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Association between the Distribution of Adipose Tissue and Outcomes in Acute Pancreatitis: A Comparison of Methods of Fat Estimation

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Abstract

Purpose To assess the correlation between abdominal fat measured at computed tomography (CT) and dual-energy X-ray absorptiometry (DXA) and association with clinical outcomes in patients with acute pancreatitis (AP).

Methods This prospective study comprised consecutive patients with AP who underwent abdominal CT and DXA. Fat estimation was done on whole-body DXA and abdominal CT. Correlations among body mass index (BMI), waist circumference (WC), DXA, and CT fat measurements were determined. The association between fat measurements and clinical outcomes was assessed.

Results Fifty-nine patients (mean age 38.2 years, 48 males) were included. There was a strong correlation ($r = 0.691–0.799$) between DXA and CT fat estimation. In addition, there was a significant association of the visceral adipose tissue (VAT) on DXA and CT with the severity of AP ($p = 0.039$ and 0.021, respectively) and the need for drainage of collections ($p = 0.026$ and 0.008, respectively). There was a weak correlation of the BMI and WC with the length of hospitalization (LOH) ($r = 0.121$, 0.190, respectively) and length of intensive care unit stay (LOICU) ($r = 0.211$, 0.197), while there was a moderate to strong correlation of the truncal fat and visceral fat on DXA and total adipose tissue and VAT on CT with LOH ($r = 0.562$, 0.532, 0.602 and 0.614, respectively) and LOICU ($r = 0.591$, 0.577, 0.636, and 0.676, respectively).

Conclusion In conclusion, fat indices measured on DXA and CT are associated with the severity of AP. In addition, the fat measurements at DXA are strongly correlated with those obtained at CT.

Keywords
- acute pancreatitis
- CT
- dual-energy X-ray absorptiometry

Introduction

Acute pancreatitis (AP), especially severe AP (SAP), causes significant morbidity and mortality.[1] SAP is commonly accompanied by systemic inflammatory response syndrome and multiple organ dysfunction.[2,3] Early detection and management of patients likely to develop SAP are imperative to prevent complications.[4,5] The incidence of obesity is increasing

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worldwide.[6] Obesity increases the incidence as well as the severity of AP.[6–8] Obesity can increase the incidence of AP by predisposing to gallstones, hypertriglyceridemia, and diabetes.[7–9] Therapeutic interventions for obesity are also associated with increased incidence of AP.[8] The increased severity of AP in obesity is explained by several mechanisms.[9]

The conventional indicators of obesity include body mass index (BMI) and waist circumference (WC). The limitation of these parameters is that they do not account for the differences in fat distribution.[10] Studies have shown that visceral fat is more closely related to the severity of AP.[11–16] Computed tomography (CT) is the most widely used method for estimating abdominal fat.[9] Dual-energy X-ray absorptiometry (DXA) allows the estimation of body composition. It has the advantage of reduced radiation exposure and hence repeatability. Although DXA has been commonly utilized for various diseases, its role has not been evaluated explicitly for fat quantification in AP.[17–20] Additionally, no published studies have compared the performance of CT and DXA for fat estimation in AP. This study explores the correlation between the body fat estimation by CT and DXA and the association of fat indices with clinical outcomes in patients with AP.

Materials and Methods

The institute ethics committee approved this prospective study. Informed written consent was obtained from all patients. Consecutive patients with AP who underwent CT scans of the abdomen and whole-body DXA between June 2017 and June 2019 were included. Patients with acute on chronic or recurrent AP were excluded.

Baseline Evaluation

Diagnosis of AP was based on the presence of at least two of the three features: pain abdomen consistent with AP, raised serum lipase (or amylase) at least three times the upper limit of the normal, and characteristic findings of AP on imaging.[21] The etiology of AP was recorded. The disease severity was assessed based on the revised Atlanta Classification.[21]The body mass index (BMI) and waist circumference (WC) were measured as per the WHO criteria and consensus statement for Asian Indians.[22,23]

CT and DXA were both performed between 5 and 7 days of pain onset.

DXA Fat Measurement

Whole-body DXA was performed using Hologic Discovery W. The DXA field of view was 195×65 cm. All DXA measurements were analyzed using the Hologic software. The software reported total body and regional fat mass and percentage fat results. In addition, DXA-visceral adipose tissue (VAT_{DXA}) was measured in a 5 cm wide region placed across the entire abdomen width just above the iliac crest.

Abdominal Fat Assessment using CT

Patients were scanned in a supine position with both arms stretched above the head. Scans were performed on multidetector-row CT scanners (Siemens Somatom Flash; Philips iCT; VCT, GE) following intravenous injection of 80 to 100 mL of non-ionic iodinated contrast (Omnipaque 300, GE healthcare). The acquisition was performed in the portal venous phase 65 seconds after the start of contrast injection. The intraabdominal visceral fat volume was measured by an abdominal radiologist with 7 years of experience in evaluating abdominal CT. The radiologist was blinded to the DXA fat estimates and the clinical outcomes. The abdominal fat estimation was done using the in-built volumetry software on the SyngoVia workstation (Siemens Medical Solutions, Erlangen, Germany). Fat measurement was done on 10-mm reconstructed slices by drawing two regions of interest (ROI) according to the protocol described previously.[24] Briefly, three non-contiguous axial sections, at T12-L1, at the umbilicus, and at L5/S1 level were utilized for fat estimation. First, ROIs were drawn to contour the entire abdomen using the skin surface as the landmark to measure the total adipose tissue (TAT). Then, another ROI was drawn, excluding the subcutaneous fat and muscles. This allowed the calculation of VAT_{CT}. The range of attenuation for automated fat estimation was set between -30 and -190 HU.

CT scans were also assessed for the presence and extent of pancreatic necrosis and the presence of local complications. CT severity index (CTSI) was calculated on baseline CT.

Management

Analgesics, oxygen, intravenous fluids, and other supportive measures were administered as per the requirement. In SAP, nasoenteric or parenteral feeding (in persistent ileus or active gastrointestinal bleeding) was administered. Antibiotics were given for suspected infection of the necrosis (suspicion was based on the presence of gas within the necrotic collection on CT and confirmed by culture of the fluid aspirated at the time of drainage) or extrapancreatic infections. A step-up approach was used for the management of pancreatic fluid collections. In the step-up approach, patients with symptomatic pancreatic fluid collections underwent percutaneous, endoscopic, or dual-modality drainage. Those not responding to the drainage underwent minimally invasive necrosectomy.

Outcome Assessment

Length of hospital stay (LOH), need for admission to the intensive care unit (ICU) as well as the length of ICU stay were recorded. Additionally, the need for drainage and surgery was noted. The number of deaths during hospital admission and within 3 months of discharge from the hospital was recorded.

Statistical Analysis

All data were entered in Microsoft Excel analyzed using IBM SPSS version 23.0 (Chicago, IL, USA). Quantitative or numerical variables are presented as mean with range. The continuous variables were compared using Student's *t*-test. Dichotomous variables were compared using the Chi-square test. The correlation between the various continuous variable was assessed using Pearson's or Spearman's correlation coefficient depending on the distribution. The area under the curve (AUC) was calculated using receiver operating characteristic (ROC)

Table 1 Baseline characteristics of patients ($n = 59$)

Parameters	Result
Age	38.27 years (range, 13–65 years)
Males/females	48/11
Mean BMI (Kg/m$^{2)}$	22.2 (range, 13.7–33.7)
Obesity (Indian)	16
Mean waist circumference (cm)	88.1 (range, 70–104)
Etiology	
Alcohol abuse	33 (55.9%)
Gallstones	14 (23.7%)
Idiopathic	6 (10.2%)
Others	6 (10.2%)
Severity	
Mild	18 (30.5%)
Moderately severe	23 (39%)
Severe	18 (30.5%)
Mean CTSI	7.03 (range, 1–10)
DEXA fat measures	
VAT volume (cm^3)	397.4 (92–974)
%fat	28 (12.8–44.6)
Truncal fat (g)	7943 (1929–15541)
CT fat measures	
Total adipose tissue (cm^3)	7521.3 (264–14530)
Visceral adipose tissue (cm^3)	2805 (128–5901)
Organ failure	18 (30.5%)

Abbreviations: BMI, body mass index; CTSI, CT severity index; VAT, visceral adipose tissue.

curves. The *p*-value of less than 0.05 was taken as statistically significant.

Results

Baseline Characteristics

A total of 59 patients were included in the study. The mean age was 38.2 years (range, 13–65 years). There were 48 (81.3%) males and 11 (18.7%) females. The most common etiologies of AP were alcohol use ($n = 33$, 55.9%) and gallstone disease ($n = 14$, 23.7%). Mild, moderately severe, and severe AP was seen in 18 (30.5%), 23 (39%), and 18 (30.5%) patients, respectively. The mean CTSI was 7.03 (range, 1–10). Eighteen (30.5%) patients had organ failure.

Fat Measures

The mean BMI was 22.2 Kg/m^2 (range, 13.7–33.7). According to the Asian cut-off, 43 (72.9%) patients were non-obese, and 16 (27.1%) cases were obese. The mean WC was 88.17 cm (range, 70–104). DXA fat estimates were mean VAT_{DXA} volume of 397.42 cm^3 (92–974), fat percentage of 28% (range 12.8–44.6), and truncal fat of 7943 g (range, 1929–15541). CT fat estimates were mean TAT volume of 7521.3 cm^3 (range, 264–14530) and VAT_{CT} volume of 2805 cm^3 (range, 128–5901)

Outcomes

Thirty-five patients (59.3%) patients required hospitalization. The mean length of hospitalization was 12.29 days (range, 0–98 days). Ten (16.9%) patients needed ICU admission, and the mean length of ICU stay was 1.8 days (range, 0–20). Eleven (18.6%) patients underwent percutaneous catheter drainage, 4 (6.8%) patients underwent endoscopic drainage, and 7 (11.9%) patients underwent dual-modality drainage. In addition, three patients underwent surgical necrosectomy. None of the patients died during the study period. ►**Table 1** shows the baseline characteristics, values of fat indices, and outcomes.

Table 2 Correlation between different fat parameters for all patients

Indices	BMI	WC	VAT_{DXA}	%Fat	Truncal fat	TAT
WC *p*-Value	0.736 (0.0002)					
VAT_{DXA} *p*-Value	0.527 (0.022)	0.353 (0.191)				
%fat *p*-Value	0.496 (0.041)	0.407 (0.056)	0.826 (0.0001)			
T.fat (g) *p*-Value	0.418 (0.091)	0.562 (0.010)	0.759 (0.0002)	0.786 (0.0001)		
TAT *p*-Value	0.610 (0.003)	0.579 (0.010)	0.799 (0.0001)	0.727 (0.0002)	0.783 (0.0001)	
VAT_{CT} *p*-Value	0.475 (0.049)	0.398 (0.102)	0.740 (0.0002)	0.691 (0.001)	0.792 (0.0001)	0.841 (0.0001)

Abbreviations: BMI, body mass index; T.fat, truncal fat on DXA; TAT, total adipose tissue on CT; VAT_{CT}, visceral adipose tissue on CT; VAT_{DXA}, visceral adipose tissue on DXA; WC, waist circumference.
p-Value $< .05$ is statistically significant.

Association/Correlation between Fat Indices and Outcomes

There was no significant association of BMI and WC with clinical outcomes. There was a significant association of VAT_{DXA} and VAT_{CT} with the severity of AP ($p = 0.021$ and 0.019, respectively) and the need for drainage of peripancreatic collection ($p = 0.038$, and 0.003, respectively). There was no significant association between any measures of fat indices and the presence of multiple or persistent OF, local complications, and need for surgery.

BMI and WC had a weak correlation for both LOH (0.121, 0.190) and length of ICU admission (0.211, 0.197). There was a moderate to strong correlation between DXA and CT fat measures and clinical outcomes. For LOH, correlation coefficients for truncal fat, VAT_{DXA}, TAT, VAT_{CT} were 0.562, 0.532, 0.602 and 0.614, respectively. For the length of ICU stay, correlation coefficients for truncal fat, VAT_{DXA}, TAT, VAT_{CT} were 0.591, 0.577, 0.636, and 0.676, respectively.

Correlation Among Various Fat Indices

There was a strong correlation between DXA (VAT and truncal fat) and CT (TAT and VAT_{CT}) fat measurements ($r = 0.691$–0.799). ►**Table 2** shows the correlations among fat indices. ►**Table 3** shows the correlations stratified for severity.

Area Under the Curve

Compared with other fat indices, VAT_{CT} had a consistently higher AUC than other indexes for predicting outcomes (►**Table 4** and ►**Fig. 1**).

Discussion

In this study evaluating CT and DXA fat estimation in AP, we found a strong correlation between DXA and CT fat indices. VAT_{DXA} and VAT_{CT} showed significant association with the severity of AP and the need for drainage of peripancreatic collections. There was a moderate to strong correlation between the LOH and length of ICU stay with the DXA and CT fat indices. VAT measured on CT showed the highest AUC for predicting the outcomes. These results suggest a potential role of fat estimation in AP and that either CT or DXA can be used for this purpose.

A few studies have suggested the association between obesity and the severity of AP.[2,3] BMI has been shown in a previous study to have a weaker relationship with severity of AP compared with visceral fat or the distribution of visceral fat and skeletal muscle.[11] BMI was weakly correlated with the length of hospitalization and length of ICU stay. However, BMI had no significant association with the severity of AP.

Previous studies have shown that the visceral adiposity measured at CT predicts the severity and other outcomes in AP.[11,13–16] Yashima et al found that peripancreatic VAT has a more robust correlation with SAP than BMI or WC and higher VAT correlates with the risk of developing pseudocyst.[14] O'Leary et al evaluated the CT fat parameters in 62 patients with AP.[15] VAT was found to have a significant

Table 3 Correlation between different fat parameters stratified for severity

Indices	BMI			WC			VAT_{DXA}			%Fat			T. fat			TAT		
	Mild	MSAP	SAP	Mild	MSAP	SAP	Mild	MSAP	SAP	Mild	MSAP	SAP	Mild	MSAP	SAP	Mild	MSAP	SAP
WC p-value	0.543 (0.020)	0.738 (0.0002)	0.707 (0.0004)															
VAT_{DXA} p-value	0.497 (0.036)	0.682 (0.0003)	0.515 (0.034)	0.350 (0.091)	0.412 (0.071)	0.364 (0.110)												
%fat p-value	0.321 (0.194)	0.610 (0.002)	0.485 (0.065)	0.398 (0.102)	0.581 (0.003)	0.419 (0.091)	0.694 (0.001)	0.828 (0.0001)	0.706 (0.0004)									
T. fat g p-value	0.539 (0.021)	0.681 (0.001)	0.750 (0.0002)	0.537 (0.021)	0.598 (0.002)	0.391 (0.101)	0.647 (0.002)	0.798 (0.0002)	0.640 (0.001)	0.758 (0.0002)	0.691 (0.001)	0.708 (0.0009)						
TAT p-value	0.454 (0.058)	0.629 (0.002)	0.512 (0.038)	0.459 (0.055)	0.598 (0.002)	0.366 (0.149)	0.573 (0.013)	0.831 (0.0001)	0.769 (0.0001)	0.621 (0.005)	0.727 (0.0002)	0.684 (0.001)	0.602 (0.008)	0.790 (0.0001)	0.755 (0.0002)			
VAT_{CT} p-value	0.419 (0.089)	0.537 (0.008)	0.492 (0.045)	0.397 (0.101)	0.520 (0.030)	0.257 (0.321)	0.604 (0.008)	0.776 (0.0002)	0.749 (0.0002)	0.609 (0.008)	0.703 (0.0003)	0.676 (0.002)	0.604 (0.008)	0.812 (0.0001)	0.569 (0.017)	0.761 (0.0002)	0.898 (0.00005)	0.773 (0.0002)

Abbreviations: BMI, body mass index; T.fat, truncal fat on DXA; TAT, total adipose tissue on CT; VAT_{CT}, visceral adipose tissue on CT; VAT_{DXA}, visceral adipose tissue on DXA; WC, waist circumference.
Note: *p*-Value < 0.05 is statistically significant.

Table 4 Area under curve for the prediction of various outcomes

Indices	OF (95% CI)	Severity (95% CI)	ICU stay (95% CI)	Surgery (95% CI)	Drainage (95% CI)
BMI	0.549 (0.182–0.844)	0.515 (0.149–0.821)	0.542 (0.167–0.879)	0.526 (0.151–0.809)	0.343 (0.129–0.703)
WC	0.529 (0.199–0.773)	0.538 (0.192–0.833)	0.583 (0.279–0.883)	0.558 (0.212–0.890)	0.345 (0.143–0.721)
VAT_{DXA}	0.701 (0.582–0.917)	0.665 (0.575–0.859)	0.621 (0.523–0.769)	0.684 (0.535–0.891)	0.618 (0.512–0.832)
%fat	0.657 (0.612–0.871)	0.572 (0.529–0.798)	0.650 (0.588–0.871)	0.789 (0.638–0.951)	0.626 (0.608–0.854)
T. fat (g)	0.652 (0.565–0.885)	0.621 (0.549–0.791)	0.716 (0.638–0.931)	0.671 (0.579–0.910)	0.631 (0.587–0.832)
TAT	0.710 (0.632–0.926)	0.669 (0.592–0.880)	0.727 (0.637–0.938)	0.719 (0.622–0.936)	0.742 (0.659–0.946)
VAT_{CT}	0.746 (0.634–0.939)	0.691 (0.591–0.890)	0.760 (0.613–0.971)	0.783 (0.654–0.976)	0.799 (0.651–0.981)

Abbreviations: BMI, body mass index; CI, confidence interval; ICU, intensive care unit; LC, local complications; OF, organ failure; TAT, total adipose tissue on CT; Trn fat, truncal fat on DXA; VAT_{CT}, visceral adipose tissue on CT; VAT_{DXA}, visceral adipose tissue on DXA; WC, waist circumference.

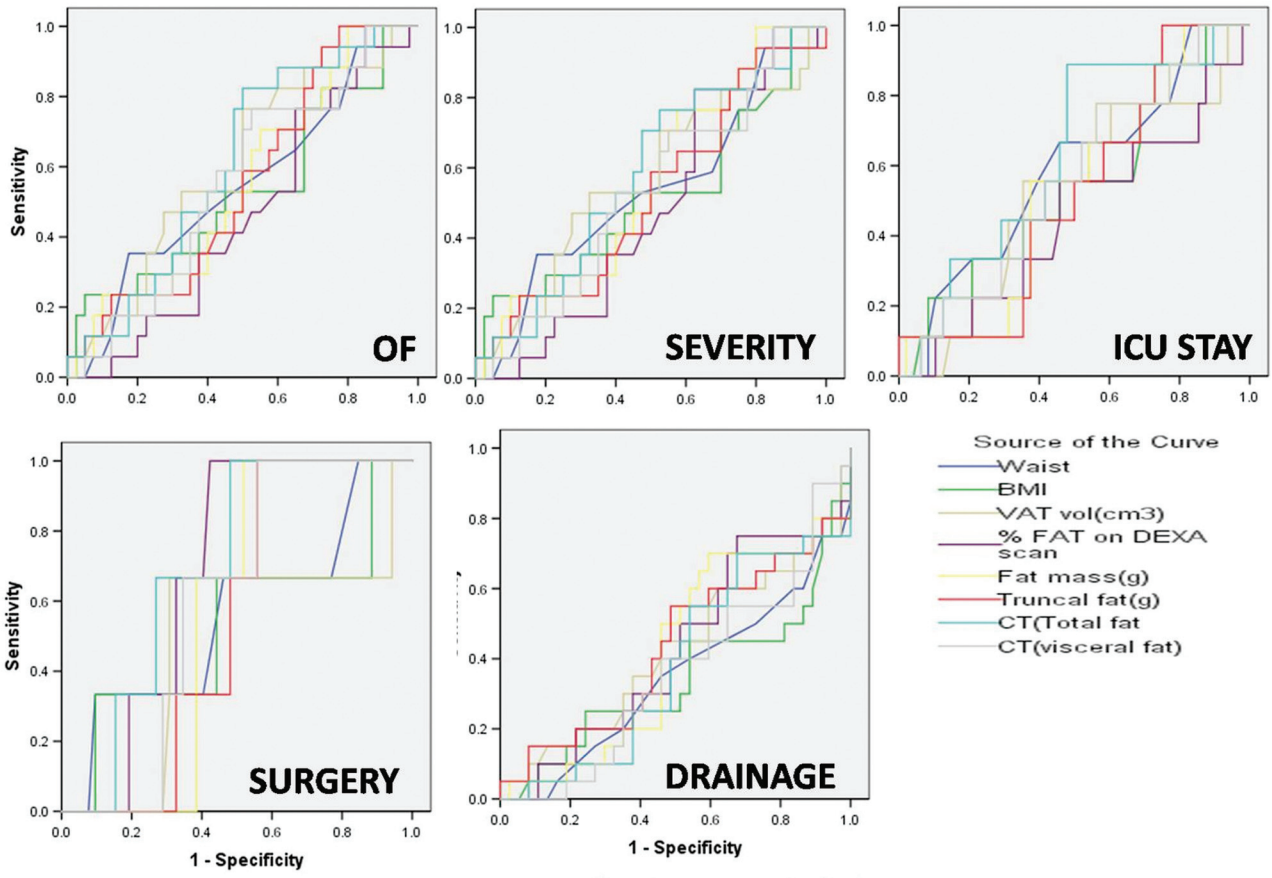

Fig. 1 Area under the curve for prediction of outcomes based on anthropometric, DXA, and CT fat estimates. OF, organ failure, ICU, intensive care unit.

association with SAP and mortality. However, on multivariate analysis, none of the fat parameters were significantly associated with SAP. Natu et al also found that patients with greater VAT area had severe disease, multiorgan failure, and necrosis.[16] Yoon et al found that the ratio of visceral fat to a skeletal muscle has the largest AUC in predicting severe AP.[11] Our results are in concordance with the previously published studies.

None of the published studies have compared the performance of the two most commonly used imaging techniques for fat estimation (CT and DXA) in patients with AP. Though CT indices had a slightly better AUC, the strong correlation between the fat indices at DXA and CT implies that either technique can be utilized. The decision to perform DXA versus CT for fat estimation may be based on the clinical status. While patients with mild AP do not routinely require CT evaluation, moderately severe and severe AP frequently undergo CT. DXA can thus be utilized in patients with clinically mild AP (at presentation) as it does not expose the patient to intravenous contrast and the relatively higher radiation dose associated with CT scan.[25]

A few studies in other diseases suggest a strong correlation between CT and DXA fat measurement. In a study by Mourtzakis et al comprising 50 patients with cancers, both CT and DXA strongly predicted whole-body fat and fat-free mass ($r = 0.86–0.94$; $p < 0.001$).[17] A study by Snijder et al compared CT and DXA for fat measurement in elderly subjects between 70 and 79 years.[18] They reported that total abdominal fat measured by DXA was strongly correlated with total abdominal fat measured by CT ($r = 0.87–0.98$). The correlation coefficient for visceral fat measured using DXA, and CT ranged from 0.65–0.79. The authors concluded that DXA is a reasonable alternative to CT for predicting total abdominal fat in elderly subjects. A study by Xia et al also showed a strong correlation ($r = 0.94–0.96$) between VAT measured at CT and DXA in 155 subjects comprising 60 females and 55 males.[19] In a study assessing the visceral adiposity among gastrointestinal and pancreatic cancer survivors, Coletta et al found that DXA and CT VAT estimates were strongly correlated. However, the authors reported that there is substantial bias in DXA measurement.[20] They suggested that further research is required to evaluate the interchangeability of the two modalities.

There were a few limitations to our study. First was the small sample size. Also, there were disproportionally more males than females and due to small sample size, the results stratified by gender could not be provided. Additionally, most patients had moderately severe AP and SAP, which a referral bias can explain. However, patients with mild AP have an excellent outcome. Hence, patients with moderately severe and SAP are better suited for the evaluation of various prognostic indices.

Conclusion

In conclusion, fat indices measured on DXA and CT is associated with the severity of AP. In addition, the fat measurements at DXA and CT are strongly correlated. This suggests that either DXA or CT may be utilized for fat estimation in patients with AP.

Conflict of Interest
None declared.

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