



Evaluation of Risk Factors and Diseases Associated with Metabolic and Atherosclerotic Disorders in Different Abdominal Fat Distribution Patterns Assessed by CT-Scan

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Abstract

Introduction: Obesity is defined as an increase in body fat composition.

Aim: The purpose of our study was to evaluate metabolic risk factors and diseases in different patterns of abdominal fat distribution.

Materials and methods: This is a cross-sectional study. Among patients aged 15 to 65 years who have had no significant weight loss in the past year and were referred to the Radiology Department to perform an abdominal CT-scan, the visceral and subcutaneous fat area (VFA and SFA) with Hounsfield units -30 to -190 (± 2 SD) was calculated at the umbilical level. Based on the VFA and SFA, patients were stratified into four groups, group 1: V(+)S(+); group 2: V(+)S(-); group 3: V(-)S(+); group 4: V(-)S(-). The following parameters were assessed in the groups: anthropometric parameters including body mass index (BMI), waist circumference (WC), waist-to-height ratio (WHtR), waist to hip ratio (WH); laboratory parameters, including fasting blood glucose (FBG), lipids profile (TG, LDL, HDL, and total cholesterol), creatinine, and liver enzymes (AST, ALT). Additionally, sensitivity, specificity, positive predictive value (PPV), and negative predictive value of study variables were assessed in predicting group 1.

Results: The study included 180 individuals (mean age 50 ± 14 years, range 15-65 years). Group 1 was the most, and group 2 was the least prevalent pattern of abdominal fat distribution. Most females (75%) had high percentage of subcutaneous fat tissue. There was a significant association between the abdominal fat distribution pattern and BMI, WC, WHtR, TG, LDL, HDL, total cholesterol, FBG, diabetes, and metabolic syndrome ($p < 0.05$).

Conclusions: Most of the metabolic factors, including BMI, WC, lipid profile, and FBG, as well as metabolic syndrome, diabetes, and impaired glucose tolerance, were highly correlated with group 1. However, most of the individuals in group 1 were normal according to the factors mentioned above. Therefore, there is a gap between the main definition of obesity (increasing body fat mass) and parameters that calculated obesity and metabolic disorders.

Keywords

abdominal fat distribution, association, CT-scan, metabolic disorders, obesity

INTRODUCTION

Obesity is currently recognized as a global issue associated with metabolic disorders and cardiovascular diseases.^[1,2] In recent years, it has been shown that accumulated abdominal adipose tissue produces abnormal metabolites that are associated with the increased risk of atherosclerotic and cardiovascular diseases.^[3] The abdominal fat tissue comprises two compartments, including visceral fat and subcutaneous fat. Visceral fat is the fat tissue that is stored internally to the abdominal wall muscles, and subcutaneous fat is the fat tissue accumulated externally to these muscles and beneath the skin.

Visceral fat accumulation is the main component of central obesity, which is essential in developing metabolic disorders such as insulin insensitivity^[4,5], type 2 diabetes, and metabolic syndrome.^[4,6,7] Abdominal fat can be quantified using either anthropometric indices such as body mass index (BMI), waist circumference (WC), waist-to-height ratio (WHtR), and waist to hip ratio (WH) or imaging. However, BMI is not a good candidate because it is not necessarily associated with high visceral fat tissue.^[8] Moreover, other anthropometric indices are not entirely reliable and often cause confusion regarding the amount of visceral and subcutaneous fat tissue.^[8-10] Therefore, imaging is the most reliable method that can be used to evaluate fat tissue and differentiate visceral from subcutaneous fat.

Abdominal CT scan is commonly used to measure abdominal fat tissue. Although there is a risk of radiation with this technique, it is widely available and highly reliable.^[9,11] It has been shown that abdominal CT scan at the umbilical level is the most accurate diagnostic method to evaluate abdominal fat tissue.^[12]

The intensity range of -30 to -190 Hounsfield units has been defined as the reference standard that indicates abdominal adipose tissue.^[9] Quantification of abdominal adipose tissue at the umbilical level has been shown to be highly reliable and quite similar to its quantification at the level of the L3-L4 intervertebral disc. High visceral adipose tissue in diabetic patients with normal BMI was recently reported to be associated with arterial stiffening.^[6] This highlights the importance of evaluating and managing visceral adipose tissue to reduce the risk of metabolic and cardiovascular diseases.

AIM

This study aimed to investigate the association of metabolic and cardiovascular risk factors with the visceral and subcutaneous fat area (VFA and SFA) measured using abdominal CT scan. Additionally, this study aimed to evaluate diagnostic sensitivity, specificity, positive predictive value (PPV), and negative predictive value and its potential to predict radiologically diagnosed obese patients (group 1).

MATERIALS AND METHODS

Settings and patients

In this cross-sectional study, 180 individuals undergoing abdominal CT scan in the Radiology Department of Valiasr Hospital (Birjand, Iran) were randomly selected. The patients aged 15 to 65 years without a history of significant weight loss (more than 5%) within the past year were included. Patients with history of weight-loss surgeries, history of surgeries causing damage to the abdominal subcutaneous or visceral fat tissue, large abdominal tumors and metastatic tumors to mesenteric and visceral adipose tissue were excluded.

Ethical approval

Informed written consent was obtained from all participants or their legal guardians (for participants under 18 years of age). Patients were assured that the study would use only the information in the CT scans taken for their primary disease and that they would not receive any extra dose of radiation. This study was approved by the ethics committee of Birjand University of Medical Sciences under the code IR.BUMS.REC.1395.170.

Data collection

The demographic data and the history of metabolic disorders were collected using a questionnaire. Fasting blood glucose (FBG), lipids profile (TG, LDL, HDL, and total cholesterol), creatinine and liver enzymes (AST, ALT) were measured. The height, weight and anthropometric variables including BMI, WC, WHtR and WH were recorded.

Based on NCEP-ATP3 criteria, metabolic syndrome was defined as high TG (>150 mg/dL); high FBG (>100 mg/dL); high WC (>80 cm for females and >90 cm for males); low HDL (<50 mg/dL in females and <40 mg/dL in males); hypertension (systolic blood pressure \geq 130 mmHg, diastolic blood pressure \geq 85 mmHg (or receiving anti-hypertensive therapy).^[13] Additionally, high LDL (>130 mg/dL) was considered abnormal.^[14]

Patients were classified according to the BMI based on WHO classification: obese (\geq 30 kg/m²), overweight (25–29.9 kg/m²), normal weight (18.5–24.9 kg/m²) and underweight (<18.5 kg/m²). Diabetes was defined as two measurements of FBG >126 mg/dL. WHtR \geq 0.5 indicated central obesity based on previous studies.^[15]

The non-contrast abdominal CT scans of the patients were investigated for the signs of fatty liver and renal stones. The border of abdominal skin at the umbilical level parallel to the intervertebral discs L3-L4 and L4-L5 was specified using a tracer. The surface area of regions with the intensities within the range of -30 to -190 Hounsfield units was calculated and recorded as the total abdominal fat area (TFA). The border of abdominal wall muscles and

the anterior surface of vertebral bodies were also specified and the visceral fat area was measured. The subcutaneous fat area was calculated by subtracting the VFA from TFA (Fig. 1, Table 1).^[12,16]

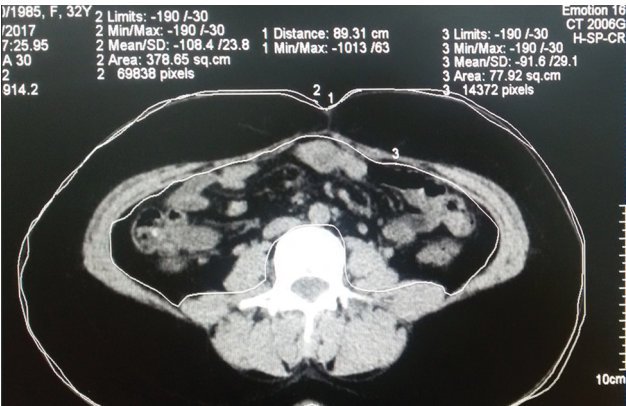


Figure 1. Axial CT-scan at the umbilical level used for the calculation of VFA and SFA.

The patients were classified into four groups: 1) V(+)S(+): VFA >100 cm² and SFA >100 cm²; 2) V(+)S(-): VFA >100 cm² and SFA <100 cm²; 3) V(-)S(+): VFA <100 cm² and SFA >100 cm²; 4) V(-)S(-): VFA <100 cm² and SFA <100 cm². We performed this categorization based on a

previous study.^[17] The diagnostic sensitivity, specificity, positive predictive value (PPV), and negative predictive value of study variables were performed to predict group 1.

It is needed to be acknowledged that the results of history and demographic data for some of our included patients were not available. The study variables were compared among the four groups using the Fisher exact test. Statistical analysis was performed using IBM SPSS 20 (IBM Corp., Armonk, NY, USA). The level of significance was set at $p<0.05$.

RESULTS

In this study, 180 patients were included. The mean age of the patients was 50 ± 14 years, and 30.6% of them were male. The patients were classified into four types of abdominal fat distributions with 38.9% in group 1, 1.6% in group 2, 30.5% in group 3, and 28.8% in group 4.

There was a significant association between abdominal fat distribution and sex ($p=0.001$) (Fig. 2).

High SFA was observed in 75% of the females, while 38% of them had high VFA, indicating a lack of association between SFA and VFA among women. High SFA and high VFA was observed in 56% and 47% of the male patients, respectively. SFA and VFA among men were highly correlated and only 11% of them had high SFA despite a normal VFA.

Table 1. Imaging parameters used to calculate abdominal fat in CT-scan

Scan position	Umbilical level parallel to L3-L4 to L4-L5 intervertebral discs
Attenuation range	-30 to -90 Hounsfield units
Tube voltage	120 kVp
Slice thickness	5-10 mm
Field of view	Includes complete border of the abdomen without any missing region
Kidney, liver, iliac bone	Are not visible at this section to avoid over- or underestimation of abdominal fat

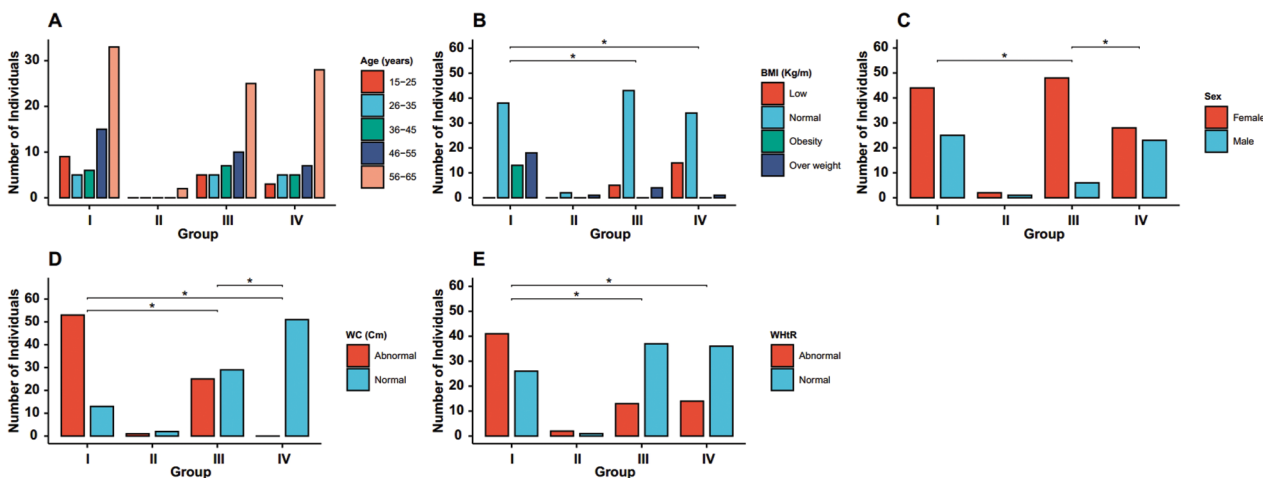


Figure 2. The association of demographic and anthropometric variables with abdominal fat distributions. A: Age (years); B: BMI (kg/m²); C: Sex; D: WC; E: WHtR. Group 1: V(+)S(+); Group 2: V(+)S(-); Group 3: V(-)S(+); Group 4: V(-)S(-). BMI: body mass index; WC: waist circumference; WHtR: waist-to-height ratio; Fisher exact test. * $p<0.05$.

No significant association was observed between the age and abdominal fat distribution. BMI was significantly associated with abdominal fat distribution. All obese patients and most of the overweight patients were in group 1, although 44.9% of patients in this group had normal BMI (Fig. 2).

Obesity was highly specific for group 1 with a positive predictive value (PPV) of 100%. Only 7% of the patients in group 3 and 2% of the patients in group 4 were overweight.

WC was also significantly associated with abdominal fat distribution. Almost all patients with high WC were in groups one and two, and WC was highly specific for these two groups. On the other hand, 80.3% of the patients in group 1 had high WC; therefore, WC was highly sensitive for this group (Table 3).

Elevated TG and FBG levels had a high specificity and PPV for group 1, and abnormal total cholesterol, LDL, and

Table 2. Comorbid diseases in different abdominal fat distributions

		Group 1	Group 2	Group 3	Group 4	Chi-square	P-value
Diabetes	Present (n=27)	74.1%	0.0%	14.8%	11.1%	16.181	0.001
	Absent (n=148)	33.1%	2.0%	33.8%	31.1%		
	Total (n=175)	39.4%	1.7%	30.9%	28.0%		
Hypertension	Present (n=94)	41.5%	1.1%	31.9%	25.5%	1.703	0.6
	Absent (n=80)	37.5%	2.5%	27.5%	32.5%		
	Total (n=174)	39.7%	1.7%	29.9%	28.7%		
Ischemic heart disease	Present (n=9)	55.6%	0.0%	11.1%	33.3%	2.074	0.5
	Absent (n=167)	38.3%	1.8%	31.7%	28.1%		
	Total (n=176)	39.2%	1.7%	30.7%	28.4%		
Stroke	Present (n=14)	28.6%	0.0%	50.0%	21.4%	2.809	0.4
	Absent (n=162)	40.1%	1.9%	29.0%	29.0%		
	Total (n=176)	39.2%	1.7%	30.7%	28.4%		
Fatty liver	Present (n=5)	20.0%	0.0%	40.0%	40.0%	0.955	0.8
	Absent (n=171)	39.8%	1.8%	29.8%	28.7%		
	Total (n=176)	39.2%	1.7%	30.1%	29.0%		
Metabolic syndrome	Present (n=21)	85.7%	0.0%	9.5%	4.8%	21.974	< 0.01
	Absent (n=156)	32.7%	1.9%	33.3%	32.1%		
	Total (n=177)	39.0%	1.7%	30.5%	28.8%		
Renal stone	Present (n=22)	31.8%	0.0%	27.3%	40.9%	2.118	0.5
	Absent (n=155)	40.0%	1.9%	30.0%	27.1%		
	Total (n=177)	39.0%	1.7%	30.5%	28.8%		

Group 1: V(+)/S(+); Group 2: V(+)/S(-); Group 3: V(-)/S(+); Group 4: V(-)/S(-). $P < 0.05$ was considered significant.

Table 3. Diagnostic accuracy of study variables to predict V+S+ group

Indexes	Specificity	Sensitivity	Positive predictive value	Negative predictive value
BMI	100%	18%	100%	65%
WC	75%	80%	67%	86%
WtHR	71%	53%	58%	74%
TG	96%	30%	84%	68%
LDL	89%	34%	69%	32%
HDL	90%	23%	61%	64%
Total cholesterol	93%	20%	66%	64%
FBG	98%	23%	88%	66%
Diabetes and impaired glucose tolerance	93%	28%	74%	66%
Metabolic syndrome	97%	26%	85%	67%

BMI: body mass index; WC: waist circumference; WtHR: waist-to-height ratio; HDL: high-density lipoprotein; LDL: low-density lipoprotein; TG: triglycerides

HDL had a high specificity for this group. The prevalence of impaired glucose tolerance (IGT) and diabetes in this study was 15.4%, and 74% of them were in group 1. Therefore, IGT and diabetes had a high specificity and PPV for group 1. There was no significant association between abdominal distribution patterns and creatinine, AST, and ALT (Fig. 3, Tables 2, 3).

The history of hypertension, ischemic heart disease, cerebral stroke, and fatty liver was also not associated with abdominal distribution patterns. Metabolic syndrome was present in 11.9% of the study population, and 85% of them were group 1. Therefore, the metabolic syndrome had a high specificity and PPV for the this group (Table 3).

DISCUSSION

Abnormalities in abdominal fat distribution, especially excessive amounts of visceral fat, which is considered an integral part of central obesity, have been linked to many adverse metabolic conditions.^[4-7] The association of visceral fat accumulation with metabolic syndrome and its major components, such as impaired glucose metabolism and insulin resistance, has been established in the literature.^[18-21] The aim of this study was to evaluate metabolic and atherosclerotic risk factors and disorders in different abdominal fat distributions in CT scans. In this study, groups 1 and 2 were the high-risk groups because they had high VFA. The prevalence of group 1 was the highest with 38.9%, followed

by group 3 with 30.5%, group 4 with 28.4% and group 2 with 6.1% (Fig. 2).

In this study, we showed that gender, probably through the effect of sex hormones, affects the abdominal fat distribution since 75.4% of female patients had high SFA and 88.9% of the group 3 patients were women (Table 2). Moreover, our study showed that, unlike women, there was a correlation between SFA and VFA among men as 45.4% and 41.8% of them were in groups 1 and 2, respectively.

Depending on the technique used to measure obesity, different results can be obtained. Based on BMI, we had 13 obese patients, who were all in group 1. Additionally, based on imaging criteria, 69 patients had high VFA and SFA levels and were considered obese patients. However, 38 (55%) of the patients in this group had low or normal levels of BMI, indicating the inability of BMI to detect obesity. Therefore, it can be inferred that BMI may not be a suitable index to detect obesity. The gap between the results of radiologically diagnosed obesity (group 1) and obesity diagnosed by other measures, e.g., anthropometric parameters (BMI, WC, and WtHR) can be referred to as the occult obesity gap (OOG).

Unlike BMI, which was highly correlated only with group one, WC was specific for both groups 1 and 2 and was a better marker of abdominal fat accumulation in the general population. The OOG for WC was nearly 20%, which is a better marker for treating obesity compared to BMI with an OOG of 55% (Fig. 2). This finding was in line with the results reported by Shen and colleagues, who

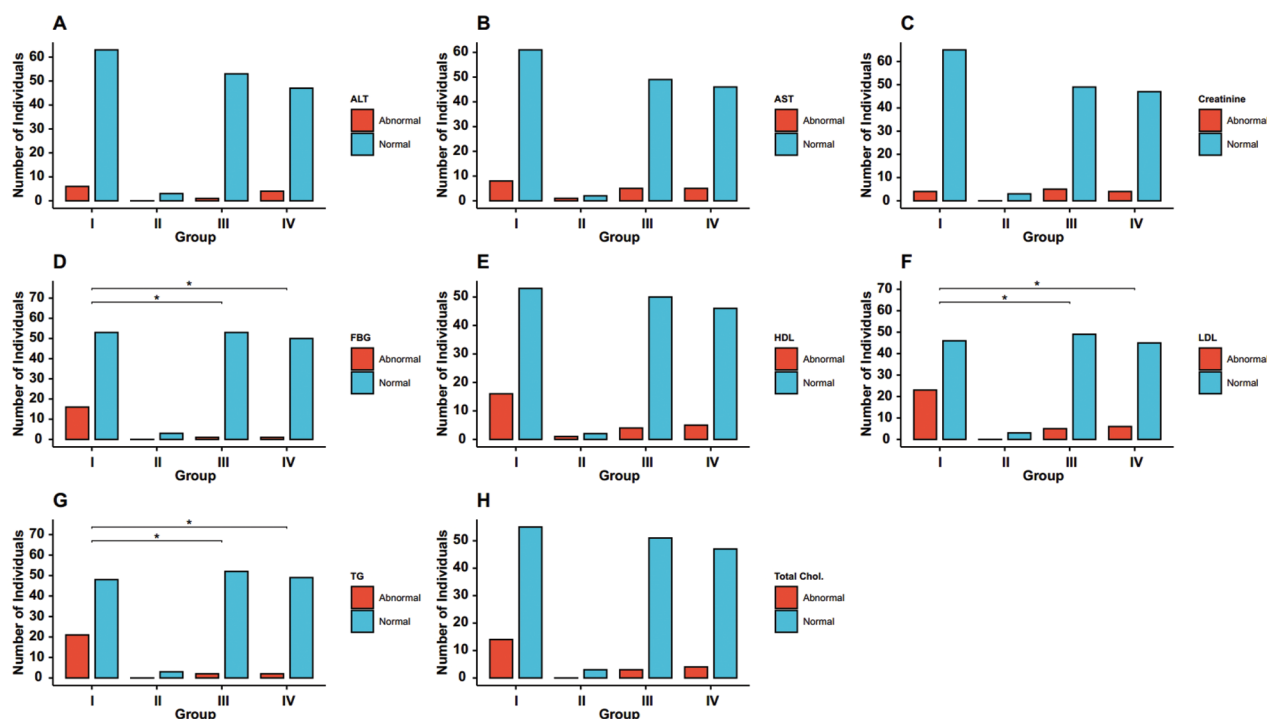


Figure 3. The association of laboratory variables with abdominal fat distributions. **A:** ALT; **B:** AST; **C:** creatinine; **D:** FBG; **E:** HDL; **F:** LDL; **G:** TG; **H:** total cholesterol. Group 1: V(+)/S(+); Group 2: V(+)/S(-); Group 3: V(-)/S(+); Group 4: V(-)/S(-). ALT: alanine aminotransferase; AST: aspartate aminotransferase; HDL: high-density lipoprotein; LDL: low-density lipoprotein; TG: triglycerides; FBG: fasting blood glucose; Fisher exact test. * $p < 0.05$.

found WC to be a better predictor of visceral obesity in the Caucasian race compared with BMI.^[22] Several other studies have reported the superiority of WC to BMI in detecting visceral obesity and predicting the risk of cardiovascular disorders and metabolic syndrome.^[23-26]

In our study, the prevalence of metabolic syndrome was 11.9%, and the prevalence of diabetes and IGT was 15.4%. Metabolic syndrome, diabetes, and impaired glucose metabolism had high specificity and positive predictive value but low sensitivity and negative predictive value for group 1 (Table 3). Previous studies have also reported similar results, indicating an association between quantities of visceral fat as measured by radiological techniques and impaired glucose metabolism and diabetes.^[20,27,28]

The prevalence of non-alcoholic fatty liver disease (NAFLD), when assessed by ultrasound exam, has been reported to be around 15.3% in Iran while ranging between 2% and 21.5% in different regions.^[29-31] However, we found the prevalence of NAFLD to be around 8% in our study, according to CT scans. This inconsistency could be due to the lower sensitivity of CT imaging for diagnosing NAFLD compared to ultrasonography. The prevalence of NAFLD in our study was similar to the figure reported for Gonabad, which could be due to the geographic proximity of the two regions and the large rural population in both regions.

This study provides evidence of sensitivity and specificity of different techniques detecting obesity in individuals; however, some limitations need to be acknowledged with regard to the research methods. Firstly, although history and demographic data for some of our patients were not available, we did not exclude them. Secondly, we conducted CT scans on individuals who visited the hospital to do CT scans for any reason; however, it is suggested to perform CT scans on healthy individuals. Therefore, continued efforts are needed to the best method for measuring abdominal fat.

CONCLUSIONS

Most of the metabolic factors, including BMI, WC, lipid profile, and FBG, as well as metabolic syndrome, diabetes, and impaired glucose tolerance, were specific for group 1 (V+S+). However, most of the individuals in group 1 were normal according to the factors mentioned above. Therefore, there is a gap between the main definition of obesity (increasing body fat mass) and parameters that calculated obesity and metabolic disorders.

Conflict of Interest

The authors declare that they have no conflict of interest.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee of Birjand Uni-

versity of Medical Sciences (reference number: ir.bums.rec.1395.170) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Data availability

The datasets generated during the present study are available from the corresponding author on reasonable request.

Author contributions

Javad Mohamadi Taze Abadi and Alireza Ehsanbakhsh conceived of the presented idea. Javad Mohamadi Taze Abadi developed the theory and performed the computations. Nasrin Khorashadizadeh and Azadeh Darabi verified the analytical methods. Alireza Ehsanbakhsh encouraged Javad Mohamadi Taze Abadi to investigate the correct way to measure abdominal fat and supervised the findings of this work. All authors discussed the results and contributed to the final manuscript.

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Оценка факторов риска и заболеваний, связанных с метаболическими и атеросклеротическими нарушениями, при различных паттернах распределения жира в брюшной полости по данным КТ

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Резюме

Введение: Ожирение определяется как увеличение состава жира в организме.

Цель: Целью нашего исследования была оценка метаболических факторов риска и заболеваний при различных паттернах распределения абдоминального жира.

Материалы и методы: Это перекрёстное исследование. Среди пациентов в возрасте от 15 до 65 лет, не имевших существенной потери массы тела за последний год и направленных в рентгенологическое отделение для выполнения КТ брюшной полости, области висцеральной и подкожной жировой клетчатки (ВЖК и ПЖК) с единицами Хаунсфилда (Hounsfield units) от -30 до -190 (± 2 SD) рассчитывали на пупочном уровне. На основании ВЖК и ПЖК пациенты были разделены на четыре группы, группа 1: В(+)/П(+); группа 2: В(+)/П(-); группа 3: В(-)/П(+); группа 4: В(-)/П(-). В группах оценивали следующие параметры: антропометрические параметры, включая индекс массы тела (ИМТ), окружность талии (ОТ), соотношение талии к росту (WHtR), соотношение талии и бёдер (WH); лабораторные параметры, в том числе уровень глюкозы в крови натощак (FBG), профиль липидов (TG, LDH, LDL и общий холестерин), креатинин и ферменты печени (AST, ALT). Кроме того, в группе прогнозирования 1 оценивали чувствительность, специфичность, положительное прогностическое значение (PPV) и отрицательное прогностическое значение переменных исследования.

Результаты: В исследование было включено 180 человек (средний возраст 50 ± 14 лет, диапазон 15-65 лет). Группа 1 была самой распространённой, а группа 2 – наименее распространённой моделью распределения абдоминального жира. Большинство женщин (75%) имели высокий процент подкожно-жировой клетчатки. Выявлена значительная связь между паттерном распределения абдоминального жира и ИМТ, ОТ, WHtR, TG, LDL, HDL, общим холестерином, FBG, диабетом и метаболическим синдромом ($p < 0.05$).

Заключение: Большинство метаболических факторов, включая ИМТ, ОТ, липидный профиль и FBG, а также метаболический синдром, диабет и нарушение толерантности к глюкозе, сильно коррелировали с группой 1. Однако большинство лиц в группе 1 были в норме, в соответствии с указанными выше факторами. Следовательно, существует разрыв между основным определением ожирения (увеличение жировой массы тела) и параметрами, по которым рассчитывают ожирение и метаболические нарушения.

Ключевые слова

распределение абдоминального жира, ассоциация, КТ, метаболические нарушения, ожирение