Subcutaneous abdominal adipose tissue is associated with an index of insulin sensitivity/resistance

Katsura Niijima, Yoko Shimoda, Tsugumichi Saito, Eijiro Yamada, Yawara Niijima, Shuichi Okada, and Masanobu Yamada

Kan-etsu Chuo Hospital, Takasaki, Gunma, Japan; Department of Medicine and Molecular Science, Gunma University Graduate School of Medicine, Maebashi, Gunma, Japan

To assess whether there is any clinical significance for determining the normal range of subcutaneous abdominal fat area, we compared fat area with insulin sensitivity. Visceral and subcutaneous abdominal fat area at the L4-L5 thoracic level was determined by computed tomography (CT). Plasma glucose and insulin levels were determined after an overnight fast and calculated by the homeostatic model assessment of insulin resistance (HOMA-IR). We analyzed 350 (180 male and 170 female) subjects whose BMI was 18.5 < BMI < 25. The subcutaneous abdominal fat area of the female subjects was 124.7 ± 46.13 cm² and that of male subjects was 77.53 ± 37.53 cm² (mean ± SD). We compared HOMA-IR between subjects whose visceral abdominal fat area was above 100 cm² and subcutaneous abdominal fat area below the mean ± 2SD (15 subjects, 6 male and 9 female) with subjects whose visceral abdominal fat area was also above 100 cm² but whose subcutaneous abdominal fat area was above the mean ± 2SD (20 subjects, 7 male and 13 female). The HOMA-IR of the former subjects group was 8.17 ± 6.22 and that of the latter subjects group was 3.37 ± 2.07 (p = 0.0486). Subjects with increased subcutaneous abdominal fat area displayed lower HOMA-IR values, demonstrating a protective effect of subcutaneous fat for individuals with visceral abdominal fat area above 100 cm².

Introduction

Multiple studies have reported that intraabdominal (visceral) adipose tissue is a major contributor to metabolic risk. On the other hand, it was reported that the Health, Aging, and Body Composition Study reported that large subcutaneous thigh fat was independently associated with more favorable glucose (in men) and lipid profile (in both genders). Similarly, Porter et al reported that subcutaneous abdominal fat plays a protective role on atherosclerosis and triglyceride unlike visceral abdominal fat. These studies suggest that determining the relative range of subcutaneous and visceral abdominal fat area may provide additional clinical significant information for deciding the appropriate treatment of patient with metabolic dysfunction. The data presented in this report clearly demonstrates that for individuals with visceral abdominal fat area > 100 cm², the amount of abdominal subcutaneous abdominal fat is a predictor of insulin sensitivity.

Methods

Our study protocol was reviewed and approved by Kan-etsu Chuo Hospital review boards according to the Declaration of Helsinki. Written informed consent was obtained from each participant. We analyzed 350 (180 male and 170 female) subjects whose BMI was 18.5 < BMI < 25 in this clinical study. They were received comprehensive medical check-up annually.

Visceral and subcutaneous abdominal fat area was determined by CT (CT) using L4-L5 level method as previously reported by Matsuzawa et al. Plasma glucose and insulin levels following an overnight fast and the homeostatic model assessment of insulin resistance (HOMA-IR) was used to estimate peripheral insulin sensitivity. Total cholesterol, leptin, and TNF-α were determined by LSI Medience Corporation.

Venous blood samples were collected into tubes containing ethylenediaminetetraacetic acid (EDTA) and fluoride. Plasma was separated from whole blood within 1 h after collection, and plasma glucose and HbA1c
concentrations were determined as previously reported [7, 8]. Brachial-ankle pulse wave velocity (baPWV) was also measured as previously reported7,8 in order to compare our results and previous results from the point of research objectivity and suitability.

The InStat 2 program was used for statistical analyses.

Results

The subcutaneous abdominal fat area of female was 124.7 +/− 46.13 (mean±SD) cm² and that of male was 77.53 +/− 37.53 cm². In this study, we considered that upper limit of standard value for the female subcutaneous abdominal fat area was 217 cm² (mean+2SD) and upper limit of standard value for male subcutaneous abdominal fat area was 153 cm² (mean+2SD).

The averages of study subjects were as follows. Age was 61.14 ± 11.35 y old, fasted blood glucose (FBS) was 97.7 ± 9.02 mg/dL, glycosylated hemoglobin (HbA1c) was 5.31 ± 0.30 %, immunoreactive Insulin (IRI) was 17.42 ± 13.88 μU/mL, the HOMA-IR was 3.51 ± 3.30, total cholesterol was 188.04 ± 28.35 mg/dL, TNF-α was 1.40 ± 0.71 pg/mL (normal range; <6 pg/mL) and Leptin was 13.75 ± 7.57 ng/mL (normal range; male 0.9–13.0, female 2.5–21.8).

We compared HOMA-IR between subjects whose visceral abdominal fat area was above 100 cm² but that the subcutaneous abdominal fat area was above the mean + 2SD (20 subjects, 7 male and 13 female) with subjects whose visceral abdominal fat area was above 100 cm² and also subcutaneous abdominal fat area was below the mean + 2SD (15 subjects, 6 male and 9 female). As shown in Table 1, the HOMA-IR of the former subjects group was 3.37 ± 2.07 and that of the latter subjects group was 8.17 ± 6.22 (p = 0.0486).

As shown in Figure 1, baPWV of subjects whose visceral abdominal fat area was above 100 cm² but with subcutaneous abdominal fat area above the mean + 2SD was significantly lower than that of subjects whose visceral abdominal fat area was above 100 cm² with subcutaneous abdominal fat area below the mean + 2SD (1,251 ± 286 vs 1,567 ± 238 cm/second, p = 0.012).

Table 1. Estimation of HOMA-IR.

| Subcutaneous abdominal fat area (cm²) | <Mean + 2SD | ≥Mean + 2SD |
|--------------------------------------|-------------|-------------|
| Visceral abdominal fat area > 100 cm² | 8.17 ± 6.22 | 3.37 ± 2.07 |

Note. 35 Subjects showed 18.5 < BMI < 25 and visceral fat area was above 100 cm². Among 35 subjects, 20 subjects (7 male and 13 female) showed that subcutaneous abdominal fat area was above the mean + 2SD and 15 subjects (6 male and 9 female) showed that subcutaneous abdominal fat area was below the mean + 2SD. The HOMA-IR between two groups was significantly different (p=0.0486).

Discussion

In this clinical study, we estimated that the subcutaneous abdominal fat area of female was 124.7 ± 46.13 cm² and that of male was 77.53 ± 37.53 cm². Also in this study, we determined that excess amount of subcutaneous abdominal fat area was larger than the upper limit of standard value (mean + 2SD). In these individuals, baPWV whose visceral abdominal fat area was above 100 cm² but with subcutaneous abdominal fat area above the mean + 2SD was significantly lower than that of subjects whose visceral abdominal fat area was above 100 cm² with subcutaneous abdominal fat area below the mean + 2SD. As baPWV assesses atrial stiffness, these data are consistent with the previous study of Porter et al reported6 supporting the role of subcutaneous abdominal fat in protection against the development of atherosclerosis.

As a parameter of insulin resistance/sensitivity, HOMA-IR was selected in this clinical study and the HOMA-IR of subjects whose visceral abdominal fat area was above 100 cm² but with subcutaneous abdominal fat area above the mean + 2SD was significantly lower than that of subjects whose visceral abdominal fat area was above 100 cm² with subcutaneous abdominal fat area below the mean + 2SD. Based on these results we considered that large amount of subcutaneous abdominal fat area was beneficial for not only atrial stiffness but also insulin resistance in the case of the population whose BMI was 18.5 < BMI < 25 and visceral fat area was above 100 cm². Thus it can be considered that identification of normal
range of subcutaneous abdominal fat area is clinically significant in comparison with the estimation of visceral abdominal fat. However it will be required to analyze larger number of subjects at younger ages and in different ethnic populations to confirm the generality of these results.

Disclosure of potential conflicts of interest
The authors declare that they have no conflicts of interest that could be perceived as prejudicing the impartiality of the information presented in this report.

Acknowledgment
We would like to thank Dr. Jeffrey E. Pessin (Albert Einstein College of Medicine, Bronx, NY, USA) for critical suggestions correcting English about our manuscript.

Funding
This research did not receive any specific grant from any funding agency in the public or commercial sector or from any of the each co-authors.

Author contributions
NK, TS, SO, and YN took care of subjects in this study. SO, EY, YN, and MY analyzed the data and prepared the manuscript.

References

[1] Garg, A. Regional adiposity and insulin resistance. J Clin Endocrinol Metab 2004; 89:4206-10; PMID:15356007; http://dx.doi.org/10.1210/jc.2004-0631

[2] Matsuzawa Y, Shimomura I, Nakamura T, Keno Y, Kotani K, Tokunaga K. Pathophysiology and pathogenesis of visceral fat obesity. Obes Res 1995; 2:1875-1945; http://dx.doi.org/10.1002/j.1550-8528.1995.tb00462.x

[3] Fujimoto WY, Abbate SL, Kahn SE, Hokanson JE, Brunzell JD. The visceral adiposity syndrome in Japanese-American men. Obes Res 1994; 2:364-71; PMID:16353583; http://dx.doi.org/10.1002/j.1550-8528.1994.tb00076.x

[4] Banerji MA, Faridi N, Atluri R, Chaiken RL, Lebovitz HE. Body composition, visceral fat, leptin, and insulin resistance in Asian Indian men. J Clin Endocrinol Metab 1999; 84:137-44; PMID:9920074

[5] Snijder MB, Visser M, Dekker JM, Goodpaster BH, Harris TB, Kritchevsky SB, De Rekeneire N, Kanaya AM, Newman AB, Tylavsky FA, Seidell JC, Health ABC Study. Low subcutaneous thigh fat is a risk factor for unfavourable glucose and lipid levels, independently of high abdominal fat. The Health ABC Study. Diabetologia 2005; 48:301-8; PMID:15660262; http://dx.doi.org/10.1007/s00125-004-1637-7

[6] Porter SA, Vasan RS, Massaro JM, O’Donnel CJ, Hoffmann UH, Fox CS. Abdominal subcutaneous adipose tissue: a protective fat depot? Diabetes care 2009; 32:1068-75; PMID:19244087; http://dx.doi.org/10.2337/dc08-2280

[7] Ando T, Okada S, Niiijima Y, Hashimoto K, Shimizu H, Tsuchiya T, Yamada M, Ohshima K, Mori M, Ono K. Impaired glucose tolerance, but not impaired fasting glucose, is a risk factor for early-stage atherosclerosis. Diabet Med 2010; 27:1430-5; PMID:21059096; http://dx.doi.org/10.1111/j.1464-5491.2010.03144.x

[8] Niiijima K, Muranaka Y, Ando T, Okada S, Niiijima Y, Hashimoto K, Yamada M, Ohshima K, Mori M, Ono K. Elevated 1-h plasma glucose following 75-g oral glucose load is a predictor of arterial stiffness in subjects with normal glucose tolerance. Diabet Med 2012; 29:e457-60; PMID:23002926; http://dx.doi.org/10.1111/dme.12026