR ($P = 0.006$), clinically significant macular edema ($P = 0.008$) and diabetes-related retinal photocoagulation ($P = 0.006$).**
- **Only the association with proliferative DR remained significant ($P = 0.028$) after adjustment for glycemic (HbA_{1c}) and nonglycemic (e.g., age, duration of T1D, blood pressure) factors.**

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ARTICLE HIGHLIGHTS

- Current eye examination guidelines recommend an initial comprehensive dilated eye examination or validated retinal imaging evaluation within 5 years of diagnosis of type 1 diabetes (T1D).
- We investigated whether individuals with T1D who develop any retinopathy prior to 5 years of diabetes duration (early diabetic retinopathy [DR]) have an increased subsequent risk of advanced retinopathy.
- Individuals with early DR had an increased subsequent risk of proliferative DR, even adjusted for glycemic (HbA_{1c}) and nonglycemic (e.g., age, duration of T1D, blood pressure) factors.
- Individuals with any sign of retinopathy within the first 5 years of T1D onset may be at higher risk of long-term development of advanced DR.

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OBJECTIVE

To determine whether individuals with type 1 diabetes (T1D) who develop any retinopathy at any time prior to 5 years of diabetes duration have an increased subsequent risk for further progression of retinopathy or onset of proliferative diabetic retinopathy (PDR), clinically significant macular edema (CSME), diabetes-related retinal photocoagulation, or anti-vascular endothelial growth factor injections. Additionally, to determine the influence of HbA_{1c} and other risk factors in these individuals.

RESEARCH DESIGN AND METHODS

Diabetic retinopathy (DR) was assessed longitudinally using standardized stereoscopic seven-field fundus photography at time intervals of 6 months to 4 years. Early-onset DR (EDR) was defined as onset prior to 5 years of T1D duration. Cox models assessed the associations of EDR with subsequent risk of outcomes.

RESULTS

In unadjusted models, individuals with EDR (*n* = 484) had an increased subsequent risk of PDR (hazard ratio [HR] 1.51 [95% CI 1.12, 2.02], *P* = 0.006), CSME (HR 1.44 [1.10, 1.88], *P* = 0.008), and diabetes-related retinal photocoagulation (HR 1.48 [1.12, 1.96], *P* = 0.006) compared with individuals without EDR (*n* = 369). These associations remained significant when adjusted for HbA_{1c}, but only the association with PDR remained significant after adjustment for age, duration of T1D, HbA_{1c}, sex, systolic/diastolic blood pressure, pulse, use of ACE inhibitors, albumin excretion rate, and estimated glomerular filtration rate (HR 1.47 [95% CI 1.04, 2.06], *P* = 0.028).

CONCLUSIONS

These data suggest that individuals with any sign of retinopathy within the first 5 years of T1D onset may be at higher risk of long-term development of advanced DR, especially PDR. Identification of early-onset DR may influence prognosis and help guide therapeutic management to reduce the risk of future visual loss in these individuals.

Diabetic retinopathy (DR) can progress to severe sight-threatening complications in both type 1 and type 2 diabetes. However, the time of onset, rate of progression, and extent of visual loss can vary widely. The Diabetes Control and Complications Trial (DCCT) (1) demonstrated the role of treatment to improve glycemic control

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**A complete list of members in the DCCT-EDIC Research Group is presented in the supplementary material online.*

See accompanying article, p. 678.

(as assessed by HbA_{1c}) on the onset and progression of DR (2). The dominant role of HbA_{1c} on the risk of more advanced retinopathy outcomes was then confirmed in the combined follow-up of the DCCT and its observational follow-up study, the Epidemiology of Diabetes Interventions and Complications (EDIC) (3).

The extent to which onset of DR prior to 5 years of diabetes duration is associated with increased risk of subsequent worsening to advanced DR has not been well elucidated but may be important since current eye care guidelines do not require annual eye examinations in individuals with type 1 diabetes (T1D) prior to 5 years' duration (4). In this study, we analyzed data collected during 37 years of the DCCT/EDIC studies to test the hypothesis that individuals with T1D with photographic evidence of microvascular abnormalities at any time prior to 5 years of diabetes duration (early DR [EDR] group) have a greater subsequent risk of progressing to advanced retinopathy than individuals with no photographic evidence of retinopathy prior to 5 years of T1D duration (no early DR [NEDR] group). We also tested whether known glycemic and nonglycemic risk factors explain any of the findings. The outcomes evaluated included development of proliferative DR (PDR), two- and three-step DR severity progression, onset of clinically significant macular edema (CSME), application of laser photocoagulation or anti-vascular endothelial growth factor (VEGF) injections for DR/CSME, and ocular surgery in the DCCT/EDIC cohort.

RESEARCH DESIGN AND METHODS

Participants

The DCCT and EDIC protocols were approved by the institutional review boards of all participating clinical centers. The methods of DCCT and EDIC have been previously described in detail (5,6). Briefly, the DCCT enrolled 1,441 participants with T1D into the primary prevention cohort (n = 726), comprising those with 1 to 5 years' diabetes duration, no retinopathy based on fundus photography, and $<$40 mg/24 h of urinary albumin excretion, or the secondary intervention cohort (n = 715), comprising those with 1 to 15 years' diabetes duration, early to mild non-PDR, and $<$200 mg/24 h of urinary albumin excretion at DCCT baseline.

Participants were randomized to receive intensive therapy (INT, n = 711) or conventional therapy (CON, n = 730) to assess the impact of glycemia on the onset and progression of diabetes-related outcomes. INT therapy was aimed at lowering glycemic levels to as close to nondiabetic levels as safely possible. In contrast, the goal of CON therapy was the absence of symptoms of hypo- or hyperglycemia without specific glucose targets. The DCCT ended in 1993 after an average of 6.5 years of follow-up, and all participants were taught INT therapy and referred to their health providers for future diabetes care. In 1994, 96% of the surviving DCCT cohort enrolled in the EDIC observational follow-up study, and 92% of the surviving cohort continues to actively participate after $>$25 years of additional follow-up.

Retinopathy and Biomedical Evaluations

Retinopathy was assessed using standardized, stereoscopic, seven-field fundus photography every 6 months during the DCCT, every 4th year during EDIC (staggered from the start of the EDIC follow-up), and in addition, all participants were assessed at EDIC years 4 and 10. Photographs were graded by a central reading center using the Early Treatment of Diabetic Retinopathy Study (ETDRS) scale (7). Graders were masked to treatment group assignment, measures of glycemic control, or presence of other diabetes complications.

Risk factors for advanced retinopathy were assessed using standardized methods in DCCT and EDIC (3). HbA_{1c} was measured using high-performance liquid chromatography quarterly in DCCT and annually in EDIC. The albumin excretion rate (AER) was measured annually in DCCT and every other year in EDIC. The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, with serum creatinine levels (collected annually), and age, sex, and race (8). Systolic and diastolic blood pressure (BP) and pulse rate were recorded during the annual medical history and physical examination. Medication use was recorded during EDIC. ACE inhibitors or angiotensin II receptor blockers (ARBs) were not used during DCCT and were not considered during baseline analyses.

Early Retinopathy

Participants who had $<$5 years of diabetes duration at DCCT randomization were included in this study (n = 853) and were separated into groups determined by photographic evidence of any retinopathy obtained by DCCT on one or more occasions at any time prior to 5 years of diabetes duration. The NEDR group included participants without any photographic evidence of microvascular retinal abnormalities at any time prior to reaching 5 years duration (n = 369), and the EDR group included participants with photographic evidence of retinal microvascular abnormalities at any point before 5 years of diabetes duration (n = 484). Median follow-up time was 29.1 years for the EDR group and 29.6 years for the NEDR group.

Retinopathy Outcomes

Retinopathy progression was based on the further progression in the participant's ETDRS score starting after 5 years of diabetes duration (1). More specifically, further two-step (three-step) progression was defined as sustained increases of two (three) or more levels in the participant's ETDRS score. PDR was defined as the presence of neovascularization seen on fundus photographs, the presence of panretinal photocoagulation, or the presence of vitreous hemorrhage (3). CSME was defined as evidence of macular thickening on fundus photography or an increase in central retinal thickness as measured by Spectralis spectral domain optical coherence tomography (starting with EDIC year 26) (3). DR-related therapy was defined as the use of any panretinal or focal retinal photocoagulation, or self-reported receipt of anti-VEGF injections (9). Ocular surgery was defined as a composite outcome including cataract extraction, vitrectomy, and/or retinal detachment surgery, glaucoma-related surgery (including laser treatment, filtering surgery, cyclocryotherapy, or other operative procedures to lower intraocular pressure), cornea- or lens-related surgery (including corneal transplant or yttrium aluminum garnet laser posterior capsulotomy), or enucleation (10).

Statistical Methods

For each participant, the initial time point (i.e., time 0 for the time-to-event models) for these analyses was the closest visit prior to 5 years duration of T1D. Separately for each of the early

retinopathy groups (EDR and NEDR), the characteristics at that 5-year period are described using mean (SD) for continuous variables and percentages for discrete variables, while the advanced retinopathy outcomes are described using the number and rate of events. The prevalence of early retinopathy was defined as the presence of DR at any time prior to 5 years duration of T1D. Kaplan-Meier curves describe the cumulative incidences for each of the retinopathy outcomes (i.e., further two- and three-step progression, PDR, CSME, ocular surgery, and DR-related therapy).

Separately for each outcome, Cox proportional hazard (PH) models assessed the association between early retinopathy status prior to 5 years of diabetes (i.e., EDR vs. NEDR) and the subsequent risk of advanced retinopathy. Models were unadjusted, minimally adjusted for mean updated HbA_{1c}, or fully adjusted for the risk factors identified previously in this cohort (current age, current duration of T1D, mean updated HbA_{1c}, sex, DCCT treatment group, cohort, mean updated systolic BP, mean updated diastolic BP, pulse, use of ACE inhibitors, AER, and eGFR) (3). Except for sex and the original DCCT treatment group and cohort, all covariates included in the model were time varying. Mean updated risk factors, such as mean updated HbA_{1c}, were calculated as the time-weighted average from randomization up to a given visit, with weights proportional to the length of time between evaluations. Interaction terms assessed whether the effect of glycemia on the retinopathy outcomes was heterogeneous across the EDR groups.

Owing to the exploratory nature of our analyses, no adjustment for multiplicity was conducted, and P values <0.05 were considered nominally significant.

Data and Resource Availability

Data collected for the DCCT/EDIC study through 30 June 2017 are available to the public through the NIDDK Central Repository (https://repository.niddk.nih.gov/studies/edic/). Data collected in the current cycle (July 2017–June 2022) will be available within 2 years after the end of the funding cycle.

RESULTS

This study evaluated the 853 DCCT/EDIC participants who had <5 years of diabetes duration at DCCT randomization with subsequent retinopathy evaluations (n = 711 from the primary prevention cohort, and n = 142 from the secondary intervention cohort). The EDR group consisted of 484 participants (57%) with retinopathy documented photographically prior to 5 years of T1D duration. Participants in the EDR group were evaluated an average of 4.8 times before 5 years' T1D duration, compared with 5.6 times among the NEDR group. On average, retinopathy was first observed in the EDR group ~3.4 years (median 3.6 [quartile 1, 2.7; quartile 3, 4.3] years) after T1D diagnosis.

Participant Characteristics and Event Rates by EDR Status

The participant characteristics at the 5-year T1D duration time point are described in Table 1*A*, separately by the presence or absence of retinopathy prior to 5 years of T1D duration. Briefly, compared with the participants in the EDR group, the participants in the NEDR group were less likely to be ≥18 years of age (88.3% in the NEDR group vs. 93.8% in the EDR group; P = 0.005), had lower systolic BP (111.8 ± 11.2 mmHg vs. 114.8 ± 11.6 mmHg in the NEDR and EDR groups, respectively; $P < 0.001$), and had lower diastolic BP (72.2 ± 8.3 mmHg vs. 73.9 ± 8.3 mmHg in the NEDR and EDR groups, respectively; P = 0.003). Other covariates were similar between groups. Participants with NEDR and EDR had mean updated HbA_{1c} levels of 8.2 ± 1.4% and 8.3 ± 1.5%, respectively. Of note, the NEDR group consisted solely of participants without retinopathy prior to 5 years' duration and were, therefore, by study design all from the original DCCT primary prevention cohort. Participants with EDR were from the primary (70.7%) or secondary cohort (29.3%).

Table 1*B* shows the number and rates of subsequent retinopathy complications separately by DR group (i.e., NEDR vs. EDR). Long-term ocular complication rates were generally lower in the NEDR group compared with the EDR group. In the NEDR group, PDR developed in 70 participants compared with 124 in

Table 1—Characteristics at the last evaluation prior to 5 years of T1D duration (*A*) and outcomes (*B*) by NEDR vs. EDR group

	NEDR group (n = 369)	EDR group (n = 484)	P value*
A: Characteristics			
Age (years)	29.3 ± 8.0	29.9 ± 7.3	0.419
Adult (≥18 years of age)	88.3	93.8	**0.005**
Female sex	49.6	43.0	0.055
Intensive group	47.4	48.8	0.699
Primary cohort	100	70.7	**<0.001**
Systolic BP (mmHg)	112 ± 11	115 ± 12	**<0.001**
Diastolic BP (mmHg)	72 ± 8	74 ± 8	**0.003**
Pulse (bpm)	74 ± 11	75 ± 11	0.121
HDL cholesterol (mg/dL)	65 ± 20	63 ± 21	0.214
LDL cholesterol (mg/dL)	91 ± 33	91.1 ± 31	0.708
Total cholesterol (mg/dL)	171 ± 41	170 ± 37	0.682
Triglycerides (mg/dL)	76 ± 55	80.5 ± 58	0.159
AER (mg/24 h)	13 ± 14	14.2 ± 16	0.171
eGFR (mL/min/1.73 m^2)	121 ± 15	121.3 ± 14	0.444
HbA_{1c} (%)	8.2 ± 1.7	8.3 ± 1.8	0.434
Mean updated HbA_{1c} (%)	8.2 ± 1.4	8.3 ± 1.5	0.259
B: Outcomes			
Further two-step progression	297 (75.2)	392 (86.7)	0.106
Further three-step progression	245 (46.0)	317 (48.1)	0.564
PDR	70 (8.2)	124 (11.9)	**0.006**
CSME†	87 (10.7)	148 (14.8)	**0.008**
Ocular surgery	79 (8.1)	116 (9.4)	0.188
DR-related therapy	77 (8.2)	138 (11.8)	**0.006**

Data are presented as the percentage of participants or as the mean ± SD (*A*) or as the number of events (event rate per 1,000 patient-years) (*B*). *P values from Wilcoxon rank sum tests for quantitative characteristics and χ^2 tests for categorical characteristics (*A*) and unadjusted Cox PH models (*B*). Associations significant at level 0.05 are presented in bold. †CSME excludes one patient with CSME before diabetes duration >5 years.

the EDR group, representing a 45% increased risk (8.2 vs. 11.9 cases/1,000 patient-years). DR onset prior to 5 years was also associated with increased rates of CSME (38%), ocular surgery (16%), and two- and three-step DR severity progression (15% and 5%, respectively).

Table 2 shows the severity of DR present before and after the 5-year duration time point. Notably, only 82 participants (22%) with NEDR had any retinopathy (including microaneurysms, mild NPDR, or moderate NPDR) at the first visit after 5 years of T1D compared with 286 (59%) in the EDR group. Thus, 41% (=100% − 59%) of the EDR group had less DR at the first visit after 5 years duration of diabetes than they had documented at least at some point before that. This is consistent with the waxing and waning of mild retinopathy findings at these early diabetes durations. Indeed, the percentage of participants in the EDR group with DR present at the first visit after 5 years duration was actually 19% less than had been identified at this group's prior visit before 5 years, a finding resulting almost entirely among those with microaneurysms only. Consistent with the primary results of DCCT, of the 484 participants in the EDR group, the participants in the INT group were more likely to have no evidence of retinopathy at the first evaluation after 5 years duration than individuals from the CON group (114 of 236 [48%] vs. 84 of 248 [34%], $P = 0.002$) (data not shown).

EDR and Risk of Long-Term Outcomes

Kaplan-Meier cumulative incidence curves are presented separately for each advanced retinopathy outcome for the NEDR versus EDR groups (Fig. 1).

The interaction effects between any early retinopathy and the mean updated HbA_{1c} were not statistically significant for any of the outcomes (data not shown), suggesting that the association between HbA_{1c} and the subsequent risk of retinopathy outcomes does not differ between participants with versus without early retinopathy.

Associations between early retinopathy and advanced outcomes are reported in Table 3. Compared with the NEDR group, the EDR group had a higher risk for PDR in all models, with hazard ratios (HRs) ranging from 1.47 to 1.53. The risk of CSME was higher in the EDR group compared with the NEDR group in the unadjusted (HR 1.44 [95% CI 1.10, 1.88], $P = 0.008$) and the minimally adjusted (HR 1.38 [95% CI 1.06, 1.81], $P = 0.017$) models, but not in the fully adjusted models (HR 1.27 [95% CI 0.93, 1.72], $P = 0.126$). Likewise, the risk of treatment for DR was higher in the EDR group compared with the NEDR group in the unadjusted (HR 1.48 [95% CI 1.12, 1.96, $P = 0.006$) and minimally adjusted (HR 1.44 [95% CI 1.12, 1.96], $P = 0.010$) models, but not in the fully adjusted model (HR 1.34 [95% CI 0.97, 1.84], $P = 0.077$).

CONCLUSIONS

These results demonstrate that individuals who develop any photographic evidence of DR prior to 5 years of T1D duration (the EDR group) have a greater subsequent risk for developing PDR, CSME, and need for treatment for DR than individuals with no photographic evidence of DR prior to 5 years of T1D (NEDR group). These associations were independent of the original treatment assignment (INT vs. CON) and of the mean updated HbA_{1c} levels. However, only the association with PDR remained statistically significant after full adjustment for other risk factors, including current age, current duration of T1D, mean updated HbA_{1c}, sex, treatment group, cohort, mean updated systolic BP, mean updated diastolic BP, pulse, use of ACE/ARB inhibitors, AER, and eGFR. The need for DR treatment was significantly increased in participants with EDR compared with NEDR after adjustment for glycemia (mean updated HbA_{1c}) and approached statistical significance when adjusted for age, duration of T1D, mean updated HbA_{1c}, sex, treatment group, cohort, mean updated systolic BP, mean updated diastolic BP, pulse, use of ACE inhibitors, AER, and eGFR. Importantly, none of the associations with two- and three-step progression on the ETDRS scale were statistically significant, suggesting that the rate of worsening is similar between the two groups.

The updated mean HbA_{1c} levels were similar between NEDR and EDR, and there was no heterogeneity in the effect of HbA_{1c} on outcomes between these two groups. This suggests potential differences in susceptibility for cellular damage at the same degree of glycemia as a potential factor. A previous statistical analysis of the DCCT cohort showed that total glycemic exposure (as captured by the mean updated HbA_{1c}) accounts for only 11% of the reduction in retinopathy risk and suggests other factors, including genetic or metabolic factors other than glycemia, may influence the severity of DR (11). As presented in Table 2, 87% of DR prior to year 5 was microaneurysms only. Furthermore, 41% of participants with DR prior to 5 years duration had no DR at the first visit subsequent to 5 years duration, demonstrating the waxing and waning of microaneurysm presence in early DR. Thus, the initial DR severity difference at 5 years duration is unlikely to account for all of the observed outcome differences. The higher rate of development of advanced DR phenotypes, such as PDR or CSME, in the EDR group could be due to higher levels of VEGF or other angiogenic factors, an inflammatory milieu that is conducive to alteration of the blood-retinal barrier and angiogenesis, or other factors. Such factors might be relatively independent of HbA_{1c}, thus explaining the limited HbA_{1c} contribution observed in the study. Whether such a difference exists and whether it is due to genetic or epigenetic factors (12,13) needs further investigation.

A major strength of our study is the detailed phenotyping of a cohort of individuals with T1D over ~30 years of follow-up, with standardized measurements of established risk factors and

Table 2—Presence of retinopathy within the NEDR and the EDR groups at the first visit after reaching 5 years' T1D duration

	NEDR (n = 369)		EDR (n = 484)	
Retinopathy	Last visit prior	First visit after	Last visit prior	First visit after
No retinopathy	369	287	167	198
Microaneurysms only	0	71	277	239
Mild NPDR	0	10	32	40
Moderate NPDR	0	1	8	7

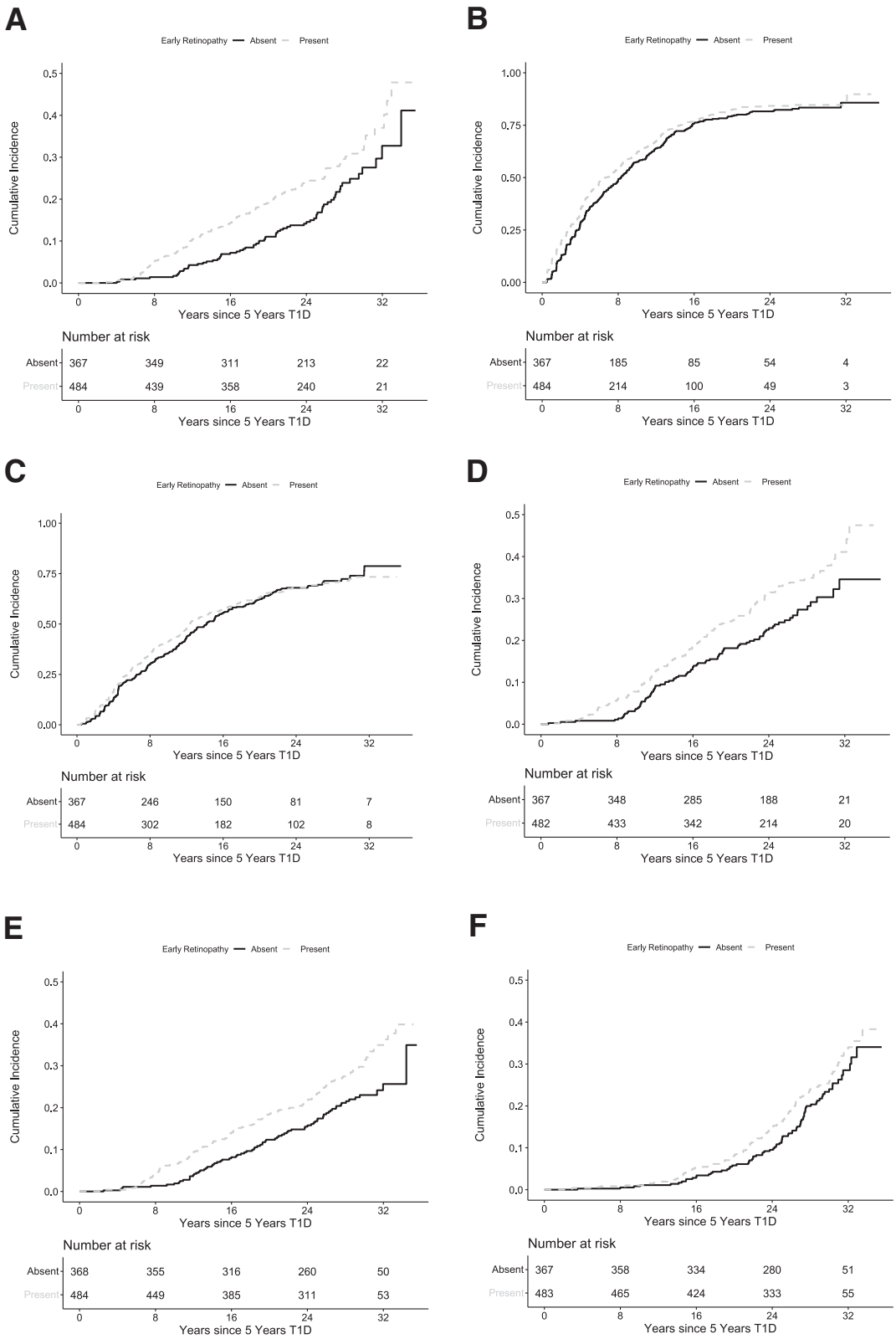

Figure 1—Cumulative incidence of DR outcomes by EDR vs. NEDR status. *A*: PDR ($P = 0.006$). *B*: Further two-step progression of DR ($P = 0.106$). *C*: Further three-step progression of DR ($P = 0.564$). *D*: CSME ($P = 0.008$). *E*: Receipt of DR-related therapy ($P = 0.006$). *F*: Ocular surgery ($P = 0.188$).

retinopathy outcomes. However, the DCCT/EDIC cohort is largely White, consistent with the ethnic distribution of T1D in the U.S., and these results need to be validated in different race/ethnicity groups and assessed against specific screening guidelines in those regions. In addition, the results were obtained in a cohort of highly motivated and highly

Table 3—Association between EDR and the risk of subsequent advanced retinopathy outcomes comparing EDR vs. NEDR

	Unadjusted		Adjusted for mean updated HbA_{1c}		Fully adjusted^	
EDR vs. NEDR	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
PDR	**1.51 (1.12, 2.02)**	**0.006**	**1.53 (1.14, 2.05)**	**0.004**	**1.47 (1.04, 2.06)**	**0.028**
Further progression						
Two-step	1.13 (0.97, 1.32)	0.106	1.09 (0.94, 1.27)	0.240	1.04 (0.87, 1.23)	0.669
Three-step	1.05 (0.89, 1.24)	0.564	1.03 (0.88, 1.22)	0.689	1.04 (0.86, 1.26)	0.656
CSME	**1.44 (1.10, 1.88)**	**0.008**	**1.38 (1.06, 1.81)**	**0.017**	1.27 (0.93, 1.72)	0.126
Ocular surgery	1.21 (0.91, 1.61)	0.188	1.20 (0.90, 1.60)	0.206	1.07 (0.77, 1.48)	0.684
DR-related therapy	**1.48 (1.12, 1.96)**	**0.006**	**1.44 (1.09, 1.91)**	**0.010**	1.34 (0.97, 1.84)	0.077

Associations significant at level 0.05 are presented in bold. ^Cox PH models adjusted for current age, current duration of T1D, mean updated HbA_{1c}, sex, treatment group, cohort, mean updated systolic BP, mean updated diastolic BP, pulse, use of ACE/ARB inhibitors, AER, and eGFR.

educated individuals participating in a demanding clinical trial, which may not reflect the general T1D population. It is important to note that the DCCT did not enroll participants at the time of diabetes diagnosis. Consequently, it is possible that some of the participants had undiagnosed DR prior to DCCT enrollment that cleared prior to study entry and remained absent prior to reaching 5 years duration of T1D. Such participants would be misclassified as NEDR. However, given that participants in the NEDR group had an average of 5.6 negative evaluations as part of the study before 5 years duration of T1D and that the first observed DR in the EDR group occurred after an average of 3.4 years duration, the probability of NEDR misclassification is likely to be low. Moreover, misclassifications are likely to bias the results toward the null (i.e., reduce the power to detect differences rather than increase the likelihood of a false-positive finding). In addition to DR status, the risk profile (e.g., HbA_{1c} levels) between T1D diagnosis and enrollment in DCCT is unknown. Finally, given the observational nature of this study, no adjustments for multiplicity were made, and therefore, the results should be interpreted with caution.

Conclusion

These data demonstrate that individuals with T1D who develop DR at any time prior to 5 years of diabetes duration have an increased risk of vision-threatening DR, including PDR, CSME, and the need for DR therapy, that is not totally dependent on glycemic levels. However, among those who developed evidence of DR at any point prior to 5 years, DR was only present at the first evaluation after the 5-year time point in 59%. These higher-risk patients therefore might have been missed by current eye examination guidelines that recommend an initial comprehensive dilated eye examination or validated retinal imaging evaluation within 5 years of T1D diagnosis but do not recommend annual evaluations (4). Thus, an annual eye examination initiated at the time of diabetes diagnosis, as currently suggested for patients with T2D, might be valuable for individuals with T1D.

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