

Human adipose tissue morphology and function

Relation to insulin sensitivity and glucose tolerance with focus on pregnancy and women with previous gestational diabetes mellitus

Akademisk avhandling

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Av

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Avhandlingen baseras på följande delarbeten:

- I. Svensson H, Odén B, Edén S, and Lönn M
Adiponectin, chemerin, cytokines and dipeptidyl peptidase 4 are released from human adipose tissue in a depot-dependent manner: an in vitro system including human serum albumin
BMC Endocrine Disorders. 2014; 14:7
- II. Svensson H, Wetterling L, Bosaeus M, Odén B, Odén A, Jennische E, Edén S, Holmäng A, and Lönn M
Body fat mass and the proportion of very large adipocytes in pregnant women are associated with gestational insulin resistance
Submitted manuscript
- III. Svensson H, Wetterling L, Odén A, Jennische E, Edén S, Holmäng A and, Lönn M
BMI, waist-to-height ratio and adipocyte volume are associated with impaired glucose metabolism and insulin resistance in women with previous gestational diabetes: A 6-year follow-up study
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UNIVERSITY OF GOTHENBURG

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ABSTRACT

Obesity is a global health problem and affects women of reproductive age. During pregnancy, obesity increases the risk for gestational diabetes mellitus (GDM), in turn predisposing for type 2 diabetes (T2D). Not only the amount and distribution of adipose tissue (AT) but also the AT morphology and function are of importance in pathogenesis of metabolic disease related to obesity. The aims of this thesis were 1) to compare subcutaneous (SC) and visceral AT regarding release of adipokines, implicated in insulin resistance/inflammation, using an in vitro system reflecting the release in vivo, and 2) to characterize AT morphology and function in normal weight (NW) and obese pregnant women in trimester 1 and 3, and in women with previous GDM, and identify AT-related factors associated with insulin resistance and impaired glucose metabolism.

AT biopsies were obtained from 1) patients undergoing surgery at Sahlgrenska University Hospital, and 2) women in the Pregnancy Obesity Nutrition and Child Health (PONCH) study. AT adipokine release and immune cell/blood vessel density, and adipocyte size/number and lipolytic activity were analyzed. Women were examined regarding insulin resistance (HOMA-IR), glucose tolerance, body composition and blood chemistry.

Chemerin, cytokines, and dipeptidyl peptidase 4 were more abundantly released from visceral than SC AT; adiponectin release was higher from the SC depot. During pregnancy, NW women accumulated fat in existing adipocytes (which became larger) and adiponectin levels were reduced. Obese women had signs of adipocyte recruitment and maintained adiponectin levels. Fat mass and the proportion of very large adipocytes were associated with HOMA-IR in trimester 3. In women with previous GDM, follow-up body mass index (BMI) was the best discriminator of normal vs impaired glucose metabolism, and waist-to-height ratio and adipocyte volume were associated with HOMA-IR.

To conclude, adipokines implicated in metabolic dysfunction are released from AT in a depot-dependent manner. AT mass/morphology contribute to gestational insulin resistance. During pregnancy, AT morphology appears to change oppositely in NW and obese women, possibly protecting obese women against even more severe insulin resistance. To prevent T2D, BMI and abdominal fat accumulation should be controlled in women after GDM.

Keywords: Adipose tissue, adipocyte, adipokines, insulin resistance, pregnancy, gestational diabetes mellitus, type 2 diabetes mellitus

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