Areas of uncertainty or controversy

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21.10.1 Diabetes mellitus and the kidney 4985 surveillance and eye screening for these patients also confers benefit in terms of limb and sight preservation. A multiple risk factor approach As the outlook for patients with diabetic nephropathy is poor, many national guidelines now suggest a multiple risk factor approach to management. However, many patients with advanced diabetic nephropathy referred to renal units in Europe and the United States of America have inadequate blood pressure control, low use of therapies of proven benefit (e.g. β-blockers, ACE inhibitors, lipid-lowering therapy, and low-dose aspirin), and poor assessment of comorbidities such as retinopathy and foot care. The Steno 2 study in 160 moderately albuminuric type 2 dia- betic patients involved a multifactorial intervention for 7 to 8 years that addressed glycaemia, blood pressure (using renin–angiotensin system blocking agents in all), serum lipid lowering, low-dose as- pirin, smoking cessation, reduction of dietary fat and salt, exercise, and antioxidant vitamins. Compared to routine care this significantly reduced the development of severely elevated albuminuria and the composite cardiovascular outcome of fatal and nonfatal myocar- dial infarction and stroke, myocardial revascularization (surgical or percutaneous), and peripheral vascular surgery or amputation. The SHARP (Study of Heart And Renal Protection) trial demonstrated a 2% absolute risk reduction in cardiovascular endpoints in patients with CKD (many of whom had diabetes) treated with a combination of simvastatin and ezetimibe. There is, therefore, a real challenge for our patients as well as their carers to implement multiple therapies in a way that will facilitate compliance and deliver long-term benefit. Prognosis Moderately albuminuric type 1 and type 2 patients have a two- to fourfold increased mortality, mainly from cardiovascular disease. The reported relative mortality for European 40-year-old type 1 pa- tients with clinical proteinuria in Denmark was between 80 and 100 times that of the nondiabetic population, while the World Health Organization study revealed a three- to fourfold excess for severely elevated albuminuric patients with type 2 diabetes. Data from the FinnDiane and Pittsburgh Epidemiology Studies and Joslin Clinic cohorts also showed that the excess cardiovascular mortality associ- ated with type 1 diabetes is confined to those patients who develop elevated albuminuria; normoalbuminuric individuals have a mor- tality risk indistinguishable from the background population. Most of these deaths are due to stroke or myocardial infarction. In Finland, type 1 patients with nephropathy have a 10-fold relative risk for both stroke and myocardial infraction compared to nondiabetic controls. The UKPDS cohort

demonstrated an annual mortality of 4.6% for those with severely increased albuminuria, and almost 20% for those with a serum creatinine greater than 175 µmol/litre or in endstage renal disease (Fig. 21.10.1.4), cardiovascular disease being the main cause of death. Pima Indians also show an increase in mortality with increasing ACR, but the causes of death are some- what different to white Europid patients; vascular disease is much less prevalent in Native Americans, although more frequent in those with diabetic nephropathy. In a largely white Europid population in the United Kingdom, a reduced eGFR of less than 60 ml/min per 1.73 m2 conferred a more than threefold increased hazard ratio for cardiovascular mortality irrespective of albuminuria status. Survival on dialysis remains worse for patients with diabetes com- pared to those without, but they are improving; around 37% are alive after 5 years in American registries compared to 44% for hyperten- sive renal disease and 54% for glomerulonephritis. Overall survival for diabetic patients is best in those who have an early successful kidney transplant. Areas of uncertainty or controversy Should we screen for diabetic nephropathy? Due to the strong associations between an increase in UAER and car- diovascular disease, a case for screening for diabetic nephropathy can

Table 21.10.1.4 Cross-tabulation of latest classification of chronic kidney disease and historical definition of diabetic kidney disease GFR stage, description and definition Albuminuria stage, description, and definition A1—(Normal) <3.0 mg/mmol
<30 mg/g A2—moderate increase (microalbuminuria) <3.0–30 mg/mmol; <30–299 mg/g
A3—severe increase (macroalbuminuria) > 30 mg/mmol; >300 mg/g G1 (normal) >90 ml/min per 1.73 m2 At risk of DKD Possible DKD (probable if DR) Probable DKD (consider other causes albuminuria in type 2) G2 (mild reduction) 60–89 ml/min per 1.73 m2 At risk of DKD Possible DKD (probable if DR) Probable DKD (consider other causes albuminuria in type 2) G3a (mild–moderate reduction)
45–59 ml/min per 1.73 m2 Possible DKD
(probable if DR) Probable DKD (definite if DR) DKD G3b (moderate–severe reduction)
30–44 ml/min per 1.73 m2 Possible DKD (probable if DR) Probable DKD (definite if DR) DKD G4 (severe reduction) 15–29 ml/min per 1.73 m2 Possible DKD (probable if DR) Probable DKD (definite if DR) DKD G5 (kidney failure) <15–29 ml/min
per 1.73 m2 Possible DKD (probable if DR) Probable DKD (definite if DR) DKD DKD, diabetic kidney disease; DR, diabetic retinopathy.

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