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The effect of the visceral adiposity index on the severity of COVID-19 disease: results of a cross-sectional study

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Abstract. – OBJECTIVE: Obesity has been identified as a contributing factor that exacerbates the severity of COVID-19 and is associated with an increased risk of mortality among hospitalized patients. Assessing visceral adipose tissue cannot be solely determined by obesity and body mass index (BMI) alone. In our study, we investigated the relationship between the visceral adiposity index (VAI) and the clinical severity of COVID-19.

PATIENTS AND METHODS: A total of 315 adult patients hospitalized with COVID-19 were included in the study. The cohort consisted of 146 male patients, and the median age was 60 (48-74) years. Comparative analyses were conducted to evaluate gender-based differences in VAI levels and the impact of VAI on the extent of radiological lung involvement.

RESULTS: The median VAI level was significantly higher in women compared to men (6.1 *vs.* 4.0, $p<0.001$). Furthermore, patients with radiologically severe lung involvement demonstrated a higher median VAI level compared to those with mild involvement (5.7 *vs.* 4.2, $p=0.003$). This difference was particularly notable among male patients, where the median VAI level was significantly higher. Logistic regression analysis revealed that each integer increase in the median VAI value was associated with a 1.1-fold (1.01-1.14) increase in the severity of radiological lung involvement ($p=0.011$).

CONCLUSIONS: Our study highlights a significant correlation between VAI and the clinical severity of COVID-19, particularly among male patients. The findings suggest that VAI, as an indicator of visceral adiposity, holds potential as a valuable tool for assessing COVID-19 severity and identifying high-risk individuals, particularly males.

Key Words:
Obesity, COVID-19, Visceral adiposity index, VAI, Visceral adipose tissue.

Introduction

Obesity has been defined as a factor that worsens the severity of COVID-19[1]. It is a risk factor that increases mortality in hospitalized patients[2-4]. Especially, a significant relationship between visceral adiposity and the need for an intensive care unit (ICU) and mechanical ventilation has been shown[5,6] in COVID-19 patients.

Obesity and body mass index (BMI) alone are not very effective in demonstrating visceral adipose tissue, and the distinction between subcutaneous adipose tissue and visceral adipose tissue is important. Visceral adipose tissue has been associated with a poor prognosis[7-9]. To calculate the ratio of visceral fat tissue, images obtained from the level of the L3 vertebra through computerized tomography (CT) and magnetic resonance imaging (MRI) methods were used. However, these methods have disadvantages such as cost, radiation exposure, and increased workload[8,9]. Consequently, research has been conducted on more practical computational methods. One such method is the visceral adiposity index (VAI), which was first reported by Amato et al[10] in 2010. Over the past decade, numerous studies in the literature have investigated the relationship between VAI and various clinical conditions. However, to date,

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no study has investigated the relationship between VAI and the clinical severity of COVID-19. The aim of our study is, to investigate the relationship between visceral adiposity index (VAI) and the clinical severity of COVID-19.

Patients and Methods

Study Design and Patients

This study was conducted simultaneously in Samsun Training and Research Hospital and Gazi State Hospital, prospectively. Informed consent was obtained from all participants.

A convenience sampling method was utilized to gather data for this study. From June 2021 to December 2021, clinical and demographic information was collected from a total of 365 hospitalized patients diagnosed with COVID-19. This included data on age, gender, body mass index, height (cm), waist circumference (cm), smoking habits, and comorbidities such as diabetes, hypertension, kidney failure, chronic lung disease, and heart failure. Additionally, information regarding the degree of radiological involvement, length of hospital stay, length of intensive care unit (ICU) stay, need for invasive mechanical ventilation (IMV), and specific treatments administered (plasma, steroid, tocilizumab) was recorded. Laboratory values at the time of admission, including white blood cell count (WBC), lymphocyte count, neutrophil count, C-reactive protein (CRP), D-dimer, ferritin, aspartate transaminase (AST), alanine transaminase (ALT), blood urea nitrogen (BUN), creatinine, fasting blood glucose, high-density lipoprotein (HDL), and triglycerides, were also documented based on comorbidities. All patient information and test results were obtained from the hospital automation system. After excluding 38 patients with incomplete data and 12 individuals who did not provide informed consent, the study was completed with a total of 315 patients, resulting in a participation rate of 86.3%

The VAI was calculated with the formula given below for male and female genders[10]:

$$\text{VAI (men)} = [(\text{Waist circumference}) / (39.68 + (1.88 \times \text{BMI}))] \times (\text{Triglyceride} / 1.03) \times (1.31 / \text{HDL})$$

$$\text{VAI (women)} = [(\text{Waist circumference}) / (36.58 + (1.89 \times \text{BMI}))] \times (\text{Triglyceride} / 0.81) \times (1.52 / \text{HDL})$$

Ethical Approval

The study was approved by the Institutional Ethics Committee of Samsun Training and Research Hospital (Date: 29/04/2021, Decision No.: GOKA/2021/10/6).

Statistical Analysis

All statistical tests were conducted using the SPSS for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to express the data, including median (Q1-Q3) and percentage (%). The Kolmogorov-Smirnov test was used to assess the distribution of numerical data. In cases where the data did not meet the assumptions of a normal distribution, the Mann-Whitney U test was employed for paired groups, and the Kruskal-Wallis analysis of variance test was utilized for groups consisting of more than two variables. The relationship between the variables was examined using the Spearman's correlation test. Logistic regression analysis was performed to evaluate the impact of VAI in specific scenarios. The Chi-square test was employed to compare quantitative data. Participants with missing data were excluded from the study. A statistical significance level of $p<0.05$ was considered for all statistical tests.

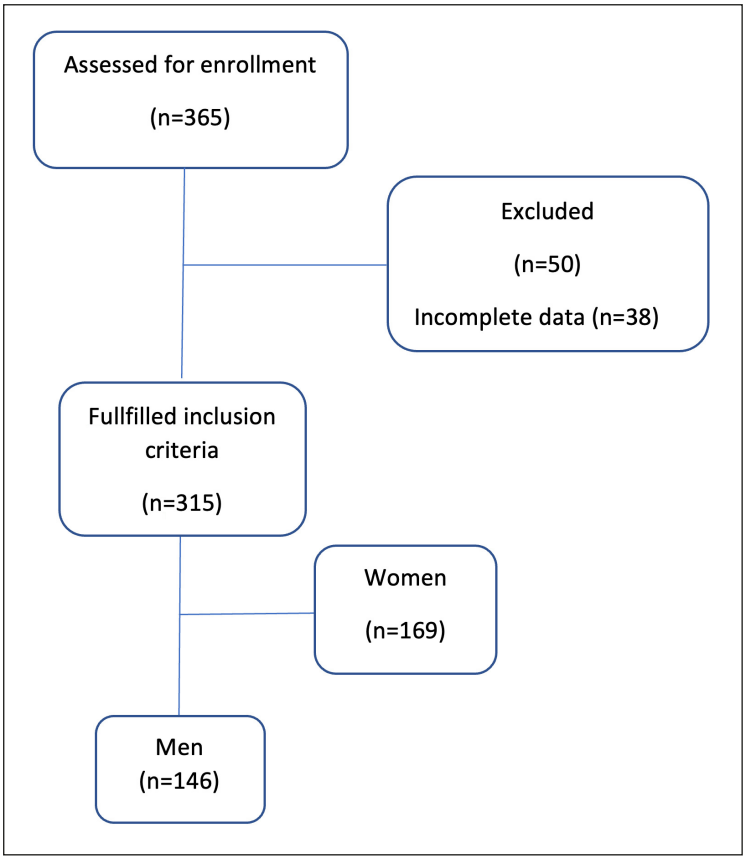
Results

A total of 365 patients were assessed for enrollment in the study, out of which 315 patients were included (Figure 1).

Of the total cases, 146 (46.3%) were males, with a median age of 60 (range: 48-74) years. Women had significantly higher BMI and waist circumference compared to men (31.1 *vs.* 27.4 Kg/m^2 and 108 cm *vs.* 101 cm, respectively) ($p<0.001$, 0.012) (Table I). The median VAI value was higher in women than in men (6.1 *vs.* 4.0) ($p<0.001$) (Table I). The prevalence of DM and HT was higher in women compared to men (36.7% *vs.* 23.3% and 54.4% *vs.* 41.8%, respectively) ($p<0.05$). The use of favipiravir, prednisolone, and tocilizumab was statistically similar between genders, although it was slightly higher in males ($p>0.05$). Gender-related mortality rates were comparable between the groups ($p=0.317$) (Table I).

The impact of median VAI value on mean length of stay, intensive care stay, need for invasive mechanical ventilation, and the use of favipiravir and prednisolone did not differ significantly between genders ($p>0.05$). However, tocilizumab

Figure 1. Patient flowchart.



use was associated with a higher median VAI level (p=0.042) (Table II). Among the cases, 101 (32.1%) showed mild involvement, while 214 (67.9%) showed moderate to severe involvement. Higher VAI levels were associated with more severe lung involvement in males (5.7 *vs.* 4.2) (p=0.007) (Table II).

In logistic regression analysis, each integer increase in median VAI value, regardless of gender, increased the risk of severe radiological involvement by 1.1 times (95% CI: 1.01-1.14) (p=0.011) (Table III). Sub-analysis revealed that a high median VAI level predicted severe radiological involvement in male COVID-19 cases but was not associated with mortality, number of intensive care unit days, or mechanical ventilation (Table IV).

Discussion

Our study demonstrates a strong correlation between VAI and the clinical severity of COVID-19, particularly among male patients. These findings emphasize the potential of VAI as a valuable marker for assessing disease severity in males and underscore its significance in evaluating clinical outcomes related to COVID-19.

Numerous studies[11,12] have investigated the relationship between VAI and diverse clinical conditions, consistently demonstrating its superior capability in reflecting adipose tissue dysfunction when compared to conventional anthropometric measures such as BMI and waist circumference. The impact of infectious diseases can vary between individuals based on their biological sex or gender due to the immunomodulatory effects of sex hormones[13]. Recent research[14] suggests that females with COVID-19 may have certain advantages over males, including higher levels of CD4+ T cells, more robust CD8+ T-cell cytotoxic activity, and increased production of B-cell-derived immunoglobulins. These findings indicate a potential immunological advantage in females when it comes to combating COVID-19. Notably, Klein[15] found that female individuals exhibit immune responses that are twice as potent as those observed in male individuals. Consequently, being male may serve as a risk factor for severe COVID-19 infection. Consistent with the existing literature, our findings demonstrate that while

Table I. Demographic, clinical and laboratory findings of the participants.

	Men (%) n=146 (46.3)	Women (n,%) N=169 (55.7)	p
Age (years)	60.0 (48.0-74.0)	59.0 (48.0-73.0)	0.989
Body mass index (kg/m^2)	27.4 (24.4-30.6)	31.1 (26.7-35.0)	**<0.001**
Waist circumference (cm)	101.0 (90.0-110.0)	108.0 (90.0-120.0)	**0.012**
Visceral adiposity index	4.0 (2.5-6.9)	6.1 (4.2-8.9)	**<0.001**
HDL (mg/dL)	40.0 (34.0-49.2)	47.0 (40.0-56.0)	**<0.001**
Triglyceride (mg/dL)	121.0 (90.0-194.7)	133.0 (100.0-194.0)	0.063
WBC	8.2 (6.0-11.5)	6.7 (5.2-9.9)	**0.004**
Neutrophyle	5.9 (4.1-9.1)	4.7 (3.2-8.1)	**0.004**
Lymphocite	1.1 (0.6-1.7)	1.1 (0.8-1.8)	0.851
Hemoglobine	13.7 (12.2-14.7)	12.2 (10.8-13.1)	**<0.001**
Platelet	196,500 (153,250-297,000)	211,000 (169,500-276,500)	0.266
C-reactive protein	61.4 (21.5-115.5)	37.0 (13.4-114.2)	**0.042**
D-Dimer	0.9 (0.4-2.0)	0.7 (0.3-1.8)	0.404
Ferritine	419.5 (210.0-772.5)	200.0 (90.0-346.0)	**<0.001**
Glucose	121.5 (102.0-176.0)	134.0 (110.0-186.5)	**0.038**
Creatinine	0.9 (0.7-1.1)	0.7 (0.6-0.9)	**<0.001**
AST	34.0 (24.0-52.2)	27.0 (21.0-37.5)	**0.002**
ALT	29.0 (18.0-52.5)	22.0 (14.0-34.0)	**<0.001**
LDH	277.5 (201.2-416.2)	270.0 (206.0-379.0)	0.453
Fibrinogen	419.5 (333.7- 534.2)	408.5 (342.5-555.5)	0.967
Comorbidity (n, %)			
Smoking	28 (19.2)	6 (3.6)	**<0.001**
Diabetes mellitus	34 (23.3)	62 (36.7)	**0.010**
Hypertension	61 (41.8)	92 (54.4)	**0.025**
Coronary artery disease	17 (11.6)	19 (11.2)	0.911
Chronic kidney disease	8 (5.5)	12 (7.1)	0.556
Hospital stay (days)	9.0 (5.7-16.0)	8.0 (6.0-14.0)	0.406
Time to onset of symtoms (days)	4.0 (1.7-7.0)	4.0 (2.0-7.0)	0.880
Favipiravir use (n, %)	127 (87.0)	146 (86.4)	0.877
Prednisolone use (n, %)	124 (84.9)	136 (80.5)	0.299
Tocilizumab use (n, %)	11 (7.5)	9 (5.3)	0.423
Mortality (n, %)	20 (13.7)	17 (10.1)	0.317

HDL: High-density lipoprotein, WBC: leukocyte, AST: Aspartate aminotransferese, ALT: Alanine aminotarnsferese, LDH: lactate dehydrogenase, HDL: high density lipoprotein.

females exhibit higher VAI rates, elevated levels of VAI exclusively correlate with the severity of COVID-19 involvement in males.

Obesity is associated with an upregulation of proinflammatory cytokines and adipokines, including tumor necrosis factor-alpha, leptin, monocytes, and interleukin-6, accompanied by a reduction in adiponectin levels, which possesses anti-inflammatory properties. These changes can adversely affect immunomodulation[2,16]. The association between higher body mass index and increased risk of intensive care follow-up, need for invasive mechanical ventilation, and severity of pneumonia further supports the inflammatory effect[4-6,17-21]. A limited number of studies[22-24] have investigated the relationship between increased visceral fat and the severity of COVID-19. One study[25] examining the impact of increased adipose tissue on COVID-19 outcomes through intramuscular adiposity found a 2.3 times higher risk of critical COVID-19 infection in individuals with high adiposity index compared to those with low adiposity. Similarly, it has been reported[20,26] that regardless of age, COVID-19 patients with morbid obesity have a higher risk of hospitalization (2.3 times), disease severity (7.4 times), need for mechanical ventilation (7.4 times), and mortality (12.1 times). Other factors contributing to the

Table II. Comparison of echocardiographic and ambulatory blood pressure parameters of the study population.

	Men			Women			Total		
	n	Median (Q1-Q3)	p*	n	Median (Q1-Q3)	p*	n	Median (Q1-Q3)	p*
ICU stay									
Yes	46	5.1 (2.3-7.4)	0.527	48	6.7 (4.6-9.4)	0.445	94	5.7 (3.6-8.0)	0.439
No	100	3.6 (2.5-6.9)		121	3.6 (2.5-6.9)		221	5.2 (3.2-8.0)	
Hospital stay (days)									
≤7	60	3.2 (2.4-6.9)	0.299	82	6.0 (4.1-8.6)	0.415	142	5.1 (3.1-8.0)	0.367
≥8	86	5.0 (2.5-7.0)		87	6.3 (4.4-9.6)		173	5.5 (3.5-8.1)	
IMV									
Yes	23	5.1 (2.3-7.4)	0.849	23	5.5 (3.2-8.1)	0.495	46	5.2 (3.3-8.1)	0.512
No	123	3.8 (2.6-6.9)		146	6.2 (4.2-9.6)		269	5.3 (2.6-7.7)	
Favipiravir use									
Yes	127	4.7 (2.5-6.9)	0.319	146	6.1 (4.2-9.0)	0.883	273	5.4 (3.4-8.0)	0.355
No	19	3.1 (2.3-6.3)		23	6.3 (3.3-8.5)		42	4.7 (2.9-7.8)	
Prednisolon use									
Yes	124	4.7 (2.5-7.7)	0.065	136	5.9 (4.1-8.8)	0.306	260	5.3 (3.3-8.0)	0.663
No	22	3.2 (2.4-5.3)		33	6.5 (4.5-9.3)		55	5.3 (3.2-8.0)	
Tocilizumab use									
Yes	11	6.7 (5.0-10.9)	0.043	9	7.6 (4.0-19.3)	0.240	20	7.5 (4.8-12.3)	0.042
No	135	3.7 (2.5-6.8)		160	6.0 (4.1-8.5)		295	5.2 (3.2-7.9)	
Severity of radiological involvement									
Mild	50	3.0 (2.3-5.1)	0.007	51	5.6 (3.9-8.5)	0.210	101	4.2 (2.8-7.2)	0.003
Severe	96	5.1 (2.8-7.9)		118	6.2 (4.3-9.9)		214	5.7 (3.6-8.6)	

ICU: Intensive care unit, IMV: Intermittant mechanical ventilation.

severity of COVID-19 include increased airway resistance, impaired gas exchange, weakened respiratory muscles, and decreased lung volume[17,27]. The concentration of Angiotensin-converting enzyme receptor-2 (ACE2) in adipose tissue has been suggested[18,28,29] to facilitate the entry of SARS-CoV-2 into cells, leading to increased hospitalization rates and a more severe clinical course of COVID-19. In our study, we did not investigate the effect of increased VAI on hospitalization rates and disease severity, as only hospitalized cases were included. When considering gender differences, women had a higher median VAI than men (6.1 *vs.* 4.0), and a correlation was found between severe radiological involvement and high median VAI level only in males (5.1 *vs.* 3.0). The most noteworthy finding of this study is that each integer increase in VAI increases the severity of radiological involvement by 1.10 times in males but does not significantly impact females.

Table III. Visceral adiposity index and relationships between clinical data.

	B	S.E.	Wald	Sig.	Odds ratio	95% C.I.	
						Lower	Upper
Mortality	-0.041	0.041	0.968	0.325	0.960	0.885	1.041
Intensive care unit stay	-0.002	0.025	0.005	0.946	0.998	0.950	1.049
Mechanical ventilation need	-0.019	0.035	0.298	0.585	0.981	0.917	1.050
Severity of radiological involvement	0.076	0.030	6.428	**0.011**	1.079	1.017	1.114

HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein; MHR, Monocytes to High-Density Lipoprotein Ratio; TSH, Thyroid Stimulating Hormone; WBC, White blood cell.

Table IV. Relationships between the VAI and clinical data according to gender.

	Men							Women						
	B	S.E.	Wald	p	Odds ratio	95% C.I.		B	S.E.	Wald	p	OR	95% C.I.	
						Lower	Upper						Lower	Upper
Mortality	-0.046	0.061	0.574	0.44	0.955	0.848	1.076	-0.023	0.056	0.162	0.68	0.978	0.875	1.092
Need for ICU stay	-0.010	0.038	0.072	0.78	0.990	0.918	1.067	0.010	0.034	0.090	0.76	1.010	0.945	1.080
Need for mechanical ventilation	-0.022	0.052	0.186	0.66	0.978	0.883	1083	-0.011	0.047	0.049	0.82	0.990	0.902	1.086
Severity of radiological involvement	0.099	0.048	4.159	0.041	1.104	1.004	1.213	0.056	0.039	2.062	0.15	1.058	0.980	1.142

VAI: Visceral adiposity index, ICU: Intensive Care Unit.

Although we did not measure pro-inflammatory cytokine and anti-inflammatory adipokine concentrations in our study, the increased need for tocilizumab, an Interleukin-6 inhibitor, and more severe radiological involvement in males suggests that increased adipose tissue mass may play a significant role in the inflammatory process, particularly in males. Further multicenter studies with larger sample sizes are needed to establish a stronger correlation between VAI levels and COVID-19 severity. While some studies[2] indicate that obesity is an independent risk factor for mortality and is associated with higher mortality rates, there are also studies[21] reporting a decrease in mortality rates and suggesting[30] no significant association between obesity and mortality. In our study, we found similar mortality rates and intensive care unit admission rates between genders. This may be attributed to the absence of a standardized national and international treatment algorithm for the COVID-19 pandemic for an extended period. Furthermore, obesity is frequently regarded as a comorbidity, prompting healthcare providers to adopt comprehensive treatment approaches in individuals with obesity.

Limitations

Our study has some limitations that need to be acknowledged. Firstly, our study focused solely on hospitalized patients, excluding individuals who were managed on an outpatient basis, those with milder cases of COVID-19, or those seen only in the emergency department, which is a hectic place due to patients' emergent nature being managed there[31]. Furthermore, the duration of data collection in our study was relatively short, which may have hindered our ability to observe long-term complications associated with VAI and COVID-19.

Conclusions

Our study, which is the first in the literature to investigate the relationship between VAI and COVID-19 clinics, demonstrates that elevated VAI values are linked to a greater severity of COVID-19 symptoms, particularly among males. These findings highlight the potential of VAI as a useful marker for assessing disease severity and risk stratification in COVID-19 patients. Clinicians should consider incorporating VAI measurements into their clinical evaluations to better manage and predict the outcomes of COVID-19 cases.

Conflict of Interest

The authors declare that they have no conflict of interests.

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Informed Consent

Informed consent was obtained from all individual participants included in the study.

Ethics Approval

The study was approved by the Institutional Ethics Committee of Samsun Training and Research Hospital (Date: 29/04/2021, Decision No.: GOKA/2021/10/6).

Availability of Data and Materials

The datasets of the current study are available upon reasonable request.

Authors' Contributions

All authors contributed to one or more of the following steps; the design of the study, data acquisition, or analysis and interpretation of data, drafting or revising the article and final approval of the manuscript to be published.

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