Nephropathy

DIABETES

Risk of ESRD low in women and young people

Readability	✓✓✓✓
Applicability to practice	✓✓
WOW! factor	✓✓✓✓

1 The authors of this study aimed to estimate the cumulative risk of developing end-stage renal disease (ESRD) due to diabetic nephropathy, and to specifically study the effects of sex and age at onset.

2 A large population-based cohort with T1D in Sweden was selected from validated research registers linked to the Swedish Renal Registry, which collects data on people who receive active uremia treatment.

3 A total of 11 681 people with a duration of T1D ≥13 years were included.

4 After a median follow-up period of 20 years, 127 people had developed ESRD due to diabetic nephropathy.

5 At 30 years, the cumulative incidence of T1D was low (4.1%; 95% confidence interval [CI], 3.1–5.3 with a male predominance (2.5%; 95% CI, 1.7–3.5).

6 In both men and women, the lowest risk of developing ESRD was associated with T1D onset before 10 years of age. Men diagnosed between the ages of 20 and 34 years had the highest risk of developing ESRD (hazard ratio, 3.0; 95% CI, 1.5–5.7) and women whose diabetes was diagnosed between the ages of 20 and 34 years carried a similar risk to those diagnosed before 10 years of age.

7 The authors concluded that the cumulative risk of ESRD is low in young people with T1D in Sweden and there is a large difference in risk between men and women.

Möllsten A, Svensson M, Waernbaum I et al (2010) Cumulative risk, age at onset, and sex-specific differences for developing end-stage renal disease in young patients with type 1 diabetes: a nationwide population-based cohort study. *Diabetes* **59**: 1803–8

Low cumulative incidence of ESRD due to nephropathy among people with type 1 diabetes in Sweden

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Epidemiological studies in the 1980s first reported changes in the natural history of diabetic nephropathy in type 1 diabetes, with earlier estimates of a cumulative incidence of nephropathy exceeding 40%, falling to around 25% in later time cohorts (Krolewski et al, 1985).

Further changes in the epidemiology of type 1 diabetes have emerged since – most notably, the rise in the incidence of the condition occurring in children at a younger age. Despite this observation, the cumulative incidence of diabetic nephropathy in type 1 diabetes appears to be continuing to fall, with recent estimates from Finland reporting a cumulative incidence of end-stage renal disease (ESRD) below 10% at 30 years' diabetes duration (Finne et al, 2005), and with a longer duration from the onset of diabetes to both development of nephropathy and ESRD. Although single-figure incidence of nephropathy at 30 years was seen in the intensive-treatment arm of the DCCT/EDIC (Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications), participants in the conventional arm still had a cumulative incidence of 25% (DCCT/EDIC Research Group et al, 2009).

Sweden has one of the highest incidences of childhood diabetes in the world, and a study from combined Swedish registry data for young people with diabetes onset since 1977 (Möllsten et al, 2010; summarised alongside), provides us with a comprehensive view of diabetic nephropathy in that country.

The authors report a strikingly low cumulative incidence of ESRD – only 3.3% at 30 years of type 1 diabetes duration. Peak incidence was again confirmed between 15 and 25 years' duration and was greater in men, particularly those with diabetes onset at 20–34 years of age. Earlier findings of a reduced risk for people diagnosed below the age of 10 years were confirmed, but the observation of relative protection for women over 20 years of age at onset is novel.

> *"It is encouraging that modern diabetes care appears to be capable of exerting a significant impact on one of the most severe complications of diabetes."*

The reasons for the falling and low incidence presumably reflect improvements in both blood glucose and blood pressure control. Möllsten et al remind us that mean HbA_{1c} levels in Sweden have fallen from 8.5% (69 mmol/mol) to 8.1% (65 mmol/mol) between 1996 and 2005. It is encouraging that modern diabetes care appears to be capable of exerting a significant impact on one of the most severe complications diabetes.

Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Research Group, Nathan DM, Zinman B et al (2009) Modern-day clinical course of type 1 diabetes mellitus after 30 years' duration: the diabetes control and complications trial/epidemiology of diabetes interventions and complications and Pittsburgh epidemiology of diabetes complications experience (1983–2005). *Arch Intern Med* **169**: 1307–16

Finne P, Reunanen A, Stenman S et al (2005) Incidence of end-stage renal disease in patients with type 1 diabetes. *JAMA* **294**: 1782–7

Krolewski AS, Warram JH, Christlieb AR et al (1985) The changing natural history of nephropathy in type I diabetes. *Am J Med* **78**: 785–94

"This study demonstrated a dose-response relationship between serum uric acid and risk of early glomerular filtration rate loss in people with T1D."

DIABETES CARE

High serum uric acid associated with early renal function loss

Readability	✓✓✓✓
Applicability to practice	✓✓
WOW! factor	✓✓✓

1 A cross-sectional association between serum uric acid and reduced glomerular filtration rate (GFR) has previously been identified in non-proteinuric people with T1D.

2 The authors of this study prospectively investigated whether baseline uric acid impacts the risk of early GFR loss.

3 A total of 355 people with elevated urinary albumin excretion were followed for 4–6 years for changes in urinary albumin excretion and GFR. Multiple determinations of serum cystatin C (GFRcystatin) and albumin:creatinine ratios (ACRs) were used to estimate the changes.

4 Baseline median values for uric acid, ACR and GFRcystatin were 4.6 mg/dL, 26.2 mg/g and 129 mL/min/1.73 m^2, respectively.

5 After 6 years of follow-up, a significant association between serum uric acid and development of early GFR loss was observed ($P<0.0002$), defined as GFRcystatin decline exceeding 3.3% per year.

6 The risk of early GFR loss increased linearly with increasing baseline uric acid concentrations. This increase corresponded to an odds ratio of 1.4 (95% confidence interval, 1.1–1.8) per 1 mg/dL increase of uric acid.

7 This study demonstrated a dose-response relationship between serum uric acid and risk of early GFR loss in people with T1D. The authors suggest that further investigation will determine whether uric acid-lowering drugs can reduce renal function decline.

Ficociello LH, Rosolowsky ET, Niewczas MA et al (2010) High-normal serum uric acid increases risk of early progressive renal function loss in type 1 diabetes: results of a 6-year follow-up. *Diabetes Care* **33**: 1337–43

DIABETES CARE

Novel assay for measurement of serum metformin

Readability	✓✓✓✓
Applicability to practice	✓✓
WOW! factor	✓✓✓

1 Treatment with metformin in people with T2D and impaired renal function can sometimes be complicated by lactic acidosis.

2 A new assay has been developed to measure trough levels of metformin in serum and the variation of levels in different individuals.

3 New technologies have been combined in the development of the new assay: liquid chromatography-tandem mass spectrometry (LCMSMS) and hydrophilic interaction liquid chromatography.

4 A total of 137 people (99 men; median age 60 years) with T2D and varying renal function had their serum metformin level measured once by LCMSMS.

5 Measurements were also taken at 0, 2, 4 and 8 weeks in 20 people (16 men) with an estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73 m^2.

6 Participants with an eGFR >60, 30–60 and <30 mL/min/1.73 m^2 had median trough metformin concentrations of 4.5, 7.71 and 8.88 µmol/L, respectively.

7 The median intra-individual overall coefficient of variation was 29.4% (range, 9.8–74.2).

8 The LCMSMS technique was found to be useful for determining serum metformin levels in people with impaired renal function treated with metformin. Few participants had values >20 µmol/L.

Frid A, Sterner GN, Löndahl M et al (2010) Novel assay of metformin levels in patients with type 2 diabetes and varying levels of renal function: clinical recommendations. *Diabetes Care* **33**: 1291–3

J HYPERTENSION

Safety and efficacy of routine BP-lowering in older people

Readability	✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 The authors assessed the efficacy and safety of routine blood pressure lowering to prevent major clinical outcomes in older people with T2D, using data from the ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron-MR Controlled Evaluation) trial.

2 A total of 11 140 people with T2D (age, ≥55 years) were randomly assigned to perindopril–indapamide or placebo. There were 4527 people aged <65 years, 5605 aged 65–74 years and 1008 aged >75 years. The primary outcome was a composite of major macrovascular or microvascular disease.

3 The primary outcome was major macrovascular disease, death and renal events across all age groups.

4 Participants were followed for a mean of 4.3 years; 1799 (16.1%) people experienced a primary outcome.

5 Similar relative risk reductions were produced by active treatment for the primary outcome, major macrovascular disease, death and renal events across all age groups.

6 Active treatment was estimated to prevent one primary outcome event in every 21 people >75 years of age, 71 people 65–74 years of age and 118 in people <65 years.

7 Similar patterns of benefit were observed for secondary outcomes (i.e. major macrovascular disease, all-cause mortality, cardiovascular events and total renal events).

8 It was concluded that these findings suggest that routine treatment with perindopril and indapamide can be recommended for older people with T2D.

Ninomiya T, Zoungas S, Neal B et al (2010) Efficacy and safety of routine blood pressure lowering in older patients with diabetes: results from the ADVANCE trial. *J Hypertens* **28**: 1141–9