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section 21 Disorders of the kidney and urinary tract 4984 Criteria for diagnosis Diabetic nephropathy is a clinical diagnosis based upon the finding of albuminuria in a patient with diabetes and in whom there is no evidence of urinary infection. The definitions of mod- erate and severe elevations are shown in Table 21.10.1.1. Current United Kingdom guidelines suggest confirming the diagnosis with one or two repeat tests over the subsequent 1 to 6 months (Fig. 21.10.1.3). Although timed urine collections remain the gold standard for diagnosis, they are cumbersome to use in routine clinical prac- tice and most definitions depend on a spot urine sample and thus a test of albumin concentration. Levels above 50 mg/litre or above 300 mg/litre define moderately and severely elevated albuminuria, respectively. Sensitivity and specificity can be im- proved by using an early morning, first-voided specimen and correcting the urinary albumin level for creatinine concentration (an albumin:creatinine ratio (ACR)). Defining levels are shown in Table 21.10.1.1. The latest modification of the classification of CKD has divided stage 3 into 3a and 3b (eGFR 45–60 and 30–45 ml/min per 1.73 m2 respectively). It also incorporates an assessment of albumin- uria as it is now acknowledged that increased urine excretion of albumin represents an independent risk factor for cardiovascular disease. This goes some way to aligning the historical classification of diabetic and CKD (Table 21.10.1.4). eGFR estimated from the MDRD equation consistently underestimates measured GFR in large diabetic cohorts, and it is not very accurate at values above 90 ml/min. The newer CKD-EPI equation has improved accuracy at higher values. However, as many newly diagnosed type 1 and type 2 patients have an elevated GFR, significant reductions over time may pass undetected. Treatment Glycaemic control and blood pressure The roles of glycaemic control and blood pressure management have been discussed earlier in this chapter. Current target HbA1c levels from the National Institute for Health and Care Excellence guidelines in the United Kingdom are less than 48 mmol/mol (6.5%) for type 1 and type 2 patients. The American Diabetes Association target is 53 mmol/mol (<7.0%) for most patients of both types. Blood pressure targets are below 130/80 mmHg for patients with elevated albuminuria. Recent analyses suggest that values lower than this are of no benefit and may cause harm. Due to the piv- otal role that angiotensin II is thought to play in diabetic nephrop- athy development, all guidelines suggest using renin–angiotensin system blocking agents as first-line treatment. However, the UKPDS has shown that most type 2 patients will require two or more agents in order to achieve the target. Following publication of the OnTARGET and ALTITUDE trials, multiple blockade of the renin–angiotensin system with the combination of an ACEi and an ARB is not recommended. Meta-analysis has shown that although dual blockade appears to be more effective at reducing albuminuria, it is also associated with more adverse events, notably hyperkalaemia and acute kidney injury. Achieving blood pressure targets is difficult, particularly in pa- tients with type 2 diabetes and systolic hypertension. Although the UKPDS showed a linear relationship between

glycaemia and blood pressure and microvascular risk, implying the lower the better, the ACCORD glycaemia and blood pressure studies failed to show benefit of reduction of HbA1c to below 48 mmol/mol (≤6.5%) and of blood pressure to less than 120/80 mmHg, suggesting that there is no benefit for patients by reducing current targets. Other aspects Low-protein diets have been shown by meta-analysis to slow the rate of decline of GFR in diabetic patients, and a study from Denmark has also shown benefit on mortality. Current dietary recommenda- tions are for an intake of between 0.7 and 0.9 g protein/kg body weight per day. Aspirin in a dose of 325 mg/day reduced myocardial infarction (relative risk 0.72; 99% confidence interval 0.55–0.95) in 3711 type 1 and 2 patients with retinopathy. Although nephropathy status was not determined in this study, the use of low-dose aspirin should be considered for all patients with an increased UAER (unless contra-indicated) because of their high risk for cardiovascular disease. Lipid-lowering therapy should also be commenced for all diabetic patients with CKD. Observational studies suggest that patients with better glycaemic control have a better overall survival on haemodialysis. Active foot Annual dipstick urinalysis for protein Positive (>300 mg/L) Previously positive on 2 or more occasions over previous 6 months Positive ACR>2.5 mg/mmol (men) ACR>3.5 mg/mmol (women) Positive No No Yes No Yes No Yes Severely increased albuminuria Moderately increased albuminuria Negative Test for moderately increased albuminuria Retest over next 1–6 months Retest over next 1–6 months Positive Fig. 21.10.1.3 Flowchart for diagnosis of moderately and severely elevated albuminuria. NB: assumes sterile urine throughout. Exclude infection when proteinuria first detected and at any time thereafter if a history of urinary tract infection.

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