e-SPEN, the European e-Journal of Clinical Nutrition and Metabolism 5 (2010) e238–e242

Contents lists available at ScienceDirect

e-SPEN, the European e-Journal of Clinical Nutrition and Metabolism

journal homepage: http://www.elsevier.com/locate/clnu

Original Article

Visceral adiposity cut-off points to indicate risk factor to develop the nonalcoholic fatty liver disease in Brazilian and Italian obese adolescents

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ARTICLE INFO

Article history:
Received 4 February 2010
Accepted 30 June 2010

Keywords:
Visceral adipose tissue
Obesity
Liver disease
Youth

SUMMARY

Background & aims: Visceral adiposity distribution also appears to influence metabolic complication. The purpose of this study was to determine a visceral adiposity cut-off points to indicate risk factor to develop NAFLD in Brazilian and Italian obese adolescents.
Methods: 151 Brazilian and 87 Italian obese adolescents were enrolled. Visceral adiposity was distributed in cut-off values using a ROC curve analysis.
Results: We verified that Brazilian obese adolescents showed a worse metabolic profile and liver function compared to Italian population. The risk factor to develop NAFLD was two fold higher in Brazilian compared with Italian obese adolescents. The corresponding OR (95%CI) was 6.66 (2.85–15.60) and 2.97 (0.61–14.47), for Brazilian and Italian population, respectively. The optimal visceral adiposity cut-off point to indicate risk factor of NAFLD development was 3.78 cm in Brazilian obese adolescents and 2.83 cm in Italian obese adolescents.
Conclusions: Brazilian obese adolescents have a higher risk to develop NAFLD compared with Italian obese adolescents, confirmed by upper odds ratio values and a higher visceral adiposity cut-off value.

1. Introduction

Current data suggest that the prevalence of overweight (body mass index, BMI >95th percentile for age and gender) among Latino-american children has approximately doubled in the past 10 years, reaching a prevalence of approximately 25% in the pubertal period.[1,2] A similar trend was also observed in several European countries, the estimated prevalence rates ranging from 10–12 up to 36%.[3]

Nonalcoholic fatty liver disease (NAFLD) has been proposed as a component of metabolic syndrome.[4] Although the pathogenesis is not clearly defined and is being actively investigated, it is believed that insulin resistance might play a predominant role.[5] In this respect, several authors suggested that NAFLD could be considered the hepatic manifestation of the insulin resistance and/or of the metabolic syndrome.[6–8]

In agreement with these findings, a recent collaborative study of our groups have demonstrated the different prevalence of metabolic syndrome (23.6% *vs* 16.5%, $p < 0.001$) and of related risk factors in Brazilian in comparison with Italian obese adolescents of both genders.[9]

Abbreviations: ALT, apartate aminotransferase; AST, alanine aminotransferase; AUC, area under curve; BMI, body mass index; CDC, Centre of Disease Control; CI, confidence interval; DBP, diastolic blood pressure; FPG, fasting plasma glucose; GGT, gamma-glutamylaminotransferase; HDL, high density lipoprotein; HOMA-IR, homeostatic model assessment insulin resistance; LDL, low density lipoprotein; QUICKI, quantitative insulin-sensitivity check index; NAFLD, nonalcoholic fatty liver disease; OR, odds ratios; ROC, Receiver Operating Curve; SBP, systolic blood pressure; TC, cholesterol total; TG, triglycerides; VLDL, very low density lipoprotein.

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1751-4991/$36.00
doi:10.1016/j.eclnm.2010.06.001

The visceral adiposity is a risk factor for pediatric diseases.[10] In addition to obesity, adipose tissue distribution also appears to influence metabolic complications and physical limitations to body composition assessment.[11,12] A strict relationship between the visceral adipose tissue and NAFLD in obese adolescents of both genders with similar body mass index (BMI) and a higher prevalence of NAFLD were demonstrated in Brazilian obese adolescents.[13]

Visceral adipose tissue cut-off points to indicate risk factor to develop NAFLD have not yet been established. Thus, the purpose of this study was to determine a visceral adiposity cut-off points to indicate risk factor to develop NAFLD in Brazilian and Italian obese adolescents.

2. Material and methods

2.1. Study group

A total of 151 Brazilian, including 57 boys and 94 girls (16.45 ± 1.57 years), and 87 Italian, including 30 boys and 57 girls obese adolescents (16.01 ± 1.36 years), were enrolled in this study. The Brazilian adolescents were recruited from the Federal University of São Paulo – Paulista Medicine School, UNIFESP, and the Italian adolescents from the Division of Auxology, Italian Institute for Auxology, IRCCS, Piancavallo (VB).

Inclusion criteria were: i. body mass index (BMI) above the 95th percentile for gender and chronological age according with the CDC growth charts,[14] ii. Tanner[15] stage more than 4 for all adolescents recruited in this study, iii. sedentary life-style. Exclusion criteria were: a) identified genetic disease, b) metabolic or endocrine disease, c) excessive chronic alcohol consumption, d) previous use of drugs, such as glucocorticoids, insulin sensitizers or psychotropics which might affect appetite regulation, e) pregnancy and f) previous hepatitis diagnostic.

The experimental protocol was conducted in accordance with the guidelines in the Declaration of Helsinki and was formally approved by the Ethical Committees of the Federal University of São Paulo – Paulista Medicine School and of the Italian Institute for Auxology, Milan and Piancavallo (VB), respectively. In addition, the purpose and objectives were carefully explained to each adolescent and their parents, as well as a written informed consent was obtained.

2.2. Anthropometric and biochemical measurements

Body mass was measured to the nearest 0.1 kg with a manual weighing scale without shoes and light clothes; height was measured to the nearest 0.5 cm on a standardized wall-mounted height board.

Body mass index (BMI) was calculated as weight (kg)/stature^2 (m). Pubertal stage was assessed by an expert auxologist in agreement with Tanner criteria.[15]

Blood samples were collected after an overnight fast in standard tubes. Triglycerides and HDL-, LDL- and total-cholesterol, as well as plasma glucose (FPG) and insulin concentrations were immediately measured with enzymatic-colorimetric methods (CELM, Barueri, Brazil and Hitachi Instrument, Japan, respectively), after appropriate processing. A comparative study performed in a small number of samples revealed no significant differences in the results obtained by using the different methods for all the parameters tested (data not shown).

Insulin resistance was assessed by homeostasis model assessment insulin resistance index (HOMA-IR) and a useful index of insulin sensitivity (QUICKI). HOMA-IR was calculated by the following formula: fasting insulin (μlU/ml) × fasting glucose (mmol/L)/22.5. QUICKI was calculated as 1/[log (Io) + log (Go)].[16,17]

2.3. Visceral, subcutaneous adiposity and nonalcoholic fatty liver disease (NAFLD)

Abdominal ultrasound (US) procedures were performed double-blinded to the medical history by two different examiners specialized in imaging diagnostic (one for each Country), using a 3.5-MHz multifrequency transducer (broad band) located 1 cm from the umbilicus. This procedure permits a reduction of margin risk for misclassification. The intra-operators coefficient of variation in the determination of visceral and subcutaneous fat of 10 different ultrasound imaging, randomly chosen among the two subgroups, was on the average lower than 5% (data not shown).

US-determined subcutaneous fat was defined as the distance between the skin and external face of the recto abdominal muscle, and visceral fat was defined as the distance between the internal face of the same muscle and the anterior wall of the aorta. Cut-off points to define adiposity visceral by ultrasonographic parameters were based on a previous method.[18]

The definition of ultrasonic fatty liver was based on previously reported diagnostic criteria, liver steatosis being classified as grade 1 (liver attenuation slightly less than spleen), grade 2 (more pronounced difference between liver and spleen and intrahepatic vessels not seen or slightly higher attenuation than liver) and grade 3 (markedly reduced liver attenuation with sharp contrast between liver and intrahepatic vessels).[19]

2.4. Blood pressure

Blood pressure was measured on the right arm using a mercury-gravity manometer with appropriate cuff size. Two blood pressure determinations were made after the subjects had been sitting for at least 5 min and the mean value was used for analyses.[9]

2.5. Statistical analysis

All data were expressed as means ± SD unless otherwise stated. Distributional assumptions were verified by Kolmogorov–Smirnov and non-parametric methods were performed when appropriate. Insulin, HOMA-IR, VLDL, blood pressure, subcutaneous fat, AST, ALT and GGT were analyzed with non-parametric tests. Comparisons between groups were made using independent *t*-tests or Mann–Whitney (non-parametric variables).

Visceral fat of obese adolescents was distributed in cut-off values using a Receiver Operating Characteristic Curve (ROC curve). ROC curve was used to determine a cut-off that suggested the best accuracy of the visceral adiposity the computed risk score values to development the nonalcoholic fatty liver (NAFLD) given as area under the curve (AUC) and 95% confidence interval (CI). An AUC of 1.0 is characteristic of perfect discrimination, whereas an AUC of 0.5 indicates chance discrimination.[20] In ROC analysis, the true-positive rate (sensitivity) is plotted against the false-positive rate (1 – specificity) across a range of values from the diagnostic test. This provides an estimate of the cut-off that corresponds to the best tradeoff between sensitivity and 1 – specificity (ie, minimal false-negative and false-positive cases), suggesting tha NAFLD. The decision threshold for the best tradeoff is the criterion value with the highest accuracy that maximizes the sum of the sensitivity and specificity. One index reflecting the overall accuracy of the diagnostic test derived from an ROC analysis is the area under curve (AUC).

SPSS 17 for Windows (SPSS, Chicago, IL) was used for statistical analyses. The prevalence of NAFLD among the groups was compared by using a chi-square test. Significance values were set at $\alpha < 0.05$. All odds ratios (OR) are expressed with 95% confidence intervals (CI).