

## Obesity



### Obesity, diabetes and kidney function

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There has been an increase in chronic kidney disease (CKD) that has, to some extent, been attributed to the increased prevalence of obesity and type 2 diabetes (Ting et al, 2009). The progression of CKD to end-stage renal disease not only has a significant impact on the affected individual's quality of life and survival but is also expensive, with the need for regular renal replacement therapy and renal transplantation.

Many studies examining the link between obesity and CKD have relied on estimated glomerular filtration rate (GFR). These calculations, however, have limitations in obese people. Nair et al (2011) studied the utility of the four-variable Modification of Diet in Renal Disease (MDRD) formula to estimate GFR in 111 people with type 2 diabetes compared with more objective GFR measurement using <sup>51</sup>chromium-labelled EDTA plasma clearance. They observed that, when adjusted for body surface area, the MDRD equation, which is commonly used in clinical practice, significantly underestimated GFR by 9.4 mL/min/1.73 m<sup>2</sup>. This discrepancy has implications for the classification of kidney disease as well as selection of renally cleared medications in obese patients.

Belhatem and colleagues, in the cross-sectional study summarised alongside, examined the relationship between extreme obesity (BMI ≥40 kg/m<sup>2</sup>) and renal function in 855 people with diabetes and 84 without the condition. They evaluated kidney function using the MDRD and Chronic Kidney Disease Epidemiology Collaboration (CKD-Epi) equations, <sup>51</sup>chromium-labelled EDTA plasma clearance and urinary albumin excretion (microalbuminuria, macroalbuminuria and albumin clearance). The MDRD and CKD-Epi estimations of GFR were not significantly different between the normal-

weight, overweight, obese and morbidly obese groups. However, GFR assessed by EDTA plasma clearance was lower in the participants with diabetes irrespective of the degree of obesity. The lowest GFR value was observed in people with type 2 diabetes and extreme obesity. An interaction between diabetes and obesity was seen for GFR. There was a significantly increased risk of microalbuminuria (odds ratio [OR], 1.99; 95% confidence interval [CI], 1.35–2.98) and macroalbuminuria (OR, 2.33; 95% CI, 1.25–4.22) in morbidly obese people after adjustment for potential confounders, including the presence of type 2 diabetes. Albumin clearance was highest in those with both type 2 diabetes and obesity. Interestingly, the severity of diabetic retinal disease increased with obesity.

This study confirms the challenges of estimating GFR in obese individuals. This is made more complex when weight loss occurs. Obesity was shown to have a significant impact on important renal parameters in people with diabetes. Several studies have shown that weight loss can be beneficial for both diabetes and renal function. Reducing body weight through medical and surgical interventions has been shown to improve renal function, albeit using less rigorous assessment methods (Bolignano and Zoccali, 2013). Managing bodyweight in people with diabetes is an important approach that has to be combined with glycaemic and blood pressure control to prevent and delay CKD. ■

Bolignano D, Zoccali C (2013) Effects of weight loss on renal function in obese CKD patients: a systematic review. *Nephrol Dial Transplant* **28**(Suppl 4): iv82–98

Nair S, Mishra V, Hayden K et al (2011) The four-variable modification of diet in renal disease formula underestimates glomerular filtration rate in obese type 2 diabetic individuals with chronic kidney disease. *Diabetologia* **54**: 1304–7

Ting SM, Nair H, Ching I et al (2009) Overweight, obesity and chronic kidney disease. *Nephron Clin Pract* **112**: c121–7

### Diabetes Res Clin Pract

#### Impact of obesity on kidney function in people with T2D

Readability ///

Applicability to practice ///

WOW! Factor ///

**1** These authors evaluated the contribution of obesity to kidney function, as defined by urinary albumin excretion (UAE) and glomerular filtration rate (GFR), in people with T2D.

**2** In a cross-sectional, prospective study, 855 people with T2D were compared with 84 volunteers without the condition, all stratified according to obesity levels.

**3** Participants with T2D had the same age, diabetes duration and HbA<sub>1c</sub> levels across BMI stages. However, UAE increased from 21 µg/mg in normal-weight people to 30, 33 and 51 µg/mg in overweight, obese and morbidly obese people, respectively ( $P < 0.001$  for trend).

**4** After adjustment for age, gender, systolic blood pressure and the presence of T2D, morbid obesity was associated with a risk of microalbuminuria (odds ratio [OR], 1.99;  $P < 0.001$ ) and macroalbuminuria (OR, 2.33;  $P = 0.006$ ).

**5** In people without T2D, body surface-adjusted GFR was not correlated with obesity stage. In people with T2D, however, GFR was lower than in the controls and reduced further as obesity levels increased ( $P < 0.001$ ).

**6** There was a significant interaction between the presence of T2D and obesity stage in terms of unadjusted GFR ( $P = 0.02$ ). For body surface-adjusted GFR, the trend approached significance ( $P = 0.07$ ).

**7** The authors conclude that obesity interacts with T2D to exacerbate kidney function, and that treatment should be targeted at both conditions in people who have them.

Belhatem N, Mohammedi K, Rouzet F et al (2015) Impact of morbid obesity on the kidney function of patients with type 2 diabetes. *Diabetes Res Clin Pract* **108**: 143–9

## Surg Obes Relat Dis

### Meta-analysis: sleeve gastrectomy versus RYGB for T2D

Readability ✓✓✓  
 Applicability to practice ✓✓✓  
 WOW! Factor ✓✓

- 1 While Roux-en-Y gastric bypass (RYGB) is viewed as the gold-standard bariatric surgery procedure, the number of sleeve gastrectomies being performed has increased in recent years, given the latter's perceived ease and lower risk of complications.
- 2 In this systematic review and meta-analysis, the authors compared the effects of sleeve gastrectomy and RYGB in terms of weight loss and T2D remission.
- 3 Overall, 11 studies (three retrospective, six prospective and two randomised controlled trials), with a total of 857 participants with T2D, were included in the final analysis.
- 4 The percentage of excess weight loss did not significantly differ between the two procedures (mean difference, 1.24%;  $P=0.67$ ).
- 5 Overall, there was a non-significant trend towards a lower rate of T2D remission with sleeve gastrectomy (odds ratio [OR], 0.90;  $P=0.07$ ); however, the results differed according to study type. In non-randomised studies, there was no significant difference, whereas in the two randomised studies remission was significantly less likely with sleeve gastrectomy (OR, 0.54;  $P<0.01$ ).
- 6 There was no significant correlation between the percentage of weight lost and the rate of T2D remission with either procedure, suggesting that T2D remission occurs through other mechanisms than weight loss.
- 7 The authors note the high heterogeneity among the studies, which may limit their conclusions.

Cho JM, Kim HJ, Menzo EL et al (2015) Effect of sleeve gastrectomy on type 2 diabetes as an alternative treatment modality to Roux-en-Y gastric bypass: systemic review and meta-analysis. *Surg Obes Relat Dis* 5 Mar [Epub ahead of print]

## J Clin Endocrinol Metab

### Endocrine-disrupting chemicals and obesity: Economic costs

Readability ✓✓✓  
 Applicability to practice ✓✓✓  
 WOW! Factor ✓✓

- 1 Endocrine-disrupting chemicals (EDCs) are associated with obesity and diabetes through their effects on a number of endocrine mechanisms.
- 2 In this study, the authors used current epidemiological data to estimate the disease burden and economic costs to the European Union associated with exposure to the three EDCs with the best documented evidence of obesogenicity.
- 3 Dichlorodiphenyldichloroethylene (DDE) was estimated to cause 1555 cases of overweight per year at the age of 10 years and 28 200 cases of adult diabetes per year.
- 4 Phthalate exposure was estimated to result in an extra 53 900 cases of obesity and 20 500 incident cases of diabetes in older women. Prenatal exposure to bisphenol A (BPA) was estimated to cause 42 400 cases of childhood obesity.
- 5 The total estimated attributable costs (both direct and indirect) were €859.6 million for DDE, €16.2 billion for phthalate and €1.54 billion for prenatal BPA exposure.
- 6 The authors point out that these costs are likely to be underestimations, as the majority of EDCs were not analysed owing to a poor evidence base.
- 7 While the effects of EDCs are small compared with the effects of diet and lifestyle, policies and regulation to limit human exposure to these agents could be executed more quickly and would be easier to implement and maintain.

Legler J, Fletcher T, Govarts E et al (2015) Obesity, diabetes, and associated costs of exposure to endocrine-disrupting chemicals in the European Union. *J Clin Endocrinol Metab* 100: 1278–88

## Diabetes Care

### Risk of colorectal cancer in T2D: Association with obesity

Readability ✓✓✓  
 Applicability to practice ✓✓✓  
 WOW! Factor ✓✓

- 1 In this study, the risk of colorectal cancer was compared between people with T2D and a reference population without the condition. Within the cohort with T2D, the associations between colorectal cancer, diabetes treatment stage and duration of obesity were also determined.
- 2 A total of 300 039 people with at least one prescription for an antidiabetes drug were compared in a 1:1 ratio with controls matched by birth year, gender and practice location.
- 3 Over a median follow-up of 4.5 years, there were 2759 cases of colorectal cancer in the population with T2D, compared with 2359 in the controls (adjusted hazard ratio [HR], 1.26; 95% confidence interval, 1.18–1.33).
- 4 People with insulin-treated T2D had a slight, non-significant increase in cancer risk compared with those receiving a single oral antidiabetes agent; however, overall, diabetes treatment stage did not affect the risk.
- 5 Among people with T2D, the duration of obesity conferred an additional risk of cancer. Compared with non-obese people with T2D, those with a recorded obesity duration of 4–8 years had an HR of 1.19, and those with a duration of >8 years had an HR of 1.28.
- 6 The authors attribute the increased risk of colorectal cancer to long-term exposure to high levels of endogenous insulin as a result of insulin resistance. Studies to determine whether weight loss can reverse the risk are warranted.

Peeters PJ, Bazelier MT, Leufkens HG et al (2015) The risk of colorectal cancer in patients with type 2 diabetes: associations with treatment stage and obesity. *Diabetes Care* 38: 495–502

“The authors conclude that obesity interacts with T2D to exacerbate kidney function, and that treatment should be targeted at both conditions in people who have them.”