

The Impact of Obesity on Urine Composition and Nephrolithiasis Management

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Abstract

Background and Purpose: Several studies have reported that obese patients have a higher risk of nephrolithiasis. The purpose of this study is to investigate the effect of overweight (OW) and obesity on stone composition, type of treatment, and urine composition.

Methods: With Institutional Review Board approval, charts of adult patients who attended our dedicated stone clinic over a 5-year period starting January 2006 were reviewed. Patients were categorized into normal (body mass index 18.5–24.9), OW (25–29.9), and obese (≥ 30). We excluded those who did not have at least one 24-hour urine analysis.

Results: OW and obese patients were more likely to have previous stones, more chance to have uric acid stones, and to be treated with shockwave lithotripsy in the community, and with ureteroscopy or percutaneous nephrolithotripsy in our center. They needed more thiazide diuretics, allopurinol, and dietitian counseling. They had statistically significant ($P < 0.05$) higher urine calcium, citrate, supersaturation calcium phosphate, uric acid, supersaturation uric acid, sodium, potassium, magnesium, phosphorus, chloride, sulfate, urine urea nitrogen, protein catabolic rate, and creatinine compared with those with normal weight.

Conclusion: OW and obese patients have different stone composition with increased excretion of stone promoters in the urine. Stone prevention measures should be introduced during metabolic syndrome evaluation.

Introduction

OBESITY IS CONSIDERED an important health problem in many countries. In the United States, there has been a significant increase in the rate of overweight (OW) and obesity during the past 20 years.^{1,2} In 2009 to 2010, 35.7% of US adults were obese (OB).³ The prevalence of nephrolithiasis has also been on the increase.⁴ Several studies reported that OB patients have a higher risk of nephrolithiasis.^{5–7} This study looks at the effect of OW and obesity on stone composition, type of treatment, metabolic evaluation, and urinary excretion of stone formation promoters and inhibitors, including dietary factors.

Methods

The study was approved by the Institutional Review Board. Charts of patients who attended our dedicated stone clinic over a 5-year period starting January 2006 were reviewed. Children (< 18 years) were excluded. Also excluded were those who did not have at least one 24-hour urine analysis during that period. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. BMI was categorized using the World Health Organization

criteria into: underweight (BMI < 18.5), normal (N) with BMI 18.5–24.9, OW (BMI 25–29.9) and OB (BMI 30 and above). Underweight patients were excluded from the analysis.

Only the first urine analysis data were included to get more representative information before any modification of patients' diet or introduction of stone preventive measures. All urine samples were analyzed through the Litholink laboratory (Litholink Corporation, Chicago, IL) to minimize discrepancy in reporting or testing methodology.

Results

Using the above criteria, 162 men and 163 women were included. The BMI groups' characteristics and their stone history are outlined in Table 1. There was a high proportion of OW and OB patients in our study group; 44.8% of women and 37.7% of men were OB. Overall, 41.2% of stone formers were OB. OB men tended to be younger than their normal weight counterparts whereas OB women tended to be older.

OB men had a higher chance of having a family history of urinary stones (23%) compared with normal (16.7%) and OW men (20%). On the contrary, more normal weight women had a family history of stone formation compared with OW and OB women. More women compared with men had a history

TABLE 1. PATIENT CHARACTERISTICS DIVIDED BY SEX AND BODY MASS INDEX GROUPS

Sex	Men			Women				All women
BMI group	Normal BMI N (%)	Overweight	Obese	All men	N (%)	OW	OB	
Number of patients	36 (22.2)	65 (40.1)	61 (37.7)	162	52 (31.9)	38 (23.3)	73 (44.8)	163
BMI (mean)	22.9	27.2	36.2		21.18	27.74	38.65	
Age: mean (range)	54.8 (18–84)	55.3 (27–78)	51.6 (22–71)		44.7 (19–68)	49.5 (20–80)	54 (26–78)	
Family history of stones	6 (16.7)	13 (20)	14 (23)	33 (20.4)	16 (30.8)	9 (23.7)	14 (19.2)	39 (23.9)
Bowel disease/surgery	2 (5.6)	3 (4.6)	3 (4.9)	8 (4.9)	5 (9.6)	2 (5.3)	8 (11)	15 (9.2)
Previous stones	22 (61.1)	47 (75.4)	47 (77.1)	106 (71.6)	31 (59.6)	34 (89.5)	48 (65.8)	116 (69.3)
Previous stone workup	9 (25)	23 (35.4)	22 (36.1)	54 (33.3)	16 (30.8)	14 (36.8)	18 (24.7)	48 (29.4)

BMI=body mass index; N=normal weight; OW=overweight; OB=obese.

of bowel diseases (Crohn or ulcerative colitis) or surgery (bowel resection, bypass); the highest was in OB women.

Surgical treatment for stones

In the community, OB and OW patients were more likely to be treated with extracorporeal shockwave lithotripsy (SWL) compared with normal weight patients in both males and females (Table 2). The next popular treatment is ureteroscopy (URS) with a small percentage undergoing percutaneous lithotripsy (PCNL). In our center, however, most patients were treated with URS followed by PCNL, and a small percentage underwent SWL (Table 3). The higher the BMI, the more chance that the patient needed intervention.

Medical treatment

At our stone clinic, more OW and OB men needed thiazide diuretics for hypercalcemia compared with those of normal

weight. In women, about a quarter needed dietitian counseling. This increased with increasing BMI from 15.4% in normal weight to 30.1% in OB women (Table 4).

Stone composition

The majority of stones were calcium based. Uric acid (UA) stones (pure or mixed) were more common in OB patients (Table 5).

Urine composition

The 24-hour urine volume tended to be higher for OW and OB patients but was not statistically significant. OW and OB patients had significantly higher calcium (Ca), citrate (Cit), supersaturation calcium phosphate, uric acid (UA), supersaturation uric acid (SSUA), sodium (Na), potassium, magnesium (Mg), phosphorus (P), chloride (Cl), sulfate (Sul), urine urea nitrogen (UUN), protein catabolic rate (PCR),

TABLE 2. SURGICAL TREATMENT IN THE COMMUNITY

Sex	Men			Women		
BMI	N (%)	OW	OB	N (%)	OW	OB
No data	7 (19.4)	7 (10.8)	4 (6.6)	2 (2.8)	1 (2.6)	4 (5.5)
None	14 (38.9)	26 (40)	22 (36.1)	30 (57.7)	12 (31.6)	33 (45.2)
SWL	8 (22.2)	19 (29.2)	23 (37.7)	13 (25)	17 (44.7)	21 (28.8)
PCNL	3 (8.3)	3 (4.6)	5 (8.2)	3 (5.8)	4 (10.5)	5 (6.8)
URS	10 (27.8)	14 (21.5)	15 (24.6)	11 (21.2)	13 (34.2)	16 (21.9)

BMI=body mass index; N=normal weight; OW=overweight; OB=obese; SWL=shockwave lithotripsy; PCNL=percutaneous nephrolithotripsy; URS=ureteroscopy.

TABLE 3. SURGICAL TREATMENT AT OUR CENTER

Sex	Men			Women		
BMI	N (%)	OW	OB	N (%)	OW	OB
Interventions at our center	25 (69.4)	51 (78.5)	52 (91)	41 (78.8)	31 (91.6)	64 (87.7)
None	11 (30.6)	14 (21.5)	9 (14.8)	11 (21.2)	7 (18.4)	9 (12.3)
SWL	4 (11.1)	2 (3)	7 (11.5)	2 (3.8)	2 (5.3)	8 (10.9)
PCNL	3 (8.3)	12 (18.5)	13 (21.3)	13 (25)	8 (21.1)	23 (31.5)
URS	17 (47.2)	41 (63.1)	44 (70.5)	29 (55.8)	23 (60.5)	47 (64.4)
Others	2 (5.6)	1 (1.5)	0	2 (3.8)	3 (7.9)	3 (4.1)

BMI=body mass index; N=normal weight; OW=overweight; OB=obese; SWL=shockwave lithotripsy; PCNL=percutaneous nephrolithotripsy; URS=ureteroscopy.

TABLE 4. PERCENTAGE OF PATIENTS WHO HAD MEDICAL TREATMENT AT OUR CENTER

Sex	Men				Women			All
BMI	N	OW	OB	All men	N	OW	OB	women
Thiazides	2.8	15.4	10	10.5	5.7	2.6	9.6	6.7
Dietitian	33.3	32.3	39	35.2	15.4	28.9	30.1	25.2
Citrate	41.66	23.1	39	33.3	36.5	21.1	31.5	30.7
Allopurinol	0	3.1	3.3	2.5	0	0	2.7	1.2
Thiola	2.8	0	1.6	1.2	0	5.3	1.4	1.8
Other	30.6	13.9	13.1		34.6	34.2	20.5	
None	2.8	21.5	16.4		13.5	21.1	17.8	

BMI=body mass index; N=normal weight; OW=overweight; OB=obese.

creatinine (Cr), and calcium per weight (Ca/kg) compared with normal weight in both men and women (Table 6).

Discussion

No state in America had a prevalence of obesity less than 20% in 2010. Some states had a prevalence of 30% or more. The prevalence of stone disease has been estimated at 10% to 15% in the United States.^{8,9} The rate of obesity in stone formers was assessed by previous studies. Siener and associates¹⁰ in Germany found that 49.6% of the 363 men and 33.5% of the 164 women with idiopathic calcium oxalate (CO) stones were OW. The OB patients with stones in their population were 9.6% of the men and 10.4% of the women. In a US based study, Ekeruo and colleagues¹¹ found 14% OB of 1021 stone former patients. In a French study,¹² of 672 stone formers, 27.1% of male and 19.6% of female stone formers were OW, and 8.4% and 13.5% were OB, respectively.

We had a much higher rate of OW and obesity in our study population; 37.7% of men and 44.8% of women were OB and 40.1% and 23.3% were OW, respectively. This might be a direct correlation to the high rate of obesity in the state of Pennsylvania (28.6%), where our center is. OB men tended to be from the younger age group whereas OB women tended to be older. Large perspective studies found direct correlation between BMI and the risk of nephrolithiasis in both sexes.^{5,7} Taylor and coworkers⁷ also indicated that obesity and weight gain were independent risk factors and the risk could not be accounted for by diet alone.

High BMI seems to increase the risk of stone recurrence, most patients had a history of stones but more so if they

were OW or OB. This has been reported before. Lee and colleagues¹³ followed 163 patients for more than 36 months. Recurrence was more common in OB (42.6%) compared with non-OB stone formers (14.9%), but this was only true in first-time stone formers and not in recurrent stone formers. They defined OB as those with a BMI of more than 25. Although most of our patients had a history of stone formation, only 33.3% of the males and 29.4% of the females had a metabolic workup for their risk of stone recurrence in the community.

UA stones (pure or mixed) were more common in OB patients compared with those of normal weight. This is in line with previous studies, which indicated that calcium-based stones, especially CO and UA stones, were the most common types of stones in OB patients. In one study, Ekeruo and associates¹¹ had stone analysis from 32 OB patients. UA was present in 63% of them compared with 11% in non-OB. Also Del Valle and coworkers¹⁴ showed higher UA-containing stones in OB males (15.2%) and females (5%) compared with normal weight males (12.5%) and females (1.7%). This has been attributed to the increased chance of hyperuricosuria and gouty diathesis (low urine pH) in OB compared with patients with normal BMI.

In the community, about half of our patients had some sort of intervention to manage stones. SWL was the most common type of treatment followed by URS. Interestingly, more OW and OB patients were treated with SWL compared with those of normal weight even though it is known that efficacy of SWL decreases with obesity because of increased skin to stone distance.¹⁵ This might be because community urologists are more familiar with SWL and they wanted to avoid the complications of URS and PCNL.

The effect of BMI on urine composition has been looked at in previous studies. The results are somewhat variable. Powell and associates¹⁶ looked at a national database from 5942 consecutive patients with urinary stones. They defined obesity as more than 120 kg in men (3.8%) and more than 100 kg in women (12.6%). Obesity was associated with increased excretion of Na, Ca, Mg, Cit, Sul, P, oxalate (OX), UA, and cysteine. When adjusting for urine volume, only Na, UA, and P were different.

Taylor and Curhan¹⁷ looked at stone-forming and non-stone-forming participants in the Health Professionals Follow-Up Study. Participants with a high BMI excreted more urinary OX, UA, Na, and P. There was an inverse relationship between BMI and urine pH. There was also a positive relation between BMI and urinary excretion of

TABLE 5. STONE COMPOSITION BASED ON BODY MASS INDEX GROUP

Sex	Men			Women		
BMI	N (%)	OW	OB	N (%)	OW	OB
CO	13 (36.1)	13 (20)	18 (29.5)	10 (19.2)	11 (28.9)	13 (17.8)
CaP	1 (2.8)	1 (1.5)	2 (3.3)	5 (9.6)	1 (2.6)	9 (12.3)
CA	16 (44.4)	33 (50.8)	20 (32.8)	29 (55.8)	20 (52.6)	32 (43.8)
UA	3 (8.3)	10 (15.4)	14 (19)	3 (5.8)	0	9 (12.3)
Brushite	2 (5.6)	2 (3.1)	0	1 (1.9)	1 (2.6)	0
Cysteine	1 (2.8)	0	2 (3.3)	0	2 (5.3)	3 (4.1)
Mixed	2 (5.6)	12 (18.4)	11 (18)	7 (13.5)	7.9	13 (17.9)

BMI=body mass index; OW=overweight; OB=obese; CO=calcium oxalate; CaP=calcium phosphate; CA=mixed CO and CaP; UA=uric acid.

TABLE 6. URINE COMPOSITION AND BODY MASS INDEX

Sex	Men			Women			P value	P value
BMI group	N	OW	OB	N	OW	OB	Compare N/OW	Compare N/OB
Vol24 (liters)	2.16	1.94	2.28	1.77	1.74	1.99	0.86	0.86
SSCa Ox	6.16	7.02	6.67	6.50	7.41	6.84	0.98	0.98
Ca24 ^a	219.59	236.50	271.11	187.13	233.35	224.29	0.04	0.04
Ox24	41.33	40.36	44.41	32.33	32.64	37.43	0.34	0.34
Cit24 ^a	553.49	624.43	796.80	536.63	588.86	650.23	<0.001	<0.001
SSCaP ^a	1.24	1.36	1.15	1.34	1.56	1.12	0.01	0.01
pH	6.10	6.01	5.95	6.23	6.16	6.06	0.34	0.34
SSUA ^a	0.87	1.22	1.25	0.69	0.91	1.01	<0.001	<0.001
UA24 ^a	0.65	0.74	0.87	0.50	0.59	0.62	<0.001	<0.001
Na24 ^a	191.86	198.94	248.77	139.19	161.65	191.69	0.001	0.001
K24 ^a	67.75	76.11	80.49	51.82	52.73	60.34	0.003	0.003
Mg24 ^a	108.62	114.86	128.25	81.15	84.34	97.64	0.005	0.005
P24 ^a	1.02	1.13	1.28	0.72	0.85	0.96	0.006	0.006
Nh424	34.18	36.09	43.79	30.28	28.70	35.13	0.27	0.27
Cl24 ^a	185.00	188.89	234.76	139.86	154.31	178.33	<0.001	<0.001
Sul24 ^a	44.76	48.70	54.17	28.75	32.03	37.46	0.037	0.037
UUN24 ^a	11.57	13.35	15.17	7.95	9.09	10.50	0.001	0.001
PCR ^a	1.20	1.15	1.02	1.06	0.97	0.84	0.042	0.042
Cr24 ^a	1599.47	1853.79	2186.68	1122.53	1230.43	1371.18	<0.001	<0.001
Cr24kg	22.42	21.31	19.39	19.65	16.75	13.77	0.27	0.27
Ca24kg ^a	3.06	2.73	2.43	3.23	3.22	2.25	0.003	0.003
Ca24Cr24	135.66	128.43	126.13	168.30	193.85	164.26	0.08	0.08

^aIndicates statistically significant difference.

BMI=body mass index; N=normal weight; OW=overweight; OB=obese; SSCa=supersaturation calcium; OX=oxalate; Ca=calcium; Cit=citrate; SSCaP=supersaturation calcium phosphate; SSUA=supersaturation uric acid; Na=sodium; K=potassium; Mg=magnesium; P=phosphorus; Nh=Ammonium; Cl=chloride; Sul=sulfate; UUN=urine urea nitrogen; PCR=protein catabolic rate; Cr=creatinine.

Ca in men and stone-forming younger women, but this did not persist after adjusting for urinary P and Na excretion. They assumed that the differences in animal protein and Na intake might have led to the positive association between Ca and BMI. Few other studies support our finding of higher Ca excretion with increasing BMI.^{10,13,18} Negri and coworkers,¹⁹ however, did not find this association significant.

Our finding of higher UA and SSUA were also reported by other studies; the latest was by Del Valle and colleagues.¹⁴ They found a higher chance of hyperuricosuria in OW and OB men of all ages and in OW and OB females younger than 50 years of age.

Several studies reported on the effect of BMI on urine pH. Maalouf and coworkers²⁰ investigated the results of ambulatory evaluation of 4883 patients with nephrolithiasis. They found that urinary pH was inversely related to body weight. Taylor and Curhan¹⁷ also reported a decrease of pH with increasing BMI. Others found this true only in males but not in females.^{14,18,19} The decrease in pH could be secondary to insulin resistance as part of the metabolic syndrome and diet that might be rich in animal protein. We did find a tendency to reduced pH with increasing BMI in both men and women, but this was not statistically significant.

OW and OB patients are at high risk of development of the full metabolic syndrome. Various strategies have been proposed to prevent such consequence. These include increased physical activity²¹ and a healthy, reduced calorie diet.²² It seems reasonable to introduce stone prevention measures as part of the metabolic syndrome risk evaluation and preven-

tion program. This will help to reduce stone occurrence and the need for intervention.

Conclusions

Significant proportions of stone-forming patients were OW or OB. In the community, only a small percentage of recurrent stone formers receives metabolic evaluation. SWL remains the mainstay of treatment in the community even for OW and OB patients. OW and OB patients excrete larger amount of stone promoters—in particular Ca and UA—making them at higher risk for stone formation. Stone preventives measure should be part of the metabolic syndrome risk evaluation and prevention program.

Disclosure Statement

No competing financial interests exist.

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Abbreviations Used

BMI	= body mass index
Ca	= calcium
Cit	= citrate
CO	= calcium oxalate
Mg	= magnesium
Na	= sodium
N	= normal weight
OB	= obese
OW	= overweight
OX	= oxalate
P	= phosphorus
PCNL	= percutaneous nephrolithotripsy
SSUA	= supersaturation uric acid
Sul	= sulfate
SWL	= shockwave lithotripsy
UA	= uric acid
URS	= ureteroscopy