Diabetes journals

Targeting cardiovascular and renal risk via reductions in microalbuminuria

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The study to the right evaluates the effects of reducing microalbuminuria in people with type 2 diabetes. In total, 116 individuals with type 2 diabetes with microalbuminuria were evaluated for an initial period of 2 years and thereafter for a further 8 years. Remission of microalbuminuria and a 50 % reduction in the level of microalbuminuria were defined as a shift to normo-albuminuria. The alteration in urinary albumin excretion rate was associated to the first occurrence of a renal or cardiovascular event, together with an annual decline rate of estimated glomerular filtration rate (eGFR). In individuals who achieved a reduction in microalbuminuria, there were 12 events in 93 participants compared with 35 events in 123 participants without a significant reduction in urinary albumin excretion rate. The cumulative incidence rate of events was significantly lower in individuals with a reduction in microalbuminuria. The risk of a cardiovascular and renal events were reduced by approximately 50 % in those demonstrating a significant improvement in microalbuminuria levels. These individuals also demonstrated a significantly lower rate of decline of eGFR.

Therefore, this study provides clinical evidence that the reduction in microalbuminuria in people with type 2 diabetes plus microalbuminuria is an integrated indicator for renal and cardiovascular risk reduction.

DIABETES

Reducing microalbuminuria in T2D reduces renal and CV risk

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

1 That microalbuminuria is a predictor for diabetic nephropathy and CVD has been previously shown. To further this understanding, the authors of this study investigated the impact of reducing microalbuminuria in type 2 diabetes on clinical risk factors.

2 This was an observational follow-up study that enrolled 216 people with type 2 diabetes and microalbuminuria (albumin excretion rate <200 µg/min) and followed them for 8 years.

3 Participants were divided into two groups: those who achieved at least a 50 % reduction in microalbuminuria (n=93) and those who did not (n=123); baseline mean eGFR for each group was 103±24 and 101±25 µg/min, respectively; baseline age was 62±8 and 61±10 years, respectively; and HbA_{1c} was 7.5 % for both.

4 The group who reduced microalbuminuria by 50 % had a significantly lower cumulative incidence of death from, and hospitalisation for, renal and CV events than those who did not (12 versus 35, respectively; *P*=0.0019).

5 Adjusted risk for CV and renal events in those who reduced microalbuminuria by 50 % was 0.41 (95 % CI 0.15–0.96) in comparison to those who did not have this degree of reduction.

6 The authors conclude that this evidence showing the improved risk profile with improved microalbuminuria demonstrates the need for aggressive multifactoral control in microalbumnuria in type 2 diabetes.

Araki S, Haneda M, Koya D et al (2007) Reduction in microalbuminuria as an integrated indicator for renal and cardiovascular risk reduction in patients with type 2 diabetes. *Diabetes* **56**: 1727–30

DIABETES CARE

Aldosteronism common in resistant hypertension in T2D

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

1 Screening for aldosteronism was carried out in 100 people with type 2 diabetes and resistant hypertension by measuring the plasma aldosterone (PAC) : plasma renin activity (PRA) ratio.

2 Resistant hypertension was defined as BP >140/90 mmHg with use of ≥3 antihypertensive agents.

3 Where PAC : PRA ratio >30 ng/ml salt-load testing was performed. Primary aldosterone was defined as when 24-h urine aldosterone >12 µg during the third day of salt loading or a PAC ≥5 ng/dl after a 4-h intravenous saline load.

4 In total, 14 % of participants were diagnosed with primary aldosteronism, indicating that in people with diabetes and resistant hypertension screening for the condition should be considered.

Umpierrez GE, Cantey P, Smiley D et al (2007) Primary aldosteronism in diabetic subjects with resistant hypertension. *Diabetes Care* **30**: 1699–703

DIABETOLOGIA

Advanced glycation endproducts predict CVD mortality in women with T2D

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

1 The authors investigated whether or not increased serum advanced glycation endproducts (AGEs) could predict the total, CVD or CHD mortality in people with type 2 diabetes.

2 Recruited to the study were 488 men and 386 women in Finland aged 45–64 years at baseline who were followed for 18 years.

3 Serum AGEs significantly correlated with total mortality (*P*=0.002) and CVD mortality (*P*=0.021) in women. This trend was not significant among men.

4 The authors conclude that it is possible that measuring serum AGEs could help identify women with type 2 diabetes at high risk of CV complications.

Kilhovd BK, Juutilainen A, Lehto S et al (2007) Increased serum levels of advanced glycation endproducts predict total, cardiovascular and coronary mortality in women with type 2 diabetes: a population-based 18 year follow-up study. *Diabetologia* **50**: 1409–17

DIABETES CARE

Diabetic retinopathy increases CV death risk 3-fold

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

1 To examine the relationship between diabetic retinopathy and incident CHD, a population-based, prospective cohort study involving 1524 individuals with type 2 diabetes was undertaken.

2 The average length of follow up was 7.8 years and mean age at baseline was 60 years.

3 Of the 1456 for whom full data were available, diabetic retinopathy (identified by retinal photographs) was found in 14.7 % of participants (12.0 % mild or moderate, 2.7 % severe).

4 A CHD event was reported in 13.7 % of the total study population. Of this number, 15.9 % were fatal.

5 When the data were adjusted to control for age, sex, race, study centre, fasting glucose, HbA_{1c}, duration of diabetes, BP, antihypertensive treatment, smoking, BMI and lipid profile, incidence of CHD events were twice as high in those with type 2 diabetes than those without (HR: 2.07 [95 % CI: 1.38–3.11]).

6 Similarly, after adjustment for the above variables, there was a three-fold higher risk of a fatal CHD event in those with type 2 diabetes (HR: 3.35 [95 % CI: 1.40–8.01]).

7 Those with severe retinopathy were found to have a higher risk of CHD than those with mild-to-moderate retinopathy (HR: 1.96 versus 2.69, respectively).

8 The data presented in this study supports the hypothesis that microvascular disease has a role in the pathogenesis of CHD in diabetes.

Cheung N, Wang JJ, Klein R et al (2007) Diabetic retinopathy and the risk of coronary heart disease: the Atherosclerosis Risk in Communities Study. *Diabetes Care* **30**: 1742–6

DIABETOLOGIA

Omega-3 decreases vLDL-c but may increase LDL-c

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

1 The objective of this study was to investigate the effects of omega-3 on lipid and lipoprotein CV risk biomarkers in individuals with type 2 diabetes.

2 A systematic review and meta-analysis was conducted on randomised, placebo-controlled trials looking at omega-3 intake in type 2 diabetes.

3 In total, 23 trials involving non-dietary supplementation of omega-3 met the inclusion criteria, comprising 1075 people with diabetes and having a mean trial duration on 8.9 weeks.

4 Compared with placebo, omega-3 reduced levels of triglycerol by, on average, 25 % (mean decrease 0.45 mmol/l; $P<0.0001$).

5 In addition, compared with placebo omega-3 supplementation reduced vLDL-c by, on average, 36 % ($P=0.04$) and vLDL-triacylglycerol by 39.7 % ($P=0.03$).

6 LDL-c was significantly elevated by 5.7 % among participants who took omega-3; this translated to an average increase of 0.11 mmol/l ($P=0.05$).

7 Levels of total cholesterol, apolipoproteins, lipid subfractions or ratios were not significantly changed by omega-3 therapy.

8 While benefits are seen in the vLDL-c and vLDL-triacylglycerol profiles in people with type 2 diabetes taking omega-3, the authors conclude that further trials are needed to assess the adverse effect seen here on LDL-c.

Hartweg J, Farmer AJ, Perera R et al (2007) Meta-analysis of the effects of n-3 polyunsaturated fatty acids on lipoproteins and other emerging lipid cardiovascular risk markers in patients with type 2 diabetes. *Diabetologia* **50**: 1593–602

DIABETES CARE

Waist circumference has limited use in calculating cardiometabolic risk

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

1 This new consensus statement was drawn up from an expert panel with representatives from the American Diabetes Association, the Association for Weight Management and Obesity and NASSO (the Obesity Society).

2 The group state that while BMI provides information regarding body volume and mass, waist circumference provides data on body shape and fat distribution. However, MRI and CT remain the gold standard.

3 The panel concur that, with appropriate training, waist circumference measurements are highly reproducible.

4 Having examined the available data, the panel agreed that waist circumference is a stronger predictor of type 2 diabetes than BMI.

5 In the management of individuals who are already clinically obese by the standard BMI definition ($\geq 30\ kg/m^2$), assessment of waist circumference would not have any effect on clinical management decisions.

6 It is still uncertain whether or not the incremental value of waist circumference predictions on cardiometabolic risk are above those offered by BMI, blood glucose, lipid profile and BP.

7 The expert panel called for more studies investigating cut-off values for waist circumference as a clinical indicator of cardiometabolic risk.

Klein S, Allison DB, Heymsfield SB et al (2007) Waist circumference and cardiometabolic risk: a consensus statement from shaping America's health: Association for Weight Management and Obesity Prevention; NAASO, the Obesity Society; the American Society for Nutrition; and the American Diabetes Association. *Diabetes Care* **30**: 1647–52

'In the management of individuals who are already clinically obese, assessment of waist circumference would not have any effect on clinical management decisions.'

'Levels of total cholesterol, apolipoproteins, lipid subfractions or ratios were not significantly changed by omega-3 therapy.'

'Encouraging children to increase their cardiorespiratory fitness could reduce the deleterious effects of having high body fat.'

'MetS increases the risk of subclinical atherosclerosis, which contributes to CVD in people with diabetes.'

DIABETOLOGIA

HOMA and fasting insulin associated with body fat in school-aged children

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

1 This study aimed to investigate the relationship between insulin resistance and body fat and waist circumference, and the effect these factors have on cardiorespiratory fitness.

2 Children (n = 873) from Estonia and Sweden with a mean age of 9.6 ± 0.4 years were assessed for height, weight, waist circumference and body fat (sum of five skinfold thicknesses).

3 Fasting insulin and glucose, and HOMA were measured to assess insulin resistance.

4 HOMA and fasting insulin were positively associated with body fat and waist circumference, when adjusted for cardiorespiratory fitness, age, pubertal status and study location ($P < 0.001$).

5 For children in the highest tertile of body fat and waist circumference, HOMA and fasting insulin significantly reduced cardiorespiratory fitness (as measured by a maximal cycle-ergometer test), regardless of sex, age, pubertal status or study location.

6 The same association was present for fasting glucose and cardiorespiratory fitness in this group of children, unless body fat was accounted for.

7 The authors speculate that encouraging children to increase their cardiorespiratory fitness could reduce the deleterious effects of having high body fat.

Ruiz JR, Rizzo NS, Ortega FB et al (2007) Markers of insulin resistance are associated with fatness and fitness in school-aged children: the European Youth Heart Study. *Diabetologia* **50**: 1401–8

DIABETIC MEDICINE

Retinopathy and macroalbuminuria increase risk of composite cardio–renal events

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

1 People with type 2 diabetes were assessed in order to establish the effect of albuminuria and retinopathy on cardiovascular and renal complications, and all-cause mortality.

2 Glomerular filtration rate (eGFR) was measured in 4416 people in China with type 2 diabetes but no macrovascular complications at baseline (mean age: 57.6 ± 13.3 years).

3 Measured outcomes were all-cause mortality, cardiovascular events (heart failure, angina, MI, lower limb amputation, re-vascularisation procedures and stroke) and renal complications (reduction in eGFR by >50 %, eGFR <15 ml/min/1.73 m^2, death from renal causes or need for dialysis).

4 Compared with people who did not develop complications, those with retinopathy and macroalbuminuria had a higher incidence of cardiovascular events (14.1 vs 2.4 %), renal events (40.4 vs 0.8 %) and death (9.3 vs 1.7 %; $P < 0.001$ for all).

5 The hazard ratio for death or cardio–renal events was 1.61 (1.05–2.47; $P = 0.04$) when retinopathy was present, 1.93 (1.38–2.69; $P < 0.001$) with macroalbuminuria alone, 4.34 (3.02–6.22; $P < 0.001$) with macroalbuminuria alone, 2.59 (1.76–3.81; $P < 0.001$) for retinopathy plus microalbuminuria and 6.83 (4.89–9.55; $P < 0.001$) for retinopathy plus macroalbuminuria.

6 Interaction between retinopathy and macroalbuminuria increased the relative excess risk by 15.31, which indicatesa biological interaction and highlights the importance of preventing the occurrence of one or both complications.

Tong PC, Kong AP, So WY et al (2007) Interactive effect of retinopathy and macroalbuminuria on all-cause mortality, cardiovascular and renal end points in Chinese patients with Type 2 diabetes mellitus. *Diabetic Medicine* **24**: 741–6

DIABETES

Metabolic syndrome increases risk of subclinical atherosclerosis

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

1 Owing to limited data on cardiovascular disease (CVD) risk in people with metabolic syndrome (MetS), this study investigated the prevalence of subclinical CVD in 1945 people who participated in the Framingham Offspring Study.

2 Mean age was 58 years and 59 % were female.

3 Electrocardiography, echocardiography, carotid ultrasound, ankle–brachial blood pressure and urinary albumin secretion measurements were taken.

4 Of the people with MetS, 51 % had subclinical disease in at least one test, a higher frequency than those without MetS (odds ratio: 2.06; 95 % CI: 1.67–2.55; $P < 0.0001$).

5 MetS was associated with an increased risk of CVD (hazard ratio [HR]: 1.61; 95 % CI: 1.12–2.33). At follow up (mean: 7.2 years), 10.2 % of people with MetS had developed CVD.

6 The presence of subclinical disease with MetS increased overt CVD risk (HR: 2.67; 95 % CI: 1.62–4.41) compared with people without diabetes, MetS or subclinical disease.

7 This association was attenuated when subclinical disease was absent (HR: 1.59; 95 % CI: 0.87–2.90).

8 Subclinical disease was also a predictor of CVD in people without MetS or diabetes (HR: 1.93; 95 % CI: 1.15–3.24).

9 MetS increases the risk of subclinical atherosclerosis, which contributes to CVD in people with diabetes.

Ingelsson E, Sullivan LM, Murabito JM et al (2007) Prevalence and prognostic impact of subclinical cardiovascular disease in individuals with the metabolic syndrome and diabetes. *Diabetes* **56**: 1718–26