Clinical characteristics in urolithiasis formation according to body mass index

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Abstract. Although urolithiasis is considered to be strongly associated with lifestyle habits, there are numerous cases in which urolithiasis develops despite a non-obese body type or healthy lifestyle habits. However, in clinical practice, the diet therapy and lifestyle changes instructed for the prevention of recurrence of urolithiasis are almost identical in numerous cases. Therefore, the present study examined the effect of body mass index (BMI) on urolithiasis and its surrounding environment in patients, by analyzing the number of normal- and high-BMI (healthy and overweight) patients with urolithiasis. The present study analyzed 63 patients with urolithiasis for whom height and weight were measured at our hospital (Tokyo Medical University Ibaraki Medical Center). BMI <25 represents healthy body types and BMI ≥25 BMI defines overweight body types. Thus, patients were then grouped by BMI-defined body type using a threshold value of 25 accordingly. It was observed that a higher percentage of males were obese compared with females. Upon comparing the normal- and high-BMI groups, no significant difference was observed in uric acid level, urine pH or calculus number between the two groups. Liver computed tomography (CT) values were significantly lower in the high-BMI group compared with the normal-BMI group. There was no significant correlation between calculus size counts and BMI. However, a significant negative correlation was observed between BMI and the liver CT value. These results suggest that liver CT values correlated negatively with BMI, but the data indicates that other mechanisms unassociated with a fatty liver may be involved in urolithiasis in non-obese patients. The results of the present study suggest that physicians should consider the mechanism involved in preventing the recurrence of urolithiasis.

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Introduction

Urolithiasis is one of the most prevalent urological diseases in the nineteenth century population in Europe is quite similar to that of the twentieth century in Asia (1). The incidence of urolithiasis in Japan has steadily increased between 1965 and 2005 (2). Urolithiasis has been reported to increase the number of patients of various dietary habits. It has been reported that 12% of people globally suffer from urolithiasis (3). The increase in urolithiasis prevalence is thought to associated with changes in dietary habits, but may be particularly associated with a higher intake of animal protein (4,5).

Urolithiasis is a metabolic syndrome that presents symptoms including hypertension, lipid metabolism disorders, diabetes, obesity, atherosclerosis, ischemic heart disease and other associated problems that have a common pathology of visceral fat accumulation and insulin resistance (6-10). This common pathology means urolithiasis is considered to be a lifestyle disease. Various studies have reported cases of urolithiasis associated with hyperlipidemia, obesity, fatty liver, hyperuricemia, diabetes, hypertension and aortic calcification (9,10).

Although urolithiasis is considered to be strongly associated with lifestyle habits, there are numerous cases in which urolithiasis develops despite a non-obese body type or healthy lifestyle habits (6-10). However, in clinical practice, diet therapy and lifestyle changes instructed for the prevention of recurrence of urolithiasis are almost identical in numerous different cases.

Therefore, the present study examined the effect of body mass index (BMI) on urolithiasis and its surrounding environment in patients, by analyzing the number of normal- and high-BMI (healthy and overweight) patients with urolithiasis. Based on their BMI, patients with urolithiasis were categorized into a standard-type patient group and an obese-type patient group, and differences in clinical factors were assessed.

Materials and methods

The present study analyzed a total of 63 patients with urolithiasis for whom height and weight were measured at our hospital (Tokyo Medical University Ibaraki Medical Center, Ibaraki, Japan) between July 2013 and June 2015. The mean age of the patients was 55.6 years (range, 59-78 years). Of the total 63 patients, 49 were male and 14 were female (Table I). Written informed consent was obtained from all patients and all procedures used in the present study were ethically approved by the Ethical Committee of our hospital (Tokyo Medical University Ibaraki Medical Center). For each patient, BMI was calculated initially. According to World Health Organization guidelines, BMI <25 is of healthy body types and BMI ≥25 represents overweight body types (11). Thus, patients were then grouped by BMI-defined body type using a threshold value of 25 accordingly (11).

The measurement of the computed tomography (CT) value was determined using the Hounsfield Unit (HU). The liver CT value was defined as the mean value of three CT values selected randomly. Two CT model types, the Brilliance iCT SP 64-Slice configuration (Philips Healthcare, Amsterdam, The Netherlands) and the SOMATOM Sensation 64-Slice configuration (Siemens AG, Munich, Germany) were used.

Statistical analysis. All statistical analyses were performed using Stat View (ver. 5.0; SAS Institute, Inc., Cary, NC, USA). Continuous variables were presented as the mean ± standard deviation. A χ^2 test was used to evaluate comparisons between the differences in sex between the BMI≥25 and BMI<25 groups (Table II). A Student's t-test was used to evaluate the comparisons between the clinical features, including BMI, calculus size, serum uric acid value, urinary pH value and liver CT value (Fig. 1). The correlations amongst the liver CT value, calculus size and BMI were determined using a Spearman's rank correlation test (Fig. 2). P<0.05 was considered to indicate a statistically significant difference. The difference between the mean values of the two groups was analyzed using a Student's t-test, and the difference between the two variables was analyzed using a χ^2 test. Regression analysis was used to identify correlations between variables.

Results

The clinical features of the 63 patients with urolithiasis are listed in Table I. The mean age of the patients was 55.6 years (range, 59-78 years). Of the total 63 patients, 49 were male and 14 were female. The mean BMI was 24.4 (range, 17.6-41.0). The mean value of the urine PH was 6.63 (range, 5.5-7.5). The mean value of the calculus size was 9.5 mm (range, 4-35). The mean value of the uric acid was 5.86 mg/dl (range, 2.3-10.1). The mean value of the liver CT was 56.2 (range, 30-70).

The comparison of the BMI between males and females revealed that the male patients with urolithiasis had a higher BMI compared with the female patients with urolithiasis. It was observed that there was a higher percentage of obesity amongst males compared with females, however this difference was not significant (P=0.2207; Table II).

Association amongst clinical characteristics and BMI in patients with urolithiasis. Upon comparing the normal- and high-BMI groups, no significant differences were observed in uric acid level (P=0.1836; Fig. 1A), urine PH (P=0.4073; Fig. 1B) or calculus size (P=0.8129; Fig. 1D) between the two groups. However, liver CT values were significantly lower in the high-BMI group compared with the normal-BMI group. (P=0.001; Fig. 1C).

Correlation between liver CT value, calculus size counts and BMI in patients with urolithiasis. There was no significant correlation between calculus size counts and BMI (P=0.9176; Fig. 2A). However, a significant negative correlation was observed between BMI and liver CT value (P=0.0004; Fig. 2B).

Discussion

The present study examined whether there exist differences in a number of variables, including body type and BMI, amongst patients with urolithiasis. The present study examined patients with urolithiasis, identified the differences between obese-type patients with urolithiasis and normal-type patients, and deduced that the CT value of the liver in obese-type patients with urolithiasis is significantly lower compared with that in standard-type patients with urolithiasis, and that obese-type urolithiasis is more common in males compared with in females. However, these were no significant differences between obese-type patients with urolithiasis and standard-type patients with urolithiasis in other factors other than liver CT values. The present study revealed that obese-type patients with urolithiasis were more common amongst males, and standard-type patients with urolithiasis were more common amongst females; and these results suggest that lifestyle-associated disease factors may not be involved in the formation of urolithiasis in females. Furthermore, these results suggest that the prevention of recurrence in females with urolithiasis may be less useful compared with that in males.

The present data indicated that liver CT values were significantly lower in obese patients (high-BMI) with urolithiasis. In abdominal CT examination, the liver CT value decreases with fat deposition in such a manner that CT value has been noted to be associated with fatty liver (12). In fact, fatty liver may be diagnosed using the CT value of the liver (13). The results of the present study suggest that only fatty liver, amongst all the symptoms of metabolic syndrome, was significantly different between normal- and high-BMI groups.

Fatty liver affects not only the liver, but also other aspects of metabolism. 'Fatty liver is a phenotype in the liver of metabolic syndrome' (14) and is closely associated with insulin resistance (15). Furthermore, it has been reported to be a predictor of coronary artery disease independent of other risk factors (16).

An increase in urolithiasis has been associated with an increase in metabolic syndrome (6-10). In particular, associations with type 2 diabetes, a high BMI, hypertension, hyperlipidemia (6) and cardiovascular diseases have been noted (7). It has been reported that the decrease in urine pH resulting from metabolic syndrome is the mechanism for the increase in urolithiasis (10). Increased acid excretion through urine and ammonium excretion disorder are considered to be responsible for decreased urinary pH; in patients with diabetes, the main cause of uric acid

Table I. Clinical features of the 63 patients with urolithiasis.

Characteristics	Value
Age, mean (range)	55.6 years (range, 59-78 years)
Sex, n	Male 49, female 14
Body Mass Index, mean (range)	24.4 (17.6-41.0)
Size of urolithiasis, mean (range)	9.5 mm (4-35)
Number of urolithiasis, n	Single 36, double 5, more than triple 22
Value of uric acid, mean (range)	5.86 mg/dl (2.3-10.1)
Value of urine pH, mean (range)	6.63 (5.5-7.5)
Value of liver computed tomography, mean (range)	56.2 Hounsfield Unit (30-70)

n, number of patients.

Table II. Comparison of BMI between male and female patients with urolithiasis.

Gender	BMI <25	BMI ≥25	Rate of high BMI (%)
Male (n=49)	26	23	46.9
Female (n=14)	10	4	28.6
Total (n=63)	36	27	42.9

n, number of patients; BMI, body mass index.

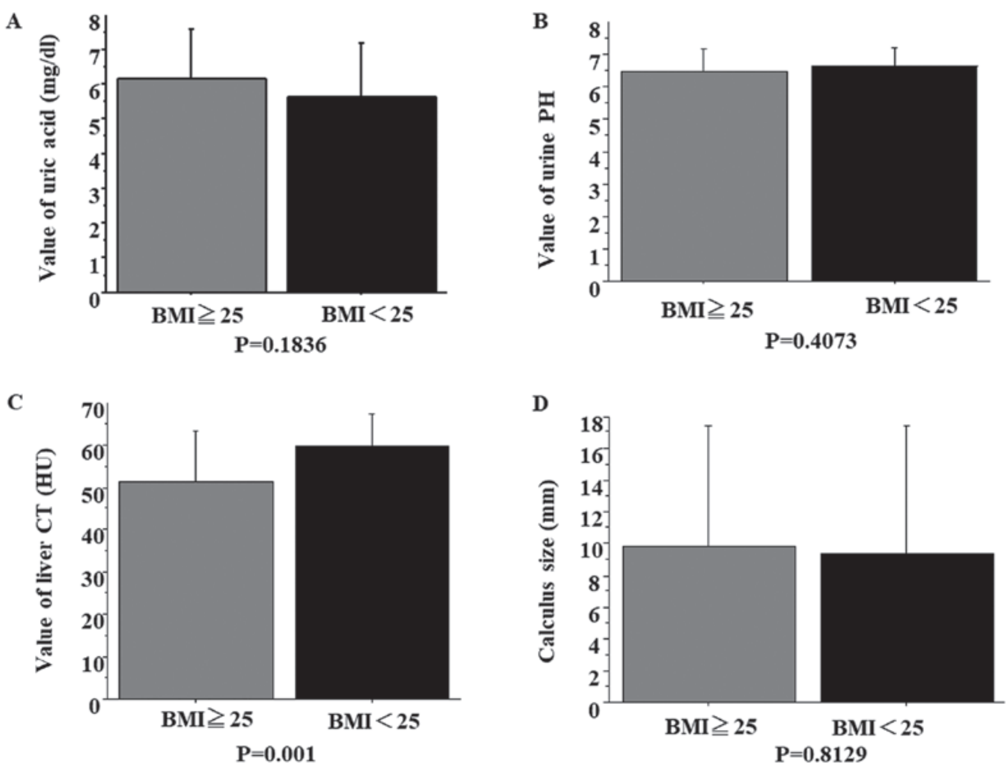

Figure 1. Comparisons between clinical characteristics and BMI in patients with urolithiasis. Continuous variables were presented as the mean ± standard deviation. (A) Comparison of the value of uric acid. (B) Comparison of the value of urine pH. (C) Comparison of the value of liver CT. (D) Comparison of calculus size. BMI, body mass index; CT, computed tomography; HU, Hounsfield Unit.

calculus, a common complication, is low urine pH (10). One study suggests that an increased intake of fructose causes metabolic syndrome, and the low urinary pH in turn results in an increase in urolithiasis (17). In particular, urine pH is

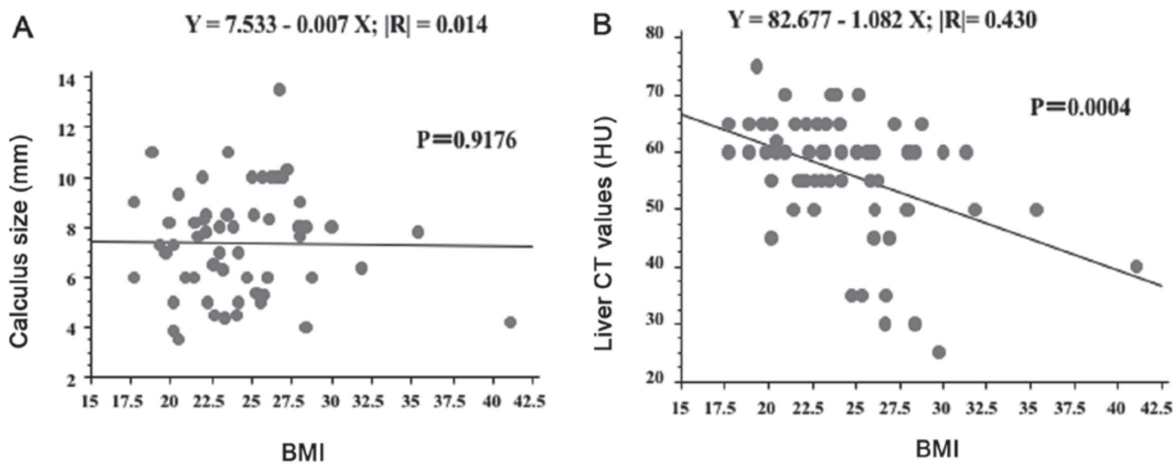

Figure 2. Correlation between liver CT value, calculus size counts and BMI in patients with urolithiasis. (A) Correlation between calculus size counts and BMI. (B) Correlation between liver CT value and BMI. CT, computed tomography; BMI, body mass index; HU, Hounsfield Unit.

persistently low (usually there is a diurnal variation with a transient rise in urine pH during the daytime). The diurnal variation of urine pH disappears in urolithiasis, uric acid becomes insoluble and is precipitated, and uric acid stones are formed (18).

A report on urolithiasis and metabolic syndrome-associated factors from Japan noted that fatty liver in male patients is a notable risk factor, an observation that the present study supports (19). However, in a large-scale cohort study in the United States it was observed that weight and BMI are associated with the onset of calculus in males and females, and that this association is stronger in females (20). In Japan, detailed cross-sectional studies on the presence or absence of insulin resistance were performed, and they determined that female patients with kidney stones had high insulin resistance and insulin values, supporting the link between obesity and urolithiasis (21). Furthermore, one study reports that urolithiasis formation (calcium phosphate) is observed in the kidney when rats receive a high cholesterol diet (22).

It has been reported that urolithiasis is similar to arteriosclerotic lesions, one of the metabolic syndromes, in cross-sectional studies and studies using mice models. In addition, in this phenomenon, the number of macrophages (Mφ) of the renal interstitium increased with the formation of calculus and an image of Mφ phagocytizing the crystal was observed (23). From these results of this previous study, the formation and disappearance of nephrolithiasis may be mostly attributed to the adhesion of crystals to the renal tubule cells, which are then transferred to the interstitial crystalline mass, the expression of chemokines/cytokines and other associated processes (23). Subsequent to adhesion to vascular endothelial cells, Mφ mature, begin phagocytosis, intracellular digestion, antigen presentation of Mφ and finally digest the crystal (24). However, M1 macrophages are pro-inflammatory, and M2 anti-inflammatory (25); M1s are associated with adipocytes and metabolic syndrome, whereas M2s are associated with organ restoration (26,27) and carcinogenesis (28). When crystals adhere to the renal tubular epithelium, M1-associated genes are highly expressed and promoted by adipocytes (29); in mice in which M2 macrophages are dysfunctional, M1 macrophages and kidney stone formation are increased (30).

There may be a number of potential limitations in the present study. Although the present study focused on BMI, urolithiasis is a multifactorial disease. Additionally, although using BMI as a marker is not the best method to measure obesity, it has been focused on in this paper as limited other studies on urolithiasis, to date, have focused on it.

Further studies, including studies with a larger number of cases, a greater number of clinical factors included, and the time course of treatment progress being taken into consideration, are warranted to rigorously examine the characteristics associated with urolithiasis formation.

Liver CT values correlated negatively with BMI, but the present data indicate that other mechanisms unassociated with fatty liver may be involved in urolithiasis in non-obese patients. It may be suggested that physicians should consider the mechanism involved in preventing the recurrence of urolithiasis.

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Availability of data and materials

Not applicable.

Authors' contributions

HT designed the study, and wrote the initial draft of the manuscript. HT contributed to analysis and interpretation of data, and assisted in the preparation of the manuscript. HT contributed to data collection and interpretation, and critically reviewed the manuscript. All authors approved the final version of the manuscript, and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics approval and consent to participate

All procedures used in this research were approved by the Ethical Committee of Tokyo Medical University Ibaraki Medical Center. Written informed consent was obtained from all patients.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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