

On the relationship between CT measured abdominal fat parameters and three metabolic risk biomarkers

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ABSTRACT

Introduction: Cardiovascular diseases are the leading cause of morbidity and mortality worldwide, and there is a need for the development of adjacent markers to assess cardiovascular risk. In this study, we examined the relationship between the areas of abdominal fat compartments, as measured by computed tomography (CT)-based planar measurements, and laboratory-validated cardiovascular risk markers.

Methods: Fat distribution was measured on CT scans in 252 patients (M: F = 1.13) who underwent routine abdominal CT, using in-house and commercially available software. The included laboratory parameters were glucose, triglycerides, and the triglyceride-glucose index.

Results: The visceral abdominal fat (VAF) area and VAF percentage were lower in females compared to the VAF area and VAF percentage in males, ($p=0.001$, and $p<0.001$ respectively). However, the total abdominal fat (TAF) area was not significantly different between genders. Visceral fat and triglyceride levels showed a weakly positive connection for females ($r=0.447$, $p=0.002$) but not for males ($r=0.229$, $p=0.09$). The glucose levels had a weak correlation with CT calculated abdominal fat parameters, with the strongest statistically significant correlation value being with TAF for females ($r=0.331$, $p=0.003$).

Conclusions: Areas of abdominal fat compartments correlate with metabolic parameters in the blood, and in the future, their assessment might be considered when constructing risk scores. Visceral fat content assessment for every abdominal computed tomography procedure might become a surrogate marker for cardio-vascular risk estimation after defining clear cut-off values and image analysis parameters.

Keywords: computed tomography, abdominal fat, glycemia, triglyceride, triglyceride glucose index

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INTRODUCTION

Cardiovascular diseases represent one of the major causes of morbidity and fatality worldwide, accounting for up to 18 million deaths every year and posing important public health challenges and economic burdens for patients [1,2].

Even if in some older populations mild forms of obesity or being overweight may act as a protective factor, obesity is typically considered a risk factor for atherosclerotic cardiovascular disease (CVD) [3,4]. Visceral adipose tissue (VAT) accumulation is closely linked to CVD, diabetes, and fatty liver disease-related increased mortality [5,6].

Body mass index (BMI) has long been considered the traditional marker for obesity and general overweight. However, promising data suggests that markers of abdominal adiposity have stronger associations with CVD and CVD risk factors, allowing for a more accurate identification of patients with these conditions. [3,7,8].

There is mounting evidence that the volume and area of abdominal fat tissue represent a significant contributor to the association between abdominal obesity and features of the metabolic syndrome and that abdominal obesity represents a major player in the overall atherothrombotic abnormalities frequently defined as the “metabolic syndrome”. The inflammatory profile linked to excess VAT may result from the relative incapacity of subcutaneous adipose tissue to expand in order to store the extra energy brought on by a positive energy balance [9].

For the evaluation of obesity multiple clinical techniques have been considered including clinical (anthropometry), paraclinical (bioelectrical impedance) and imaging tests (ultrasound, dual-energy X-ray absorptiometry (DEXA), computed tomography (CT), and magnetic resonance imaging (MRI)) [5]. However, only CT and MRI represent reference techniques for the evaluation of all compartments of abdominal adiposity, as they can completely assess VAT areas and volumes. While

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MRI is preferred to CT due to the lack of ionizing radiation, such techniques are less standardized and the acquisition is time consuming; moreover, the majority of MRI systems have a small bore of up to 60 cm, making it less suitable for obese patients.[10]. Due to their ease of use and ability to reduce radiation exposure in CT scans, techniques relying on the acquisition of a single slice are increasingly frequent used to quantify adiposity in the abdomen.[5,11,12].

New tools and algorithms are currently being developed in order to extend the information obtained through routine CT examinations as there is a need for the development of adjacent surrogate markers to assess cardiovascular risk.

Since primary prevention of cardiovascular events currently recommends screening for the four traditional cardiovascular risk factors, which are strongly related to lifestyle, multiple clinical and new-media[13] tools have been considered for the evaluation of obesity and nutrition, despite evidence that cardiovascular events occur in subjects without such factors [14].

Although neither glucose nor triglyceride levels are considered traditional cardiovascular risk factors, both represent routine laboratory markers and have been shown to increase the risk of cardiovascular disease [15–21].

The triglyceride-glucose index, considered a marker of insulin resistance, also shows evidence of being a reliable alternative cardiovascular disease prognostic marker [22,23], although validation studies are still needed in this regard. However, the relationship of these metabolic markers with abdominal CT determined parameters is still a matter of debate [7].

Previously, we demonstrated that routine abdominal computed tomography data can be used to assess obesity in healthy adults [24]. The objective of this study was to assess the relationship between abdominal fat compartments assessed through CT-based planar measurements and blood markers of insulin resistance/metabolic risk.

METHODS

Materials

This is a single-center, retrospective, observational, cross-sectional study with a convenience sample of 252 patients who had a native abdominal CT exam at the Radiology service of the Mureș County Emergency Clinical Hospital between March 2013 and October 2016.

Inclusion criteria: examinations without movement artifacts and without detectable changes at the abdominal level.

Exclusion criteria: Slices with pathological alterations that may impede abdominal fat assessment (e.g., space occupying lesions, hemorrhage, diffuse abdominal diseases, etc.).

Ethical aspects

Before examination or admission, each patient signed a standard consent form regarding the educational and scientific use of examination results. The study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of the Emergency Clinical County Hospital of Târgu Mureș (approval number 20075/2013).

Variables

The following variables were recorded or calculated: Age (years), gender (male/female), abdominal circumference (cm), visceral abdominal fat area (VAF) (square cm), total abdominal fat area (TAF) (square cm), visceral abdominal fat to total abdominal fat ratio, antero-posterior (sagittal) abdominal diameter (AP) (cm), transversal latero-lateral abdominal diameter (LL) (cm), blood glucose (mg/dl), triglycerides (mg/dl), triglyceride and glucose index (TyG).

CT Image

An oblique slice was generated, using the umbilicus as the anterior landmark and the L4/L5 intervertebral space as the posterior landmark from submillimeter non-contrast CT slices acquired in the supine position at late inspiration (Figure 1). The reconstructions were performed using a Siemens-HP workstation with the v. 11b, 2013 version of the Syngo via software.

Abdominal fat segmentation

A dedicated software was developed using Matlab 2013b (The MathWorks Inc., Natick, Massachusetts). Based on the CT numbers stored in the DICOM images, the Hounsfield unit values were calculated at pixel level. Using a threshold of (-190:-30)[25] a binary image was generated, with fat/non-fat pixels (Figure 2).

The binary files were manually processed using ImageJ 1.48 [26]. A board-certified radiologist performed the outlining of the visceral abdominal fat and of the abdominal contour (total abdominal fat); based on the pixel count and pixel spacing, the total and abdominal fat parameters were calculated.

The abdominal circumference was retrospectively calculated using the methodology described by Ciudin et



Fig. 1. Sagittal reconstruction used to identify the posterior margin of the L4/L5 intervertebral space and umbilicus. The white line represents the reconstruction plane for the slices used for abdominal fat segmentation.



Fig. 2. DICOM images before and after post-processing. A. DICOM image displayed before processing in the densitometric window of the abdomen. B. Binary Image. White pixels represent fat tissue (values between -190 and -30 HU)

al [27], based on the antero-posterior and latero-lateral diameters of the slice and Ramanujan' formula [28].

Laboratory data

The fasting values of blood glucose and triglycerides were collected from the hospital database when they were available for the same admission. The triglyceride-glucose index (TyG) was calculated as $\ln [TG (mg/dL) \times FBG (mg/dL) / 2]$, obtained from previous studies [29].

Statistical analysis

Microsoft Office Excel software was used for data collection. All statistical analyses were performed using the Statistical Package for Social Sciences, version 25 [30]. To evaluate normality, the Kolmogorov-Smirnov test was applied, and continuous variables are presented as median [interquartile range]. The two-tailed Spearman rho coefficient was utilized to assess correlations. For the multivariate regression analysis, we considered the abdominal fat CT-derived parameters independent of each other. All statistical calculations were carried out at a significance level of $\alpha = 0.05$.

RESULTS

Cohort summary and demographics

A total of 252 patients with a median age of 63.5 years were enrolled. The sample had a male predominance with a male to female ratio of 1.13, the males being younger than the females (61 vs 66 years). There were no differences in terms of laboratory analysis values between genders.

There is a strong, positive correlation between waist circumference and VAT, with a Spearman rank-order correlation coefficient of 0.624, $p < 0.01$.

Table 1 provides a summary of the demographic, CT parameter, and laboratory analysis of all patients, broken down by gender.

The difference in computed tomography calculated abdominal fat parameters according to gender

VAF area and VAF percentage (calculated as $VAF / TAF \times 100$) were lower in females compared to the VAF area and VAF percentage in males, ($p = 0.001$, and $p < 0.001$ respectively). However, the TAF area was not significantly different between genders.

Table 1. Demographic, CT determined parameters and laboratory analysis by gender

Parameter	Male (n=134)	Female (n=118)	p-value
Age (years)	61 (43.7-78.2)	66 (46.7-85.2)	0.029
AP (cm)	24.1 (18.3-29.9)	23.7 (17.5-29.9)	0.468
LL (cm)	34.1 (28.8-39.4)	35.1 (28.9-41.3)	0.221
Waist circumference (cm)	92.3 (76.7-107.9)	92.9 (74.7-111.1)	0.703
TAF area (cm ²)	458.5 (226.6-690.4)	456.5 (187.8-725.2)	0.479
VAF area (cm ²)	208 (46.2-369.8)	155.1 (38.4-271.8)	0.001
VAF percentage	47.5 (33.2-61.8)	35.2 (24.4-46)	<0.001
Glucose (mg/dl)	106 (81.8-130.2)	109 (69.9-197.5)	0.425
Cholesterol (mg/dl)	176.5 (95.6-257.4)	174.1 (88-260.2)	0.993
Triglycerides (mg/dl)	110 (49.8-170.2)	118.2 (38.9-197.5)	0.555
Triglyceride glucose index (mg ² /dl ²)	8.67 (7.9-9.4)	8.78 (5.9-11.6)	0.589

AP: antero-posterior (sagittal) abdominal diameter; LL: transversal latero-lateral abdominal diameter; VAF: Visceral Abdominal Fat area; TAF: Total Abdominal Fat area; TyG: Triglyceride and Glucose index.

Correlations between computed tomography determined parameters and laboratory values

A Spearman's rank-order correlation test was used to examine the connection between triglyceride values and CT determined parameters. Visceral fat area and triglyceride levels showed a weak positive connection for females ($r=0.447$, $p=0.002$) but not for males ($r=0.229$, $p=0.09$).

Additionally, the same Spearman's rank-order correlation was used to examine the connection between glucose levels and CT parameters. For females, there was a weak positive correlation between VAF area and glucose levels ($r=0.263$, $p=0.018$), but it was not statistically significant for males ($r=0.02$, $p>0.05$). The total abdominal fat area for females had the strongest correlation value that was statistically significant ($r=0.331$, $p=0.003$).

For the relation between the TyG index and CT calculated parameters the Spearman rho correlation found a weak correlation between the TyG index and VAF area in females, ($r=0.377$, $p=0.01$), while in males the correlation was weak and not significant ($r=0.207$, $p=0.137$).

Multivariable regression analysis between computed tomography determined parameters and laboratory values

Triglyceride values were predicted using a multiple regression model based on abdominal diameters (antero-posterior, latero-lateral), TAF and VAF area. These variables predicted triglyceride levels with statistical significance, $F(4, 96) = 2.809$, $p = 0.03$, $R^2 = 0.105$. Statistically, lateral diameter and total abdominal fat area contributed significantly to the prediction, $p < 0.05$.

To predict blood glucose values from abdominal diameters (antero-posterior, latero-lateral), TAF area, and VAF area, a multiple regression analysis was carried out. These variables showed a certain trend towards significance into predicting glicemic values, $F(4, 96) = 2.068$, $p = 0.08$, $R^2 = 0.048$. The contribution of lateral diameter and total abdominal fat area to the prediction was marginally statistically significant, $p = .05$.

The triglyceride-glucose index values were predicted using multiple regression on the basis of abdominal diameters (antero-posterior and latero-lateral) and total

Table 2. Correlations between computed tomography determined parameters and laboratory values

		Triglycerides	Triglycerides	Glicemia	Glicemia	TyG index	TyG index
		males	females	males	females	Males	Females
AP	Correlation Coefficient	0.155	0,334*	0.042	0,247*	0.207	0,299*
	Sig. (2-tailed)	0.259	0.023	0.697	0.026	0.137	0.043
LL	Correlation Coefficient	0.175	0.184	0.009	0,249*	0.206	0.174
	Sig. (2-tailed)	0.202	0.220	0.934	0.025	0.138	0.247
Abdominal circumference	Correlation Coefficient	0.173	0.266	0.026	0,251*	0.211	0.247
	Sig. (2-tailed)	0.208	0.074	0.808	0.024	0.129	0.098
VAF as percentage of TAF	Correlation Coefficient	0.036	0.156	0.140	-0.118	-0.008	0.047
	Sig. (2-tailed)	0.796	0.301	0.196	0.293	0.957	0.755
TAF Area (cm ²)	Correlation Coefficient	0.223	0,371*	-0.006	0,331**	0.258	0,345*
	Sig. (2-tailed)	0.103	0.011	0.956	0.003	0.062	0.019
VAF Area (cm ²)	Correlation Coefficient	0.229	0,447**	0.021	0,263*	0.207	0,377**
	Sig. (2-tailed)	0.093	0.002	0.847	0.018	0.137	0.010

*. Correlation is significant at the 0.05 level (2-tailed); **. Correlation is significant at the 0.01 level (2-tailed); AP: antero-posterior (sagittal) abdominal diameter; LL: transversal latero-lateral abdominal diameter; VAF: Visceral Abdominal Fat; TAF: Total Abdominal Fat.

Table 3. Multivariable regression analysis between triglyceride values and CT determined parameters.

	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
(Constant)	213.625	75.940		2.813	0.006
AP	2.562	2.689	0.150	0.953	0.343
LL	-6.625	3.143	-0.406	-2.108	0.038
TAF Area (cm2)	0.208	0.091	0.553	2.301	0.024
VAF Area (cm2)	-0.072	0.138	-0.094	-0.524	0.602

AP: antero-posterior (sagittal) abdominal diameter; LL: transversal latero-lateral abdominal diameter; VAF: Visceral Abdominal Fat; TAF: Total Abdominal Fat.

Table 4. Multivariable regression analysis between glucose values and CT determined parameters.

	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
(Constant)	157.286	42.346		3.714	0.000
AP	2.303	1.631	0.195	1.412	0.160
LL	-3.490	1.774	-0.298	-1.967	0.051
TAF Area (cm2)	0.095	0.049	0.376	1.925	0.056
VAF Area (cm2)	-0.082	0.088	-0.149	-0.938	0.350

AP: antero-posterior (sagittal) abdominal diameter; LL: transversal latero-lateral abdominal diameter; VAF: Visceral Abdominal Fat; TAF: Total Abdominal Fat.

Table 5. Multivariable regression analysis between triglyceride- glucose index values and CT determined parameters.

	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
(Constant)	4.850	0.315		15.385	0.000
AP	0.019	0.011	0.268	1.743	0.085
LL	-0.028	0.013	-0.396	-2.113	0.037
TAF Area (cm2)	0.001	0.000	0.620	2.632	0.010
VAF Area (cm2)	-0.001	0.001	-0.181	-1.020	0.311

AP: antero-posterior (sagittal) abdominal diameter; LL: transversal latero-lateral abdominal diameter; VAF: Visceral Abdominal Fat; TAF: Total Abdominal Fat.

abdominal and visceral fat area. These variables predicted the triglyceride-glucose index with statistical significance, $F(4, 94) = 4.576$, $p=0.02$, $R^2 = 0.1$. With a p value <0.05 , the lateral diameter and total abdominal fat area were found to contribute statistically to the prediction.

DISCUSSION

In this study, the relationship between abdominal fat compartments, as measured by CT-based planar measurements, and blood markers of insulin resistance/ metabolic risk was investigated.

Although CT measurement of abdominal visceral fat has been regarded as the most precise and reproducible method for determining abdominal fat [31], the lack of standardized reference range for fat HU makes it challenging to compare results from different studies.

Typical HU reference intervals for abdominal fat include (-190:-30), (-140:-40), (-250:-50), (-250:-20), and (-150:-50) [13,32–34] owing to the fact that it depends on the window level and range used to define and extract fat-corresponding pixels from the images. For abdominal fat segmentation we used the -190 to -30 range

as it represents one of the oldest and currently validated reference range.

We observed that both triglycerides and TyG show a correlation with total abdominal fat area, which, even if low, concurs with previous studies on Caucasian [35] and in large-scale Japanese general population [36]. While the VAF area showed a weak correlation with laboratory values, its average areas were higher than the previously reported thresholds for associations with cardiovascular risk- Anderson et al.[37] or Després et al.[35] and it should be considered for further analysis.

In this study, visceral abdominal fat parameters determined from computed tomography images were found to display a statistically significant correlation with triglycerides, glucose and TyG in females but not in males. While previous studies [38] found a statistically significant gender-specific correlation between visceral fat and various laboratory parameters those were about low HDL-C levels- which were found to be significantly associated with visceral obesity in men, and elevated HbA1c levels were found to be significantly associated with visceral obesity in women. Other studies using bioelectrical impedance analysis to evaluate visceral fat [39] found

that in females it had positive correlation with triglycerides while in males it was a negative correlation.

We can only assume that the presence of a positive correlation between fat compartments determined by CT and triglycerides, glucose, and TyG was due to the presence, in the aforementioned age group, of an estrogen protection decline characteristic of menopausal females, given that postmenopausal women have almost twice as much visceral adipose tissue as compared to premenopausal women [40].

In studies measuring visceral fat using magnetic resonance [41] the correlation coefficient between triglycerides and total abdominal fat was found to be lower than the ones we found using CT images, they were 0.3 ($p < 0.05$) in women and 0.14 ($p > 0.05$) in men. Nonetheless, they found that the correlation coefficient between visceral fat area and triglyceride values was greater than that found using CT, 0.49 ($p < 0.001$) for females and 0.35 ($p < 0.05$) for males. We hypothesize that the differences stem from the technical image acquisition parameters, as the CT resolution is four times greater than that of magnetic resonance images [42], and as a result of the slice positioning, which in our case followed the line used for abdominal circumference measurement more closely, rather than relying on the pure axial arrangement of image acquisition.

Multiple software packages [43–45] are used for computing visceral abdominal fat area from routine abdominal CT examinations and the growth in the field of artificial intelligence may be a potential future direction for providing precise and fully automated 3D segmentation of adipose tissue deposits [46].

Limitations

Important limitations exist in this study. Firstly, as a convenience sample from a single-center the selection bias cannot be completely ignored, therefore our cohort cannot be considered nationally or internationally representative. Secondly, the small sample size for analysis may necessitate additional validation of the research results on a larger cohort. Thirdly, the values computed from abdominal CT protocols were not compared to clinical outcomes nor did we evaluate the effect of acquisition parameters or the BMI on these measurements. Moreover, the absence of data regarding the status of the patients analyzed in the study, in terms of the presence of a disease with an impact on the metabolic balance, might have produced data with high variability. Given the retrospective nature of this study and the small sample size, it is recommended that future research should involve longitudinal studies with larger samples to provide reli-

able data for determining the cause of the correlation between abdominal components and laboratory values.

CONCLUSIONS

This study demonstrated the presence of a weak positive correlation between triglyceride and tryglyceride glucose index values and total fat surface area determined by computed tomography.

Areas of abdominal fat compartments correlate with metabolic parameters in the blood, and in the future, their assessment might be considered when constructing risk scores.

ABBREVIATIONS

AP: Antero-Posterior (sagittal) abdominal diameter

CT: Computed tomography

HU: Hounsfield unit

LL: Latero-Lateral (transversal) abdominal diameter

MRI: Magnetic Resonance Imaging

TAF: Total Abdominal Fat area

TyG: Triglyceride and Glucose index.

VAF: Visceral Abdominal Fat area

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AUTHORS' CONTRIBUTION

M.P. – Writing draft; analysis, data visualization

R-M.P. – Writing draft; analysis, data management

CONFLICT OF INTEREST

None to declare.

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