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Adjustment for Body Mass Index and Calcitrophic Hormone Levels Improves the Diagnostic Accuracy of the Spot Urine Calcium-to-Creatinine Ratio

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Abstract

Purpose—Hypercalciuria is a risk factor for osteoporosis and nephrolithiasis. 24-hour urine calcium (24HUC) measurement is the gold standard to diagnose hypercalciuria, but the spot urine calcium-to-creatinine ratio (SUCCR) is more convenient. Although authors claim they are interchangeable, we observed inconsistencies during conduct of a clinical trial. Therefore, we systematically evaluated agreement between the tests.

Methods—During 28 inpatient calcium absorption studies in 16 postmenopausal women, we simultaneously collected paired fasting morning and 24-hour urine specimens.

Results—We found moderate correlation between paired SUCCR and 24HUC specimens ($r = 0.57$, $p = 0.002$), but the SUCCR underestimated 24HUC by a mean of 83 mg (Bland-Altman). We diagnosed hypercalciuria (24HUC >250 mg) in eight specimens using the 24HUC but only two specimens using the SUCCR (25% sensitivity). We developed a regression model to predict 24HUC using SUCCR, parathyroid hormone, body mass index and 1,25(OH)₂D. The model improved diagnostic sensitivity to 100% and decreased Bland-Altman bias of the SUCCR to +0.06 mg/kg/24-hour.

Conclusions—We conclude the SUCCR underestimates urine calcium loss and does not reliably diagnose hypercalciuria. A formula derived from multivariate regression incorporating other readily measurable variables greatly improved the SUCCR's accuracy. Future studies must verify this correction before clinical implementation.

Keywords

calcium; diagnosis; hypercalciuria; nephrolithiasis; osteoporosis; urine

Introduction

Hypercalciuria is a common clinical problem whose presence increases the risk of nephrolithiasis and osteoporosis [1]. The diagnosis of hypercalciuria influences management of osteoporosis and stone disease [2]. Thus, clinicians need a screening test with high sensitivity for detecting hypercalciuria.

Providers diagnose hypercalciuria using the 24-hour urine collection or the spot urine-calcium-to-creatinine ratio (SUCCR). The 24-hour urine calcium (24HUC) is considered the gold standard test because of diurnal variation in urinary clearance and fractional excretion of calcium [3,4]. Two different approaches establish cut-points for 24HUC levels. One method uses a numerical threshold, while the other method normalizes excretion to body mass (20). However, patients often find the 24HUC inconvenient and might not provide a complete urine collection, yielding inaccurate test results.

A 1991 study [5] reported a strong linear correlation ($r = 0.946$, $p < 0.001$) between the SUCCR and 24HUC in 67 adults and concluded the SUCCR was a simple, cost-effective and reliable means of estimating 24HUC. These authors further asserted that the SUCCR value could be substituted, without a conversion factor, for the 24HUC in grams. However, study limitations included collection of urine as outpatients, inclusion of subjects with renal failure and other conditions affecting urinary calcium excretion, and limited statistical analysis of test agreement. Nevertheless, based on this publication [5] and a study in children [6], a SUCCR ≥ 0.25 is often used to diagnose hypercalciuria based on a 24HUC level ≥ 250 mg.

Some experts recommend using the SUCCR to diagnose hypercalciuria [7-9]. Such recommendations influence clinical practice. For example, providers at the University of Wisconsin (UW) Hospital and Clinics ordered twice as many SUCCR tests compared to 24HUC tests in 2007 (personal communication, Donald A. Wiebe, UW Hospital and Clinics Clinical Pathology Department).

In the course of studying relationships between vitamin D and calcium absorption [10], we observed that some subjects with a normal SUCCR at the screening visit had hypercalciuria based on 24HUC tests conducted during inpatient calcium absorption study visits. At that point, we began to systematically evaluate the accuracy of the SUCCR, compared to carefully timed and collected 24HUC measurements performed during inpatient admissions to the research ward. Herein, we report that 24HUC values vary as a function of not only SUCCR but also $1,25(\text{OH})_2\text{D}$, body mass index and parathyroid hormone levels. Further, we find that adjustment for these covariates substantially improves diagnostic performance of the SUCCR.

Methods

Patients

We recruited twenty post-menopausal women to assess their calcium absorption [10] and bone mineral density before and after correction of vitamin D insufficiency. The University of Wisconsin (UW) Human Subjects Committee approved the study protocol and all participants provided written informed consent. Participants were greater than five years

postmenopausal with a baseline serum 25(OH)D of 16-24 ng/mL and an estimated calcium intake less than 1,100 mg daily. Because our primary objective was to evaluate the effect of high-dose vitamin D on calcium absorption, we excluded women who might experience harm from vitamin D therapy due to preexisting hypercalciuria, hypercalcemia or nephrolithiasis. We diagnosed hypercalciuria based on a SUCCR greater than 0.25. Because we planned to treat women with vitamin D for one year to assess whether correction of vitamin D insufficiency influenced bone mineral density, we also excluded women who, due to other conditions, might not respond to vitamin D. We also excluded women whom we felt should begin prescription medication for osteoporosis or osteomalacia, instead of participating in a vitamin D research study. We thus excluded women with osteomalacia [11], adult fragility fracture, T-score below -3.0 at the lumbar spine or hip, renal insufficiency, disorders of malabsorption and use of medications known to interfere with vitamin D or calcium metabolism.

Protocol

In brief, subjects came to the UW General Clinical Research Center (GCRC) for two 24-hour inpatient stays, first when vitamin D insufficient and later when vitamin D replete. We prescribed ergocalciferol 50,000 IU daily for 15 days [10] and verified vitamin D repletion before the second calcium absorption study visit. The second absorption study occurred a mean of 36 ± 8 days following the first, as the Food and Nutrition Board [12] recommends a dietary adaptation period of at least 12 days between calcium studies. After the second calcium absorption study visit, women commenced maintenance vitamin D therapy as 50,000 IU twice monthly for the next eleven months. Below, we report the procedures related to calcium absorption study visits, as paired SUCCR and 24HUC measurements were collected at these study visits only.

Women fasted after midnight, the day prior to each scheduled calcium absorption study visit. The morning of the study visit, subjects arose from bed, emptied their bladder, dressed and came to the research ward at approximately 0700. Upon arrival, each subject provided a fasting second void morning urine specimen.

Subjects then received dual stable calcium isotopes to trace calcium absorption. We administered tiny doses (~ 21 mg) of calcium tracers, thus avoiding alterations in calcium intake that could alter subjects' calcium homeostasis [13]. We replicated each woman's research diet using 7-day diet diaries, thus any calcium ingested during the stays matched participants' normal intake.

During each inpatient calcium absorption study visit, research nurses supervised a carefully timed 24-hour urine collection from each participant. The timed collection began immediately after subjects voided to provide the fasting urine specimen. Nurses collected and refrigerated urine in plastic preservative-free, acid-free jugs. We used acid and preservative free jugs based on direct communications with the laboratory personnel analyzing urine calcium levels, who stated that preservatives and acid were not required so long as specimens were refrigerated until analysis. This policy is supported by a study in which researchers found no significant differences between calcium measurements from urine specimens analyzed before and after acidification [14]. At the end of the 24-hour interval, nurses mixed all urine, recorded the total volume and removed an aliquot for analysis.

Because trained nurses supervised carefully timed and collected 24HUC, we did not assess 24-hour urine creatinine. Some experts do not recommend urine creatinine measurement to verify a complete 24-hour urine collection, due to high within-subject coefficients of

variation attributed to daily changes in diet and exercise [3,15-18]. Thus, we deemed it both unnecessary and of questionable utility to measure urine creatinine.

Laboratory

Meriter Laboratories (Madison, WI, [USA](#)) analyzed all urine specimens to determine calcium content, using a COBAS Integra 400 Analyzer o-cresolphthalein complexone assay (Roche Diagnostics, Indianapolis, IN, [USA](#)). The within and between run coefficients of variation were 2.2% and 3.8%, respectively. Meriter Laboratories analyzed urine creatinine levels using a COBAS Integra 700 Analyzers enzymatic assay (Roche Diagnostics, Indianapolis, IN, [USA](#)). The within and between run coefficients of variation for creatinine measurements were 1.8% and 3.9%, respectively. Meriter Laboratories measured intact parathyroid hormone by electrochemiluminescence (reference range 15-65 pg/mL). The reported intra- and inter-assay coefficients of variation were 1.5% to 4.1% and 2.6% to 6.5%, respectively. The UW Institute on Aging measured serum 25(OH)D by high performance liquid chromatography. Between-run assay coefficients of variation were 2.6% to 4.9% for 25(OH)D₃ and 3.2% to 12.6% for 25(OH)D₂.

Statistical Analysis

For the present study, our primary objective was to assess relationships between the SUCCR, defined as the ratio of calcium in mg/dL to creatinine in mg/dL times 1000 [5] and the 24HUC, defined as mg calcium in a 24-hour urine collection. We performed forward stepwise linear regression of 24HUC on other clinical variables, using a criterion of $F > 4.00$ for inclusion and $F < 3.90$ for removal. Demographic variables included age, height, weight, body surface area (BSA) and body mass index (BMI). Laboratory variables included serum calcium, creatinine, parathyroid hormone (PTH), 1,25(OH)₂D, 25(OH)D and spot urine calcium and creatinine. Nutritional variables included fractional calcium absorption [10] and dietary calcium, kilocalories, protein, carbohydrate, fat, fiber, vitamin D, sodium, magnesium, iron, caffeine and oxalate. We initially used univariate regression to examine relationships between 24HUC and the variables listed above, and included those variables with $p < 0.05$ in the stepwise regression model.

We further assessed sensitivity of SUCCR results as a means of diagnosing hypercalciuria based on the gold-standard 24HUC. We assessed test agreement using the Bland Altman method [19]. We used 3 criteria to define hypercalciuria; >250 mg calcium in a 24-hour urine collection [20], >4 mg/kg/24-hour [21] and above normal limits established from a reference population (over 252 mg, 286 mg and 357 mg in 24 hours for low, medium and high calcium intake respectively) [22].

Results

In total, we collected 28 paired SUCCR and 24HUC measurements from sixteen subjects for analysis [10]. All sixteen women were Caucasian with a mean age, body mass index and daily calcium intake of 59 ± 7 years, 30 ± 7 and 810 ± 200 mg, respectively. We obtained twelve paired samples at the initial calcium absorption study visit during vitamin D insufficiency and sixteen paired samples during the second calcium absorption study visit following vitamin D repletion (Table 1).

Hypercalciuria was present in eight 24HUC samples based on a 250 mg/24-hour threshold [20], six 24HUC samples using a normal upper limit of 4 mg/kg/24-hour [21] and eight 24HUC samples using upper normal limits from a reference population [22]. By contrast, hypercalciuria was present in two SUCCR samples based on a 250 mg/24-hour threshold [20], two SUCCR samples using a normal upper limit of 4 kg/mg/24-hour [21] and one

SUCCR sample using upper normal limits from a reference population [22]. Thus, the sensitivity of the SUCCR for diagnosis of hypercalciuria was 25% using an upper normal limit of 250 mg/24-hour [20], 33% using a normal upper limit of 4 kg/mg/24-hour [21] and 13% using upper normal limits from a reference population [22].

We found a positive correlation ($r = 0.73$, $p < 0.001$) between 24HUC and SUCCR results from 28 paired urine samples. However, one subject's paired sample, with a SUCCR of 360 mg and a 24HUC value of 542 mg, excessively influenced the correlation and we excluded these data in subsequent analyses. Without this outlier, the SUCCR only moderately correlated with 24HUC test results ($r = 0.57$, $p = 0.002$, Figure 1). Additionally, a Bland Altman analysis (Figure 2) revealed that SUCCR systematically underestimated 24HUC (130 ± 73 mg versus 212 ± 106 mg, $p < 0.001$, average Bland Altman bias of 83 ± 14 mg). When we corrected the SUCCR using a published adjustment method ($\text{SUCCR} = 0.92 * 24\text{HUC} - 0.002$ [5]), the SUCCR continued to underestimate the 24HUC content by an average of 69 mg and provided a diagnostic sensitivity of 25%.

Vitamin D status did not influence agreement between SUCCR and 24HUC test results (Table 1). In 28 paired specimens, the mean difference in 24HUC and SUCCR results was 97 ± 84 mg when vitamin D insufficient and 72 ± 63 mg when vitamin D replete ($p = 0.37$, independent t-test). We noted similar findings when excluding the outlier. Among 27 paired specimens the average difference between 24HUC and SUCCR levels was 90 ± 84 mg when vitamin D insufficient and 72 ± 63 mg when vitamin D replete ($p = 0.53$, independent t-test).

Similarly, vitamin D status did not influence diagnostic sensitivity of the SUCCR for hypercalciuria. Among twelve samples collected during vitamin D insufficiency, 33% ($n=4$) revealed hypercalciuria based on 24HUC results >250 mg while 17% ($n=2$) showed hypercalciuria based on SUCCR results ≥ 0.25 . In the sixteen samples collected after vitamin D repletion, 4 (25%) revealed hypercalciuria based on 24HUC results but none showed hypercalciuria based on SUCCR results.

We built a regression model using the SUCCR and additional variables described under "Methods" to predict 24HUC values in mg. When used as the sole predictor variable in a linear regression analysis, the SUCCR accounted for 53% of the variability in 24HUC measurements among 28 samples. However, without the outlier (SUCCR 360 mg and a 24HUC value of 542 mg), the SUCCR accounted for only 32% of the variability ($p = 0.002$) in 24HUC measurements in 27 samples. In individual regressions (27 samples), the variables that significantly associated ($p < 0.05$) with 24HUC included the SUCCR, PTH, $1,25(\text{OH})_2\text{D}$ and dietary intake of iron, magnesium, fiber and carbohydrate (Table 2).

In stepwise multivariate linear regression models predicting 24HUC, the SUCCR, PTH and dietary calcium significantly influenced significantly influenced ($p < 0.05$) the model ($r^2 = 0.81$) (Table 3). However, dietary calcium data was determined using cumbersome 7-day diet diaries. As 7-day diaries are impractical in a clinical setting, we re-analyzed our linear model without dietary variables. We found that the SUCCR, PTH and height significantly influenced the model ($p < 0.05$, $r = 0.73$), yielding the formula:

$$24\text{-Hour Urine Calcium (mg)} = -983 + [1.1 \times (\text{SUCCR} \times 1000)] + (14 \times \text{Inches}) + (2 \times \text{PTH})$$

We estimated 24HUC values using the formula derived above and compared them to our measured 24HUC values. The Bland-Altman bias decreased to -23 mg, the Pearson's correlation coefficient increased to 0.85 ($p < 0.001$) and the diagnostic sensitivity (based on a 250 mg/24-hour threshold) improved to 57%.

We then constructed a regression model using the SUCCR and additional variables described under “Methods” to predict 24HUC values in mg/kg/24-hour (Table 2). When used as the sole predictor variable in linear regression analysis of 27 samples, the SUCCR accounted for 41% ($p < 0.001$) of the variation in mg/kg/24-hour urine calcium excretion. Additionally, BMI, BSA, dietary intake of fat, fiber, magnesium, iron and sodium, serum creatinine and 1,25(OH)₂D significantly ($p < 0.05$) associated with urine calcium loss in mg/kg/24-hour in univariate analyses.

In step-wise multivariate linear regression models the SUCCR, 1,25(OH)₂D, PTH, dietary vitamin D and BMI significantly influenced mg/kg/24-hour urine calcium ($p < 0.05$, $r = 0.81$) (Table 3). Again, dietary measurement of vitamin D requires a seven-day diet diary, thus limiting clinical use of this model. After removing dietary vitamin D, a model incorporating the SUCCR, BMI, PTH and 1,25(OH)₂D accounted for 75% of the variation in mg/kg/24-hour urine calcium and yielded the formula:

$$\begin{aligned} \text{mg/kg/24-Hour Urine Calcium} = & 0.33 + [0.014 \times (\text{SUCCR} \times 1000)] \\ & + (-0.052 \times \text{BMI}) \\ & + (0.026 \times \text{PTH}) \\ & + (0.016 \times 1,25(\text{OH})_2\text{D}) \end{aligned}$$

We used the formula above to estimate mg/kg/24-hour urine calcium loss and compared calculated values to measured values. We found a high correlation between calculated and measured values ($R = 0.86$, $p < 0.001$). Bland Altman analysis revealed no significant difference between estimated versus measured values ($p = 0.69$) and a positive bias of 0.06 mg/kg/24-hour using the formula to estimate actual mg/kg/24-hour (Figure 3). The formula performed similarly across all ranges of values including high urine calcium levels, where a diagnosis of hypercalciuria should occur. The diagnostic sensitivity of the estimated values was 100% based on a 4 mg/kg/24-hour urine calcium threshold.

Discussion

Clinicians and researchers commonly use the SUCCR to diagnose hypercalciuria [7]. However, we observed that the SUCCR was normal when 24HUC values were high, during an ongoing clinical research study [10]. During the remainder of the study, we systematically collected paired SUCCR and 24HUC specimens during each calcium absorption study visit and tested their agreement. Although the two measurements showed a positive correlation, the SUCCR underestimated 24-hour urine calcium loss by a mean of 83 mg and had an unacceptably low diagnostic sensitivity, ranging from 13% to 33%. Multiple regression models increased diagnostic sensitivity to 100% and demonstrated a positive Bland Altman bias of only 0.06 mg/kg/24-hour.

Surprisingly, few research studies compared the accuracy of the SUCCR to the 24HUC. A 1959 publication first proposed using the SUCCR to assess hypercalciuria but described a wide range of normal results [23]. Others reported large intra-individual variations in SUCCR test results over a 24-hour interval [24]. Another group emphasized test inaccuracy and proposed a higher upper limit of normal [25]. A 1987 study showed good correlation between the SUCCR and 24HUC, but only in subjects with hypercalciuria [26]. A more recent study [5] suggested the SUCCR was interchangeable with 24HUC test results. Although one group [3] proposed collecting two fasting and two post-prandial SUCCR specimens to estimate urine calcium loss, four samples limit test convenience.

Our multivariate analyses revealed associations between 24HUC and PTH, BMI and 1,25(OH)₂D. PTH affects urine calcium levels by stimulating calcium re-absorption in the proximal tubules and promoting excretion in the distal nephron [27]. In our model, PTH levels positively associated with urine calcium loss, suggesting a greater effect of PTH at the distal than the proximal nephron. Our study's positive association between BMI and urine calcium loss is congruent with other reports [28,29], although the mechanism by which this occurs is uncertain. 1,25(OH)₂D promotes intestinal calcium absorption, thus explaining our observation that 1,25(OH)₂D positively associates with urine calcium loss [30]. Although dietary calcium did not significantly associate with 24HUC values [22], we excluded subjects reporting high calcium intake, thus limiting variability in dietary calcium.

Our study has some limitations. Because we excluded patients with nephrolithiasis or a high SUCCR at screening, we decreased the potential number of subjects with hypercalciuria and thus have insufficient data to comment on the specificity of our proposed adjustment of SUCCR results. The number of subjects was relatively small and was limited to Caucasian women at least five years past menopause. Furthermore, our study results might not apply to men, children, premenopausal women and those of other ethnic backgrounds, and stone formers. We did not measure 24-hour urine creatinine. However, experts do not recommend 24-hour creatinine measurements to verify a complete urine collection [15-18]. Thus, a major strength of this study is highly supervised collection of 24-hour urine samples by trained research nurses.

We conclude that the SUCCR alone underestimates urine calcium loss in postmenopausal women, demonstrating an unacceptably low diagnostic sensitivity for hypercalciuria. It is not surprising that fasting SUCCR specimens alone poorly predict 24HUC results, as SUCCR measurements do not capture fluxes in calcium intake and excretion over a 24-hour period [4]. Further, urine calcium excretion also depends on age, race, gender, estrogen status, calcium intake and many other factors [22,31]. Therefore, using a uniform SUCCR threshold of ≥ 0.25 to diagnose hypercalciuria seems simplistic.

Providers need accurate diagnostic tests for hypercalciuria, as detection influences the care of patients with osteoporosis and nephrolithiasis. We developed a regression model to accurately predict 24HUC in mg/kg/24-hour using the SUCCR and readily available clinical data including BMI, PTH and 1,25(OH)₂D. Moreover, in the screening setting, it is desirable to maximize sensitivity even if this entails some loss of specificity. Future studies must confirm our formula prior to its widespread incorporation into clinical practice. Until validation of our regression-based formula to correct the SUCCR, we call for caution when using a single SUCCR test to exclude hypercalciuria in postmenopausal women.

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Fig. 1.
Correlation Between 24-Hour Urine Calcium and the Spot Urine Calcium to Creatinine Ratio

- ▲ Vitamin D Insufficient: 25(OH)D <30 ng/mL
- Vitamin D Replete: 25(OH)D >30ng.mL
- Outlier (Vitamin D Insufficient)
- Line of Regression
- - Line of Identity

Fig. 2.
 Bland Altman Plot of Differences Between the Spot Urine Calcium to Creatinine Ratio (SUCCR) and the 24-Hour Urine Calcium (24HUC)
 — Bias (-83)
 - Identity
 - - 95% Limits of agreement (-225 to 60)

Fig. 3. Measured Urine Calcium Loss in mg/kg/24-hour Compared to Estimated Urine Calcium Loss Using a Multivariate Model

Table 1

Test Agreement According to Vitamin D Status

Subject	Vitamin D Insufficient ¹ n=12			Vitamin D Replete ² n=16			
	SUCCR ³	24HUC ⁴	25(OH)D	SUCCR ³	24HUC ⁴	25(OH)D	
1				168	166	47	
2				50	149	58	
3				186	122	68	
4				214	287	81	
5	147	151	19	129	151	72	
6	360	542	21	191	370	48	
7	144	296	25	122	286	50	
8	131	248	21	227	307	62	
9	126	144	21	162	188	36	
10	100	138	14	71	110	46	
11				76	166	54	
12	71	56	25	75	114	81	
13 ⁵	260	363	23				
	93	367	24				
14	79	118	23	72	154	129	
15 ⁶	80	206	28	66	210	33	
				44	162	55	
16	57	186	22	131	189	60	
Average SD	137	234	22	124	196	61	
	88	137	3	61	76	23	

¹ Vitamin D insufficiency was a serum 25(OH)D level <30 ng/mL² Vitamin D repletion was a serum 25(OH)D level >30 ng/mL³ SUCCR indicates the spot urine calcium to creatinine ratio times 1000⁴ 24HUC indicates mg of calcium in a 24-hour urine collection

⁵ We diagnosed hypercalciuria on subject 13 at her first calcium absorption study visit and thus, did not prescribe vitamin D but did repeat a second absorption study to evaluate the monthly change in calcium absorption without vitamin D repletion.

⁶ The first diet diary for subject 15 was incomplete, rendering data from her first calcium absorption study visit questionable. She completed a full 7-day diet diary and underwent a second "baseline" calcium absorption study visit, but between visits 1 and 2 had an increment in 25(OH)D levels with summer sun exposure.

Table 2

Univariate Analysis Predicting Urine Calcium Loss

Independent Variable	Predicting Urine Calcium Loss (mg/24-hour)					Predicting Urine Calcium Loss (mg/kg/24-hour)				
	Intercept	β	SE	R ²	p	Intercept	β	SE	R ²	p
Demographic										
Age	278	-1.33	2.44	0.012	0.59	2.60	-3.5E-08	0.041	2.9E-08	0.99
Height (inches)	-810	15.5	9.52	0.096	0.12	6.80	-0.064	0.170	0.006	0.71
Weight (kilograms)	251	-0.61	0.797	0.023	0.45	5.74	-0.038	0.011	0.310	0.003
Body Surface Area	282	-42.2	65.6	0.016	0.53	8.59	-3.080	0.930	0.305	0.003
Body Mass Index	296	-3.18	2.45	0.063	0.21	6.59	-0.133	0.034	0.380	0.001
Laboratory										
Serum Calcium, mg/dL	391	-20.5	58.5	0.005	0.73	1.07	0.164	0.990	0.001	0.87
Serum Creatinine, mg/dL	418	-266	150	0.111	0.09	7.08	-5.483	2.456	0.166	0.04
Parathyroid Hormone, pg/mL	93.9	1.91	0.792	0.194	0.02	1.40	0.020	0.014	0.084	0.15
1,25(OH) ₂ D, pg/mL	116	1.88	0.838	0.168	0.03	0.76	0.041	0.013	0.284	0.004
25(OH)D, ng/mL	217	-0.367	0.651	0.013	0.58	2.81	-0.005	0.011	0.008	0.67
Spot Urine Calcium	204	-0.346	2.16	0.001	0.87	2.33	0.023	0.036	0.015	0.54
Spot Urine Creatinine	243	0.397	0.237	0.101	0.11	3.18	-0.005	0.004	0.067	0.19
SUCCR * 1000	98.7	0.837	0.242	0.323	0.002	0.67	0.016	0.004	0.407	<0.001

Independent Variable	Predicting Urine Calcium Loss (mg/24-hour)					Predicting Urine Calcium Loss (mg/kg/24-hour)				
	Intercept	β	SE	R ²	p	Intercept	β	SE	R ²	p
Fractional Calcium Absorption	233	-150	145	0.041	0.31	3.00	-1.855	2.477	0.022	0.46
Nutritional ¹										
Calcium	115	0.104	0.075	0.071	0.18	2.31	3.4E-04	0.001	0.002	0.80
Kilocalories	85.0	0.071	0.046	0.086	0.14	3.07	-2.9E-04	0.001	0.005	0.72
Protein	104	1.30	1.20	0.044	0.29	3.05	-0.006	0.021	0.003	0.77
Carbohydrate	23.3	0.92	0.276	0.309	0.003	0.78	0.009	0.005	0.114	0.09
Fat	227	-0.42	0.832	0.010	0.62	4.64	-0.032	0.013	0.205	0.02
Fiber	98.7	6.11	2.44	0.201	0.02	0.61	0.120	0.039	0.270	0.005
Vitamin D	159	0.39	0.193	0.140	0.05	2.29	0.003	0.003	0.028	0.41
Sodium	280	-0.033	0.029	0.048	0.27	5.87	-0.001	4.3E-04	0.280	0.005
Magnesium	2.57	0.74	0.200	0.357	<0.001	-0.63	0.012	0.003	0.334	0.002
Iron	-112	26.7	4.68	0.566	<0.001	-0.95	0.303	0.103	0.255	0.007
Caffeine	200	-0.078	6.22	6.3E-0.6	0.99	2.74	-0.063	0.104	0.014	0.55
Oxalate	179	29.1	19.8	0.080	0.15	2.12	0.636	0.324	0.134	0.06

¹ Nutritional intake was determined by analysis of 7-day diet diaries.

Table 3

Step-Wise Multivariate Linear Model Predicting Urine Calcium Loss

Predicting Urine Calcium Loss (mg/24-hour)						
Step	Variables	Beta	St. Error	p	Intercept	R ²
1	SUCCR * 1000	0.84	0.24	0.002	99	0.32
	PTH, ng/mL	2.6	0.54	<0.001	-67	0.66
2	SUCCR * 1000	1.03	0.18	<0.001		
	PTH, ng/mL	2.6	0.54	<0.001		
3	SUCCR * 1000	1.2	0.14	<0.001	-204	0.81
	PTH, ng/mL	2.5	0.41	<0.001		
	Dietary calcium	0.15	0.04	<0.001		
4	SUCCR * 1000	1.06	0.17	<0.001	-983	0.73
	PTH, ng/mL	2.1	0.54	<0.001		
	Height (inches)	14	6.4	0.034		

Predicting Urine Calcium Loss (mg/kg/24-hour)						
Step	Variables	Beta	St. Error	p	Intercept	R ²
1	SUCCR * 1000	0.016	0.0038	<0.001	0.67	0.41
	SUCCR * 1000	0.013	0.0035	<0.001	-0.36	0.55
2	1,25(OH) ₂ D, pg/mL	0.030	0.011	0.011		
	SUCCR * 1000	0.016	0.0030	<0.001	-1.74	0.70
3	1,25(OH) ₂ D, pg/mL	0.020	0.0093	0.047		
	PTH, ng/mL	0.026	0.0087	0.006		
4	SUCCR * 1000	0.016	0.0029	<0.001	-2.03	0.74
	1,25(OH) ₂ D, pg/mL	0.021	0.0089	0.03		
	PTH, ng/mL	0.023	0.0085	0.01		
5	Dietary Vitamin D	0.0034	0.0019	0.09		
	SUCCR * 1000	0.012	0.0021	<0.001		
	1,25(OH) ₂ D, pg/mL	0.014	0.0062	0.04	2.15	0.89
	PTH, ng/mL	0.019	0.0058	0.005		
	Dietary Vitamin D	0.0078	0.0016	<0.001		
	Body Mass Index, kg/m ²	-0.11	0.023	<0.001		

Predicting Urine Calcium Loss (mg/kg/24-hour)					
6	SUCCR * 1000	0.014	0.0031	<0.001	0.33
	1,25(OH) ₂ D, pg/mL	0.016	0.0091	0.10	
	PTH, ng/mL	0.026	0.0082	0.005	0.75
	Body Mass Index, kg/m ²	-0.052	0.027	0.07	