Obesity

Obesity – a modifiable factor in peripheral vascular disease?

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There is increasingly convincing evidence that the incidence of both coronary artery and cerebrovascular disease can be reduced in people with diabetes by various interventions targeting dysglycaemia, lipid profiles, blood pressure and thrombosis. By contrast, the evidence for potential reversibility of peripheral vascular disease (PVD) – a common and difficult problem, requiring medical intervention – has been less forthcoming.

In the article abstracted alongside, Golledge et al found that increasing obesity was associated with a greater likelihood of worse outcomes in those with established PVD. While this was a relatively small prospective study in people with known PVD, the results suggest that obesity might be a significant reversible risk factor for PVD, or that obesity worsens the prognosis in established PVD. This is hardly surprising since obesity and the metabolic syndrome increase cardiovascular work substantially.

While Golledge et al do not report an intervention study, their data still suggest that prognosis may be more favourable in non-obese people with fewer cardiovascular risk factors, which in turn implies that weight loss might be beneficial. Therefore, these data add to the current understanding of PVD and suggest that favourable medical interventions may include smoking cessation, antithrombotic therapy with anticoagulants, intensive lipid lowering therapy and weight loss.

While this observation needs to be followed up and properly corroborated by intervention studies, it may nevertheless be an important finding. People with diabetes often have diffuse PVD, with a low likelihood of salvage through surgical revascularisation. It is important that all potentially reversible factors for disease progression are identified.

JOURNAL OF ENDOCRINOLOGICAL INVESTIGATION

ARBs improve metabolic profile

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

1 The insulin resistance syndrome comprises obesity, hypertension, dyslipidaemia and glucose intolerance.

2 Irbesartan and telmisartan are angiotensin II receptor blockers that reduce insulin resistance. Telmisartan also stimulates peroxisome proliferator activated receptor (PPAR) γ.

3 Insulin resistant, hypertensive and obese individuals without diabetes (n = 46) were assessed to determine variations in metabolic parameters following pharmacological intervention.

4 For 6 months, irbesartan 150 mg/day was administered to 23 individuals and a further 23 received telmisartan 80 mg/day.

5 At baseline and the end of the study period, adiponectin, glucose, cholesterol, triglycerides, free fatty acids, plasma insulin and glucose, and 24-hour blood pressure were measured.

6 Insulin sensitivity was ameliorated, adiponectin increased and blood pressure reduced with both drugs.

7 The amelioration of metabolic parameters was greater following telmisartan therapy. This agent also demonstrated an inverse correlation between adiponectin levels and blood pressure.

8 The authors suggest that this is probably due to the action of telmisartan as a PPARγ agonist.

Negro R, Formoso G, Hassan H (2007) The effects of irbesartan and telmisartan on metabolic parameters and blood pressure in obese, insulin resistant, hypertensive patients. *Journal of Endocrinological Investigation* **29**: 957–61

JOURNAL OF VASCULAR SURGERY

Intermittent claudication, diabetes and obesity

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

1 This study aimed to assess the association between obesity and peripheral arterial disease (PAD) given that obesity is a well-recognised risk factor for coronary artery disease.

2 The International Diabetes Federation definition was used to identify obesity and metabolic syndrome in 60 individuals with intermittent claudication.

3 When PAD was measured by the ankle–brachial pressure index, it was significantly associated with obesity ($P=0.03$) and serum adiponectin levels ($P=0.001$).

4 Obesity and serum adiponectin levels were also associated with initial claudication distance ($P= 0.009$ and 0.03, respectively) and graded treadmill-measured maximum walking distance ($P=0.001$ and 0.04, respectively).

5 Only maximum walking distance was significantly related to the metabolic syndrome ($P=0.02$).

6 At 24 months, outcome measures of death, cardiovascular events or revascularisation requirement were reported in 37 ± 7% of individuals with metabolic syndrome and 43 ± 9% of obese participants. This was greater than 0% and 11 ± 6%, respectively, for those who were not diagnosed with either metabolic syndrome or obesity.

7 The authors conclude that treating obesity in people with intermittent claudication might be important. They add that serum adiponectin concentrations might predict the response of these individuals to treatment.

Golledge J, Leicht A, Crowther RG et al (2007) Association of obesity and metabolic syndrome with the severity and outcome of intermittent claudication. *Journal of Vascular Surgery* **45**: 40–6

"Insulin resistance might be a factor in the pathogenesis of latent autoimmune diabetes."

"When orlistat is administered in addition to lifestyle counselling, weight loss is more easily maintained."

DIABETES, OBESITY AND METABOLISM

Insulin glargine benefits when oral treatment is insufficient

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

1 The aim of this study was to investigate if people with type 2 diabetes benefit from the addition of insulin glargine to inadequate oral antidiabetic treatment.

2 In a 9-month, open-label, multicentre, observational study, the safety and efficacy of insulin glargine was assessed in 12216 individuals with diabetes (mean age was 63.9±11.3 years).

3 Fasting blood glucose, insulin dose and HbA_{1c} were recorded at baseline, 6 months, 3 months and 9 months. BMI was also recorded to monitor any changes in weight.

4 Diabetes duration was >5 years in 47% of individuals, 1–5 years in 39%, <1 year in 10% and newly diagnosed in 4%.

5 Of the 12110012 enrolled in the study, 2789 had a BMI > 30 kg/m^2 and <35 kg/m^2; and 1055 had a BMI ≥ 35 kg/m^2.

6 Insulin glargine treatment reduced HbA_{1c} by on average 1.5% at 3 months, down from 8.7% and reduced fasting blood glucose by on average 3.8 mmol/l from 11.1 mmol/l. This effect was maintained at 9 and 20 months.

7 A total of 47 adverse events were reported in 26 individuals (0.02%), 19 of which were as a result of hypoglycaemia.

8 In everyday practice, the addition of insulin glargine to inadequate oral antidiabetic treatment improves glycaemic control with few side effects and little or no weight gain.

Schreiber SA, Haak T (2007) Insulin glargine benefits patients with type 2 diabetes inadequately controlled on oral antidiabetic treatment: an observational study of everyday practice in 12,216 patients. *Diabetes, Obesity and Metabolism* **9**: 31–8

DIABETES CARE

Orlistat maintains weight loss and reduces diabetes occurrence

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

1 Obese individuals with metabolic risk factors including type 2 diabetes controlled by diet alone, dyslipidaemia and impaired fasting glucose (n=383) were followed while undertaking an 8-week very-low-energy diet (VLED).

2 A VLED involves restriction of food intake to a maximum of 600–800 kcal/day.

3 In the 3 years following the VLED, those who achieved a ≥5% reduction in body weight (80.7%) received lifestyle counselling. In addition, they were randomised to either orlistat 120 mg three times daily or placebo.

4 The mean weight loss during the VLED was 14.4±2.0 kg. At 3 years, weight regain with orlistat (4.6±8.6 kg) was significantly less than the placebo group (7.0±7.1 kg; $P<0.02$).

5 A significantly smaller waist circumference was maintained in the orlistat group; 7.7 cm compared with 5.4 cm in the placebo group ($P<0.05$).

6 Orlistat significantly reduced the incidence of type 2 diabetes; 17 individuals developed diabetes while taking placebo compared with 8 using orlistat ($P=0.041$).

7 The results demonstrate that when orlistat is administered in addition to lifestyle counselling, weight loss is more easily maintained and the frequency of new onset type 2 diabetes is reduced.

Richelsen B, Tonstad S, Rossner S et al (2007) Effect of orlistat on weight regain and cardiovascular risk factors following a very-low-energy diet in abdominally obese patients: a 3-year randomized, placebo-controlled study. *Diabetes Care* **30**: 27–32

DIABETOLOGIA

Age, weight and inactivity increase the risk of latent autoimmune diabetes

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

1 The risk factors for latent autoimmune diabetes (LADA) are not well recognised, despite the fact that it is a common form of diabetes.

2 This study assessed age, weight and physical inactivity as possible indications of LADA.

3 Between 1984 and 1986, and 1995 and 1997, data were collected from 38800 volunteers as part of the Nord–Trøndelag Health Survey in Norway.

4 The results for 738 people with type 2 diabetes and 18 with type 1 diabetes were compared against 81 people with LADA.

5 Incidence of LADA was more likely in individuals with a BMI over 30 kg/m^2 (RR: 15.0; 95% CI: 7.51–29.97) or an age of at least 60 years (RR: 5.62; 95% CI: 2.36–13.4).

6 Similarly, type 2 diabetes was strongly associated with obesity (RR: 15.37; 95% CI: 12.07–19.57) and age (RR: 6.78; 95% CI: 5.07–9.06).

7 LADA and type 2 diabetes were also associated with physical inactivity.

8 In contrast, age, weight and inactivity were not predictive in those with type 1 diabetes.

9 The authors suggested that insulin resistance might be a factor in the pathogenesis of LADA in susceptible individuals with autoimmunity.

Carlsson S, Midthjell K, Tesfamarian MY, Grill V (2007) Age, overweight and physical inactivity increase the risk of latent autoimmune diabetes in adults: results from the Nord-Trondelag health study. *Diabetologia* **50**: 55–8