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Original research

Beyond central adiposity: Liver fat and visceral fat area are associated with metabolic syndrome in morbidly obese patients

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HIGHLIGHTS

- BMI and waist circumference were not useful in discriminating between morbidly obese with and without Metabolic Syndrome.
- In morbidly obese, the expression of MetS is related to higher liver fat and increased visceral adipose tissue area.
- CT scan measures 2 important markers of metabolic syndrome: liver fat and visceral adipose tissue.
- The prevalence of metabolic syndrome in patients with both liver fat and visceral obesity is 100%.

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ABSTRACT

Background: Despite its widespread clinical use, both body mass index (BMI) and waist circumference have been reported as inaccurate methods to measure abdominal obesity. The main objective of this study was to determine the relation between visceral fat area and fatty liver infiltration with the expression of metabolic syndrome (MS) in morbidly obese patients.

Methods: We recruited a random selection of 100 morbidly obese patients on pre-operative evaluation for bariatric surgery. A pre-operative CT slice at L4-L5 level, was performed to measure visceral fat and at T12 level to measure hepatic attenuation.

Results: Patients with MS had lower hepatic attenuation values (median 49.9 vs 55.5HU; $p = .018$) and had more VAT (242 vs 172 cm^2;$p = .001$). Conventional measures (BMI: $p = .729$ and waist circumference: $p = .356$), were not useful in discriminating morbidly obese patients with MS. By multivariable logistic regression, fatty liver infiltration (OR = 5.3; $p = .03$) and age (OR = 1.08; $p = .04$) were the only factors independently related to the presence of MS. MS prevalence was 100%, 71% and 55%, respectively for patients with both fatty liver and visceral adiposity; one; or none of this findings (AUC − .715; $p = .016$).

Conclusion: CT scan seems to measure 2 important markers of MS: visceral adiposity and hepatic fatty infiltration. In morbidly obese patients, both visceral adiposity and hepatic fatty infiltration increase the risk for the presence of MS.

1. Background

Obesity is strongly associated with a cluster of cardiovascular risk factors named metabolic syndrome (MS) [1,2]. However, a significant number of obese patients do not express overt metabolic disease [1,3,4] and understanding which patients are at risk for MS might render novel insights on the pathophysiology of this disease

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and change the clinical management of patients “at risk” for metabolic disease.

Even if obesity is one of the strongest risk factors for MS, its expression is not directly dependent on body mass index [BMI] [1] and the site of fat accumulation seems to be a more important risk factor than obesity in itself [5,6].

Despite its widespread clinical use, both BMI and waist circumference are considered inaccurate methods to measure abdominal obesity, especially in morbidly obese patients [7–10]. Previous reports have concluded that VAT level was more important than liver fat in developing metabolic syndrome at lower obesity levels and that liver fat was more important than visceral adiposity in overweight and obese individuals [6].

The visceral fat area has been reported to be more discriminant for the presence of MS than waist circumference or BMI [11–14]. There is not a defined threshold for visceral fat “obesity”, but it seems that higher visceral fat areas are associated with increased prevalence of MS. Therefore, there is a clinical need to accurately measure the visceral fat area and discriminate between visceral and subcutaneous fat. Also, liver fat has been related to insulin resistance, which is one of the most important pathways in the development of metabolic syndrome [6].

An unenhanced computed tomography (CT) scan, can easily measure both fatty liver disease and visceral fat area [13,15] and CT scan protocols have became the gold-standard technique for these purposes [10,16]. A decreased liver attenuation is highly specific for hepatic steatosis [15] and hepatic attenuation <48 Hounsfield Units (HU) is 100% specific for a histopathologic moderate-severe steatosis [13].

It is not yet defined the role of the interaction of both these findings in the association with metabolic syndrome and further studies are required in morbidly obese subjects to understand if these assumptions hold true for this particular group of patients.

As such, the main objective of this study was to determine the relation between visceral fat area and fatty liver infiltration with the expression of metabolic syndrome in morbidly obese patients.

2. Methods

We recruited a random selection of 100 morbidly obese patients on pre-operative evaluation for bariatric surgery. The Institutional Ethics Review Board approved the research protocol, and patients were proposed for clinical, laboratory and CT examination. Of the 100 recruited patients, 97 completed the study protocol.

A pre-operative CT slice at L4-L5 level, was performed to measure visceral fat and at T12 level to measure hepatic attenuation.

The cross-sectional surface areas of the different abdominal fat compartments were calculated, using a previously validated method [17]. Total fat area was measured inside a line drawn around a skin surface and visceral fat area was measured inside a line drawn at the inner layer of the abdominal wall muscles. An automatic algorithm based on a Hounsfield threshold value between −50 and −150 was used to measure the fat content in cm^2. Liver fat content was measured in a representative area of the right lobe, avoiding vessels and focal lesions, using Hounsfield units attenuation as previously reported [18]. Values of HU < 50 [13] were considered as having high liver fat infiltration (division according to the sample median). All CT measures were carried out by an independent and blinded radiologist.

Patients were classified has having MS, according to the Harmonized Criteria [2] if 3 out of the following five measures were present: (i) abdominal obesity (waist circumference ≥ 102 cm for men or ≥ 88 cm for women or BMI ≥ 35); (ii) elevated triglycerides (>150 mg/dL); (iii) reduced HDL-c (<40 mg/dL for males and <50 mg/dL for females); (iv) high blood pressure (HBP); (v) fasting blood glucose ≥ 100 mg/dL. Treatment for any of these conditions was also considered a positive result.

Venous blood samples were collected after an overnight fasting and all analytical parameters were measured at the São João Medical Center Clinical Pathology Department.

Blood glucose, total cholesterol, high-density lipoprotein cholesterol (HDL-cholesterol), triglycerides, AST, ALT and alkaline phosphatase were measured with an Olympus AU5400 automated analyzer (Beckman–Coulter, Portugal), using conventional methods. Serum C-reactive protein (CRP) was assayed using an immuno turbidimetric assay also on an Olympus AU5400. Low-density lipoprotein cholesterol (LDL-cholesterol) was calculated according to Friedewald's equation [19].Insulin was measured by an electrochemiluminescent immunoassay using a Cobas e411 automated analyzer (Roche, Portugal) and HbA1c was determined by an ion-exchange HPLC system with a D-10™ Bio-Rad analyzer (Bio-Rad, Portugal).

Patients' weight was recorded during the clinical examinations using light clothing and abdominal circumference was measured at midway between the costal margin and the iliac spines. Obesity onset was self-reported by the patients.

The statistical analysis was performed with the PASW statistics version 18.0.

A post-hoc power analysis to detect an OR>1.5 with a sample size of 100 patients, determined the achieved power to be of .867.

CT measurements, age, BMI and obesity duration presented a highly skewed non-normal distribution, such that we decided to compare distributions with non-parametric tests.

Fatty liver disease was considered for attenuations lower than 50HU and visceral obesity was defined at the sample median (209 cm^2). The median visceral/total fat area ratio was .25. Significant values were considered for p values < .05.

3. Results

Most patients were female (86.8%), with a median age of 42 years and a BMI of 45.1 kg/m^2. Type 2 diabetes mellitus (T2DM) was present in 30% of the patients, HBP in 53% and MS in 68%. The median fasting glucose was 93 mg/dL and HOMA-IR was 2.08. Hepatic attenuation median value was 52.5 and the median visceral fat area was 209 cm^2 (Table 1).

Patients with MS had lower hepatic attenuation values (median 49.9 vs 55.5HU; p = .018) - which translates higher fatty infiltration - and had more VAT (242 vs 172 cm^2; p = .001) but not overall adipose tissue (838 vs 811 cm^2; p = .368). The ratio between visceral and total abdominal fat was significantly higher in patients

Table 1
Patients' characteristics.

Female sex	86.8%
T2DM	29.9%
Metabolic syndrome	68.0%
Central obesity	100%
HBP	52.6%
Dysglycemia	61.9%
Low HDL	50.5%
High triglycerides	56.7%
	Median [IQR]
Age (years)	42 [33–53]
Obesity evolution (years)	18 [12–27]
BMI (kg/m^2)	45.1 [42.0–48.6]
Fasting glucose (mg/dL)	93 [83–106]
Hepatic attenuation (HU)	52.5 [40.5–57.0]
VAT (cm^2)	209.2 [162.1–287.9]
TAT (cm^2)	824.1 [734.0–934.2]
VAT/TAT (×100)	25.6 [19.9–32.3]