Nephropathy

Is retinopathy linked to nephropathy?

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This meta-analysis builds upon a systematic review from the National Kidney Foundation (2007 and 2012). Essentially it says that the detection of one microvascular complication makes it more likely that others will be present. As the precision of retinopathy detection is so high with digital photography, its presence should prompt careful surveillance for diabetic nephropathy (DN) and perhaps neuropathy. If a person with retinopathy and T2D has albuminuria, then it is highly likely that they will have DN. Why is this important?

We know that diabetic kidney disease is progressive and leads to end stage renal disease if the patient survives the increased cardiovascular disease (CVD) risk (Adler et al, 2003). Historically, GFR declined by 10 mL/min/year (Viberti et al, 1993) but recently these rates have decreased by 2–4 mL/min/year in patients with well-controlled blood pressure (Evans et al, 2011). Those with non-diabetic glomerulopathology decline more slowly (Nosadini et al, 2000). Thus, the detection of retinopathy in someone with T2D and albuminuria should prompt correction of CVD risk factors, surveillance for anaemia and consideration of nephrology referral.

One limitation is the lack of information on biopsy appearances in people with T2D, reduced GFR and normal albuminuria. Could retinopathy help discriminate diabetic from non-diabetic nephropathology? As 15% of participants in the UK Prospective Diabetes Study (UKPDS) didn't demonstrate albuminuria despite having an eGFR <60 mL/min this is an important question (Retnakaran et al, 2006). In T1D, retinopathy did predict glomerulopathy severity in 252 patients with normal albuminuria (Klein et al, 2005). Previous retinopathy was associated with microalbuminuria and reduced eGFR in the UKPDS but there were no data on rates of progressive loss of function. Increased albuminuria and reduced GFR in T2D identify those at greater risk of progressive renal and CVD (Retnakaran et al, 2006; National Kidney Foundation, 2007) but it is not known whether retinopathy detection would improve predictability of progression.

Does this mean that detection of retinopathy in people with increased albuminuria and T2D excludes a role for renal biopsy for diagnosis? Perhaps partly, but clinicians need to be alert to atypical features such as rapidly deteriorating renal function (>5 mL/min/year); nephrotic range proteinuria; an active urinary sediment or haematuria; and systemic symptoms/signs of disease known to affect the kidneys. Any of these should prompt specialist referral and possible biopsy.

The advent of the UK National Screening Programme for diabetic retinopathy has brought real benefit for our patients but should not mean that we forget to examine the eyes of our patients when indicated, or, worse, lose the skills to do so.

Adler AI, Stevens RJ, Manley SE et al (2003) *Kidney Int* **63**: 225–32
Evans M, Bain SC, Hogan S, Bilous RW (2011) *Nephrol Dial Transplant* doi: 10.1093/ndt/gfr696
Klein R, Zinman B, Gardiner R et al (2005) Diabetes **54**: 527–33
National Kidney Foundation (2007) *Am J Kidney Dis* **49**: S1–80
National Kidney Foundation (2012) *Am J Kidney* Dis **60**: 850–86
Nosadini R, Velussi M, Brocco E et al (2000) *Diabetes* **49**: 476–84
Retnakaran R, Cull CA, Thorne KI, et al (2006) *Diabetes* **55**: 1832–9
Viberti GC, Bilous RW, Mackintosh D et al (1983) *Am J Med* **74**: 256–64

DIABETOLOGIA

Diabetic retinopathy can predict DN

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

1 A meta-analysis was conducted to determine if diabetic retinopathy (DR) can predict diabetic nephropathy (DN) in people with T2D and non-diabetic renal disease (NDRD). Searches of MEDLINE and EMBASE identified data from 2012 participants from 26 studies.

2 Pooled positive and negative predictive values of DR for DN were 0.72 (95% CI, 0.68–0.75) and 0.69 (95% CI, 0.67–0.72). Pooled sensitivity and specificity for proliferative DR differentiating DN from NDRD were 0.35 and 0.98, compared to 0.75 and 0.69 for non-proliferative DR.

3 The authors concluded that DR is predictive of DN in people with T2D and renal disease with proliferative DR being a highly specific predictor of DN.

He F, Xia X, Wu XF et al (2013) Diabetic retinopathy in predicting diabetic nephropathy in patients with type 2 diabetes and renal disease: a meta-analysis. *Diabetologia* **56**: 457–66

DIABETES CARE

T2D and chronic kidney disease: Sitagliptin versus glipizide

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

1 People with T2D and chronic kidney disease have limited antihyperglycaemic treatment options and an increased risk of developing micro- and macrovascular disease.

2 The aim of this study was to assess the tolerability and efficacy of sitagliptin compared to glipizide, in a cohort of people with poorly controlled T2D and moderate-to-severe chronic kidney disease.

3 A total of 426 patients were randomised to receive either sitagliptin (50 mg every day [qd] for moderate renal insufficiency and 25 mg qd for severe renal insufficiency) or glipizide (2.5 mg qd, adjusted according to individual glycaemic control) for 54 weeks.

4 Sitagliptin treatment was found to be noninferior to glipizide, as reflected in the similar HbA_{1c} change from baseline between the two groups (-0.8 versus -0.6%; between-group difference -0.11%; 95% CI, -0.29 to 0.06).

5 Hypoglycaemic events were less frequent in people treated with sitagliptin versus glipizide (6.2 and 17.0%, respectively; $P=0.001$). A decrease in body weight (-0.6 kg) was observed in people taking sitagliptin compared to a notable increase (1.2 kg) in people treated with glipizide (difference, -1.8 kg; $P<0.001$).

6 The authors concluded that sitagliptin was well tolerated in people with T2D and chronic renal insufficiency, and produced similar HbA_{1c}-lowering efficacy compared to glipizide.

Arjona Ferreira JC, Marre M, Barzilai N et al (2012) Efficacy and safety of sitagliptin versus glipizide in patients with type 2 diabetes and moderate-to-severe chronic renal insufficiency. *Diabetes Care* 17 Dec [Epub ahead of print]

DIABETOLOGIA

HbA_{1c} variability is associated with microalbuminuria in T2D

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

1 Variation in HbA_{1c} is thought to increase the risk of nephropathy in T1D, but evidence of this association in people with T2D is lacking.

2 The authors aimed to prospectively investigate the relationship between HbA_{1c} variability and the onset of microalbuminuria. The authors' second aim was to determine the clinical value of serial HbA_{1c} measurements in this risk assessment.

3 Serial HbA_{1c} measurements were collected from middle-aged, normoalbuminuric individuals with T2D (n=821) over 2 years. HbA_{1c} variation was calculated using the standard deviation (SD) of HbA_{1c} measurements. A Cox proportional hazards model was used to evaluate the relationship between HbA_{1c} SD quartile and microalbuminuria.

4 Participants were followed for an average of 6.2 years. The incidence of microalbuminuria in the highest adjusted HbA_{1c} SD quartile, Q4 was 91.9 per 1000 person-years compared to 58.4 in the lowest quartile, Q1 (P=0.042). Those from Q4 were 48% more likely to develop microalbuminuria compared to Q1 (P<0.05).

5 The graded correlation between HbA_{1c} quartile and microalbuminuria was consistent and only marginally affected by follow-up time (2 versus ≤7 years).

6 The authors concluded that high HbA_{1c} variability correlates to microalbuminuria development in T2D, even if quantified at 2 years.

Hsu CC, Chang HY, Huang MC et al (2012) HbA1c variability is associated with microalbuminuria development in type 2 diabetes: a 7-year prospective cohort study. *Diabetologia* **55**: 3163–72

DIABETES CARE

Visit-to-visit SBP variation and diabetic nephropathy

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

1 The authors aimed to determine the association between visit-to-visit variation in systolic blood pressure (SBP) and diabetic nephropathy.

2 SBP was measured in a total of 354 patients with T2D. Change in urinary albumin excretion (UAE) or extent of albuminuria was assessed during a mean interval of 3.76 ±0.71 years.

3 SBP variation was found to be independently associated with UAE progression (b=0.1758; P=0.0108). Coefficient of SBP variation correlated with an increased risk of developing albuminuria (hazard ratio 1.143, 95% CI, 1.008–1.302)

4 The authors concluded that visit-to-visit variation in SBP could be a risk factor for the onset and progression of diabetic nephropathy.

Okada H, Fukui M, Tanaka M, Matsumoto S (2013) Visit-to-visit blood pressure variability is a novel risk factor for the development and progression of diabetic nephropathy in patients with type 2 diabetes. *Diabetes Care* 22 Jan [Epub ahead of print]

DIABETES

Proteome analysis detects early risk of DN

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

1 Diabetic nephropathy (DN) is one of the most common causes of chronic kidney disease (CKD) in Western countries. The authors aimed to investigate the clinical value of urinary proteome analysis for prediction of DN, with the use of capillary electrophoresis–coupled mass spectrometry.

2 The peptide content of urine samples from 35 people with T1D or T2D were analysed using a CKD biomarker classifier. Collagen fragments were found to be notable biomarkers 3 to 5 years prior to the onset of macroalbuminuria (area under the curve [AUC] 0.93) when compared to urinary albumin (AUC 0.67), which is currently used for diagnosis.

3 The authors concluded that the classification of specific collagen fragments with urinary proteomics enables an early noninvasive risk assessment of DN.

Zürbig P, Jerums G, Hovind P et al (2012) Urinary proteomics for early diagnosis in diabetic nephropathy. *Diabetes* **61**: 3304–13

DIABETES CARE

Ethnic differences in DKD incidence

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

1 The authors aimed to establish the incidence of proteinuric and nonproteinuric diabetic kidney disease (DKD) in an ethically diverse cohort of people with T2D (n=15 683).

2 Electronic health records of primary care outpatients from non-Hispanic white (NHW), Asian Indian, Chinese, Filipino, Hispanic and non-Hispanic black (NHB) backgrounds were analysed.

3 Ethnic minorities were found to have higher rates of proteinuric DKD compared to NHWs (24.8–37.9 versus 24.8%) and lower rates of nonproteinuric DKD (6.3–9.8 versus 11.7%).

4 The authors concluded that differences existed in the incidence of DKD in people with T2D, emphasising the importance of targeted prevention.

Bhalla V, Zhao B, Azar KM et al (2012) Racial/ethnic differences in the prevalence of proteinuric and nonproteinuric diabetic kidney disease. *Diabetes Care* 13 Dec [Epub ahead of print]

> *"The authors concluded that differences existed in the incidence of diabetic kidney disease in people with T2D, emphasising the importance of targeted prevention."*