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UROLITHIASIS

Visceral adiposity index in kidney stone patients who have undergone surgery

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Introduction The visceral adiposity index (VAI) is a gender-specific metabolic index that indirectly measures visceral adipose function and distribution using waist circumference, body mass index (BMI), and triglyceride and high-density lipoprotein (HDL) cholesterol values. To assess visceral fat in the diagnostic pathway of urinary stone patients, we investigated the relationship between the VAI and nephrolithiasis as well as the relationship between the VAI and stone and surgery-related parameters.

Material and methods Patients who underwent percutaneous nephrolithotomy and retrograde intrarenal surgery for kidney stones were included in the study. The control group comprised of healthy individuals who volunteered to take part in study and did not have urolithiasis as confirmed by abdominal computed tomography imaging. A total of 148 patients were divided into the nephrolithiasis (n = 103) and the control (n = 45) groups. Weight, height, BMI, waist circumference measurements, and VAI were among the metabolic parameters measured. Stone and surgical parameters were evaluated.

Results VAI (4.57 vs 2.76), waist circumference (92.1 vs 87.1), and BMI (28.31 vs 26.51) values were higher in the nephrolithiasis group(p = 0.02,p = 0.04, p <0.001,respectively). The VAI was statistically significant in the multivariate analysis for the presence of nephrolithiasis (p <0.001). The VAI negatively correlated with the stone Hounsfield unit (HU) and positively correlated with very-low-density lipoprotein (VLDL), blood creatinine, and calcium levels. The relationship between VAI and surgical parameters was not significant.

Conclusions A significant relationship was detected between nephrolithiasis and VAI, a new gender-specific metabolic index that distinguishes between subcutaneous and visceral adipose mass and demonstrates metabolic syndrome. No significant effect of this relationship on surgical parameters was demonstrated in the present study.

Key Words: body mass index ‹› nephrolithiasis ‹› stone surgery ‹› visceral adiposity index

INTRODUCTION

Urolithiasis is the third most common urological disease affecting the urinary system after urinary tract infections and prostatic pathologies; its prevalence varies between 2% and 20% worldwide. It is a multifactorial disease resulting from complex interactions between environmental and genetic factors [1, 2]. It has been shown to have a significant relationship with obesity and metabolic syndrome, which are common in countries with a high standard of living [3, 4, 5], where obesity gradually increases due to dietary factors and inactive lifestyles caused by technological development. The number of obese and overweight individuals is expected to double in the next ten years [6].

Many studies have used anthropometric indices such as body mass index (BMI), waist circumference

(WC), and waist-to-height ratio (WHtR) to identify obesity when linking obesity with urolithiasis. Similar assessments have been used in studies investigating urinary system stone diseases [4, 5, 6]. However, these indexes provide limited information on fat distribution and cannot distinguish between subcutaneous fat and visceral fat masses, which is important because it is known that visceral adipose tissue accumulation contributes to the development of metabolic disorders, unlike subcutaneous fat. In fact, there is no standard method of evaluating visceral fat in the diagnostic pathway of urinary stone patients who have undergone surgery or of estimating the effect of obesity on the results of kidney stone surgery.

The visceral adiposity index (VAI) is a gender-specific metabolic index that indirectly measures visceral adipose function and distribution using waist circumference, body mass index (BMI), and triglyceride and high-density lipoprotein (HDL) cholesterol values. VAI has been shown to be significantly correlated to all of the constituents of metabolic syndrome [7]. In previous studies, the relationship between VAI and many diseases such as diabetes mellitus (DM), hypertension (HT), coronary artery disease (CAD), and erectile dysfunction (ED) has been investigated [8, 9, 10].

For nephrolithiasis associated with metabolic syndrome [11], VAI may be a useful tool to better understand the underlying mechanism. This study evaluated the relationship between the VAI and nephrolithiasis and the VAI's effect on stone and related surgery parameters. To our knowledge, the relationship between VAI and nephrolithiasis has not been investigated previously, and this is the first report in this field.

MATERIAL AND METHODS

The study's primary objective was to analyze the difference in VAI in patients with nephrolithiasis and the control group. The secondary objective was to investigate the relationship between VAI and stone and surgical parameters. Prospectively, patients living in the same geographical region with similar nutrition characteristics who underwent percutaneous nephrolithotomy (PCNL) and retrograde intrarenal surgery (RIRS) for kidney stones in a university hospital urology department between January 2017 and December 2019 were included. Kidney stones were demonstrated by computed tomography in all patients.

The control group comprised of healthy individuals who volunteered to take part in study and did not have urolithiasis confirmed by abdominal computed tomography (CT) imaging. They were living in the same geographical region as the intervention group and had similar nutrition habits. All the participants in the study provided their informed consent.

Patients were excluded from the study if they were under 18 years of age, had any malignancy or any urinary system disease such as a cyst, tumor, anomaly, etc., other than stones shown through imaging methods, or who had kidney failure or used tobacco.

Demographic data such as age, sex, and comorbidity were recorded for the patients included in the study. Weight, height, BMI, waist circumference, and VAI were among the metabolic parameters measured. The following formulas were used:

Body mass index: Weight/Height^2 (kg/m^2)

Visceral adiposity index [7]

Men: Waist circumference $[39.68 + (1.88 \times \text{BMI})] \times \text{triglyceride}/1.03 \times 1.31/\text{HDL}$

Women: Waist circumference $[36.58 + (1.89 \times \text{BMI})] \times \text{triglyceride}/0.81 \times 1.52/\text{HDL}$

Previous stone history, kidney stone size, stone density (Hounsfield unit), and stone localization were also evaluated for the patients who would have surgery due to kidney stones. Details of the surgical method, operation time, hospitalization time, and complications were recorded after the surgery.

Stone analysis was conducted using Fourier-transform infrared spectroscopy (FTIR) for patients who had undergone surgery due to nephrolithiasis. Following the European Urology Association Urolithiasis Guidelines [12]. A 24-hour urine analysis was performed for specific metabolic evaluation of people at high risk for stone formation (familial stone formation, Brushite-containing stone, uric acid, cystine and infection stones, solitary kidney, stone recurrence, early onset of urolithiasis). In the urine analysis, creatinine, calcium oxalate, uric acid, cystine, and citrate levels were measured, and the relationship of these parameters with VAI was investigated.

As a result, one hundred and forty-eight patients were included in the study. These patients were separated into the nephrolithiasis group (n = 103) and the control group (n = 45). Demographic, metabolic, and laboratory parameters were compared among these two groups.

Blood sampling and measurement of laboratory parameters

Peripheral venous blood samples (5 mL) were taken into serum separator tubes (Vacuette, Greiner Bio-One, Kremsmuenster, Austria) in the morning between 9:00 am and 10:00 am after 8 h of fasting. Sera samples were set aside for 30 to 60 min to form clots prior to centrifugation at 1500 g for 10 min at room temperature.

Routine biochemical, hematological, and urine analysis results were obtained by reviewing the patients' records. Hematological analyses were performed using an XN-1000 Sysmex (Sysmex Corporation, Kobe, Japan) hematology analyzer. All biochemical parameters were analyzed using Abbott kits (Abbott Laboratories, Chicago, IL, USA), which are manufactured for use with an Architect c16000 Auto-Analyzer. Urine samples were analyzed using a Dirui FUS-200 (Dirui Industrial Co. Ltd., China) automatic urine sediment analyzer.

Statistical analysis

Statistical analysis was performed with SPSS v.23.0 statistical software (SPSS, Inc., Chicago, IL, USA). Continuous variables are presented as mean and standard deviations. Categorical variables are given as frequencies and percentages. The independent samples t-test or Mann-Whitney U test was used when comparing continuous variables among groups. Chi-square tests were used to compare the two groups in terms of categorical variables. The Pearson correlation coefficients of continuous variables were calculated. An ordinal logistic regression model was formed to find variables associated with group membership. The area under the curve (AUC), sensitivity, specificity, and cut-off values were calculated for BMI and VAI using receiver operating characteristic (ROC) regression analyses. A p value <0.05 was considered statistically significant.

RESULTS

In terms of demographic parameters, no difference was observed in age, sex, or comorbidity between the nephrolithiasis and control groups (all parameters $p > 0.05$).

The most common comorbidities in the nephrolithiasis group were coronary artery disease (12.6%), diabetes mellitus (12.6%), hypertension (8.7%) and chronic obstructive pulmonary disease (COPD) (1.94%); the most common comorbidities in the control group were coronary artery disease (17.7%), diabetes mellitus (15.5%), hypertension (11.1%), and COPD (2.2%).

Blood lipid profile, including triglycerides, LDL, and very-low-density lipoproteins (VLDL) ($p < 0.001$, $p = 0.009$, $p = 0.02$, respectively), and laboratory parameters including urine density, creatinine, and calcium values ($p = 0.01$, $p = 0.001$, $p = 0.048$, respectively) were significantly high in the nephrolithiasis group, while urine pH values were low in the nephrolithiasis group ($p < 0.001$).

VAI values (Figure 1), waist circumference, and BMI values were higher in the nephrolithiasis group ($p = 0.02$, $p = 0.04$, $p < 0.001$, respectively).

Details of the demographic, metabolic, and laboratory parameters of the nephrolithiasis and control groups are provided in Table 1.

In the multivariate analysis for the presence of nephrolithiasis; only VAI was statistically significant (1.52 OR [(95% CI 1.21–1.9)], $p < 0.001$) while the other metabolic parameters 'height, weight, waist circumference, body mass index' were not significant ($p = 0.44$, $p = 0.61$, $p = 0.45$, $p = 0.09$ respectively). Analysis results were similar for lipid parameters ($p > 0.05$ all lipid parameters). In addition, in the

Table 1. *Details on demographic, metabolic and laboratory parameters of Nephrolithiasis and Control groups*

Parameters	Nephrolithiasis Group n = 103	Control Group n = 45	P
Demographics			
Age (mean ±SD)	48.21 ±15.8	48.97 ±17.86	0.79
Sex (men) n (%)	72 (69.9)	34 (75.6)	0.48
Comorbidity n (%)	23 (22.3)	12 (26.7)	0.56
Metabolic parameters (mean ±SD)			
Height (cm)	167.3 ±7.9	169.8 ±9.5	0.12
Weight (kg)	79.1 ±14.5	76.4 ±12.2	0.28
Waist circumference (cm)	92.1 ±12.7	87.1 ±10.1	0.02
Body mass index (kg/m^2)	28.31 ±5.31	26.51 ±3.65	0.04
Visceral adiposity index	4.57 ±2.83	2.76 ±1.41	<0.001
Blood lipid profile (mean ±SD)			
Triglyceride (mg/dL)	145.06 ±70	96.96 ±36.45	<0.001
Cholesterol (mg/dL)	179.8 ±53.4	169.5 ±31.9	0.15
Low-density lipoprotein (LDL) (mg/dL)	114.9 ±35.1	100.8 ±25.4	0.009
Very-low-density lipoproteins (VLDL) (mg/dL)	28.7 ±13.26	23.27 ±13.22	0.02
High-density lipoprotein (HDL) (mg/dL)	43.92 ±9.6	46.96 ±10.5	0.08
Laboratory parameters (mean ±SD)			
Glucose	106.38 ±27.5	99.53 ±25.2	0.15
Creatinine (mg/dL)	0.95 ±0.29	0.88 ±0.15	0.11
Sodium (mmol/L)	140.2 ±2.32	138.7 ±2.35	0.001
Calcium (mg/dL)	9.28 ±0.48	9.11 ±0.55	0.048
Potassium (mmol/L)	4.32 ±0.6	4.19 ±0.53	0.21
Uric acid (mg/dL)	5.13 ±0.87	5.09 ±0.96	0.77
Hemoglobin (g/dL)	13.3 ±1.8	13.44 ±1.6	0.85
Urine pH	5.75 ±0.4	6.22 ±0.57	<0.001
Urine density	1015.5 ±6.2	1013 ±5.1	0.01

P – probability value; SD – standard deviation

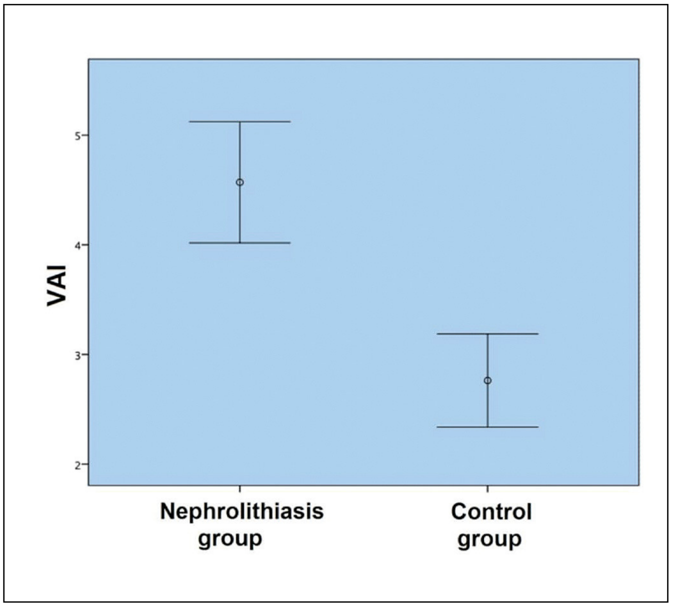

Figure 1. *VAI and groups (mean ±SD).*

VAI – visceral adiposity index; SD – standard deviation

ROC analysis for VAI and BMI, AUC: 0.708 vs 0.604, sensitivity: 69.9% vs 64.1%, specificity: 60% vs 57.8%, and cut-off values: 2.62 vs 26.37, (p <0.001, p <0.04 respectively) were calculated (Table 2, Figure 2).

Stone frequency was 1.79 ±1.19, stone size was 23.57 ±16.8 mm, and stone density was 842.4 ±345.9 Hounsfield unit (HU) in the nephrolithiasis group. Fifty-six (54.4%) patients had RIRS, and 47 (45.6%) patients had PCNL due to kidney stone. The mean stone size was higher in patients who underwent PCNL compare to those who underwent RIRS (19.4 ±13 vs 27.2 ±19.1, p = 0.017). No complications were observed in 92.6% of the patients. The mean hospitalization time was 2.64 days. Stone composition was available for 69.9% (n = 72) of the patients. Calcium oxalate (52%) and uric acid (10%) components were higher than other stone types. A 24-hour urine analysis was performed in 43 (41.7%) patients with a high risk for stone formation. Stone and surgical parameters are provided in Table 3.

Table 2. *Details of ROC analysis for BMI and VAI*

Parameters	Cutoff point	Sensitivity (%)	Specificity (%)	Area under ROC curve	SE	95% CI	p
VAI	2.62	69.9	60	0.708	0.04	0.602-0.795	<0.001
BMI	26.37	64.1	57.8	0.604	0.04	0.510-0.690	0.04

ROC – receiver operating characteristic curve; BMI – body mass index; VAI – visceral adiposity index; p – probability value; SE – standard error

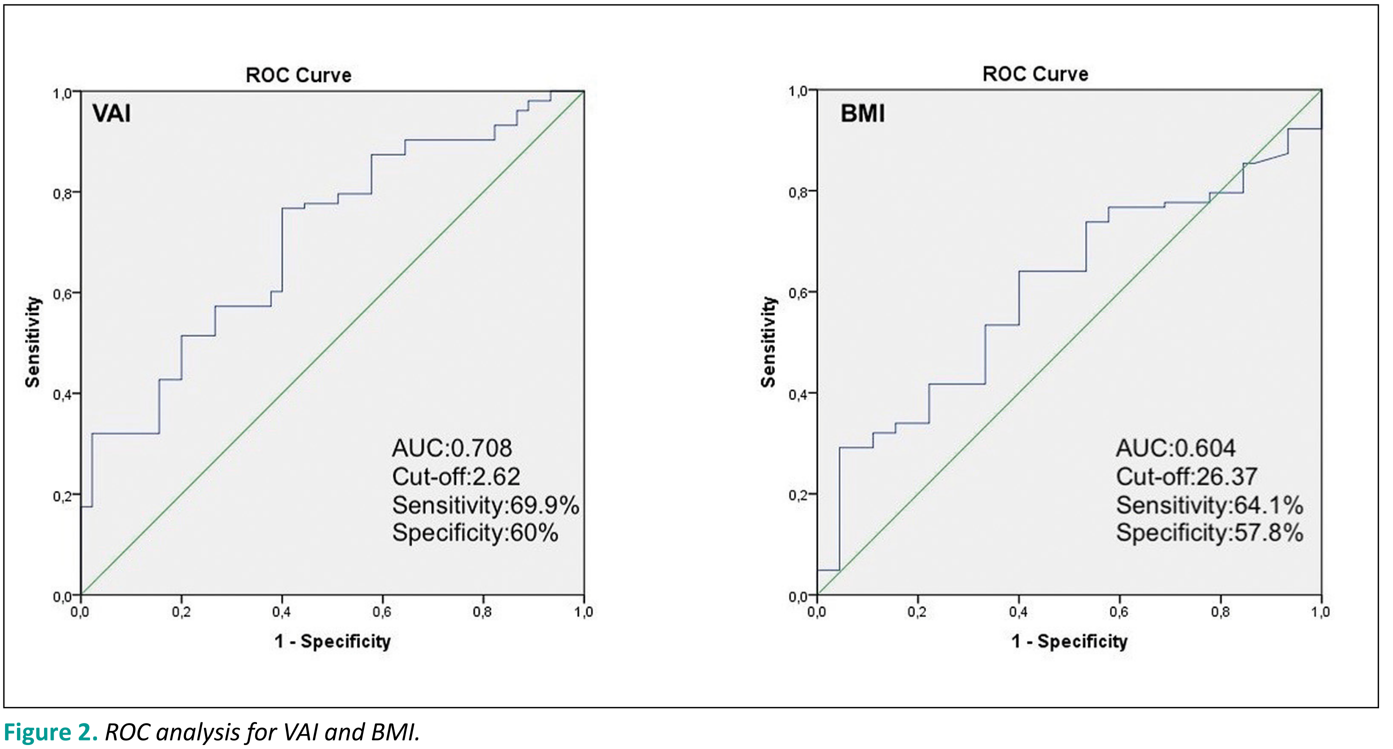

Figure 2. *ROC analysis for VAI and BMI.*

VAI – visceral adiposity index; ROC – receiver operating characteristic curve; AUC – area under the curve; BMI – body mass index

In the univariate analysis performed in the nephrolithiasis group, VAI had a negative correlation with stone HU (p = 0.047, r = -0.20) and a positive correlation with VLDL (p = 0.012, r = 0.25) creatinine (p = 0.007, r = 0.26), and calcium values (p = 0.018, r = 0.23) (Figure 3). A significant relationship was not found among VAI and stone size, stone frequency, surgical method, operation time, hospitalization time, and complications (p = 0.91, p = 0.54, p = 0.9, p = 0.64, p = 0.9, and p = 0.32, respectively). In addition, no significant correlation was found between the 24-hour urine analysis parameters and VAI (all parameters p >0.05).

DISCUSSION

The incidence and prevalence of nephrolithiasis is increasing globally according to data from the U.S., Europe, and Japan [13]. The prevalence of kidney stone increases with increasing obesity in both developed and developing countries. Kidney stone prevalence is seen more in obese (11.2%) and overweight individuals (9.1%) compared to individuals with normal weight (6.1%). Also, a significant relationship was detected between kidney stone formation and obesity in the multivariate analyses. In general, insulin resistance, acid-base balance anomalies, urine chemistry changes, and dietary factors are the basic mechanisms that increase the risk of nephrolithiasis [5, 13, 14, 15].

Obesity and metabolic syndrome have been shown to be important factors in stone formation. Yoshimura et al. detected BMI as an independent risk factor related to kidney stone incidence in a study that followed more than 4,000 male patients for 19 years [16]. In two other large prospective cohort studies that included both males and females, the prevalence of stone disease was directly related to weight and body mass index in both genders [3, 17]. Metabolic syndrome, including hyperlipidemia,

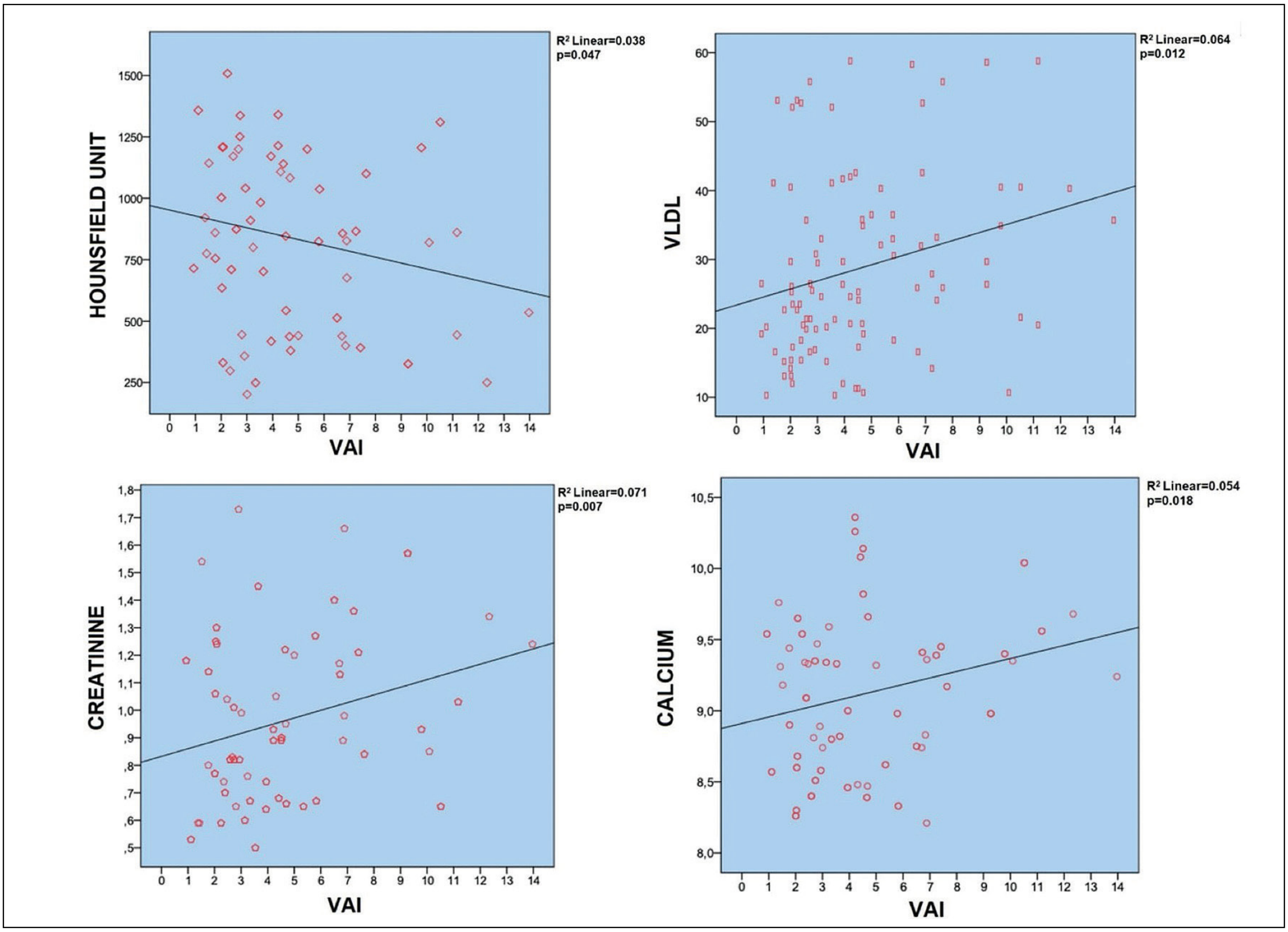

Figure 3. *VAI-related scatter plots.*

VAI – visceral adiposity index; VLDL – very-low-density lipoprotein; p – probability value

Table 3. *Parameters related to stone and surgery*

Stone parameters	
Stone size (mm) (mean ±SD)	23.57 ±16.8
Stone density (Hounsfield unit) (mean ±SD)	842.4 ±345.9
Stone side (right) (%)	66 (64.1)
Stone localization n (%)	
Upper calyx	10 (9.7)
Medium calyx	12 (11.7)
Lower calyx	18 (17.4)
Pelvis	35 (34)
Multiple localization	28 (27.2)
Average stone frequency (mean ±SD)	1.79 ±1.15
Stone analysis 69.9% (n = 72) n (%)	
Calcium-oxalate	52 (72.2)
Uric acid	10 (13.9)
Calcium-phosphate	5 (6.95)
Magnesium ammonium phosphate	4 (5.56)
Cystine	1 (1.39)
24-h urine analysis parameters (n = 43) (mmol/day) (mean ±SD)	
Urine creatinine	13 ±2.82
Urine calcium	5.71 ±1.89
Urine oxalate	0.53 ±0.51
Urine uric acid	3.5 ±2.2
Urine cystine	0.24 ±0.2
Urine citrate	2.46 ±1.11
Surgery related parameters	
Surgical method applied n(%)	
RIRS	56 (54.4)
PCNL	47 (45.6)
Operation time (min) (mean ±SD)	87.72 ±35.3
Hospitalization time (day) (mean ±SD)	2.64 ±2.93
Complications n (%) (Clavien-Dindo)	
None	92 (92.6)
1	8 (5.7)
2	2 (1.4)
3B	1 (0.7)

SD – standard deviation; n – sample size; RIRS – retrograde intrarenal surgery; PCNL – percutaneous nephrolithotomy

hypertriglyceridemia, hyperglycemia, and hypertension, together with abdominal obesity was also related to an increased kidney stone risk. West et al. found that the chance of patients diagnosed with metabolic syndrome reporting kidney stone was higher than that of healthy individuals. Kidney stone prevalence was reported as 3% in adult patients without metabolic syndrome parameters, as 7.5% in those with three parameters, and as 9.8% in those with five parameters. The risk of kidney stone was found to increase twofold in patients with four or more parameters of metabolic syndrome [18]. In our study, consistent with previous reports, waist circumference and triglyceride and dyslipidemia values, which are three sub-parameters of metabolic syndrome, were significantly higher in the nephrolithiasis group than in the control group. Based on these findings, it can be stated that metabolic syndrome is more common in nephrolithiasis patients.

Metabolic syndrome is also a potential precursor for type 2 DM and cardiovascular diseases. Thus, the detection of urolithiasis is more frequent in individuals with DM and cardiovascular disease [19, 20]. Although the factors responsible for the relationship between nephrolithiasis and cardiovascular disease have not yet been clarified, high total cholesterol, high triglycerides, and low high-density lipoprotein (HDL) have been found to be related to the changes that may cause a predisposition to kidney stone formation in urine chemistry [21]. In our study, a significant difference was not found in blood glucose, DM, HT, and CAD between the two groups, which is likely due to the limited number of patients in our study.

Waist circumference measurement and BMI are the parameters used to identify obesity and visceral adiposity. However, these measurements by themselves are not helpful in distinguishing between subcutaneous and visceral adipose mass [22, 23]. For these reasons, Amato et al. defined VAI, which is a new, gender-specific index that indirectly evaluates visceral adipose function and distribution using waist circumference and body mass index along with triglyceride, HDL, and cholesterol values [7]. As the VAI includes metabolic parameters in addition to physical parameters, its relationship with diabetes mellitus and cardiovascular diseases was found to be stronger than its relationship with waist circumference and BMI. This new index has also been found to be significantly correlated to all of the components of metabolic syndrome and cardiovascular diseases [7–10, 24].

It has been shown that calcium oxalate and uric acid excretion also increase as body size and BMI increase and that individuals with a high BMI also consume more animal protein and sodium and, thus, excrete more calcium. Urine PH values are more acidic in obese individuals compared to individuals with normal weight. Hypocitraturia and low urine volume (due to diet, secondary loss, and increase of body surface area) were detected in more than 50% of obese patients with nephrolithiasis. All of these metabolic, physiological, and dietary mechanisms contribute to the formation and growth of nephrolithiasis [4, 5, 15]. In our study, urine PH was found to be lower; urine density, blood calcium, and sodium values were found to be higher; and waist circumference, BMI, and VAI values, which are obesity-related parameters, were found to be significantly higher in the nephrolithiasis group. These parameters are in line with pathophysiological factors that have been shown to cause stone formation. However, interestingly, there was no significant relationship between

24-hour urine analysis parameters and VAI, which may be a result of the small number of patients analyzed (n = 43).

Calcium oxalate and uric acid are observed more commonly as stone components in obese patients [4]. This result is in line with our study, in which a significantly negative correlation was found between VAI and HU. We think that this may be related to stone formation being faster due to previously explained pathological causes. A significant relationship was also detected between VAI and calcium and creatinine. Attention should be paid to stone formation and kidney failure in these patients.

An ideal surgical method for nephrolithiasis in obese patients has not yet been determined. Stone size and localization are generally used to determine the surgical approach [14], and this was our approach, as well. Obesity may make surgeries requiring position change, especially PCNL, more complicated and increase the risk of complications. However, in our research, a significant relationship was not found between VAI and surgical method, operation time, hospitalization time, and complication.

CONCLUSIONS

The visceral adiposity index (VAI), a gender-specific metabolic index that indirectly identifies visceral adipose function and distribution, was significantly higher in patients with nephrolithiasis compared to the control group. The addition of triglyceride and HDL cholesterol values to the conventional assessment parameters (i.e., waist circumference, body mass index, and waist–height ratio) allowed for more comprehensive parameters to be considered. Our study demonstrated the relationship between VAI and nephrolithiasis for the first time, although no significant effect of this relationship on surgical parameters was demonstrated in the present study. Studies involving larger numbers of patients are needed to investigate the possible effects of visceral fat on surgical method and the type of surgery performed.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

ETHICS APPROVAL

All procedures performed in this study involving human participants were conducted in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Consent according to the Helsinki declaration was taken from Necmettin Erbakan University Meram Faculty of Medicine ethics committee before the study (No: 20202585).

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