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Higher visceral to subcutaneous fat ratio is associated with small intestinal bacterial overgrowth

A. Fialho [a,*], A. Fialho [a], P. Thota [b], A. McCullough [b], B. Shen [b]

[a] Department of Internal Medicine, The Cleveland Clinic Foundation, Cleveland, OH, USA
[b] Department of Gastroenterology and Hepatology, The Cleveland Clinic Foundation, Cleveland, OH, USA

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Abstract *Background and Aims:* There is a lack of studies evaluating the association between small intestinal bacterial overgrowth (SIBO) and abdominal fat. The aim of this study was to evaluate whether visceral fat area (VFA), subcutaneous fat area (SFA) or visceral to subcutaneous fat ratio (VFA/SFA ratio) were associated with SIBO.
Methods and Results: In this case–control study, 152 eligible patients submitted to glucose hydrogen/methane breath test who also had computed tomography (CT) of the abdomen performed were included. Clinical and demographic information was obtained. VFA and SFA were measured using Image J software at lumbar 3 level on CT cross-sectional image of the 152 patients included in this study, 68 patients (44.7%) tested positive for SIBO. In the univariate analysis, the presence of SIBO was associated with older age (65.2 ± 1.5 vs. 59.3 ± 1.5, $p = 0.007$); type 2 diabetes mellitus (33.8% vs. 17.9%; $p = 0.019$); hypertension (63.2% vs. 39.3%; $p = 0.003$); metabolic syndrome (85.3% vs. 64.3%; $p = 0.003$); and higher VFA/SFA ratio (1.0 ± 0.1 vs. 0.7 ± 0.1; $p < 0.001$). In multivariate analysis, metabolic syndrome (odds ratio [OR]: 2.5; 95% confidence interval [CI]: 1.1–5.7; $p = 0.035$) and higher VFA/SFA ratio (OR: 3.3; 95% CI: 1.6–7.2; $p = 0.002$) remained independently associated with SIBO.
Conclusion: The presence of SIBO was found to be associated with high VFA/SFA ratio measured from cross-sectional CT image.

Introduction

Obesity defined as a body mass index (BMI) > 30 m^2/kg is a well-known risk factor for hypertension, type 2 diabetes mellitus (DM), obstructive sleep apnea and cardiovascular disease [1–4]. Both visceral and subcutaneous fat along with height contribute to BMI, which is calculated by dividing weight in kg to the square of the height in meters. More recently the accumulation of visceral fat has been pointed as the body fat compartment mostly associated

Abbreviations: BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; CT, computer tomography; DM, diabetes mellitus; HGF, hepatocyte growth factor; IL-1Ra, interleukin-1 receptor antagonist; IL-6, INTERLUKIN-6; IL-8, interlukin-8; IQR, interquartile range; MCP-1, monocyte chemoattractant protein-1; OR, odds ratio; SFA, subcutaneous fat area; SIBO, small intestine bacterial overgrowth; SD, standard deviation; TLRs, Toll-like receptors; TNF-α, tumor necrosis factor-α; VEGF, vascular endothelial growth factor; VFA, visceral fat area; VFA/SFA, visceral to subcutaneous fat ratio.

* Corresponding author. Department of Internal Medicine, The Cleveland Clinic Foundation, 9500 Euclid Ave, Cleveland, OH 44195, USA. Tel.: +1 216 444 9252; fax: +1 216 444 6305.
E-mail address: fialhoa@ccf.org (A. Fialho).

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with a negative cardio-metabolic profile, the development of chronic kidney disease and a higher surgical risk in patients with inflammatory bowel disease [5,6]. Increased visceral fat area (VFA) has been implicated as an important metabolic risk factor for the development of coronary atherosclerosis, independent from subcutaneous fat area (SFA) or overall obesity [6–8]. In addition, visceral to subcutaneous fat ratio (VFA/SFA ratio) has been associated with cardio-metabolic disease [9,10].

Small intestinal bacterial overgrowth (SIBO), a condition caused by excessive proliferation of small intestinal bacteria, is responsible for a diverse array of symptoms such as bloating, flatulence, abdominal pain and diarrhea [11]. SIBO and intestinal microbiota have been associated with various disease conditions, such as fatty liver, irritable bowel syndrome (IBS), type 2 DM, hypertension and obesity [12–16]. The association between SIBO and obesity has not been quantified. There is a lack of studies evaluating the association between visceral or subcutaneous fat and SIBO. We hypothesized that SIBO is associated with increased mesenteric fat. Therefore the aim of the study was to evaluate whether VFA, SFA or VFA/SFA ratio were associated with SIBO.

Methods

Patients were identified from the databank of the Gastrointestinal Motility Lab at the Cleveland Clinic. A total of 152 consecutive eligible patients tested for SIBO using glucose hydrogen (H_2)/methane (CH_4) breath test who also had computed tomography (CT) of the abdomen performed at our institution were evaluated in this retrospective case–control study. VFA and SFA were measured at lumbar 3 (L3) level on cross-sectional CT image and VFA/SFA ratio was calculated for each individual. Demographic and clinical data pertaining to SIBO were obtained. The study was approved by our Institutional Review Board.

Inclusion and exclusion criteria

Inclusion criteria were patients with 1) glucose H_2/CH_4 breath test for evaluation of SIBO and 2) CT of the abdomen at our institution. Patients who did not have abdominal CT imaging were excluded.

Study and control groups

The study group consisted of patients with SIBO and the control group were those without SIBO.

Diagnosis of SIBO

The diagnosis of SIBO was made by glucose H_2/CH_4 breath test. A standard protocol was applied to all patients included. The H_2/CH_4 breath concentration was expressed in parts per million (p.p.m.) and measured by gas chromatography in basal conditions and every 15 min for at least 3 hours after the administration of an oral loading dose of glucose (50 g in 250 ml of sterile water). The test was considered positive for SIBO when one or more of the criteria was present: H_2 and/or CH_4 increase $>$ 20 p.p.m. above basal value or H_2 and/or CH_4 increase $>$ 12 p.p.m. between the minimum and maximum values after glucose ingestion [12].

Measurement of the visceral and subcutaneous fat

VFA and SFA were determined by CT of the abdomen with patients in decubitus dorsal. A single slice at lumbar 3 (L3) level was used to determine the measurements as it has been shown that this level has the strongest correlation with visceral adipose tissue volume [17]. Images acquired were processed with Image J software (http://rsb.info.nih.gov/ij/). The pixels in densities between −190 and −30 Hounsfield units (HU) were used to define an area in square decimeters (dm^2) for the visceral and subcutaneous fat compartments [18]. The same methodology has been used in a previous study by our group [5].

Study variables

Clinical variables included were age, sex, BMI, type 2 DM, hypertension, dyslipidemia and metabolic syndrome. Metabolic syndrome was defined as the presence of 3 out of 5 of the following criteria according to the Adult Treatment Panel III: 1) obesity (body mass index $\geq$ 30), 2) triglycerides $\geq$ 150 mg/dL, 3) HDL cholesterol $<$ 40 mg/dL in men and $<$50 mg/dL in women, 4) blood pressure $\geq$ 130/85 mmHg and 5) fasting glucose $\geq$ 110 mg/dL [19]. Dyslipidemia was defined as presence of either triglycerides $\geq$ 150 mg/dL and/or HDL cholesterol $<$ 40 mg/dL in men and $<$50 mg/dL in women.

Outcome measurements

The primary outcomes were to evaluate whether VFA, SFA, or VFA/SFA ratio were associated with SIBO independently of the individual BMI.

Statistical analysis

The SPSS software version 22 was used to perform all statistical analysis (SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. 2013). Continuous variables were presented as mean ± standard deviation (SD) or N%. Univariate analysis was performed to identify potential variables associated with SIBO. Student t-test or the non-parametric Wilcoxon rank sum test were used for continuous factors. The Pearson chi-square test was used for categorical variables. Risk factors associated with SIBO wre assessed using the multivariate logistic regression analysis. A $p < 0.05$ was considered statistically significant.