Microvascular Complications

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Retinopathy
Prevalence of Diabetic Retinopathy in Type 1 Diabetes

Wisconsin Epidemiological Study of Diabetic Retinopathy: WESDR

DRS: Cumulative Rates of Severe Visual Loss From Proliferative Diabetic Retinopathy

Ophthalmology 1981;88:583-600
DRS High Risk Criteria Defining Need for Pan-Retinal Photocoagulation

- Neovascularization on the disc (NVD) > 25% disc diameter
Diabetic Retinopathy Study Standard Photograph 10A
Showing NVD Approximately 1/4 disc diameter
DRS High Risk Criteria Defining Need for Pan-Retinal Photocoagulation

- Neovascularization on the disc (NVD) > 25% disc diameter
- Neovascularization on the disc (NVD) associated with pre-retinal hemorrhage
- Neovascularization elsewhere (NVE) only if associated with pre-retinal hemorrhage
Standard Format for Pan-Retinal Argon Laser Photocoagulation
Cumulative Incidence of Severe Retinopathy in Childhood T1D According To Long-Term Glycemia

Nordwall et al. Ped Diab 2009;10:168-76
Cumulative Incidence of Laser-Rx’d DR in T1D with Onset Age < 15 Years, According To Year of Onset

Overall $p = 0.006$

Nordwall et al. Diabetologia 2004;47:1266-74
Cumulative Incidence of Laser Rx in Patients with T1D by Duration & Period of Diagnosis in FinnDiane Study.

Number at risk

Duration of diabetes (years)

Cumulative incidence of severe diabetic retinopathy (%)

<1975: 1,400 1,440 1,108 615 190
1975-79: 517 508 353 24
1980-84: 506 498 260
≥1985: 1,318 774 43

Diabetes Care 2011;34:2005-2007
Cumulative Incidence of Laser Rx in T1D in Different Quartiles of HbA1c Variability in the FinnDiane study

5-year incidence 19% highest quartile vs 10% lowest quartile
p<0.001
DCCT
A1c During DCCT

DCCT Intervention

Conventional – DCCT mean 9.1%

Intensive – DCCT mean 7.2%
DCCT Retinopathy Progression
Primary Prevention Cohort

Cumulative Incidence (%)

Years

p<0.001

Conventional Group

Intensive Group

DCCT. NEJM 1993; 329:977
DCCT Retinopathy Progression Secondary Intervention Cohort

DCCT. NEJM 1993; 329:977
Study Time Line of the DCCT/EDIC Study

National Commission
RFA
DCCT Planning
Feasibility
Recruitment

DCCT
10 years


DCCT end
EDIC start
EDIC
2005 2013

EDIC
20 years

A1c During DCCT & EDIC

DCCT Intervention

Conventional – DCCT mean 9.1%

Intensive – EDIC mean 8.0%

Intensive – DCCT mean 7.2%

EDIC Observation

Conventional – EDIC mean 8.0%

Intensive – EDIC mean 8.0%

Study year

Glycated Hemoglobin (Percent)

Further Three-step Progression of Retinopathy From DCCT Close-out through EDIC Year 8

Risk reduction with intensive therapy: 63%
p < .0001

JAMA 2002; 287:2563-2569
Clinic vs ‘Real-world’ Data: Incidence of Proliferative Retinopathy (DCCT-EDIC/EDC)

Cumulative incidence of proliferative retinopathy or worse

Nephropathy
Renal Biopsies:
Normal Glomerulus & Diabetic Nephropathy
Prevalence of Microalbuminuria in Children with T1D, in Relation to Mean Lifetime HbA₁c

Incidence Rate of End-stage Renal Disease According To Time Period of Diagnosis of Type 1 Diabetes


Finland

Incidence Rate, Cases Per 1000 Patients (years)

Years After Diagnosis of Type 1 Diabetes

Period of Diagnosis of Type 1 Diabetes
- 1965-1969
- 1970-1974
- 1975-1979
- 1980-1999

Cumulative incidence of diabetic nephropathy in type 1 diabetes

Hovind et al. Diabetes Care 2003;26:1258–1264
Cumulative Incidence of Nephropathy Among Patients In Whom T1D Began Before Age 15 Years, According To Year of Onset

Overall $p<0.001$

Cumulative Incidence of Overt Nephropathy In Childhood T1D According To Long-Term Glycemic Control

DCCT: Microalbuminuria & Macroalbuminuria
Primary Prevention Cohort

Microalbuminuria
> 40 mg/24 h

Albuminuria
≥ 300 mg/24 h

Conventional
Intensive

P= 0.4
P< 0.04

DCCT: Microalbuminurina and Macroalbuminurina Secondary Intervention Cohort

Microalbuminurina ≥ 40 mg/24 h

P = 0.001

Conventional
Intensive

Albuminurina ≥ 300 mg/24 h

P = 0.01

Nephropathy defined as albumin excretion rate \( \geq 300 \text{ mg/24 h} \), serum Cr \( \geq 2 \text{ mg/dl} \), dialysis or renal transplant

Clinic vs ‘Real-world’ Data: Incidence of Nephropathy (DCCT-EDIC/EDC)

Nephropathy defined as albumin excretion rate \( \geq 300 \text{ mg/24 h} \), serum Cr \( \geq 2 \text{ mg/dl} \), dialysis or renal transplant

Diabetic Nephropathy and Mortality in Patients with Type 1 Diabetes

![Graph showing adjusted survival with different albuminuria stages over duration of follow-up.](image)

The FinnDiane Study

- Macroalbuminuria
- Microalbuminuria
- Normoalbuminuria

Groop et al. Diabetes 2009; 58, 1651-1658
Diabetic Nephropathy and Mortality in Patients with Type 1 Diabetes

The FinnDiane Study

Groop et al. Diabetes 2009; 58, 1651-1658
Pittsburgh EDC 20-yr Mortality Risk in T1D Related to Renal Disease

Unadjusted Survival (%)

Duration of follow-up (years) (%)

Normal
MA
ON
ESRD

Orchard et al. Diabetologia 2010;53:2312-19
Pittsburgh EDC 20-yr Mortality Risk in T1D Related to Renal Disease

Adjusted Hazard Ratio
SMR

Orchard et al. Diabetologia 2010;53:2312-19
Improved Outcomes

Gregg EW et al. NEJM. 2014;370:1514-23.
Change in 8-year Incidence of Major Diabetes Outcomes by Diagnosis Cohort – Pittsburgh Epidemiology Study

Year of T1D diagnosis

% Incidence

- T1D-related death
- CAD
- ESRD
- Blindness
- Cerebrovascular
- Amputation

Diabetes Care 2013;36:3999-4006