## Clinical DIGEST 6

### **Nephropathy**

## QJM

# Diabetic nephropathy increases relative risk of death

Readability	<b>///</b>
Applicability to practice	11
WOW! factor	11

- This study was undertaken due to the increasing incidence of people with diabetic nephropathy.
- A retrospective cohort study design was chosen in order to investigate the survival and characteristics of people with diabetic nephropathy undergoing renal replacement therapy (RRT) in the UK.
- The authors compared survival, social deprivation, ethnicity, gender and age of people with and without diabetic nephropathy (n=20 532) who underwent RRT in centres participating in the Renal Association UK Renal Registry between 1997 and 2004.
- The most common renal complication among the total number of people undergoing RRT was diabetic nephropathy (19 %) and 77 % of individuals were Caucasian.
- Of the Caucasian population, people with diabetic nephropathy were significantly more likely to be from a socially deprived area (*P*<0.0001).
- There was late referral for RRT (<90 days before initiation of therapy) in 20 % of the population with diabetic nephropathy.
- The difference in 5-year survival rate was greatest between younger individuals (aged 18–54 years; 56% in those with diabetic nephropathy versus 85% in those without). In older people (age ≥65 years) 5-year survival rate was 17% in those with diabetic nephropathy versus 28%.
- The results indicate that people with diabetic nephropathy who are starting RRT are more likely to come from deprived areas and relative risk of death is greatest between ages 18–54 years.

  Nitsch D, Burden R, Steenkamp R et al (2007) Patients with diabetic nephropathy on renal replacement therapy in England and Wales. *QJM* 100: 551–60

#### Dialysis and diabetes



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hirty years ago, people with diabetes were largely excluded from renal replacement therapy (RRT) programmes on the grounds that their greater number of complications and comorbidities resulted in a

poorer quality of life, so offering them RRT was less justifiable. Rationing dialysis in this way has changed dramatically in the past 15–20 years, with diabetes becoming the single most important (at almost 1 in 5) cause of end stage renal failure leading to RRT in the UK. However, life on dialysis is more difficult for many individuals with diabetes.

The UK Renal Registry (UKRR; Nitsch et al, summarised on the left) offers us an overview of the characteristics and survival of people with diabetes on RRT in England and Wales. These individuals are more likely to receive peritoneal dialysis and only half as likely to be transplanted in the first year of RRT. Caucasians with diabetes, the largest ethnic group (making up 77 %) of the population with diabetes, are more likely to come from a socially deprived background than those without diabetes. In spite of increased awareness among physicians and published recommendations, only 50 % were referred more than 1 year before dialysis was initiated. CVD is manifest in 50 % of these individuals and is much more common than in those without diabetes. Almost 20 % are smokers. Although there was no increased early (within 90 days) mortality associated with diabetes, that was not the case after 90 days. Younger (18-54 year-old) people with diabetes had the greatest relative mortality, with 87 % survival at 1 year, falling to 56 % 5 years after RRT. Survival for people with diabetes at 1 year was the same as those without the condition at 5 years. The reasons for this are not clear but may reflect lower efficacy of CV interventions in people with diabetes. The UKRR only provides us with data on survival, and not morbidity or quality of life — important considerations when informing individuals about treatments.

The Copenhagen study (Sørenson et al, see overleaf) provides some insights into these, albeit in a cohort of patients most of whom had type 1 diabetes and were receiving haemodialysis. Poor blood glucose control was a recognised predictor of increased mortality, largely a result of CVD; over 75 % had sustained a myocardial infarction and 50 % a stroke. Interestingly, level of education, as judged by time spent at school, was lower compared to matched control people with diabetes with normal renal function and the proportion of smokers was higher than both dialysis patients without diabetes and control patients with diabetes. Dialysis-related quality of life scores were similar in people on RRT, with or without diabetes, but those with the condition scored lower for physical function and health, with limitation of daily activities and role functioning strongly influenced by amputation and angina.

These two studies do serve to reinforce the earlier view of life on dialysis for the person with diabetes. Socioeconomic and educational factors are difficult to influence, but smoking cessation is something we must continue to emphasise in the context of such a heavy burden of CVD.

Higher doses of valsartan are well tolerated and reduced albuminuria more than the standard dose,

#### **DIABETOLOGIA**

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# People with diabetes on dialysis have poor self-rated health

- This study was undertaken in people with diabetes on dialysis in order to examine the prevalence of complications, health-related quality of life (HRQOL) and the influence of beliefs about control.
- 2 of the 53 individuals with diabetes on dialysis during 2004 in the authors' clinic, 38 completed a kidney-specific HRQOL questionnaire (SF-36). These people were then grouped in terms of CV diseases and diabetes-related complications.
- Two groups served as controls: one group of people on dialysis without diabetes (matched for age, dialysis modality and duration of end-stage renal disease; n=40) and one group of people with diabetes and normal renal function (matched for age and type of diabetes; n=38). HRQOL was also compared with the general population of Denmark.
- The results showed that there was a significantly higher frequency of micro- and macrovascular complications in people with diabetes on dialysis than in those with diabetes and normal kidney function.
- Compared with both other groups and the general population, self-rated physical health was significantly worse in people with diabetes on dialysis (P<0.01).
- People with diabetes in both the control and dialysis groups had a better mental health if they believed that they controlled their diabetes rather than relying on chance.
- People with diabetes on dialysis are characterised by high prevalence of micro- and macrovascular complications, low self-rated physical health but relatively good mental health.

Sørensen VR, Mathiesen ER, Watt T et al (2007) Diabetic patients treated with dialysis: complications and quality of life. *Diabetologia* **50**: 2254–62

#### JOURNAL OF HYPERTENSION

# High-dose valsartan reduces UAER more than standard dose

- The authors of this paper aimed to determine whether urinary albumin excretion rate (UAER) is reduced more by high doses of valsartan are compared to conventional doses.
- This was a multicentre randomised study across 75 centres in the US. People with hypertension, type 2 diabetes and UAER 20–700µg/min (n=391) were randomised to valsartan (160mg, 320mg or 640mg).
- All received 160mg valsartan for 4 weeks and the dose was then

#### JOURNAL OF HYPERTENSION

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# Non-dippers are at higher risk of death

- The authors of this study investigated the prognostic sigificance of CV risk factors for all-cause mortality in people with type 2 diabetes.
- Two groups of people with type 2 diabetes were followed from 1991–2004 (or until death) in this prospective

increased in two groups for 30 weeks.

- In order to assess proteinuria, overnight urine collections were taken at baseline, 4, 16 and 30 weeks.
- There were similar reductions in UAER at week 4 (*P*<0.001). At week 16 there was a significant decrease in UAER using the higher doses compared with 160mg (*P*<0.001) which was maintained until week 30.
- At week 30, 12% of those on valsartan 160mg acheived normal levels of albuminuria compared with 19% of those on 320mg and 24% of those on 640mg (*P*<0.05 for 160mg versus 640mg).
- These results indicate that, in type 2 diabetes, higher doses of valsartan reduced albuminuria more than the standard dose. The authors also noted that the higher doses were well tolerated. Hollenberg NK, Parving HH, Viberti G et al (2007) Albuminuria response to very high-dose valsartan in type 2 diabetes mellitus. *Journal of Hypertension* 25: 1921–6

observational study. One group with diabetic nephropathy (n=51), and the other with normoalbuminuria (n=53).

- The results showed that those whose blood pressure did not dip (average reduction in blood pressure >10% from day to night) were at a higher risk of death, independent of other risk factors (P=0.001).
- The authors recommend that 24-h ambulatory blood pressure be used to assess risk in non-dipping people with type diabetes.

Astrup AS, Nielsen FS, Rossing P et al (2007) Predictors of mortality in patients with type 2 diabetes with or without diabetic nephropathy: a follow-up study. *Journal of Hypertension* **25**: 2479–85

### CLINICAL NEPHROLOGY In the first individual there was a

## SKPT almost completely diminishes proteinuria

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Readability /
Applicability to practice /
WOW! factor / / /

The aim of the study was to determine the impact of a successful simultaneous kidney—pancreas transplant (SKPT) on proteinuria and kidney function. Two individuals with type 1 diabetes and nephrotic syndrome received pre-emptive (SKPT) despite having near-normal kidney function.

- near-normal protein excretion of 0.20g/24-h urine with a creatinine clearance of 82ml/min after 3 months.
- In the second individual there was a near-normal protein excretion of 0.18g/24-h urine with a creatinine clearance of 80ml/min after 3 months.
- The authors conclude that SKPT leads to rapid reduction of proteinuria in people with diabetes with nephrotic syndrome and near-normal kidney function.

Sedlak M, Biesenbach G, Margreiter R (2007) Proteinuria disappears promptly after simultaneous kidney-pancreas transplantation in nephrotic diabetic patients with near-normal GFR. *Clinical Nephrology* **68**: 330–4

Self-rated physical health was significantly worse (P<0.01) in people with diabetes on dialysis.