ADIPOCYTE SIZE IN MORBIDLY OBESE WOMEN AND ITS RELATION TO TYPE 2 DIABETES

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Abstract

Aim of the study: The aim was to perform a morphometric analysis of subcutaneous and visceral adipose tissue of morbidly obese women and to determine the relationship between adipocyte size and the development of type 2 diabetes (T2D).

Materials and methods: White adipose tissue of morbidly obese women was obtained from subcutaneous and omental adipose tissue during bariatric surgery. The same tissues were obtained at judicial autopsy in non-obese (lean) non-diabetic patients. The harvested tissue was embedded in paraffin and 5 μm thick hematoxylin-eosin stained sections were analyzed by the Olympus cellSens system. Statistical evaluation was performed by GraphPad Prism 6.1 software.

Results: We found a relationship between adipocyte size and the presence of T2D. The most pronounced changes were seen in visceral adipocytes (cell diameter increased from 61.9 μm in controls to 79.5 μm in patients with T2D). Also, the size of the subcutaneous adipocytes increased against the control. A statistically significant difference between diabetic and non-diabetic patients was not proven in subcutaneous adipocytes. We also observed differences in the distribution of adipocyte mean diameters. Whilst in the control group there was a normal (Gaussian) distribution, in the morbidly obese we found an asymmetric distribution with a positive skewness to the right.

Conclusion: We have demonstrated that in morbidly obese women a significant increase in visceral adipocyte size is associated with the development of both insulin resistance and T2D.

Key words: morbid obese, diabetes type 2, adipocyte size

INTRODUCTION

Adipocyte size can be easily measured and compared. Their change is considered to be a sign of their dysfunction. Enlarged adipocytes exhibit abnormal expression and secretion of adipokins (1, 2, 3, 4, 5). Large adipocytes are also considered a marker of insulin resistance (6, 7). Conversely, other authors consider a greater proportion of small adipocytes to cause inflammatory changes in adipose tissue and insulin resistance (8, 9). The aim of our study was to analyze the cells in subcutaneous and visceral adipose tissue in morbidly obese women and to evaluate their changes in size in relation to the T2D.

MATERIAL AND METHODS

The studied material was obtained by intraoperative biopsy in patients, some with T2D and others not diabetic, who were undergoing bariatric surgery for obesity. The same tissues were obtained at judicial autopsy of non-obese non-diabetic patients. The study group

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included 30 women. In the control group the mean BMI was 24.3 and the average age of 38 years, in the non-diabetic women the mean BMI was 45.2 and the average age of 41 years, in the diabetic group the mean BMI was 44 and the average age was 43 years. All patients gave their written informed consent. The study was approved by the local ethics committee of Vitkovice Hospital a.s., Ostrava – Vitkovice, Czech Republic, and was performed in accordance with the Helsinki Declaration (Fortaleza 2013).

We investigated both subcutaneous (taken from the umbilicus region) and omental white adipose tissues. Tissue samples were immediately fixed in 10% buffered formalin, dehydrated, and embedded in paraffin. Paraffin sections (5μm thick) were stained with hematoxylin-eosin. Morphometric analysis was performed using the Olympus cellSens system.

Statistical Analysis
The obtained results were evaluated by the Mann-Whitney test to find differences between the studied groups at the level of significance $P < 0.05$. All calculations were performed by GraphPad Prism 6.1 software.

RESULTS
We demonstrated a statistically significant increase in adipocyte size, both in subcutaneous and visceral adipose tissues, compared to their size in subjects with body mass index in the physiological (non-obese) range (Fig. 1–3). The largest mean values of the diameters of the adipocytes were found in the subcutaneous tissue (85.0 μm in patients with T2D and 83.5 μm in patients without T2D), these values were of statistically significant difference compared to the control group (70.2 μm).

Fig. 1. White adipose tissues: (a) visceral; (b) subcutaneous. The size of adipocytes is significantly smaller in visceral adipose tissue. Women, BMI 27. Magnification 20× HE.

Fig. 2. White adipose tissues: (a) visceral; (b) subcutaneous. A significant increase of the size of adipocytes in both visceral and subcutaneous adipose tissues. Women, BMI 40, T2D. Magnification 20× HE.
The measured values for adipocytes in visceral adipose tissue were smaller compared to the subcutaneous adipocytes, but showed a significantly greater increase compared to the control. Whilst the average size of the controls was 61.6 μm, in obese non-diabetic women it was 70.3 μm and 79.5 μm in the T2D group. All the differences were of high statistical significance. (Fig. 4).

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The distribution of measured values also differs (Fig. 5). While we have found a normal Gaussian distribution for the control, the population of the smaller adipocytes was not present in the obese group, whereas the hypertrofic adipocytes are more numerous (asymmetric distribution with positive skewness).
DISCUSSION

Adipocyte size is generally considered an important indicator of adipose tissue health (7,10). In our study we demonstrated the most significant changes in the size of visceral adipocytes in the morbidly obese women with T2D. Their size was significantly higher from those of obese size without diabetes. There were no similar differences in subcutaneous adipose tissue. We have demonstrated identical trend in our previous study when we investigated macrophage infiltration of adipose tissue. The highest number of macrophages was found in visceral adipose tissue of women with T2D.

The enlargement of adipocytes found in the obese is well known (2,11,12,13), and a difference in size of subcutaneous and visceral adipocytes has also been reported (5,10,11,12,14,15,16). The increase in size is caused by the accumulation of triglycerides, due to a high level of energy sources. After saturating the storage capacity of adipocytes, ectopic fat depots are formed in the liver, muscles, and elsewhere (14,17,18). There is a change in chemokine production, particularly an increase of pro-inflammatory cytokine secretion (2), in enlarged adipocytes. Hypertrophic adipocytes express and secrete increased amounts of leptin and are also more likely to undergo cell death (18).

The size of visceral adipocytes is considered to be a marker of insulin resistance and metabolic syndrome. Large adipocytes are resistant to the antilipolytic effect of insulin (6,7,14). When body weight is reduced (e.g. by surgery, diet, etc.), adipocyte size decreases, insulin sensitivity is improved, and adipokine production is adjusted (19,20).

Bredela et al. found a reduction in subcutaneous adipocyte size and an improvement in glucose tolerance after administration of growth hormone 2 mg/kg/day (21).

Hoffsted et al. state that an increased number of small adipocytes (hyperplasia) results in a protective influence on the development of changes in lipid metabolism, glucose and cell sensitivity to insulin (14).

The absence of small adipocytes in the morbidly obese patients can be explained by a defect in the formation of new fat cells, leading to a greater deposition of triglycerides into already differentiated cells, resulting in their hypertrophy as well as in the other metabolic changes described above (8,9,11,22). Lessars et al. explain hypertrophy of visceral adipocytes by the limited ability of preadipocyte adipogenesis in subcutaneous adipose tissue, preventing the accumulation of subcutaneous fat, causing lipid overflow of the visceral compartment (12).
In conclusion, the size of adipocytes is an important marker of development of insulin resistance in morbidly obese women. The largest adipocytes were found in the visceral tissue of women with T2D. In the morbidly obese women we did not identify the presence of a population of small adipocytes.

REFERENCES


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