The Effect of Falsely Highlighted Intestinal Intraluminal Areas and the Fat in Paraspinal Muscles on Abdominal Adipose Tissue Measurements Using Computed Tomography

İntestinal Lümen İçerisinde Hatalı Olarak Boyunan Alanların ve Paraspinal Kaslar İçerisindeki Yağ Alanlarının Bilgisayarlı Tomografi ile Abdominal Yağ Ölçümü Üzerindeki Etkisi

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Abstract

Objective: The measurement of abdominal fat using computed tomography (CT) is a reliable method for evaluating metabolic disorders. However, some limitations exist with the current CT measurement methods. One of them is falsely highlighted intestinal intraluminal areas and the other one is fat in paraspinal muscles. We aimed to investigate the effects of highlighted intestinal intraluminal areas and fat in paraspinal muscles on the measured values of abdominal fat. Material and Methods: Measurements were performed on 246 abdominal CT scans of 129 patients using dedicated quantitative CT software. Visceral and subcutaneous fats were measured at the level of L1-L2 disc space using two different methods. Method 1 included the highlighted intestinal intraluminal areas and fat in paraspinal muscles for measurements, whereas method 2 excluded them. The values measured using two methods were compared for a statistically significant difference. In addition, the correlation between anthropometric data and subcutaneous adipose tissue measurement methods was analyzed. Results: The mean age of patients was 53 years, and the mean body mass index was 29.73 kg/m². The waist circumference data were available of 91 patients, and the mean waist circumference was 94 cm. The Wilcoxon signed-rank sum test showed a statistically significant difference between methods 1 and 2 (p<0.0001). Although the measurements performed using methods 1 and 2 were strongly correlated (r=0.9), the Passing-Bablok regression analysis indicated a systematic and proportional error between measurements. Conclusion: Falsely highlighted intestinal intraluminal areas should be excluded for accurate visceral adipose tissue measurements, and the fat in paraspinal muscles affects subcutaneous fat measurement results.

Keywords: Multidetector computed tomography; visceral fat; subcutaneous fat; abdominal adipose tissue

Özet

Amaç: Bilgisayarlı tomografi (BT) ile abdominal yağ ölçümü, metabolik hastalık değerlendirmesi açısından oldukça güvenilir bir metotdur. Mevcut BT ölçüm metotlarının bazı kısıtlıkları vardır. Bu kısıtlıklardan biri, intestinal lümen içerisinde yanılı olarak boyanan alanlardan. Bir diğer ise paraspinal kaslar içerisindeki yağ doku anlamıdır. Çalışmanın amacı, intestinal lümen içerisinde yanılı olarak boyanan alanların ve paraspinal kaslar arasındaki yağ alanlarının abdominal yağ ölçümlerini üzerindeki etkisinin araştırılmasıdır. Gereç ve Yöntemler: Yağ ölçümü yönelik geliştirilmiş kantitatif BT yazılımı kullanılarak 129 hastanın 246 abdomen BT tettikindeki yağ ölçümlerini değerlendirilmiştir. Viseral ve subkütan yağ ölçümleri, L1-L2 disk düzeyi için faklı yöntem kullanılarak gerçekleştirilmiştir. Metot 1’de, intestinal lümen içerisinde yanılı olarak boyanan alanlar ve paraspinal kaslar arasındaki yağ alandı, abdominal yağ ölçümü dahiil edilmiş, Metot 2’de ise edilmemiştir. İkinci metot ile ölçulen değerlener istatistiksel anlamlı fark açısından karşılaştırılmıştır. Ayrıca antropometrik ölçümler ile subkütanöz yağ dokusu ölçüm metodu arasındaki korelasyonu da değerlendirilmiştir. Bulgular: Ortalama hasta yaşısı 53 yıl ve ortalamalı beden kitle indeksi 29.73 kg/m² olarak bulunmaktadır. Bel çevresi ölçümleri 91 hastada mevcut olup, ortalamalı bel çevresi 94 cm’dir. Wilcoxon işaretli sıralar testi uygulandığında, Metot 1 ve Metot 2 arasında istatistiksel olarak anlamlı farklı saptanmıştır (p<0.0001). İkinci metot ölçümleri arasında güçlü bir korelasyon bulunmaktadır birlikte (r=0.9), Passing-Bablok analizi ile ikinci metot arasında sistematik ve orantılı hata saptanmıştır. Sonuç: İntestinal lümen içerisinde yanılı olarak boyanan alanlar viseral yağ ölçümü uygulamalarının çıkartılmalıdır. Paraspinal kaslar içerisindeki yağ ise subkütan yağ ölçüm sonuçlarının etkileyeccek düzeydedir.

Anahat kelimeler: Multidektör bilgisayarlı tomografi; viseral yağ; subkütanöz yağ; abdominal yağ dokusu

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Introduction

Body fat is distributed into two main compartments: subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT). These two tissue compartments have different metabolic characteristics. The VAT is of particular interest because of its unique biochemical characteristics that influence several normal and pathological processes. Moreover, it is associated with metabolic syndrome, cardiovascular disease, and several malignancies, including prostate, breast, and colorectal cancers (1-5). The quantitative assessment of VAT is crucial in evaluating the risk of developing these pathologic conditions and in providing an accurate prognosis (1).

Computed tomography (CT) is a useful and validated technique to quantitatively assess VAT and SAT (1,2,6-8). Compared with other techniques that evaluate VAT and SAT, CT generates the most accurate, specific, and comprehensive data (1). However, the current CT quantification technique has its limitations and pitfalls, some of which are not yet addressed in the present literature. In CT, some areas within the intestinal lumen are falsely highlighted because of predefined Hounsfield unit (HU) ranges for fat measurement. These falsely highlighted areas are generally fecal material, liquid with intermediate density (bowel content), or an air-fluid interface with average density (9). To the best of our knowledge, only three studies exist in the literature that excluded falsely highlighted intestinal intraluminal areas (FHIIs) while performing VAT measurement (9-11). However, neither these three studies nor the others have focused on VAT and addressed the effect of FHIIs on measurements. In contrast, the majority of the studies measuring VAT did not exclude FHIIs (2,7,8,12-15). Therefore, whether to include or exclude FHIIs while performing VAT measurements is unclear. A similar confusion also exists with the fat within paraspinal muscles (FPM) while performing SAT measurements, as some of the studies in the literature include FPM, and some exclude them (7-11). The fatty infiltration of the FPM, secondary to muscle atrophy, obesity, or other reasons, is another drawback of the current CT quantification technique. The confusion about whether to include or exclude FPM in the SAT measurement method can be associated with this drawback.

However, whether these FHIIs and FPM affect VAT and SAT measurements, respectively, remain unknown. The aim of this study was to investigate the effect of FHIIs and FPM on VAT and SAT measurements, respectively.

Material and Methods

Study Participants

This retrospective study was approved by the institutional review board, and no informed consent was needed (Dokuz Eylül University Non-Interventional Research Ethics Committee, file no: 2017/19-13, date 27.07.2017). This study was conducted in accordance with the Helsinki Declaration. We included patients admitted to our university hospital between 2008 and 2017 who were evaluated using CT for the routine workup of their incidental adrenal lesions. Patients with malignancy were excluded from this study.

A flowchart of patient selection details is given in Figure 1. Given the alteration of bowel segment position and contents over time, more than one CT scans of any single patient were included. The VAT measurements were performed on 246 CT scans of 129 patients. In 11 scans, an accurate SAT measurement was excluded due to because of the inability to evaluate peripheral abdominal subcutaneous fat because of the limited visualization of these parts in the CT scans performed with an inadequate field of view. Therefore, the statistical analysis of SAT measurements was performed for 235 scans, excluding the 11 scans.

Fat Measurement Method

The VAT and SAT measurements were performed by two experienced radiologists. An axial view was used, with the patient lying in the supine position. Measurements were performed on a Philips Extended Brilliance Workspace (software version V3.5.0.22.54 Philips Medical Systems, Amsterdam, The Netherlands) using the quantitative CT software (Philips Medical Systems, Amsterdam, The Netherlands). The L1-L2 intervertebral disk level was selected for performing fat
measurements as described in the literature, indicating that VAT measurements at this level were more strongly associated with the metabolic syndrome than at other sites (16). A region of interest (ROI) of 100-200 mm² was drawn on pararenal visceral fat to determine the reference HU values for fat area measurements. An attenuation range of -60 to -165 HU in pararenal reference ROIs was achieved in line with the literature (2,3,7). Using this ROI as a fat density reference, the software automatically provided fat tissue mask values and fat area values. The total adipose tissue (TAT) area was measured by drawing a contour around the skin on a CT scan image. To determine VAT, another contour was drawn around the visceral fat by identifying the innermost abdominal wall muscles and the anterior aspect of the vertebral column. The subcutaneous fat was defined as the area of adipose tissue between the skin and the outermost aspect of the abdominal wall muscles. These borders were defined in line with the literature (17). The SAT area was calculated by subtracting the VAT area from the TAT area. To account for FHIIAs in each VAT measurement (so as to exclude it from the total VAT measurement), ROIs were drawn around the intestinal lumen by identifying the innermost intestinal wall (Figure 2A). Using the same method, an additional ROI was drawn around the FPM to calculate FPM, so that it can be excluded from the total SAT measurement in the slice (Figure 2B).

Two measurement methods were used to evaluate the effect of FHIIAs and FPM on VAT and SAT, respectively. Method 1 included FHIIAs in VAT measurements and FPM in SAT measurements, whereas method 2 excluded them. The results of the two methods were statistically compared. In addition, Pearson’s correlation test was performed to evaluate whether adding or removing FPM from SAT measurement was more correlated with clinical data (body mass index (BMI) and waist circumference).

Statistical Analysis
The differences between the results of the two methods (methods 1 and 2) were tested using the Passing-Bablok regression analysis using MedCalc software (MedCalc software Ltd., Ostend, Belgium) and SPSS version 15.0 (SPSS Inc, Chicago, Illinois, USA). The correlation between the results of the two measurement methods was analyzed using SPSS version 15.0. The normality test (Kolmogorov-Smirnov) was performed to evaluate the normal distribution. The Wilcoxon signed-rank sum test and the Spearman’s correlation test were used.

Intraobserver and interobserver variability between the two investigators were tested. To assess interobserver variability, additional 74 consecutive CT scans of another patient group were evaluated by both radiologists, and to assess intraobserver variability, each investigator performed fat area measurements in 18 consecutive CT scans six months apart.

Results
A total of 246 abdominal CT scans of 129 patients (99 women and 30 men) were statistically evaluated. The mean patient age was 53 years. The youngest patient aged 24 years and oldest 76 years. BMI data were available of 115 patients. Mean BMI was 29.73 kg/m² (minimum 17.48 and maximum 51.9). Waist circumference data were obtained for 91 patients. Mean waist circumference was 94 cm (minimum 64 cm and maximum 140 cm).
Moreover, 118 patients had two CT scans at different times, and only 11 had one CT scan. In three scans, FHIIA measurements were “zero.”

The results of fat measurements are summarized in Table 1.

As the normality test did not show a normal distribution, the Wilcoxon signed-rank sum test was used, which showed a statistically significant difference between the two methods for VAT (p<0.0001) and SAT measurements (p<0.0001).

Although the results of methods 1 and 2 are strongly correlated (r>0.9), the Passing-Bablok regression analysis showed a systematic and proportional error between measurements; the 95% confidence interval (CI) for intercept A does not contain 0 and that for slope B does not contain 1 in the regression model (http://www.medcalc.org/manual/passing-bablok_regression.php). The Passing-Bablok regression analysis indicated that these two methods could not be substituted for each other.

A strong intraobserver and interobserver agreement was detected; the 95% CI for intercept A contains 0 and that for slope B contains 1 in all regression models. The regression coefficient was >0.9 in all regression models.

Pearson’s correlation test performed to test whether adding or removing FPM in SAT measurement was more correlated with clinical data (BMI and waist circumference) showed similar results. Both the measurement methods were highly correlated with BMI (Method 1: r=0.789; Method 2: r=0.787) and waist circumference (Method 1: r=0.682; Method 2: r=0.682).

Discussion

CT is a validated technique for fat measurement (2). Shuster et al. have stated that the evaluation of the abdominal fat using CT generates the most accurate, specific, and comprehensive data than other techniques (1). However, CT has its own limitations because of predefined HU ranges for fat density mask, as seen in falsely highlighted areas of the intestinal lumen. Our study results demonstrated a statistically significant difference in VAT values depending upon the inclusion or exclusion of FHIIAs in the measurements. The minimum FHIIA was 0.03 cm², and maximum was 23.09 cm², indicating that the FHIIA measurement varies because of the density of intraluminal contents. The FHIIAs are very small com-
pared to VAT. However, if a larger number of patients are involved, the variability of FHIIA values widens, creating an overall inaccurate VAT measurement.

It is unclear whether adding or removing FHIIAs in VAT measurement was more correlated with clinical data. However, FHIIAs are definitely not a part of VAT; it is a misregistered area produced by fecal material, liquid with intermediate density, or an interface of air, fluid, and bowel content with average density (9). Although adding FHIIAs to VAT was found to be more correlated with clinical data, adding a misregistered area to a fat tissue measurement would be a methodological mistake. We can question whether it is really necessary to remove FHIIAs from VAT because it is a small amount of misregistered data. The answer to this question provided by this study was that it is necessary to remove FHIIA as it causes a statistically significant difference. Thus, FHIIAs should be excluded when calculating VAT regardless of its correlation with clinical data.

To the best of our knowledge, a few studies in the literature have excluded FHIIAs while measuring VAT (9-11). One of them was Hung et al.’s study, where they manually excluded FHIIAs to measure VAT (9). Moreover, Delivanis et al. have used semiautomated software to exclude FHIIAs to measure VAT (9). Lastly and recently, Akay et al. have used an oral contrast agent to prevent any intestinal involvement in the automated VAT measurement process and also excluded the remnant intestinal involvement manually, if any (11). In contrast, a majority of studies measuring VAT have not excluded FHIIAs (2,7-8-15). This methodological approach indicates that the effect of FHIIAs on the abdominal fat measurement is an underestimated problem in the literature, thus enhancing the importance of this study. This study was the first to show that FHIIAs may affect VAT measurement and highlight a problem that the majority of the studies missed.

Similarly, several previous studies have included FPM in SAT measurement (7,8). However, Hung et al., Delivanis et al., and Akay et al. have excluded FPM in their studies (9-11). In this study, a statistically significant difference was obtained between including and excluding FPM in SAT measurements. Although Pearson’s correlation test showed that both the measurement methods for SAT measurement were correlated with clinical data at the same degree, the Passing-Bablok regression analysis indicated that these two methods could not be substituted for each other. Therefore, studies with larger patient groups are needed to reveal which measurement method is more correlated with the clinical data.

One minor limitation of this study was performing two-dimensional fat measurements on a single slice selected at a specific level rather than using three-dimensional measurements as the volume was measured across several slices. However, several studies have revealed that measuring VAT on a single CT or magnetic resonance imaging slice is a reliable method (2,8,11,15,16,18-20). Given the limitation of obtaining two-dimensional measurements in a three-dimensional patient, the validity of this method has been previously established by comparing the two-dimensional and three-dimensional VAT measurements in a different patient population (21). The association between the adipose tissue area and

| Table 1. Results of fat measurement. |
|-------------------------------------|
|                                    |
| **Min. (cm²)/Max (cm²)** | **Mean (cm²)±sd:** | **Median (cm²)/(25th-75th)** | **p** |
| VAT (n=246) Method 1 | 7.84/551.37 | 130.60±90.04 | 112.13/(65.05-179.15) | p<0.0001 |
| VAT (n=246) Method 2 | 6.38/536.91 | 127.81±88.72 | 110.68/(62.79-175.60) | p<0.0001 |
| SAT (n=235) Method 1 | 21.30/560.88 | 171.54±95.82 | 150.84/(103.37-224.87) | p<0.0001 |
| SAT (n=235) Method 2 | 20.81/556.72 | 169.37±95.02 | 150.14/(99.84-223.14) | p<0.0001 |
| FHIIA (n=246) | 0.00/23.09 | 2.78±3.64 | 1.45/(0.67-3.19) |
| FPM (n=33) | 0.01/34.32 | 2.16±3.36 | 1.18/(0.61-2.53) |

FHIIA: Falsely highlighted intestinal intraluminal areas, FPM: Fat in paraspinal muscles, VAT: Visceral adipose tissue, SAT: Subcutaneous adipose tissue.
the corresponding adipose tissue volume was significant ($r=0.961; p<0.001$) (21).

The main limitation of this study was the lack of data indicating that which the SAT measurement method is more consistent with anthropometric measurements and more accurately reflects metabolic disorders. However, this study was designed to highlight the drawbacks of measuring fat using CT and determine whether FHIIAs and FPM have any statistically significant effect on VAT and SAT measurements; therefore, the correlation with anthropometric SAT measurements was not studied. In addition, including FHIIAs in VAT measurement would be a methodological mistake because of its nonadipose origin, and its correlation with anthropometric measurements would make no sense. Moreover, this study is significant because it showed that measurements with methods 1 and 2 were different, and the methods cannot be substituted for each other.

Conclusion

In conclusion, this study was the first to demonstrate that including FHIIAs in VAT measurements and FPM in SAT measurements led to statistically significant differences in VAT and SAT measurements. FHIIAs should be excluded for accurate VAT measurements. FPM inclusion in SAT measurements should be considered only if supported by anthropometric measurements.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Mustafa M. Barış, Ahmet Peker; Design: Mustafa M. Barış, Ahmet Peker, Mustafa Seçil; Control/Supervision: Mustafa M. Barış, Ahmet Peker, Mustafa Seçil; Data Collection and/or Processing: Mustafa M. Barış, Ahmet Peker, Abdullah S. Yener; Analysis and/or Interpretation: Naciye S. Gezer, Mustafa Seçil, Abdullah S. Yener; Literature Review: Mustafa M. Barış, Naciye S. Gezer; Writing the Article: Mustafa M. Barış, Naciye S. Gezer; Critical Review: Mustafa Seçil, Abdullah S. Yener, Naciye S. Gezer; Materials: Abdullah S. Yener.

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