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The association between visceral adiposity index levels and the change of the glomerular filtration rate in patients with chronic kidney disease

Zelal Adibelli

Usak University, Faculty of Medicine, Department of Internal Medicine, Usak, Turkey

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Abstract

Obesity is an expanding health challenge due to its increasing prevalence across the world. Obesity is associated with chronic kidney disease (CKD) with the advancement of diabetes mellitus (DM) and hypertension (HT), causing CKD by affecting the kidneys directly. The visceral adiposity index (VAI) has recently been developed to assess the metabolic function of visceral adipose tissue (VAT). Previous studies demonstrated that the prevalence of VAI was associated with CKD. The present study aimed to investigate the association between the decline of estimated glomerular filtration rate (eGFR) and VAT. Followed in the Nephrology Department of Research and Training Hospital for one year, 129 patients aged between 18-80 years with stages 2-5 CKD and not on dialysis were enrolled into the study. Sixty-three (40.6%) patients were females, and the mean age was 66.8 years. The averages of decreased eGFR and VAI values were also found as 12.8±19.0 mL/min/1.73 m2 and 2.86±1.63, respectively. The values of VAI were not correlated with the decrease in eGFR. The VAI values (p=0.03) and eGFR decrease (p=0.04) were higher in those with DM. Developed to indicate the metabolic effect of VAT, VAI has shown no association with the one-year decrease of eGFR in those with CKD.

Keywords: Chronic kidney disease, diabetes mellitus, obesity, visceral adiposity

Introduction

As well as an expanding healthcare problem, obesity has risen in recent years worldwide, and the obesity prevalence was found to be 40.4% among women and 35% among men in the adult population in the United States (US) in 2013-2014 [1]. It is estimated that 38% of the adult population will be overweight, and 20% population will be obese around the world by 2030 [2]. However, the obesity prevalence was reported to be 33.2% in females and 18.2% in males in Turkey by Ural et al. [3]. Obesity gives rise to chronic kidney disease (CKD) by catalyzing the evolution of hypertension (HT) and diabetes mellitus (DM), which cause CKD, and affecting the kidneys by producing adiponectin, leptin and resistin, promoting inflammation, insulin resistance (IR), renin-angiotensin-aldosterone system activation and lipid metabolism disorder [4, 5]. Such metabolic changes result in an increased risk of CKD, a phenomenon known as obesity-related glomerulopathy (ORG). Previous studies have shown that a higher body mass index (BMI) was associated with the incidence and progression of CKD [6]. Although BMI is generally used to define obesity, such an entity is not sufficient to demonstrate the visceral fat, which is considered more metabolically active. Therefore, novel parameters have been developed to demonstrate visceral fat, such as waist circumference (WC) and waist to hip ratio (WHR). Even so, as even these parameters are not good enough to differentiate between subcutaneous and visceral fat, various methods have been developed to measure visceral adipose tissue (VAT), such as computer tomography (CT) and magnetic resonance imaging (MRI). However, such modalities are expensive procedures and cause patients to be exposed to ionizing radiation [7]. Thus, the visceral adiposity index (VAI) has recently been developed as an indicator of VAT and its function. VAI is used to determine the cardiometabolic risk before the metabolic syndrome develops [8]. As another advantage, VAI can easily be calculated from BMI, WC, blood high-density lipoprotein (HDL), and triglyceride (TG) levels. In previous studies, the association between CKD

***Corresponding Author:** Zelal Adibelli, Usak University, Faculty of Medicine, Department of Internal Medicine,Usak, Turkey
E-mail: zelalad21@gmail.com

prevalence and VAI has been investigated. In a cross-sectional epidemiologic study performed in China with 1.581 adults over 40 years of age, VAI was found to be highly correlated with the prevalence of CKD [9]. In another study carried out with 2.142 participants by Huang et al., an association was found between VAI and CKD in female patients, and similar results were found in another study conducted on rural populations in northern China [10, 11]. To the best of our knowledge, there are few studies evaluating the effects of VAI on the incidence of CKD. In the present study, we attempted to search for the association between the decline of estimated glomerular filtration rate (eGFR) and visceral adiposity assessed through the values of VAI.

Materials and Methods

The data in the study were collected from stage 2-5 CKD patients, not on dialysis between 18 and 80 years of age. The patients were followed in the Nephrology Department of Research and Training Hospital for at least one year between December 2017 and November 2018. The study was approved by the local ethics committee of the School of Medicine in Usak University (Approval number is 009). Of 218 stage 2-5 CKD patients, only 129 were seen to be eligible for the study criteria. As the exclusion criteria, those with missing data, older than 80 years of age, taking cholesterol- and lipid-lowering drugs, and steroids were ruled out of the study. The demographic data related to the patients' age, gender, and medical history, such as DM, HT, and medications were detected from the hospital electronic records. On physical examinations, as well as measuring blood pressure (BP) five minutes after the rest, the measurements of height, weight, and WC were also performed at the midway from the iliac crest and the lower rib margin through the midaxillary line while the patients were standing with each foot 25-30 cm apart from the other. The samples collected from the patients were transported to the laboratory and stored at -80°C until analysis. The levels of hemoglobin A1c (HbA1c) were measured using the high-performance liquid chromatography system (Variant II Turbo HbA1c analyzer, Bio-Rad Laboratories, Hercules, CA, USA). TG, HDL, uric acid, calcium, phosphorus, bicarbonate, urine protein, and creatinine levels were also analyzed with the spectrophotometric method using the Architect c8000 automated analyzer and original Abbott kits (Abbott Diagnostics Inc, Park City, IL, USA). Two milliliters of blood were added to ethylenediaminetetraacetic acid (EDTA) (1 mg/mL blood) and mixed thoroughly to perform a complete blood count by the Mindray BC 6800 device (Mindray Bio-Medical Electronics Co., Ltd, Shenzhen, China). Parathyroid hormone (PTH) was analyzed with the electrochemiluminescence method using the ADVIA Centaur analyzer (Siemens Healthcare Diagnostics, Munich, Germany). Serum creatinine levels were measured over a one-year interval. The equation of Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) was used to calculate eGFR. The stages of CKD were defined under the values of eGFR as stage 2 (eGFR=89-60 mL/min/1.73m^2), stage 3a (eGFR=45-59 mL/min/1.73m^2), stage 3b (eGFR=30-44 mL/min/1.73m^2), stage 4 (eGFR=15-29 mL/min/1.73m^2), and stage 5 (eGFR=<15 mL/min/1.73m^2). The change of eGFR values was calculated as the percentage of the change in eGFR within one year to baseline eGFR. VAI was also estimated by using the following formula: (WC/36.8+(1.89xBMI)) x (TG/0.81) x (1.52/HDL) for women, and (WC/39.68+(1.88xBMI)) x (TG/1.03) x (1.31/HDL) for men. To calculate BMI, patients' weights in kilograms were divided by the square of the height based on the formula of BMI=kg/m^2.

In analyzing the data, the Statistical Package for Social Sciences (SPSS) for Windows 22.0 program was used to perform the statistical analyses (SPSS Inc., Chicago, IL, USA). The descriptive statistics were applied to define the main characteristics of the patients. The Shapiro-Wilk and Kolmogorov-Smirnoff statistical tests were carried out to assess the normality of the data. All parameters, except for PTH levels, were found to be normally distributed. The correlation between the difference of eGFR, VAI values, and other parameters was tested with the Pearson correlation test. The difference between the patients with different CKD stages under the change of eGFR and VAI values was tested by the one-way ANOVA test. The independent samples t-test was utilized to investigate the difference between those with and without DM and HT in terms of VAI values and eGFR change. The partial correlation was used to investigate the correlation between the two variables, where the effect of other variables was kept constant for both variables. A p-value less than 0.05 was accepted to be significant.

Results

A total of 129 stage 2-5 CKD patients were included in the study. Sixty-six (59.4%) patients were males, and 63 (40.6%) were females. The mean age was 66.8 years, with a range between 35-80 years. The mean VAI levels and mean eGFR decline were found to be 2.86±1.63 and -12.8±19.0 mL/min/1.73m^2, respectively. Of 129 patients, while 86.7% had HT, 46.5% were found to have DM. Among CKD patients, while six and 28 had stages 2 and 3a CKD, 43, 35, and 17 patients were detected to have stage 3b, stage 4, and stage 5 CKD, respectively. The basic characteristics of the participants are shown in Table 1. Additionally, no correlation was determined between the decline in eGFR in one year and VAI values (Table 2), and no difference was also observed between the decline in eGFR and VAI values in different stages of CKD (Figure 1). In the study, other factors that may have had effects on eGFR decline and VAI values were also investigated, and it was seen that there was a correlation only between the VAI values and age. While another correlation was detected between eGFR decline, and the values of bicarbonate, calcium, hemoglobin, phosphorus, albumin, and urine protein/creatinine, no correlation was observed between eGFR decline and the values of age, BMI, HbA1c, PTH, and vitamin D (Table 3). Diabetic patients were seen to have a significant decrease in eGFR (p=0.04) and higher values of VAI (p=0.03), compared to those without DM (Figure 2). There was no significant difference between the hypertensive and normotensive patients in terms of VAI values (p=0.292) and eGFR change (p=0.193) (Figure 3). Moreover, no significant difference was also observed between eGFR change in one year among those receiving and not receiving angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) (p>0.05). Considering the effects of such variables as DM, HT, gender, age, use of ACE inhibitors or ARBs, HbA1c levels, and CKD stages, it was found out there was no significant correlation between the VAI values and eGFR change within one year (p>0.05).

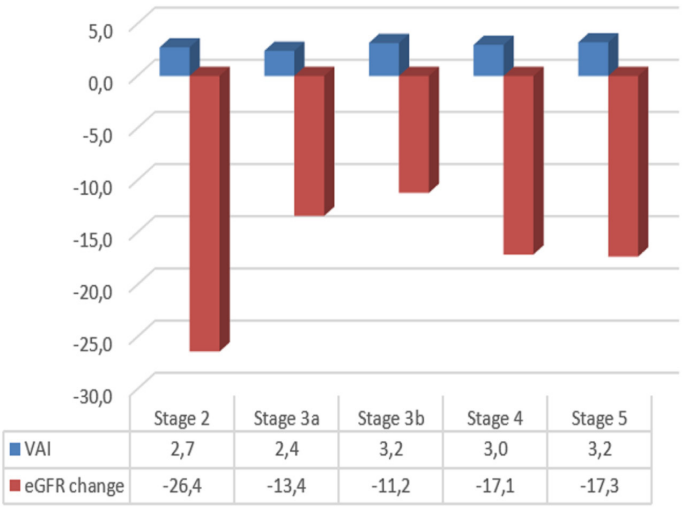

Figure 3. VAI values and eGFR change under CKD stages. (eGFR: Estimated glomerular filtration rate, VAI: Visceral adiposity index)

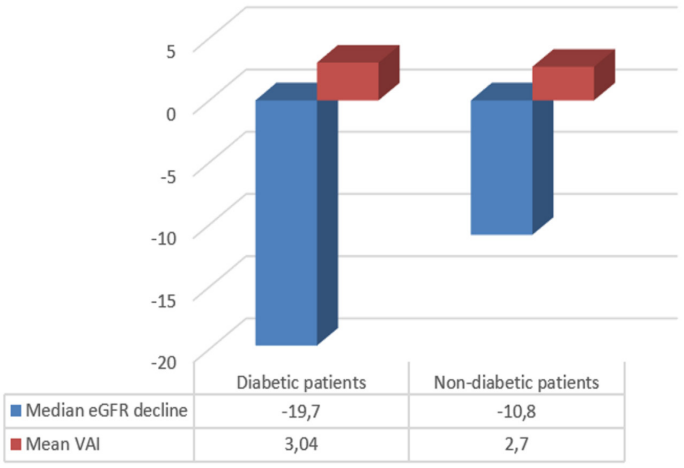

Figure 2. Difference between eGFR decline and VAI in diabetic and non-diabetic patients. (eGFR: Estimated glomerular filtration rate, VAI: Visceral adiposity index)

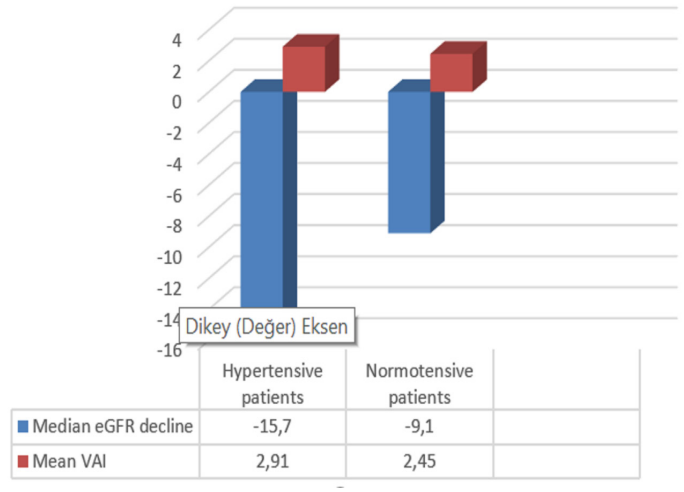

Figure 3. Difference between eGFR decline and VAI in hypertensive and normotensive patients. (eGFR: Estimated glomerular filtration rate, VAI: Visceral adiposity index)

Table 1. Basic characteristics of patients

Gender (M/F) (%)	66/63 (59.4/40.6)
Age (years)	66.8±9.9 (35-80)
Duration of CKD (months)	51.3±28.5
BMI (kg/m²)	30.1±5.5
WC (cm)	105±12.0
VAI	2.86±1.63
Systolic BP (mmHg)	136±18
Diastolic BP (mmHg)	76±13
Creatinine (mg/dL)	1.8±0.86
eGFR (CKD-EPI) (mL/min/1.73m²)	32.8±15.5
eGFR change in one year (%)	-12.8±19.0
Triglyceride (mg/dL)	157±78.6
HDL cholesterol (mg/dL)	45±12.8
HbA1c (%)	7.6±1.6
PCR	0.8± (2.2)
Hemoglobin (g/dL)	12.2±1.9
Uric acid (mg/dL)	7.2±1.7
PTH (pg/dL) (Median/min-max)	208 (12.5-1275.6)
Calcium (mg/dL)	9.1±0.5
Phosphorus (mg/dL)	3.7±0.8
Albumin (g/dL)	4.1±0.4
Vitamin D (ng/mL)	14.2±9.5

BMI: Body mass index, BP: Blood pressure, CKD: Chronic kidney disease, CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration, eGFR: Estimated glomerular filtration rate, HDL: High-density lipoprotein, HbA1c: Hemoglobin A1c, M/F: Male/Female, PCR: Protein/creatinine ratio, PTH: Parathyroid hormone, VAI: Visceral adiposity index, WC: Waist circumference

Table 2. Correlation between eGFR change and VAI values

	eGFR change in one year	P value
VAI	0.009	0.916

eGFR: Estimated glomerular filtration rate, VAI: Visceral adiposity index

Discussion

In the study, we searched whether the VAI values, indicating the metabolic activity of VAT and CKD progression (eGFR decline) in those with CKD, were correlated or not and also found no correlation between these two parameters, even when the effects of such variables as the presence of DM or HT, gender, age, use of ACE inhibitors or ARBs, HbA1c levels and CKD stages were controlled. In previous studies, although the association has been investigated and demonstrated between the prevalence of CKD and VAI, no study has investigated the relationship between CKD progression and VAI [9-11]. Furthermore, several studies have

Table 3. Correlations between other factors affecting eGFR change and VAI values

	eGFR change	P value	VAI	P value
Age (years)	-0.171	0.053	-0.290	0.001*
BMI	0.009	0.919	0.120	0.179
HbA1c	-0.116	0.414	0.135	0.339
Bicarbonate	0.298	0.001*	-0.105	0.254
Hemoglobin	0.344	0.000*	-0.167	0.061
Calcium	0.244	0.006*	-0.121	0.174
Phosphorus	-0.490	0.000*	0.077	0.405
PTH	-0.141	0.130	0.101	0.227
Albumin	0.338	0.000*	-0.013	0.888
Vitamin D	-0.091	0.318	-0.097	0.287
Urine PCR	-0.365	0.000*	0.068	0.461
Systolic BP	-0.070	0.434	0.106	0.231
Diastolic BP	-0.008	0.928	0.158	0.075

BP: Blood pressure, eGFR: Estimated glomerular filtration rate, HbA1c: Hemoglobin A1c, PCR: Protein/creatinine ratio, PTH: Parathyroid hormone, VAI: Visceral adiposity index

investigated the effects of BMI on the development of end-stage renal disease (ESRD) or progression of CKD and found that BMI is related to the enhanced risk for the development of ESRD in men [12]. In another study, BMI was reported to be an independent risk factor for the evolvement of ESRD without pre-existing DM or HT [13]. A study performed on patients with CKD also showed that BMI had a U-shaped relation with the disease progression and mortality, and those with BMI of < 25 kg/m^2 and ≥ 35 kg/m^2 had the worst outcomes [14]. Elevated WC, which is a better indicator for abdominal obesity, was stated to be associated with ESRD, but not with BMI [15]. The limited number of cases and a short follow-up period may have affected the results found in this study. Even so, we found that VAI values were negatively correlated with age, and eGFR decline showed that a positive correlation existed between the presence of DM and the levels of bicarbonate, hemoglobin, calcium, and albumin, but was negatively correlated with the protein/creatinine ratio and phosphorus levels. Such an entity may be because advanced CKD is associated with lower bicarbonate, hemoglobin, albumin, and calcium levels, and elevated phosphorus levels. As consistent with our findings, Zoppini et al. found that lower eGFR and albuminuria can predict the decrease of eGFR in one year for the diabetic population with normal kidney function [16]. Decreased plasma albumin was found to accelerate the loss of renal function in CKD patients with type 2 DM [17]. In observational studies, serum phosphorus was shown to be a major risk factor for the advancement of CKD [18, 19]. In another study, it was also demonstrated that uncontrolled HT is a potent risk factor leading to the advancement of CKD [20]. A study from Japan with 729 patients revealed that high systolic BP gives rise to the decline of eGFR [21]. Other studies showed that systolic BP is a major risk factor for the advancement of nephropathy, especially in diabetic and hypertensive patients [22-24]. In the present study, no correlation was found between eGFR change and BP, and this may have stemmed from the limited size of our patients or the short follow-up duration. In our study, HbA1c levels were observed not to be associated with eGFR decline although HbA1c was reported to be related to the enhancement of CKD in previous studies [21, 25]. In a previous study, intensive glucose control was reported to decrease the development of ESRD risk by 65%; however, no data were provided on preventing eGFR decline [26]. In our study, no significant difference was observed in eGFR change in one year between the patients receiving and not receiving ARBs and ACE inhibitors. Based on the literature, the use of ARBs and ACE inhibitors were found to be effective in decelerating the progression of kidney disease for patients with CKD [22, 27-29]. The purpose of the present study was to investigate the relationship between VAI used to validate the metabolic effects of VAT and the progression of CKD through eGFR change within one year. Although no significant relationship was found in the study, we consider that further studies with a longer follow-up duration and larger populations are needed to elucidate and understand the issue better.

Conflict of interests
The authors declare that they have no competing interests.

Financial Disclosure
All authors declare no financial support.

Ethical approval
The patients were followed in the Nephrology Department of Research and Training Hospital for at least one year between December 2017 and November 2018. The

study was approved by the local ethics committee of the School of Medicine in University (Approval number is 009).

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