

Nephropathy

Pressures are changing for people with nephropathy



Colin Close,
Consultant Physician,
Taunton and
Somerset Hospital

Studies employing ambulatory blood pressure readings have shown much closer correlations than clinic readings with both the risks of hypertensive cardiovascular complications and the progression to end-stage renal disease. Ambulatory blood pressure measurement yields important information about the circadian rhythm of blood pressure; and in particular the impact of the nocturnal blood pressure burden, and impairment of the usual blood pressure fall during sleep, a phenomenon known as ‘non-dipping’. The Steno Diabetes Centre study (Astrup et al; summarised below) is the first prospective evaluation of the impact of non-dipping on mortality in type 2 diabetes. They followed 104 individuals, 51 of whom had nephropathy, over a mean period of 9.2 years. Eighty per cent of those with nephropathy, compared to 25% with normoalbuminuria, died during follow up. 24-hour blood pressure correlated with daytime blood pressure, and was a better predictor of mortality. Non-dipping was a strong independent predictor of all cause mortality in all patients. There were close correlations between 24-hour blood pressure, glomerular filtration rate and left ventricular hypertrophy. More individuals with

nephropathy were either non-dippers (57% vs 40%) or had a reversed circadian blood pressure rhythm, with higher night time blood pressure (20% vs 2%) and 88% of those with a reversed rhythm died during follow up. Reduced heart rate variability was also more common in those with non-dipping.

The study by Tamura et al (summarised alongside) of people with diabetic and non-diabetic glomerulopathy, found higher night time systolic blood pressure in diabetes – however, the study lacked the power to examine the prevalence of non-dipping in the diabetic group, although reduced heart rate variability was again seen in the people with diabetes.

So how might this information influence our clinical practice? We need to know whether the use of therapies that can modify these abnormal blood pressure rhythms, ‘chronotherapies’, will translate into meaningful clinical outcomes for high-risk patients. Contemporaneous data from the Steno study and the ONTARGET investigators, however, give us little current indication that there may exist a specific benefit for any agent that reverses abnormal blood pressure rhythms (for example, beta- or angiotensin-receptor blockers) in reducing cardiovascular mortality in people with hypertension.

ONTARGET investigators et al (2008) Telmisartan, ramipril, or both in patients at high risk for vascular events. *NEJM* **358**: 1547–59

CLINICAL AND EXPERIMENTAL HYPERTENSION

Lowering night time BP may reduce proteinuria

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

1 This Japan-based study was undertaken in order to ascertain whether there was a difference in 24-hour blood pressure profile between people with hypertension and diabetic nephropathy (DN) and people with hypertension and non-diabetic glomerulopathy (non-DN).

2 Sixty-eight individuals, 34 with DN and 34 with non-DN, had their 24h ambulatory blood pressure measured.

3 The authors found that there was no significant difference, in terms of 24h and daytime systolic blood pressure, between the DN group (143mmHg versus 136mmHg) and the non-DN group (143mmHg versus 138mmHg).

4 It was, however, noted that although both groups had an attenuated decrease in nocturnal blood pressure, those in the DN group had a significantly higher night time systolic blood pressure than the non-DN group (142mmHg versus 132mmHg; $P=0.0217$).

5 Those in the DN group also had a significantly increased urinary protein excretion ($P=0.0095$), which was significantly correlated with night time systolic blood pressure ($P=0.0031$).

6 The authors conclude that an elevated nocturnal blood pressure may contribute to the increased proteinuria in people with hypertension and diabetic nephropathy.

Tamura K, Yamauchi J, Tsurumi-Ikeya Y et al (2008) Ambulatory blood pressure and heart rate in hypertensives with renal failure: comparison between diabetic nephropathy and non-diabetic glomerulopathy. *Clinical and Experimental Hypertension* **30**: 33–43

JOURNAL OF HYPERTENSION

Non-dipping profile increases mortality risk in diabetes

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

1 This study followed 104 people with type 2 diabetes (51 with nephropathy and 53 with persistent normoalbuminuria) to determine the prognostic significance of cardiovascular (CV) risk factors for all-cause mortality in type 2 diabetes.

2 After a mean follow up of 9.2 years, 54/104 people died (41 with diabetic nephropathy and 13 with normoalbuminuria).

3 Of the 16 people who had higher blood pressure at night than in the day (non-dipping profile), 14 (88%) died (cf 40/88 [45%] people with reduced or normal dipping profiles).

4 Ambulatory blood pressure should be used to detect non-dipping profiles and increased mortality risk in people with type 2 diabetes.

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

KIDNEY INTERNATIONAL

Rosiglitazone therapy decreases albuminuria

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

1 Thiazolidinediones are insulin sensitizers that decrease plasma glucose and improve the lipid profile in people with type 2 diabetes.

2 This placebo-controlled study examined the effect of rosiglitazone on microalbumin excretion and changes in insulin sensitivity in 15 people with type 2 diabetes; 14 people with type 2 diabetes were randomised to receive placebo for 12 weeks.

3 Measures included weekly fasting plasma glucose, fasting plasma lipids, HbA_{1c}, urinary creatinine and albumin concentrations and blood pressure.

4 After 12 weeks of rosiglitazone treatment, the urinary albumin–creatinine ratio was significantly decreased ($P<0.01$) and the glucose metabolic clearance rate (during insulin clamp) was significantly increased compared with the placebo group.

5 Additionally, rosiglitazone significantly decreased fasting free fatty acid ($P<0.01$) and tumour necrosis factor- α (TNF- α) levels ($P<0.05$) and increased fasting plasma adiponectin ($P<0.001$) vs baseline and placebo.

6 This decrease in albuminuria after rosiglitazone treatment correlated with improved metabolic control and decreased circulating adipocytokine levels; only decreased TNF- α and increased adiponectin were independently associated with decreased albuminuria.

7 Thus, thiazolidinediones may be useful to prevent nephropathy in people with type 2 diabetes.

Miyazaki Y, Cersosimo E, Triplitt C, DeFronzo RA (2007) Rosiglitazone decreases albuminuria in type 2 diabetic patients. *Kidney International* **72**: 1367–73

AMERICAN JOURNAL OF KIDNEY DISEASES

BP and glycaemic control affect risk of renal disease

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

1 As family history is a strong risk factor for diabetic nephropathy, the study determined the risk factors for renal disease in 295 people with diabetes and siblings with diabetic kidney disease.

2 Estimated glomerular filtration rate, urinary albumin–creatinine ratio, blood pressure (BP) and HbA_{1c} were measured.

3 Mean duration of diabetes was 14.6 years; 46% of participants had albuminuria.

4 Additionally, 64.7% of people had systolic BP ≥ 130 mmHg and 57.4% had HbA_{1c} $\geq 7\%$.

5 Better BP and glycaemic control are needed to prevent or slow diabetic kidney disease in this high-risk group.

Bleyer AJ, Sedor JR, Freedman BI et al (2008) Risk factors for development and progression of diabetic kidney disease and treatment patterns among diabetic siblings of patients with diabetic kidney disease. *American Journal of Kidney Diseases* **51**: 29–37

DIABETES CARE

LTPA scores vary with diabetes complications

Readability	✓✓
Applicability to practice	N/A
WOW! factor	✓✓

1 Although much is known about the importance of physical activity in people with diabetes, little is known about its relationship with diabetes complications.

2 In total, 1945 people with type 1 diabetes were assessed for level of physical activity (by self-reported leisure-time physical activity [LTPA]

score), renal function, retinopathy and cardiovascular disease [CVD].

3 Low-frequency and low-intensity LTPA were associated with diabetic nephropathy; low-intensity LTPA was associated with proliferative retinopathy and CVD.

4 Patients with diabetes complications reported different patterns of LTPA; the main difference was the intensity of the LTPA as low-intensity LTPA was associated with impaired renal function and increasing degree of proteinuria, retinopathy and CVD.

5 However, diabetes complications may affect the person's ability to exercise and thus reduce LTPA score.

Wadén J, Forsblom C, Thorn LM et al (2008) Physical activity and diabetes complications in patients with type 1 diabetes. *Diabetes Care* **31**: 230–2

DIABETOLOGIA

Lipid abnormalities relate to abnormal AER

Readability	✓✓
Applicability to practice	N/A
WOW! factor	✓✓

1 The authors looked at the relationship between lipid variables, estimated glomerular filtration rate (eGFR) and albumin excretion rate (AER) in people with type 1 diabetes.

2 Lipid profiles were available for 2927 adults with type 1 diabetes from the Finnish Diabetic Nephropathy Study; eGFR was also calculated.

3 Results showed that people with impaired renal function (eGFR < 60 ml/min/1.73m²) had higher total cholesterol, low-density lipoprotein (LDL) cholesterol, triacylglycerol and apolipoprotein B, and lower high-density lipoprotein cholesterol than people with normal renal function (eGFR > 90 ml/min/1.73m²) or mildly impaired renal function (eGFR 60–90 ml/min/1.73m²) ($P<0.001$ for all).

4 Lipid abnormalities are present in people with type 1 diabetes with an abnormal AER as well as in those with impaired renal function.

Tolonen N, Forsblom C, Thorn L et al (2008) Relationship between lipid profiles and kidney function in patients with type 1 diabetes. *Diabetologia* **51**: 12–20

‘TZDs may be useful to prevent nephropathy in people with type 2 diabetes.’