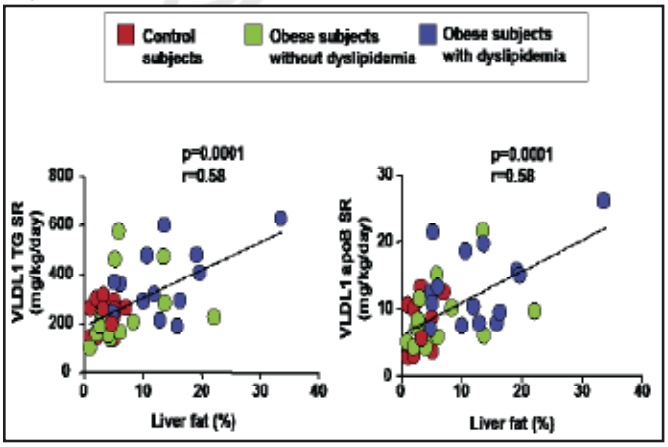
obesity [Taskinen MR et al. *Arterioscler Thromb Vasc Biol* 2011]. In those who do, nonalcoholic fatty liver disease, especially in its more severe forms, is linked to an increased risk of CVD, independent of underlying cardiometabolic risk factors [Stefan N et al. *Endocr Rev* 2008; Gastaldelli A et al. *Hepatology* 2009; Speliotes EK et al. *Hepatology* 2010].

Taskinen and colleagues investigated if hypertriglyceridemia (HTG) in obese men with similar body mass indexes, waist circumferences, and levels of visceral adiposity is caused by increased hepatic secretion induced by increased liver fat. Results showed that dual metabolic defects are required to produce HTG in obese subjects with similar levels of visceral adiposity, ie, the combination of increased secretion driven by liver fat content and severely impaired clearance of triglyceride-rich $VLDL_1$ particles linked to the elevation of apolipoprotein CIII. Notably, there was an overproduction of large VLDL particles associated with small dense LDL and lowering of HDL as seen in the atherogenic lipid triad. The data suggest that overproduction of VLDL particles is a mechanism to export extra fat out of the liver (Figure 2) [Taskinen MR et al. *Arterioscler Thromb Vasc Biol* 2011]. The data highlights the clinical importance of assessing hypertriglyceridemic waist to indentify obese subjects at high cardiometabolic risk.

Figure 2. Liver Fat Drives Production of VLDL1.



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Strategies that decrease liver fat and improve insulin sensitivity may boost whole-body insulin sensitivity [Byrne CD. *Diabet Med* 2012] and reduce CVD risk factors and lipotoxicity related to contractile, mitochondrial, and endoplasmic reticulum dysfunction; steatosis; and apoptosis [Wende AR, Abel ED. *Biochim Biophys Acta* 2010].

Beyond Weight Loss: Rethinking Treatment Strategies for Obesity

Written by Rita Buckley

Can physical activity with little or no weight loss deliver health benefits? Robert Ross, PhD, Queen's University, Kingston, Ontario, Canada, answered this question and discussed the role of physical activity/exercise in the management of abdominal obesity.

The global prevalence of obesity (BMI≥30 kg/m^2) almost doubled between 1980 and 2008, bringing the number of obese people to half a billion [World Health Organization. *World Health Statistics: A Snapshot of Global Health* 2012]. This rapid growth indicates an urgent need to identify effective interventions that can reduce or eliminate the high personal, societal, and healthcare costs associated with obesity.

Anti-obesity programs to date have focused on weight loss through lifestyle interventions, ie, changes in diet and exercise. However, the emphasis on weight loss may be misleading, diverting efforts from other approaches that may also help to achieve public health objectives. According to Prof. Ross, it is time to rethink our lifestyle management targets. To manage obesity and related health risks, clinicians must look beyond weight loss as the only indicator of therapeutic/treatment success.

Data indicate that obesity and its associated health risks can be reduced by increased physical activity with or without weight loss [Ross R, Bradshaw AJ. *Nat Rev Endocrinol* 2009]. A study of premenopausal women with abdominal obesity showed that equivalent diet- or exercise-induced weight loss and exercise without weight loss produced similar decreases in visceral fat in all treatment groups ($p<0.008$) [Ross R et al. *Obes Res* 2004]. A study of obese men also found decreased abdominal and visceral fat in the weight-loss group ($p<0.001$) as well as in the exercise-without-weight-loss group ($p=0.001$) [Ross R et al. *Ann Intern Med* 2000].

Janiszewski and Ross [*Appl Physiol Nutr Metab* 2007] identified a dose-response relationship between minutes per week of exercise and decreases in subcutaneous and visceral adipose tissue (VAT). Similarly, Coker et al. [*Metab Syndr Relat Disord* 2009] reported significant reductions in the abdominal/visceral fat of elderly adults with high-intensity exercise (-39 cm^2) compared with the medium-intensity exercise group and the control group.

More recently, a systematic review and meta-analysis by Ismail et al [*Obes Rev* 2012] reported a significant pooled effect size (ES) in a comparison of aerobic therapy versus control (ES -0.33; 95% CI, –0.52 to –0.14; p<0.01), suggesting that aerobic exercise is central for exercise programs aimed at reducing visceral adipose tissue (VAT) and that levels below current recommendations for overweight/obesity management may be sufficient for beneficial VAT modification.

Translating these findings into effective treatment within primary-care settings may be a challenge. In a randomized controlled trial that compared a behavioral intervention (individual counseling from health educators to promote physical activity with a healthful diet) to usual care (advice from physicians), outcomes showed that the former was associated with modest reductions in waist circumference in men but not women [Ross R et al. *Arch Intern Med* 2012].

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