

Urolithiasis

# Differences in Urinary Stone Composition according to Body Habitus

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**Purpose:** We analyzed differences in urinary stone composition according to body mass index (BMI).

**Materials and Methods:** Between January 2007 and December 2010, 505 ureteral or renal stones were collected from 505 patients who underwent surgical intervention. Data on patient age, gender, BMI, urinary pH, and stone composition were collected.

**Results:** The patients' mean age was 49.2 years (range, 20 to 83 years). Of the 505 patients, 196 (38.7%) had calcium oxalate (CO) stones, 172 (33.9%) had mixed calcium oxalate and calcium phosphate (COP) stones, 72 (14.2%) had calcium phosphate (CP) stones, 50 (9.8%) had uric acid (UA) stones, and 15 (2.9%) had struvite stones. We excluded struvite stones in the statistical analysis because of the small number of patients; a total of 490 patients were included in this study. In the multinomial logistic regression analysis, obesity was found to be associated with UA stones compared with COP stones (odds ratio [OR] 3.488; 95% confidence interval [CI] 1.732-7.025;  $p < 0.001$ ) and CP stones (OR 2.765; 95% CI 1.222-6.259;  $p = 0.015$ ). Similar results were observed for CO stones compared with COP stones (OR 2.682; 95% CI 1.727-4.164;  $p < 0.001$ ) and CP stones (OR 2.126; 95% CI 1.176-3.843;  $p < 0.013$ ).

**Conclusions:** Obesity was associated with UA and CO stones compared with the occurrence of COP and CP stones.

**Key Words:** Body mass index; Obesity; Urinary calculi

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## INTRODUCTION

The etiology of urinary stone disease is multifactorial and not completely well understood [1,2]. Obesity appears to play an important role in the etiology of some well-known diseases, such as diabetes, hypertension, coronary artery disease, thromboembolism, lower back pain, osteoarthritis, and depression [3]. In addition, studies performed in recent years have demonstrated that people who are overweight or obese might also be prone to increased urinary stone formation [4-8]. Obesity is associated with insulin resistance and compensatory hyperinsulinemia, metabolic derangements that may lead to overly acidic urine [8,9]. A persistently low urinary pH ( $\leq 5.5$ ) is a distinctive feature of idiopathic uric acid (UA) stones [10].

Impaired ability to excrete acid in low urinary pH could result in hypocitraturia, which is an important risk factor for calcium stones [11]. Also, calcium oxalate (CO) stones may develop by heterogeneous nucleation of CO by UA [12,13]. In addition to a lower urinary pH, recent studies have shown that obesity is associated with unique changes in serum and urinary chemistry such as increased urinary excretion of calcium, citrate, sulfate, phosphate, oxalate, UA, and cystine in stone formers [14-17].

Herein, we evaluated differences in urinary stone composition according to body habitus by use of body mass index (BMI).

**TABLE 1.** Characteristics of the study population by body habitus

Variables	Total	Nonobese	Obese	p-value
Patients, No. (%)	490 (100)	284 (58.0)	206 (42.0)	-
Mean age (yr)	49.1±13.9	48.8±14.5	49.5±13.1	0.583
Male, No. (%)	288	160 (56.3)	128 (62.1)	0.227
BMI (kg/m <sup>2</sup> )	24.69±3.49	22.38±1.95	27.88±2.49	<0.001
Urinary pH	6.20±0.90	6.39±0.88	6.04±0.83	<0.001

## MATERIALS AND METHODS

Between January 2007 and December 2010, we collected 505 urinary stones (ureteral or renal) from 505 adult patients who underwent surgical intervention (ureteroscopy, percutaneous nephrolithotomy, laparoscopic ureterolithotomy) at two hospitals located in the metropolitan area of South Korea. The composition of the collected stones was analyzed by spectroscopy. Each stone sample was washed and dried. A small portion (1 mg) of each stone sample was mixed with potassium bromide (200 mg KBr), which was powdered and then pressed into a small tablet. The tablet was then analyzed by spectroscopy. We classified the specimens as CO stones, mixed CO and calcium phosphate (COP) stones, or calcium phosphate (CP) stones according to the results of the analysis, which indicated the presence of calcium, oxalate, or phosphate regardless of mixed UA components. If the results revealed the presence of UA components only, or UA mixed with calcium components only, those stones were classified as UA stones.

The patients' data including age, gender, BMI, first urinary pH before surgical intervention, and urinary stone composition were recorded in a retrospective database. BMI was calculated by dividing the weight (kilograms) by the square of the height (meters). Individual BMI values were stratified into two categories (obese  $\geq$ , non-obese  $< 25 \text{ kg/m}^2$ ) developed for Asia-Oceanian populations [18]. Statistical analysis was performed by using SPSS ver. 14.0 (SPSS Inc., Chicago, IL, USA). A p-value was calculated by using the independent t-test for continuous variables and the Pearson chi-square test for categorical variables. Multinomial logistic regression was used to determine the associated factors for each urinary stone component. A p-value of less than 0.05 was considered statistically significant.

## RESULTS

The patients' mean age was 49.2 years (range, 20 to 83 years). Of the 505 patients, 196 (38.7%) had CO stones, 172 (33.9%) had COP stones, 72 (14.2%) had CP stones, 50 (9.8%) had UA stones, and 15 (2.9%) had struvite stones. Among the CO and COP stone formers, 20 (10.2%) and 4 (2.3%) patients had UA components in their specimens, respectively. Among 50 patients having UA stones, 34 (68%) had pure UA stones, whereas the remaining 16 (32%) pa-

**TABLE 2.** Univariate analysis between stone components and other clinical parameters

	Age ( $\geq 50$ years)	Gender (male)	Urinary pH ( $\leq 5.5$ )	Obesity
UA (%)	36 (72.0)	34 (68.0)	37 (74.0)	31 (62.0)
CO (%)	106 (54.1)	117 (59.7)	69 (35.2)	104 (53.1)
COP (%)	72 (41.9)	103 (59.9)	43 (25.0)	49 (28.5)
CP (%)	30 (41.7)	34 (47.2)	7 (9.7)	22 (30.6)
p-value	0.001	0.118	<0.001	<0.001

UA: uric acid, CO: calcium oxalate, COP: mixed calcium oxalate and calcium phosphate, CP: calcium phosphate stones

tients had mixed calcium components only besides UA.

We did not include struvite stones in the statistical analysis because of the small number of patients; a total of 490 patients were included in this study. The urinary pH of obese patients was significantly lower than that of non-obese patients ( $p < 0.001$ ) (Table 1). According to the univariate analysis, UA stones were significantly correlated with older age ( $\geq 50$  years), lower urinary pH ( $\leq 5.5$ ), and obesity. The stone composition differed significantly among the nonobese and obese groups. Obese patients tended to have a greater percentage of UA and CO stones but a lower percentage of COP and CP stones (Table 2).

Multinomial logistic regression analysis revealed obesity to be associated with UA stones compared with COP stones (odds ratio [OR] 3.488; 95% confidence interval [CI] 1.732-7.025;  $p < 0.001$ ) and CP stones (OR 2.765, 95% CI 1.222-6.259;  $p = 0.015$ ) (Table 3). Similar results were observed for CO stones compared with COP stones (OR 2.682; 95% CI 1.727-4.164;  $p < 0.001$ ) and CP stones (OR 2.126; 95% CI 1.176-3.843;  $p < 0.013$ ). Lower urinary pH ( $\leq 5.5$ ) was associated with UA stones compared with COP, CP, and even CO stones (OR 4.040; 95% CI 2.044-7.985;  $p < 0.001$ ). Increased age was associated with UA stones compared with all other types of urinary stones (Table 3).

## DISCUSSION

The incidence of urinary stones has markedly increased during the past several decades, and studies have demonstrated that inappropriate dietary habits and the increasing prevalence of overweight people may be important in the etiology of stone formation [4-8]. Urinary stones can have different components such as CO, CP, UA, struvite, and a mixture of these. An association between the different urinary stone component types and obesity has not previously been well documented.

Recent studies have revealed that obesity is associated with change in the chemical components of serum and urine such as citrate, phosphate, oxalate, and UA. Above all, obesity are associated with acidic urine. In this study, the mean urinary pH of obese patients (6.04) was significantly lower than that of nonobese patients (6.39;  $p < 0.001$ ). Although the exact mechanism is unclear, a possi-

**TABLE 3.** Multinomial logistic regression analysis between components of urinary stones and various clinical parameters

		Age ( $\geq 50$ years)	Gender (male)	Urinary pH ( $\leq 5.5$ )	Obesity
UA/CP	$\beta$	1.759	0.945	2.931	1.017
	Exp (B)	5.805	2.574	18.750	2.765
	95% CI	2.454-13.732	1.108-5.980	6.823-51.528	1.222-6.259
	p-value	<0.001	0.028	<0.001	0.015
UA/COP	$\beta$	1.568	0.456	1.823	1.249
	Exp (B)	4.795	1.578	6.190	3.488
	95% CI	2.257-10.187	0.749-3.324	3.001-12.768	1.732-7.025
	p-value	<0.001	0.230	<0.001	<0.001
UA/CO	$\beta$	1.057	0.438	1.396	0.263
	Exp (B)	2.877	1.550	4.040	1.301
	95% CI	1.395-5.934	0.761-3.156	2.044-7.985	0.669-2.531
	p-value	0.004	0.227	<0.001	0.439
CO/CP	$\beta$	0.702	0.507	1.535	0.754
	Exp (B)	2.017	1.660	4.641	2.126
	95% CI	1.120-3.633	0.925-2.982	1.989-10.827	1.176-3.843
	p-value	0.019	0.090	<0.001	0.013
CO/COP	$\beta$	0.511	0.018	0.427	0.986
	Exp (B)	1.666	1.018	1.532	2.682
	95% CI	1.073-2.587	0.649-1.595	0.955-2.459	1.727-4.164
	p-value	0.023	0.938	0.077	<0.001
COP/CP	$\beta$	0.191	0.489	1.108	-0.232
	Exp (B)	1.211	1.631	3.029	0.793
	95% CI	0.675-2.170	0.915-2.908	1.280-7.167	0.429-1.464
	p-value	0.521	0.097	0.012	0.458

UA/CP: uric acid stones compared with calcium phosphate stones, UA/COP: uric acid stones compared with calcium oxalate and calcium phosphate stones

ble explanation for the decline in urinary pH with obesity is insulin resistance, which decreases renal ammonia excretion and impairs hydrogen ion buffering. Low insulin bioactivity (due to insulin resistance from obesity) in the renal proximal tubule can theoretically lead to defective ammonium production or excretion, thus affecting urinary pH [20]. A low urinary pH ( $\leq 5.5$ ) is a distinctive feature of UA stones [10]. The low urinary pH characteristic of idiopathic UA stone formers was shown by Sakhaee and Maalouf to be associated with decreased ammonium excretion, which by itself may be a renal manifestation of insulin resistance [21]. Confirming this hypothesis, our data provide evidence of the significant influence of increasing BMI on the risk of forming UA stones compared with COP and CP stones according to the multinomial logistic regression analysis. The proportion of UA stones was over two times higher in obese patients than in lean patients. In addition, older age ( $\geq 50$  years) was found to be another factor significantly associated with UA stones. Because decreased ammonium excretion resulting in a lower urinary pH is frequently seen in the elderly, age-associated defective urinary acidification may be the major contributing factor for older subjects [22,23]. The prevalence of insulin resistance also increases with age [24].

This study also revealed that a higher BMI was significantly associated with CO stone formation compared with COP and CP stones. The common hypothesis was that

obese patients, due to high food intake, may have higher urinary excretion of lithogenic solutes, especially oxalate, calcium, and UA. Increased urinary UA excretion is not only associated with UA stone formation, but also poses a risk factor for CO stone formation because CO stones may develop by the salting-out effect in a hyperuricosuria environment [25,26]. A decrease in urine pH leads to decreased production of CP crystals, which results in a relative increase in the formation of CO stones [27]. Our analysis revealed a correlation between the prevalence of CO stones and lower urinary pH compared with CP (OR 4.641; 95% CI 1.989-10.827;  $p < 0.001$ ).

The current study has several limitations. First, our sample population included only patients who underwent surgical intervention, which does not reflect the vast majority of patients with urinary stone disease. Second, the patients' serum and urine biochemical profiles were not investigated. Also, urinary pH had a diurnal variation. Urine collected in the morning had a significantly lower pH than urine collected in the day or evening [28]. We used a single urine sample collected at a variable time, which could have distorted the results. Third, the International Association for the Study of Obesity proposed the criterion for obesity as a BMI above  $30 \text{ kg/m}^2$ , which was based on Caucasian data [29]. In contrast, for people from Asia-Oceania, where the main energy intake comes from carbohydrates, obesity is defined as a BMI above  $25 \text{ kg/m}^2$  [18].

This disparity between the cutoff points is quite large; therefore, we believe our conclusion may not be applicable to other ethnic populations. If we adopted the Western criterion for obesity in this study, only 7.1% (35/490) of the participants would have been classified as obese, compared with 42.0% according to the Asian criterion.

## CONCLUSIONS

This study revealed obesity to be associated with UA and CO stones compared with COP and CP stones. This finding suggests that clinicians should encourage urinary stone patients to reduce their weight, especially those with history of CO and UA stones.

## Conflicts of Interest

The authors have nothing to disclose.

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