

## Variations between two 24-hour urine collections in patients presenting to a tertiary stone clinic

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### Abstract

**Introduction:** The current Canadian Urological Association (CUA) guideline recommends two 24-hour urine collections in the metabolic evaluation for patients with urolithiasis. The aim of the present study was to compare two consecutive 24-hour urine collections in patients with a history of urolithiasis presenting to a tertiary stone clinic.

**Methods:** We retrospectively reviewed 188 patients who had two 24-hour collections upon presentation between January 2010 and December 2010. Samples were collected on consecutive days and examined for the following 11 urinary parameters: volume, creatinine, sodium, calcium, uric acid, citrate, oxalate, potassium, phosphorous, magnesium and urea nitrogen. For each parameter, the absolute value of the difference between the two samples rather than the direct difference was compared with zero. Similarly, the percent difference between samples was calculated for each parameter.

**Results:** The means of the absolute differences between the two samples were significantly different for all 11 urinary parameters ( $p < 0.0001$ ). The percent differences for all urinary parameters ranged from 20.5% to 34.2%. Furthermore, 17.1% to 47.6% of patients had a change from a value within normal limits to an abnormal value, or vice-versa. Significance was maintained when patients with incomplete or over-collections were excluded.

**Conclusions:** Significant variations among the two 24-hour urine collections were observed in all of the 11 urinary parameters analyzed. This variation may change clinical decision-making in up to 47.6% of patients if only a single 24-hour urine collection is obtained. The present study supports the CUA guideline of performing two 24-hour urine collections.

### Introduction

Urolithiasis is the third most common problem affecting the urinary tract. A thorough metabolic evaluation can lead to

targeted medical therapy and lifestyle changes to reduce the recurrence of stone disease.<sup>1-3</sup> Without appropriate follow-up and medical intervention, stone recurrence can be as high as 50% at 5 years.<sup>4</sup> The current Canadian Urological Association (CUA) guideline recommends two 24-hour urine collections in the workup of patients with urolithiasis.<sup>5</sup> However, there is considerable debate whether two collections are actually required. Some studies have suggested that a single urine collection is sufficient and would help reduce costs and time spent by patients and physicians.<sup>6,7</sup> Conversely, others have shown that obtaining two consecutive urine collections leads to an improved diagnostic yield resulting in more directed therapy for patients with urolithiasis.<sup>8,9</sup> Therefore, the aim of the present study was to compare two consecutive 24-hour urine collections in patients with a history of urolithiasis presenting to a tertiary stone clinic.

### Methods

A retrospective review was performed for 202 patients who presented to a tertiary stone clinic between January 2010 and December 2010 for a workup of urolithiasis and had two consecutive 24-hour urine collections. Patients were instructed (in English and/or French) on how to collect the two 24-hour urine collections by a urology nurse. Furthermore, written instructions in both English and French were given out together with the collection bottles. Urine was collected on consecutive days (on Saturday and Sunday) without dietary restrictions and was brought to the stone clinic on Monday morning. All urine collections were analyzed at a single laboratory. Patients who had previous 24-hour urine collections were excluded from the study. A total of 188 patients comprised of 67 women (36%) and 121 men (64%) met the inclusion criteria and their urine collections were analyzed for the following 24-hour parameters: volume, citrate, oxalate, calcium, potassium, phosphorous, magnesium, sodium, creatinine, urea nitrogen and uric acid.

These urinary parameters were compared between the two samples for significant variations. The absolute value of the difference between the samples for each urinary parameter was calculated rather than the direct difference between the samples. This avoids positive and negative differences of individual patients from cancelling each other out when determining the mean difference for each urinary parameter. The percent difference for each urinary parameter was also calculated using the following formula:

$$\% \text{ difference} = (|\text{sample 1} - \text{sample 2}| / [(\text{sample 1} + \text{sample 2})/2]) \times 100\%.$$

The means of the absolute differences and percent differences were compared with the value 0, which represented no change between sample 1 and 2.

Data were analyzed using SPSS 16.0 software (SPSS Inc, Chicago, IL). Descriptive data were presented in terms of mean, percentages and 95% confidence intervals, while the Student *t*-test was used to compare the means of different urinary parameters. A two-tailed *p*-value of <0.05 was considered statistically significant.

## Results

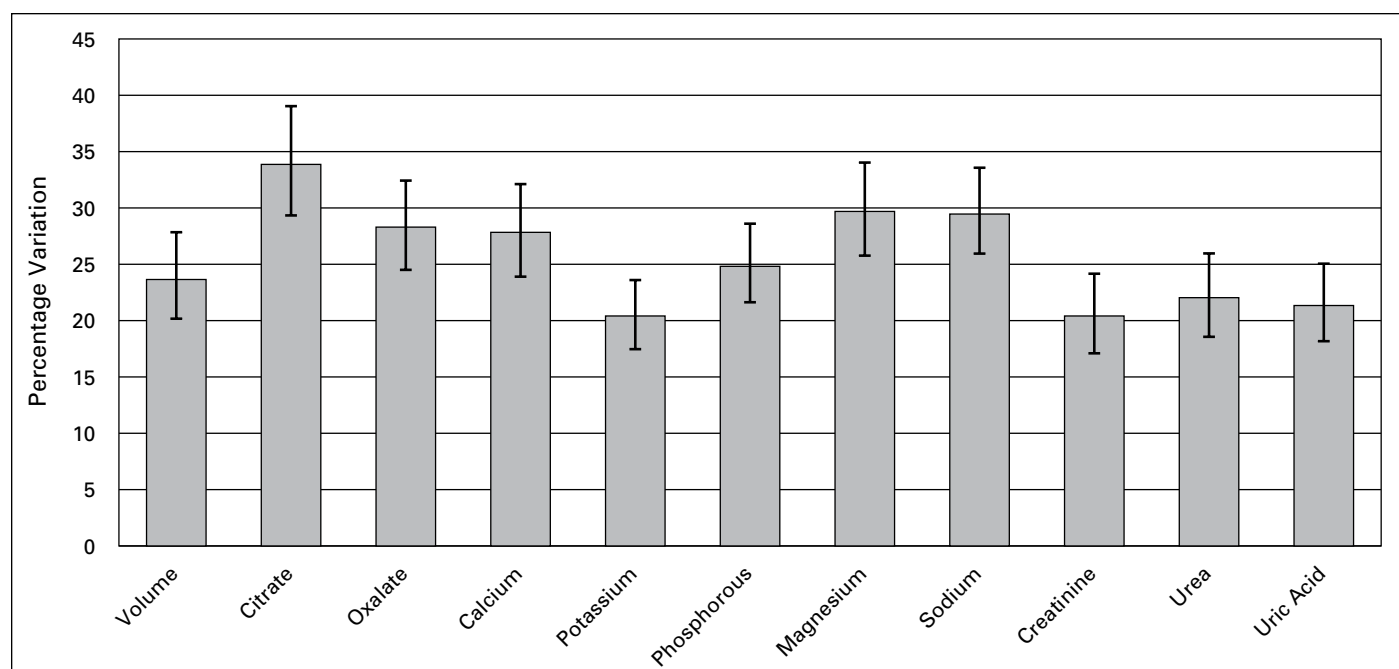
A total of 188 patients underwent a metabolic workup for urolithiasis and had two consecutive 24-hour urine collections. The means of the absolute difference and percentage variation between the two 24-hour urine collections were compared to zero. There were significant differences between the two samples in all of the analyzed variables, including urinary volume, citrate, oxalate, calcium, potas-

**Table 1. The mean absolute differences between the two consecutive 24-hour urine collections**

Urinary parameter	Mean absolute difference	95% CI	<i>p</i> value
Volume (mL)	385.4	334.3-436.5	<0.0001
Creatinine (mmol)	2.51	2.08-2.94	<0.0001
Sodium (mmol)	42.0	36.6-47.5	<0.0001
Calcium (mmol)	1.30	1.09-1.50	<0.0001
Uric Acid (mmol)	0.698	0.590-0.807	<0.0001
Citrate (mmol)	0.810	0.681-0.940	<0.0001
Oxalate (μmol)	101.1	86.4-115.8	<0.0001
Potassium (mmol)	12.6	10.6-14.7	<0.0001
Phosphorous (mmol)	5.80	5.00-6.60	<0.0001
Magnesium (mmol)	1.13	0.977-1.29	<0.0001
Urea nitrogen (mmol)	76.0	64.5-87.4	<0.0001

CI: confidence interval.

sium, phosphorous, magnesium, sodium, creatinine, urea nitrogen and uric acid (*p* < 0.0001) (Table 1). This translated to a 20.5% to 34.2% difference between the two collections (*p* < 0.0001) (Fig. 1). Furthermore, a creatinine difference of greater than 50% between the two 24-hour measurements was used to indicate over-collected or incomplete samples. When over-collected or incomplete samples were excluded, significant differences between the two samples were maintained for absolute difference and percentage variation for all parameters measured (*p* < 0.0001). To assess the clinical significance of these differences, changes from a normal 24-hour urinary parameter value to an abnormal value, or vice-versa, were examined. Clinically significant changes



**Fig. 1.** Percentage differences between the two consecutive 24-hour urine collections.

in 24-hour parameters were found in 17.1% to 47.6% of patients (Fig. 2).

## Discussion

A comprehensive metabolic evaluation of patients with urolithiasis can help identify risk factors which can be modified with appropriate management to prevent recurrence of stone disease.<sup>1-3</sup> The current CUA guideline recommends two consecutive 24-hour urine collections in patients undergoing a comprehensive metabolic evaluation for urolithiasis.<sup>5</sup> However, some studies have suggested that a single collection is adequate.<sup>6,7</sup> The present study compared two 24-hour urine collections in patients undergoing a metabolic workup at a tertiary stone clinic and demonstrated that there was a significant absolute difference and percent variation ( $p < 0.0001$ ) between the two urine collections. Furthermore, the present study is the first study evaluating 24-hour urinary parameters with or without exclusion of patients with incomplete or over-collections. When these collections were excluded from the analysis, significance was maintained for all urinary parameters ( $p < 0.0001$ ), which further emphasizes the importance of obtaining two 24-hour urine collections in all patients and not only in patients with improper collections.

The findings of the present study are in contrast to those by Castle and colleagues and Pak and colleagues who compared the variations between consecutive 24-hour urine collections using the paired *t*-test.<sup>6,7</sup> Castle and colleagues

found that none of the urinary parameters tested showed a statistically significant difference between collections, while Pak and colleagues found only magnesium and ammonium to be significantly lower in the second collection with magnesium differing by only 4%.<sup>6,7</sup> Castle and colleagues also compared the mean of individual patients' differences between collections 1 and 2 to the value of 0 and demonstrated that 6 of the 12 parameters, namely calcium, citrate, potassium, phosphorus, ammonium and creatinine, showed no significant difference. Although the differences for urinary oxalate, uric acid, sodium, magnesium, chloride and urine urea nitrogen were statistically significant when compared to 0, the authors concluded they were not clinically significant as the percent variation for all parameters was less than 5%. The discrepancy between the present results and that of Pak and Castle may be the result of different statistical methods used to compare differences between collections. Their studies relied on the paired *t*-test and compared the means of individual differences with 0. However, these methods may not be suitable in this context given the fact that positive and negative differences would cancel each other out rendering differences between collections statistically insignificant. For illustrative purposes, suppose that half of the patients had an increase of 4 mmol/day in urinary calcium excretion in the second collection and half of the patients had a 4 mmol/day decrease in the second collection, the paired *t*-test and comparing the mean difference between collections with 0 would show that the difference is statistically insignificant, yet clearly a 4 mmol/day increase or decrease is clinically

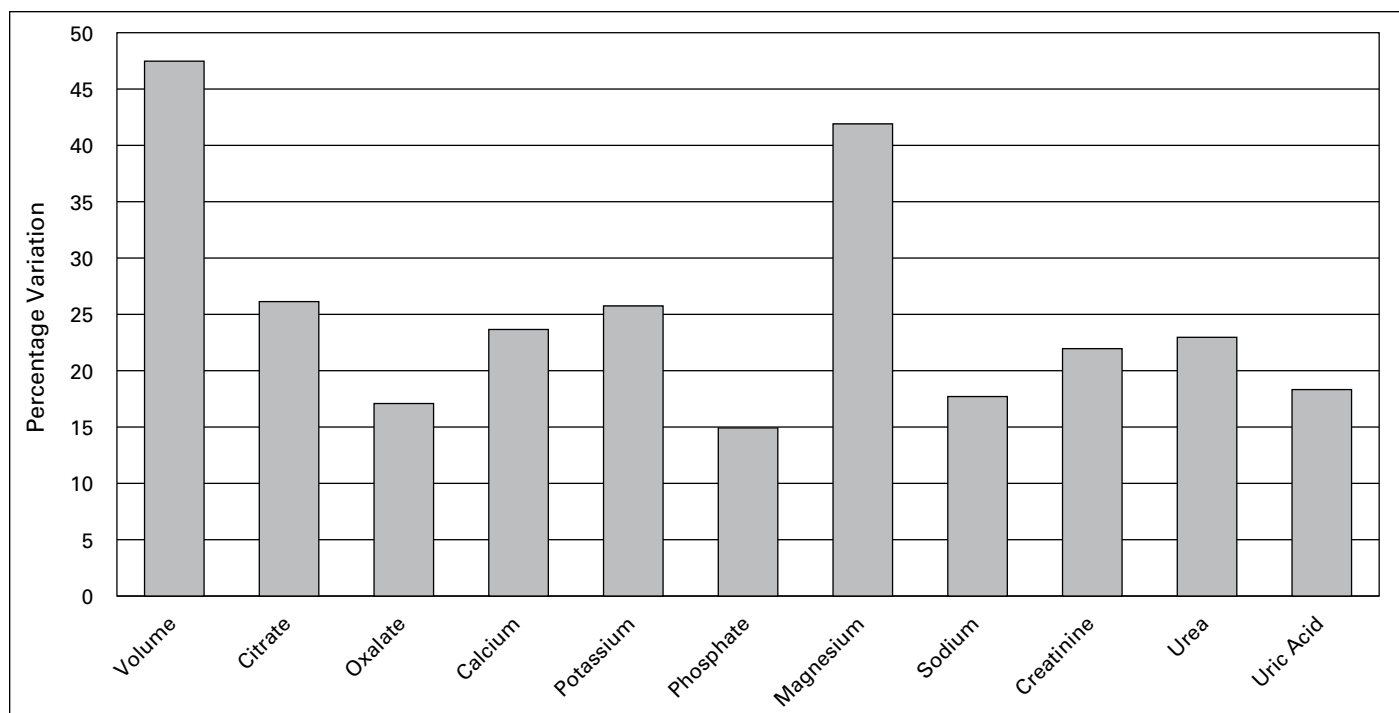


Fig. 2. Percentage of patients with clinically significant change.

significant. In the present study, with respect to calcium, 41.5% of patients had a positive difference and 49.5% had a negative difference. Similar proportions of positive and negative differences were noted for other urinary parameters. For this reason, the absolute difference between the two collections was compared to avoid individual differences from cancelling each other out in the mean. With this comparison, the present study shows that the absolute differences and percent variations, which ranged from 20.5% to 34.2%, were statistically significant when compared to 0 for all urinary parameters.

With regard to clinical practice, perhaps the most important indicator whether one or two collections are required would be evaluating the percentage of patients with whom a single collection would have resulted in improper treatment. This clinically significant change would be assessed by evaluating patients who have a value within normal limits for one collection and an abnormal value in the other. Castle and colleagues reported a clinically significant difference in 9.3% to 28.6% of patients depending on the urinary parameter.<sup>6</sup> The present study found the percentage of patients with clinically significant changes to be higher in the range of 17.1% to 47.6%. These findings are consistent with Parks and colleagues who evaluated 1142 patients in two different practices and showed that a single urine collection would underestimate or overestimate values by a large enough margin such that there would be inappropriate treatment in a significant proportion of patients.<sup>9</sup> Their conclusions were based on the large standard deviation values for the differences between consecutive samples, rather than assessing consistency of normalcy or abnormality between samples. Furthermore, Yagisawa and colleagues reported that two 24-hour collections resulted in a significantly higher ( $p < 0.05$ ) number of abnormalities diagnosed compared to a single urine collection.<sup>8</sup> Although their study only evaluated patients with calcium stones, it is nonetheless an important finding given that these stones represent most patients presenting with urolithiasis. Therefore, while obtaining a single 24-hour urine collection in the workup of patients with urolithiasis may save time and costs, the inconvenience and higher costs associated with a repeat 24-hour collection are justified to improve diagnosis and provide adequate management of urolithiasis.

Although the present study is based on a relatively limited number of patients, the differences between samples are quite significant such that increasing the sample size is unlikely to render the differences insignificant. Furthermore, patients assessed at the tertiary stone clinic may have undergone a basic evaluation elsewhere and been given some instructions to prevent recurrence of stone disease prior to obtaining the two 24-hour urine collections. Another confounding factor is that there may have been dietary differences between the two days of collection. However, these dietary variations

are natural and would further validate the value of obtaining two collections rather than relying on one single collection. Finally, while the current data suggest that obtaining two 24-hour urine collections may lead to more appropriate management, a randomized controlled trial would help clarify if two collections actually reduce the recurrence of stone disease when compared with a single collection.

## Conclusion

Significant variations among the two 24-hour urine collections were observed in all of the 11 urinary parameters analyzed. This variation may change clinical decision-making in up to 47.6% of patients if only a single 24-hour urine collection is obtained. The present study supports the current CUA guideline of performing two 24-hour urine collections in patients undergoing a comprehensive evaluation for urolithiasis.

**Competing interests:** None declared.

This paper has been peer-reviewed.

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