ORIGINAL ARTICLE

ASSOCIATION BETWEEN URINARY STONE DISEASE AND PERIRENAL TISSUE THICKNESS

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ABSTRACT

Introduction: Urinary stone disease is an important morbidity. Metabolic factors such as obesity and diabetes mellitus have been associated with stone disease. Because obesity and increased body mass index, which are characterized by thickening of subcutaneous and visceral tissue, are associated with kidney stones, we investigated subcutaneous and perirenal tissue thickness and stone size in patients with kidney stone disease and compared them with healthy subjects.

Methods: A total of 209 subjects who had undergone a stone computerized tomography protocol due to urological symptoms between February2010 and March2012 were included.

Results: No significant differences in age or sex between patients and control subjects were observed. Similarly, no significant differences between the study and control groups were observed in terms of the thickness, area and density of subcutaneous tissue, density of visceral tissue, urinary pH, or neutrophil and lymphocyte counts. The visceral tissue area was significantly larger (p= 0.014) and the neutrophil/lymphocyte ratio was significantly elevated (p=0.021) in patients with kidney stones compared to those in controls. The perirenal tissue area of the kidney with a stone increased significantly compared to the opposite kidney without stones (p=0.021).

Conclusion: The results suggest that an increased surface area of perirenal visceral adipose tissue detected by imaging studies might be a risk factor for the development of kidney stones. However, prospective studies with a larger cohort are needed to translate our results to clinical practice.

Keywords: Kidney stone, perirenal tissue, visceral tissue, neutrophil/lymphocyte ratio

INTRODUCTION

Urinary stone disease is an important morbidity. About 10% of males and 5% of females suffer from symptomatic kidney stones during their life[1]. The annual cost of managing kidney stones is estimated to be ca. 2 billion USD[2]. Most kidney stones contain calcium, and calcium oxalate is the most common type of kidney stone[3]. Urinary oxalate excretion has been reported to be associated with body size [4]. Therefore, formation of calcium oxalate stones increases with increasing body size.

Metabolic factors—such as obesity and diabetes mellitus—have been associated with kidney stone disease[5,6]. Moreover, an increased body mass index (BMI) has been suggested to be related to kidney stones [7]Obesity has been associated with abdominal subcutaneous fat tissue [8].Both abdominal subcutaneous and visceral adipose tissue contribute to the metabolic complications of obesity [9-12].

Because obesity and an increased BMI, which are characterized by thickening of subcutaneous and visceral tissue, are associated with kidney stones, we investigated subcutaneous and perirenal tissue thickness and stone size in patients with kidney stone disease and compared them with healthy subjects.

METHODS

We included 209 subjects who had undergone a stone computerized tomography (CT) protocol due to urological symptoms between February 2010 and March 2012.

Exclusion Criteria: Exclusion criteria includedstones < 4mm in the longest diameter, history of abdominal surgery, acute and chronic renal failure, renal agenesis or hypoplasia, history of acute or chronic pyelonephritis, hydronephrosis, or umbilical hernia.

Imaging: The kidney stone CT examination was performed in the supine position without the use of intravenous enhancing contrast agent. The area from the superior limit of the kidneys to the basement of the

bladder was screened at 130 kV and 60 mAS with a 3-mm slice thickness.

Stone area measurements were performed on CT images using the longest diameter slice of the stone and by signing the circumference of the stone.

Attenuation values were defined as−30 to−190 and measured using the 'two-dimensional growing region of interest' technique. According to the pixel density of the selected point, similar densities in the same slice were signed and the density of a large area was calculated. The surface area and Hounsfield units (HU) were assessed simultaneously using this technique [13,14]. Perirenal adipose tissue measurements were performed using the hilus level slice (Figure 1).

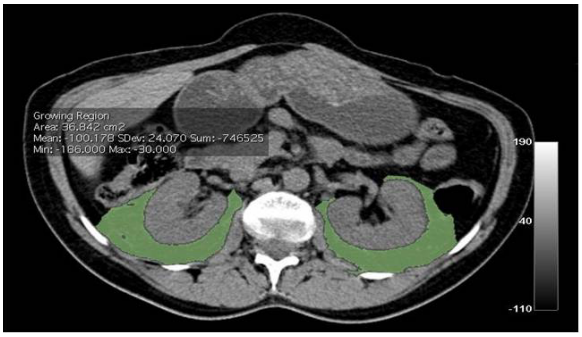

Figure 1: Perirenal adipose tissue measurement

The subcutaneous and visceral adipose tissue areas and HU measurements were performed using the umbliculusslice by the same technique.

All defined measurements were performed using the OsiriXDicom Viewer software ver. 3.6.

Statistical Analysis

Statistical analyses were conducted with IBM SPSS Statistics for Windows ver. 20.0 (IBM Corp., Armonk, NY, USA.). Continuous variables were tested for normality with the Kolmogorov–Smirnov test. Normally distributed data are presented as means ± standard deviations. The rates and proportions of discrete variables were calculated by the chi-square test. Medians and ranges were used for data not normally distributed. The independent sample t-test and Mann–Whitney U-test were used for parametric and nonparametric data, respectively. Perirenal tissue density and perirenal tissue thickness in patients with and without stones were compared by Wilcoxon's signed-rank test. A p-value <0.05 was considered to indicate significance.

RESULTS

A total of 209 subjects were enrolled in the study (147with kidney stones and 62 healthy volunteers). No significant differences were observed between patients and control subjects in terms of age or sex. Similarly, no significant differences were observed between subjects with and without kidney stones in terms of thickness, area and density of subcutaneous tissue, density of visceral tissue, urinary pH, or neutrophil and lymphocyte counts. Visceral tissue area was significantly larger (p= 0.014), and the neutrophil/lymphocyte ratio was significantly elevated (p=0.021) in patients with kidney stones compared to those in controls. The study group data are summarized in Table 1.

Table 1: Data of subjects with and without kidney stones

	Kidney Stone present	Kidney Stone absent	p value
	Mean ± Standard deviation		
Thickness of SC tissue	2.24 ± 0.84	2.29 ± 0.98	0.74
	Median (Min-Max)		
Area of SC tissue	195 (32-639)	213 (20-547)	0.83
Density of SC tissue	101 ([-107]-[110])	103 ([-109]-[110])	0.38
Area of visceral tissue	159 (9.3-384)	121 (11-266)	**0.014**
Density of visceral tissue	96 (-117-107)	93 (-121-106)	0.076
Urinary pH	5.5 (5-8.5)	5 (5-8.5)	0.097
Neutrophil count	4.8 (1.9-18.4)	4.1 (2.4-10.8)	0.073
Lymphocyte count	1.9 (0.8-4.3)	2.1 (0.5-4)	0.23
N/L ratio	2.5 (0.7-8.4)	1.9 (0.9-13)	**0.021**

Table 2: Data of subjects with kidney stones

	Kidney with stone	Counterside kidney without stone	p
Perirenal tissue area	17.2 (0.9-8.7)	16.6 (0.9-71.4)	**0.021**
Perirenal tissue density	91 (-112-114)	91 (-111-111)	0.27

We also compared the perirenal tissue area in patients with unilateral kidney stones to that of the kidney without stones. The perirenal tissue area of the kidney with stones was significantly compared greater than that of the kidney without stones (Table 2).

DISCUSSION

The main finding of our study was that kidney stones were associated with an increased area of visceral adipose tissue. In patients with unilateral kidney stones, the perirenal tissue area was increased compared to that of the opposite kidney.

Complications related to obesity are mainly associated with visceral fat depots[15]. Obesity provokes fat storage in the perirenal area. Because obesity is associated with perirenal fat deposition[16] and kidney stones[5,17-20], the increased perirenal tissue surface area in patients with urolithiasis is unsurprising.

Taylor et al. reported that the risk of kidney stone formation is increased in the presence of obesity [5]. Both subcutaneous and visceral adipose tissue areas are increased in patients with obesity. However, an increase in visceral adipose tissue poses a greater metabolic risk than an increase in subcutaneous fat[21,22]. Indeed, although the subcutaneous tissue measurements were similar, our patients with kidney stones had an increased visceral adipose tissue area compared to that in control subjects.

Why does visceral adipose tissue increase in subjects with kidney stones? Insulin-mediated glucose disposal is mainly determined by visceral adipose tissue[23]. The incidence of insulin resistance increases with increased visceral adipose tissue [24].Insulin resistance, which is characterized by increased serum insulin levels, is related to an increased risk of kidney stones [25].Our findings suggest that increased visceral adipose tissue is associated with an increased risk of urolithiasis.

Adipokines represent another possible explanation. The visceral adipose tissue-derived serine protease inhibitor (vaspin) level is elevated in patients with polycystic ovary syndrome, which is also associated with insulin resistance [26,27]. Increased visceral perirenal adipose tissue may cause an elevation in circulating caspin levels, which may promote insulin resistance and, as a consequence, kidney stone development.

Inflammation is likely responsible for stone formation in the pathogenesis of urolithiasis[28]. We shall speculate that either cell injury promotes development of kidney stones or the stones are responsible of the inflammation. Moreover, crystal deposits are associated with renal inflammation [29].The neutrophil/lymphocyte ratio has been proposed as an index of systemic inflammation[30]. Therefore, we compared the neutrophil/lymphocyte ratios of the study and control groups retrospectively and found a significantly higher ratio in the study group. Our results are in agreement with those in the literature, suggesting an association between inflammation and kidney stones.

Our study had two major limitations. First was the retrospective design. Second, we did not compare anthropometric (waist circumference and body mass index) measures of the study and control groups due to the retrospective nature of this work.

In conclusion, we suggest that increased surface area of perirenal visceral adipose tissue detected by imaging studies might be a risk factor for kidney stone development. These subjects should be evaluated and followed up for urolithiasis. However, prospective studies with a larger cohort are needed to translate our results to clinical practice.

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