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A large waist circumference is associated with higher liver fat in healthy pre-menopausal women in the absence of classical biochemical risk factors for CVD

L. Hodson[1], R. Banerjee[2], J. Cheeseman[1], F. Karpe[1] and B. A. Fielding[1,3]
[1]*Oxford Centre for Diabetes, Endocrinology and Metabolism, University of Oxford, Churchill Hospital, OX3 7LJ, UK,*
[2]*Oxford Centre for Magnetic Resonance Research, University of Oxford, John Radcliffe Hospital, OX3 9DU, UK*
and [3]*Postgraduate Medical School, University of Surrey, GU2 7WG, UK*

Epidemiological data have shown that a large waist circumference is associated with CVD[(1)], and that risk of CVD is greater in post- than pre-menopausal women. However, few detailed metabolic studies have investigated these relationships in women. The association between waist size and CVD may be mediated by liver fat. Therefore, we aimed to measure liver fat in healthy pre-menopausal women, using a sensitive imaging technique, and look for evidence of early metabolic changes.

We recruited healthy white Caucasian women aged 35–45 with a waist circumference <80 cm, *n* 11, or 80–110 cm, *n* 15. Women in the higher waist group had a significantly higher ratio of upper body fat (android) to lower body fat (gynoid), $P<0.05$, as measured by DEXA, and a greater proportion of fat-to-lean tissue ($P<0.05$). We used magnetic resonance spectroscopy to measure liver fat (intrahepatocellular lipid, IHCL) and adipose tissue area at the level of the L4 vertebra. We analysed the fatty acid composition of VLDL-TAG after overnight fasting to investigate hepatic fatty acid metabolism. We measured $16:1n-7/16:0$ in VLDL–TAG as an index of hepatic stearoyl CoA desaturase mRNA expression and hepatic lipid composition[(2)] and also $18:1n-9/18:0$[(3)]. Women with a waist <80 cm had very little IHCL (geometric mean (GM), 0.85 range 0.44–1.81 %, *n* 11), whereas those with a waist ≥ 80 cm had significantly more IHCL over a wide range (GM, 2.59 range 1.18–14.8 %, *n* 7, $P<0.01$). IHCL was significantly correlated with waist circumference ($r_s = 0.67$, $P<0.01$), visceral fat ($r_s = 0.67$, $P = 0.01$) and plasma insulin ($r_s = 0.69$, $P<0.01$). There were no significant differences between groups for plasma biochemical variables such as glucose, TG, cholesterol and NEFA. However, our results suggested differences in hepatic fatty-acid metabolism. All SCD ratios were lower in the high waist group for example, $16:1n-7/16:0$ in $VLDL_1$-TAG was 0.19 (SE 0.014, *n* 9) *v.* 0.15 (SE 0.013, *n* 13) $P = 0.061$ and in $VLDL_2$ was 0.18 (SE 0.013) *v.* 0.14 (SE 0.013), $P<0.05$. Measurements of both $18:1n-9/18:0$ and 16:1n-7/16:0 were highly correlated between $VLDL_1$ and $VLDL_2$ ($r_s = 0.93$, $P<0.001$ and $r_s = 0.96$, $P<0.001$, respectively).

Women are relatively protected against CVD before the menopause but above a waist circumference of 80 cm, there is greater intra-hepatic fat accumulation and subtle differences in VLDL–TAG metabolism. These may represent early events associated with the pathogenesis of CVD that are not apparent in classical biochemical risk factors.

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