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The relative contributions of visceral fat and liver fat to insulin resistance and beta-cell function:  
The NEO study

Abstract

Background:

Obesity is associated with insulin resistance (IR) and impaired insulin secretion. It is unclear whether these associations are mainly due to total body fat (TBF), intra-abdominal visceral adipose tissue (VAT), or liver fat. The aim of this study was to investigate the relative contributions of TBF, visceral fat and liver fat to insulin resistance and  $\beta$ -cell function.

Methods:

In this cross-sectional analysis of the Netherlands Epidemiology of Obesity (NEO) study, a population-based cohort of 6,671 men and women aged 45 - 65 years, VAT was assessed by MRI in combination with <sup>1</sup>H-MR spectroscopy of hepatic triglyceride content (HTGC) in 2,076 participants, in addition to TBF with bioelectrical impedance analysis and fasting glucose and insulin concentrations. We calculated the Homeostasis Model Assessment (HOMA) of IR and  $\beta$ -cell function (B). We performed a linear regression of VAT, HTGC and TBF on HOMA-IR and HOMA-B, adjusted for age, ethnicity, education, alcohol consumption, smoking status, physical activity, dietary energy intake and hormonal therapy, and stratified by sex.

Results:

After exclusion of participants with glucose lowering therapy (n=88), alcohol abuse (n=109), and missing data (n=96), 1,783 participants (55% women) were analysed, with a mean and standard deviation (SD) of age: 55 (6) years, BMI: 26 (4) kg/m<sup>2</sup>, TBF: men 25% (5), women 36% (6), VAT: men 111 cm<sup>2</sup> (54), women 65 cm<sup>2</sup> (41), HTGC: men 6,6% (7.5), women 4,5% (7.5). In a joint model including VAT, HTGC and TBF, and confounding factors in men, per SD VAT HOMA-IR was 16.1% (95% CI: 9.9, 22.6) higher, per SD HTGC 15.6% (9.1, 22.4), and per SD TBF 18.7% (12.0, 25.7). In women, per SD VAT HOMA-IR was 27.5% (17.4, 38.5) higher, per SD HTGC 9.7% (2.5, 17.4), and per SD TBF 15.5% (5.9, 26.1). In the multivariate joint model in men, HOMA-B was 5.7% (-0.1, 11.9) higher per SD VAT, 6.6% (0.4, 13.1) per SD HTGC, and 15.1% (7.4, 23.3) per SD TBF. In women, HOMA-B was 13.6% (4.8, 23.1) higher per SD VAT, 2.7% (-2.1, 7.8) per SD HTGC, and 10.1% (0.7, 20.4) per SD TBF.

Conclusion:

All markers of total and regional adiposity were associated with insulin resistance and  $\beta$ cell function. Joint models showed that VAT was most strongly associated with both HOMA-IR and HOMA-B in women, whereas in men all markers of total and regional adiposity were similarly associated with HOMA-IR and HOMA-B. Visceral fat accumulation may in particular be detrimental in women.