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Relationship between Patient's Demographics and Stone Composition in Men and Women

Mohamed Omar[1], Manoj Monga[2] and Juan C Calle[3]*

[1]Research fellow, Cleveland Clinic, Cleveland, USA
[2]Professor of Surgery/Urology, Stevan Streem Center of Endourology & Stone Disease, Cleveland Clinic, USA
[3]Departments of Urology & Nephrology, Cleveland Clinic Foundation, Cleveland, USA

Abstract

Purpose: To detect the differences in age, weight and height between three major stone groups.

Materials and Methods: We retrospectively reviewed all patients with a diagnosis of nephrolithiasis in a large healthcare network from January 2000 to July 2014, for whom information on stone composition, age, sex, weight and height was available. Patients less than 18 years were excluded. Patients were characterized by gender and the major component of their stone analysis. We used Wilcoxon rank-sum test for continuous variables to detect the significant differences and multiple logistic regression analysis to evaluate the relative risk between stone groups.

Results: 14,961 adult patients were identified. The Distribution of pure (≥ 90%) calcium oxalate, phosphate and uric acid stones in men, was (71%), (7%) and (22%) while in women it was (65%), (19%) and (16%) respectively. Males with calcium oxalate stones were taller than those with calcium phosphate by 2 cm (p=0.0006). Women with calcium phosphate stones were younger than those with calcium oxalate stones by 5 years (p=0.0001).

Conclusions: Calcium phosphate stone composition is associated with a shorter stature in men and younger age in women in relation to those with calcium oxalate stones.

Keywords: Calcium oxalate; Calcium phosphate; Height; PTH

Background

Nephrolithiasis poses a significant health problem in the United States and worldwide, thus an understanding of the epidemiology, particularly the interactions among different risk factors may lead to approaches that reduce the risk of stone formation [1]. Stone disease is common with a lifetime risk of stone formation in the US of 8.4% (95% CI, 7.7–9.0). Men are more likely to report a history of stone disease than women [2].

Prevalence of stone disease varies by geographic location within the US. A study of over 1 million individuals found a north-south and west-east gradient such that the highest prevalence of stone disease occurred in the Southeastern US [3]. As with prevalence, the incidence rates are highest in white males.

Among obese males the prevalence of stone disease was 13.0% (95% CI, 11.0–15.1), and among obese females the prevalence was 9.6% (95% CI, 8.3–10.8). Although a larger body size was shown to be associated with an increased prevalence and incidence of kidney stone disease in both genders [4]; and was confirmed to be associated with uric acid stones, and not calcium containing stones [5], studies have not disclosed a relationship between body height and the type of stones.

Methods

We retrospectively reviewed all patients with a diagnosis of nephrolithiasis in a large healthcare network from January 2000 to July 2014, for whom information on stone composition, age, sex, weight and height was available. All weight and height measurement were taken by the same standard equipment Detecto™. Body mass index (BMI) was calculated by dividing the weight (in kg) by the squared height (in meters). We excluded patient less than 18 years old at time of stone analysis.

Patients were characterized by gender and the major component of their stone analysis. Major stones composition was defined as ≥90% of stone content, with no distinction between calcium oxalate (CaOx) monohydrate and CaOx dihydrate, or calcium phosphate (CaP) subtypes; calcium apatite and brushite. Those stones with <90% of one composition were classified as mixed stones.

Data was presented as a mean, standard deviation and number of patients for every different group. The relationship between gender, age, serum parathyroid hormone (PTH), height, weight and BMI and the three major stone groups (calcium oxalate, calcium phosphate and uric acid) was then evaluated.

For the calcium oxalate, calcium phosphate and uric acid groups, a statistical analysis was performed using Wilcoxon rank-sum test for continuous variables and multiple logistic regression analysis was used to evaluate the relative risk, estimated by the odds ratio of age, height and weight on the occurrence of the various types of stones in both genders.

Results

A total of 14,961 adult patients were retrospectively identified who had a stone composition, sex, body weight and height available. The distribution of main stone component ≥90% was the determinant for grouping (calcium oxalate, calcium phosphate, uric acid, struvite, amorphous urate, cystine and mixed stones) are presented (Table1).

***Corresponding author:** Juan C Calle, Co-Director Kidney Stones Clinic, Glickman Urology and Kidney Institute, Department of Nephrology and Hypertension, Cleveland Clinic, 9500 Euclid Avenue, Q7-153, Cleveland, OH 44195, USA, Tel: 216 318 7105; E-mail: callej@ccf.org

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The Distribution of pure (≥90%) calcium oxalate, phosphate and uric acid stones in men, was (71%), (7%) and (22 %) while in women it was (65 %), (19 %) and (16 %) respectively.

The relationship between gender, age, serum parathyroid hormone (PTH), height, weight and BMI and the three major stone groups (calcium oxalate, calcium phosphate and uric acid) was performed using Wilcoxon rank-sum test for continuous variables and multiple logistic regression analysis was used to evaluate the relative risk (Table 2 and Figure 1).

Male patients with calcium oxalate stone are 2 cm taller than males with calcium phosphate stone and females with calcium oxalate stones are 5 years older than females with calcium phosphate stones.

Serum PTH levels were available for 872 male patients. No significant difference was found in serum PTH between calcium oxalate (n=796, 48 ± 28.8) and calcium phosphate (n=76, 43.6 ± 27.3) stone formers, (P=0.0633). Serum PTH levels were available for 611 female patients. No significant difference was found in serum PTH between calcium oxalate (n=458, 52 ± 36.2) and calcium phosphate (n=153, 49.7 ± 37.5) stone formers, (P=0.2151).

Discussion

Nephrolithiasis is considered a recurrent, painful disease for which prevention may be cost-effective for the national healthcare system. Identification of stone composition is a fundamental step in the metabolic evaluation of kidney stones and subsequent management of the disease. Delineating predisposing factors to certain stone compositions can open avenues for further investigation into the pathophysiology of the disease.

In this study, we identify a link between shorter stature and calcium phosphate stones, suggesting a potential relationship between bone health and stone disease.

Melton et al. showed evidence that fracture risk is increased among patients with kidney stones [6]. This increased risk was confined to vertebral fractures but the authors did not define the pathophysiology associated with this observation.

In our study the difference between the mean height of the patient in the CaOx and CaP groups could not be linked to a difference in PTH level (P= 0.0633).

	Number of Patients		Height /Cm (mean)		Weight/Kg (mean)		BMI (mean)		Age (mean)	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Ca Ox	3749	1888	178 ± 7.6	162.6 ± 7.2	93.5 ± 23.5	78.5 ± 22.5	29.4 ± 6.9	29.7 ± 9.6	55 ± 14	50 ± 15
Ca P	353	541	176 ± 10.6	162.2 ± 8.3	90.9 ± 22.7	77.6 ± 22.3	29.5 ± 9.3	30.2 ± 25.3	54.5 ± 16	45 ± 16
Uric Acid	1207	445	177.8 ± 7.9	162.1 ± 6.8	101.3 ± 26.6	96.1 ± 27.9	31.9 ± 7.6	36.5 ± 9.9	62 ± 13	60 ± 13
Mixed	3727	2843	177.4 ± 7.7	162 ± 7.8	93.5 ± 27.6	78.7 ± 23.3	29.6 ± 8.3	30.1 ± 14.5	55 ± 14	49.5 ± 16
Cystine	47	41	173.6 ± 6.5	163.2 ± 7	94.7 ± 19.6	87.7 ± 24.6	31.4 ± 6.6	32.6 ± 7.8	43.5 ± 14	39 ± 11
Struvite	1	0	175.2	-	73	-	23.7	-	69	-
Abnormal	41	51	174.6 ± 6.3	161.3 ± 5.4	85 ± 18.2	73.3 ± 17.5	27.8 ± 5.8	28.1 ± 6.4	59 ± 12	52 ± 17
Amorphous urate	17	10	179.6 ± 7.2	161 ± 6.2	99 ± 20	75.4 ± 32.1	30.7 ± 6.2	29.3 ± 13	57.5 ± 16	51 ± 12

Table1: Mean Height, Weight, BMI and age in different Stone Groups

Gender	Stone Composition	Height		Weight		BMI	Age	
		Univariate	Multivariate	Univariate	Multivariate	Univariate	Univariate	Multivariate
Male	CAOX VS. CAPH	0.0006	0.0007	0.0048	0.4721	0.1493	0.8169	0.6952
	UA VS. CAPH	0.0026	0.9404	0.0001	<.0001	0.0001	0.0001	<.0001
	UA VS. CAOX	0.7813	<.0001	0.0001	<.0001	0.0001	0.0001	<.0001
Female	CAOX VS. CAPH	0.352	0.1382	0.2384	0.9744	0.43	0.0001	<.0001
	UA VS. CAPH	0.4798	0.0644	0.0001	<.0001	0.0001	0.0001	<.0001
	UA VS. CAOX	0.0878	0.0002	0.0001	<.0001	0.0001	0.0001	<.0001

Table 2: Comparison between Major 3 Groups in Males and Females

In another study by Gault et al. [7], 35% of patients with idiopathic calcium phosphate stone formers had an incomplete form of distal renal tubular acidosis (idRTA). Patients with (idRTA) have a persistently high urine pH, but are able to maintain net acid excretion under basal conditions. Thus, idRTA does not manifest in overt systemic acidosis, but may cause recurrent positive acid loads in periods of increased protein intake or catabolic stress triggering alkali release from the bone and thus leading to greater bone resorption [8,9].

Sharma et al. [10] demonstrated in a cross-sectional study of children evaluated for idRTA that incomplete dRTA affects children height with significant short stature prevalence more than with those without dRTA.

In another study by Osther et al. biochemical markers of bone formation (serum osteocalcin) and bone resorption (urinary hydroxyproline) were significantly increased in idRTA compared with normal urinary acidifier and normal control (P<0.0l), indicating increased bone turnover in stone formers with idRTA [11].

Our study showed that male patients with calcium phosphate stones are 2 cm shorter than those with calcium oxalate. Other studies have linked calcium phosphate stones and a shorter stature to the higher incidence of idRTA, in both children [10] and adults [8,9].

Though the incidence of idRTA is higher in women, it is possible that they are protected from bone resorption by estrogen activity [12].

Our study also demonstrated that women with calcium phosphate stones are younger than those with calcium oxalate stones.

In a study by Kohri et al. the incidence of urinary stones was similar among men of three different generations (<29, 29-60, >60years), although that of uric acid stones increased with patient age. In women, however, there was a remarkable difference between the three

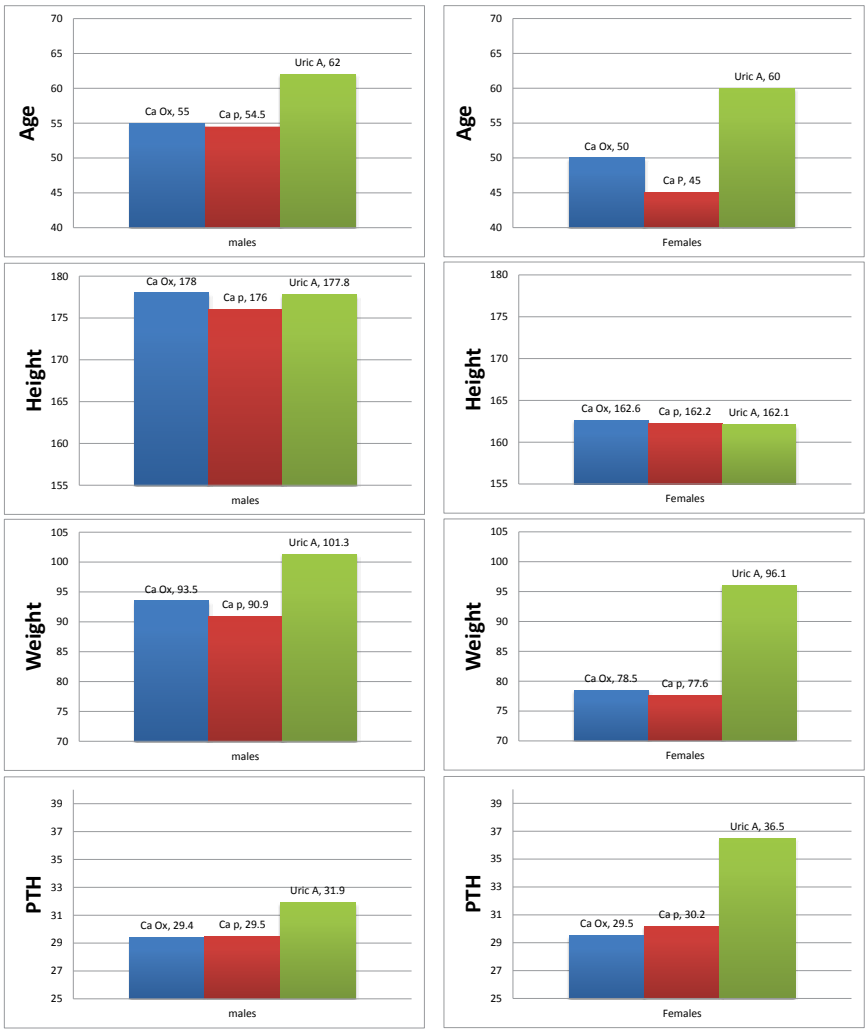

Figure 1: Differences in Age, Height, Weight and PTH between the major 3 stone groups.

generation groups. The incidence of calcium oxalate was high in both the young and old generations, while that of calcium phosphate was highest in the middle-aged and lowest in the old [13].

Kohri et al. reported that middle-aged women had milder metabolic acidosis and alkaline urine, while the elderly had a similar normal acid-base balance as men [14].

Progesterone may induce metabolic acidosis or respiratory alkalosis. It seems that metabolic acidosis or respiratory alkalosis and alkaline urine induced by progesterone facilitate calcium phosphate stone formation while suppressing calcium oxalate stone formation.

Our observations of a relationship between uric acid stones and age, weight and BMI are not new. Obesity has been linked with an increased predisposition to uric acid and calcium oxalate stones [15].

Several epidemiological studies confirmed the relation between the body size and nephrolithiasis. Based on two large cohorts in the US (the Nurse's Health Study I, or NHS I, and the Health Professionals Follow-up Study, or HPFS), Curhan et al. [16] found the prevalence of stone history and the incidence of stone episodes to be directly associated with BMI, the magnitude of the association being greater among women.

Subsequently, Michel et al. [17] concluded that obesity is associated with a high proportion of uric acid stones in patients less than 60 years of age, whereas beyond this limit, advancing age is the main risk factor.

The pathophysiologic mechanism(s) accounting for this increased acid excretion appears to be related to obesity and/or insulin resistance. Obesity itself is associated with low urine pH in patients with nephrolithiasis [18].

Limitations of our study include its retrospective nature, single institutional evaluation, small proportion of patients having PTH evaluations, and 24 hour urine results; (urinary calcium, pH, citrate, oxalare etc.); were not available for all patients.

Conclusion

In conclusion, while it's well known that uric acid patients are heavier and older than calcium oxalate and calcium phosphate patients, our study identifies demographic differences between CaP and CaOx stone formers – men with CaP stones are shorter and women are younger. These observations open the door to further inquiry as to the

pathophysiology of CaP stone formation.

Conflict of Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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