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Cross-sectional and prospective data on urinary calcium and urinary stone disease

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Cross-sectional and prospective data on urinary calcium and urinary stone disease.

Background. Urinary calcium is considered a risk factor for urinary stone disease (USD), although prospective data are missing. This epidemiologic study investigates cross-sectionally and longitudinally the relation of urinary calcium excretion to USD.

Methods. In the Gubbio Population Study, data on USD were collected by questionnaire during medical examinations from 1989 to 1992 (baseline) and telephone interviews in 1997 to 1998 (follow-up). Baseline data collection included overnight urinary calcium excretion and use of medications. Study cohort was made of 1458 men and 1799 women, age 25 to 74 years, and not on treatment with diuretics at baseline. USD was diagnosed by: excretion of stone(s), and/or radiographic or ultrasonic evidence, and/or surgical or endoscopic removal of stone(s).

Results. At baseline, urinary calcium excretion was higher in persons with than without USD (215 and 182 μmol/hour, $P < 0.001$) and related to USD prevalence independent of gender, age, and other variables ($P < 0.001$). Among persons without USD at baseline, baseline urinary calcium excretion was higher in persons with than without incident USD at follow-up (202 and 181 μmol/hour, $P = 0.034$) and related to incident USD independent of gender, age, and other variables. A difference of 100 μmol/hour (about 1 SD) in urinary calcium excretion related to a difference in USD risk of 1.32 for prevalence and 1.21 for incidence (95% CI = 1.15/1.52 and 1.01/1.45, respectively) in multivariate analyses controlled for gender, age, body mass index, parental history of USD, urinary excretion of urea, sodium, and potassium.

Conclusion. Cross-sectional and prospective data show that urinary calcium excretion is a risk factor for USD.

Urinary stone disease (USD) is a common and costly medical problem in industrialized countries [1, 2]. Several evidences support the idea that high urinary calcium excretion is a risk factor for USD. First, USD is mainly due to calcium-rich stone in the upper urinary tract [3]. Second, urinary calcium affects the saturation and the rate of crystallization of calcium salts in urine, hence urinary stone formation [3–5]. Third, urinary calcium excretion is high in persons with USD, as reported first by Albright et al [6] and later by others [7, 8]. However, prospective data are missing (i.e., there are not data showing that persons without USD and with high urinary calcium excretion develop USD more frequently than persons with low-normal urinary calcium). In the absence of these data, the possibility cannot be excluded that high urinary calcium is a secondary disorder in USD, for instance due to increased fluid intake, in turn leading to reduced antidiuretic hormone–dependent tubular calcium reabsorption [9, 10]. In the absence of prospective data, also the definition of hypercalciuria appears arbitrary due to the continuous distribution of urinary calcium excretion in the population [7]. The present study reports cross-sectional and longitudinal data on the relation of urinary calcium excretion to USD in a sample of an Italian population.

Key words: hypercalciuria, risk factor, urolithiasis.

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METHODS

The Gubbio Study is an investigation on a sample of an Italian population—both genders, aged 5 to 99 years old—residing in the town of Gubbio in central Italy. Previous papers describe aims of the investigation, time of examinations, response rates, responders and nonresponders, and methods for follow-up of lethal and nonlethal events [11–16]. Data on USD were collected with use of a questionnaire during medical examinations from 1989 to 1992 (baseline) and telephone interviews in 1997 to 1998 (follow-up). Baseline examination included the collection of timed overnight urine as previously described [13, 16] and information on personal use of medications and parental history of USD. Target cohorts for present analyses were 3776 participants with ages 25 to 74 years at baseline (1733 men and 2043 women). A

total of 13.7% of the target cohort was excluded from analyses (275 men and 244 women) because 4.2% were deceased before 1997 (105 men and 53 women); 5,7% did not participate in telephone interviews (122 men and 92 women); and 3.9% reported at baseline regular treatment with diuretics (48 men and 99 women). Persons on diuretics were excluded to avoid confounding of the drugs on urinary calcium excretion and/or USD [17, 18]. Thus, study cohort comprised 3257 persons (1458 men and 1799 women) with information on baseline urinary calcium excretion and USD at baseline and follow-up. Reported information was used for diagnosis of USD according to these criteria: (*1*) urinary excretion of stone(s) and/or (*2*) radiographic or ultrasonic evidence of urinary stone(s) and/or (*3*) surgical or endoscopic operative removal of urinary stone(s). The urinary concentration of calcium, sodium, potassium, and urea was measured by automated procedures. The variation coefficient was <5% of the average in blind duplicates [13, 16]. Urinary excretion was calculated as concentration × urine flow. Data of different studies show low risk of misclassifying urinary calcium excretion due to use of overnight instead of 24-hour collections [19, 20]. In both these previous studies, overnight urinary calcium excretion was highly correlated with and precisely predicted 24-hour urinary calcium excretion since daytime and nighttime urinary calcium excretion of the same day are highly correlated [19, 20]. Analyses on overnight and 24-hour urinary calcium excretion of two different days were done in a subgroup of participants. Urinary excretion of urea, sodium, and potassium were used as markers of dietary intake of total protein, salt, and potassium [21–23].

Statistical procedures included an analysis of variance (ANOVA) without and with adjustment for covariates, multivariate logistic regression analyses, chi-square analysis for linear trends along groups, Student *t* test for paired observation, and Spearman correlation. The difference in the relative risk of USD for a given difference in urinary calcium was calculated with 95% CI by exponentiation of logistic regression coefficients (±SE × 1.96).

Table 1. Descriptive statistics at baseline: Mean ± SD or prevalence

	Men	Women	Men and women
Number of persons	1458	1799	3257
Age *years*	48.6 ± 13.5	49.7 ± 13.4	49.2 ± 13.5
Weight *kg*	77.9 ± 11.4	65.5 ± 11.4	71.1 ± 13.0
Height *m*	1.69 ± 0.07	1.57 ± 0.06	1.62 ± 0.09
Body mass index kg/m^2	27.1 ± 3.6	26.8 ± 4.8	26.9 ± 4.3
Duration of overnight urine collection *hours*	8.23 ± 1.15	8.29 ± 1.03	8.26 ± 1.09
Urine flow *mL/hour*	56.2 ± 27.8	54.2 ± 29.6	55.1 ± 28.9
Urinary calcium concentration *mmol/L*	3.88 ± 2.20	3.66 ± 2.15	3.78 ± 2.17
Urinary calcium excretion *μmol/hour*	198 ± 116	173 ± 103	183 ± 109
Urinary sodium excretion *mmol/hour*	7.62 ± 4.52	6.27 ± 3.84	6.87 ± 4.21
Urinary potassium excretion *mmol/hour*	1.80 ± 0.95	1.51 ± 1.02	1.64 ± 1.00
Urinary urea excretion *mmol/hour*	18.0 ± 7.0	16.5 ± 6.8	16.6 ± 7.0
With urinary stone disease *number* (%)	108 (7.4%)	79 (4.4%)	187 (5.7%)
With parental history of urinary stone *number* (%)	134 (9.2%)	151 (8.4%)	285 (8.8%)

Urinary calcium excretion can be converted to mg/hour with use of the multiplier 0.04; urinary calcium concentration can be converted to mg/L with use of the multiplier 40.

RESULTS

Descriptive statistics, overnight, and 24-hour urinary calcium excretion

Table 1 reports descriptive statistics at baseline. Due to skewed distribution (skewed/SE ratio >2), urinary calcium excretion was logarithm (log)-transformed in some analyses. Mean ± SD of log-transformed urinary calcium excretion was 2.22 ± 0.27 in men, 2.16 ± 0.26 in women, and 2.19 ± 0.27 in men and women combined (μmol/hour). Median and range of urinary calcium excretion and of other urinary variables were similar to reported data (not shown) [16].

Overnight urinary calcium excretion may be used as index of 24-hour urinary calcium excretion since the correlation coefficient between overnight and 24-hour urinary calcium excretion of the same day ranges from 0.7 to 0.9 [19, 20]. To analyze the use of overnight values as predictor of 24-hour values, urinary calcium excretion was measured in overnight and 24-hour collections of two different days in a subgroup of the study cohort (72 men and 76 women; mean ± SD of age = 45.0 ± 10.7 years old). Mean ± SD was 0.184 ± 0.099 mmol/hour for overnight urinary calcium and 4.70 ± 1.93 mmol for 24-hour urinary calcium excretion. On the basis of sample size ($N = 148$) and SD in 24-hour urinary calcium excretion (1.93 mmol), the study had a power ≥95% to detect differences in mean urinary calcium excretion ≥0.58 mmol/24 hours between measured 24-hour urinary calcium excretion and 24-hour urinary calcium excretion predicted with use of overnight urine. Predicted 24-hour urinary calcium excretion was calculated as overnight urinary calcium (mmol/hour) × 24. Measured 24-hour urinary calcium excretion and predicted 24-hour urinary calcium excretion were not significantly different (4.70 ± 1.93 mmol and 4.42 ± 2.38 mmol, $P = 0.141$ in paired Student *t* test). Correlation coefficient between overnight and 24-hour urinary calcium for collections of two different days (Fig. 1) was lower than reported for collections of the same day [19] since it reflected daytime-to-nighttime variability combined with day-to-day variability [20]. Data of overnight and 24-hour collections of two different days were correlated also for urinary calcium concentration and urine flow ($r = 0.422$ and 0.321, $P < 0.001$).

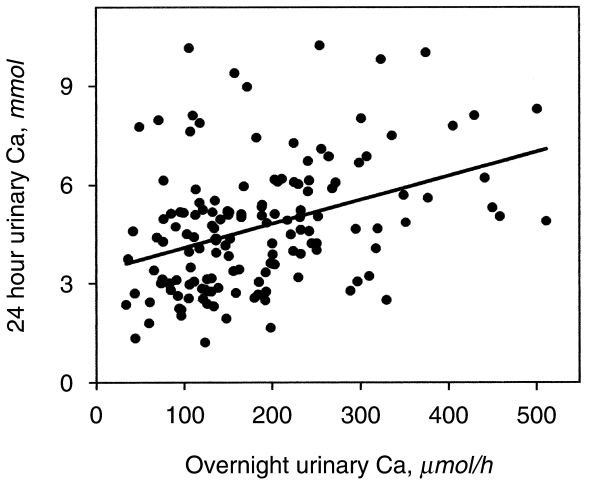

Fig. 1. Overnight urinary calcium (Ca) excretion and measured 24-hour urinary calcium excretion of two different days in a subgroup of the study cohort (72 men and 76 women). Rank order correlation coefficient = 0.387, $P < 0.001$.

Findings were similar in analyses separate by gender (not shown).

Cross-sectional analyses: Urinary calcium excretion and USD at baseline

Comparison between persons with and without USD. Table 2 shows USD prevalence by age in men and women combined; findings were similar in separate analyses for men and women (not shown). Urinary calcium excretion was higher in persons with USD than without for all ages in analyses for men and women combined and control for gender (Table 2). Urinary calcium excretion was higher in persons with USD than without also in age-controlled ANOVA done separately for men (237 and 196 μmol/hour, $P = 0.002$) and women (198 and 171 μmol/hour, $P = 0.023$).

In gender- and age-controlled ANOVA, men and women with USD compared to those without had higher urinary calcium concentration (4.21 and 3.73 mmol/L, $P = 0.003$) and urine flow (58.0 and 54.9 mL/hour, $P = 0.144$). Findings were similar in separate analyses for men and women (not shown).

Logistic analyses. Regression coefficients of urinary calcium excretion to USD were positive for all strata of age in analyses for men and women combined with control for gender and other variables (not shown). Table 2 shows for age stratum and for the entire cohort the differences in relative risk of USD prevalence calculated for a difference of 100 μmol/hour in urinary calcium excretion (about 1 SD for men and women combined) in models with control only for gender and with control for gender and other variables. Findings for urinary calcium excretion were similar in the two sets of models. In addition to gender (related to USD, $P < 0.001$), only age and parental history of USD related to USD ($P < 0.001$). Findings were similar and statistically significant with use of log-transformed urinary calcium excretion or urinary calcium concentration as independent variable (not shown).

In models analyzed separately in the two genders and controlled for age, logistic coefficients of urinary calcium excretion to USD prevalence were similarly positive in men and women (+0.00267 and +0.00242, respectively). With exponentiation of these coefficients, a difference of 100 μmol/hour in urinary calcium excretion related to a difference in USD prevalence of 1.31 for men (95% CI = 1.12/1.52), 1.27 for women (95% CI = 1.05/1.54).

Quartile analyses. The shape of the relation between urinary calcium excretion and USD prevalence was analyzed in quartiles of urinary calcium excretion. Mean urinary calcium excretion (μmol/hour) per quartile (1 to 4) was 79, 146, 211, and 359 in men, and 71, 124, 182, and 314 in women. Figure 2 shows that USD prevalence was significantly higher along quartiles in men and women. In Figure 3, the risk of USD prevalence is plotted over the mean of urinary calcium excretion in quartiles 2 to 4 compared to quartile 1 with control for gender and other variables. The relative risk was significantly increased in quartiles 3 and 4. Findings were similar in analyses by gender (not shown).

Prospective analyses: Baseline urinary calcium excretion and USD incidence

Only persons without USD at baseline were included in this set of analyses (1350 men and 1720 women). Duration of interval from baseline to follow-up (mean ± SD) was 8.45 ± 0.93 years in men and 8.45 ± 0.94 years in women. A total of 121 cases of incident USD were found (71 in men, 50 in women). Annual incidence of USD was 0.62% in men and 0.34% in women. Table 3 shows persons with USD incidence by age in men and women combined. In men and women, USD incidence was the highest for ages 35 to 44 years, the lowest for ages 65 to 74 years (not shown).

Comparison between persons with and without USD incidence. Baseline urinary calcium excretion was higher in persons with USD incidence than without for all ages in analyses for men and women combined with control for gender (Table 3). Urinary calcium excretion was higher in persons with incident USD than without in age-controlled ANOVA done separately for men (215 and 195 μmol/hour, $P = 0.144$) and women (193 and 170 μmol/hour, $P = 0.116$).

In gender- and age-controlled ANOVA, men and women with USD incidence compared to those without had higher urinary calcium concentration (4.29 and 3.72 mmol/L, $P = 0.004$) and not significantly different urine flow (53.5 and 54.7 mL/hour, $P = 0.649$). Findings were similar in analyses by gender (not shown).

Table 2. Urinary calcium excretion and urinary stone disease (USD) at baseline, men and women combined by baseline age: Mean of urinary calcium excretion in persons without and with USD, and difference in relative risk of USD prevalence associated with a difference of 100 μmol/hour in urinary calcium excretion[a]

Age	Number	With USD		Urinary calcium excretion *μmol/hour*		Difference in relative risk[b] (95%CI)	
		Number	%	Without USD	With USD	Gender-controlled models	Multivariate models[c]
25–34	592	8	1.4	156	289[e]	1.99 (1.32/3.00)	3.32 (1.78/6.21)
35–44	631	15	2.4	180	285[e]	1.80 (1.28/2.52)	1.85 (1.18/2.90)
45–54	774	43	5.6	200	251[d]	1.37 (1.09/1.72)	1.34 (1.03/1.73)
55–64	726	66	9.1	190	205	1.13 (0.91/1.41)	1.07 (0.82/1.40)
65–74	534	55	10.3	178	182	1.03 (0.79/1.34)	1.10 (0.82/1.47)
25–74	3257	187	6.5	182	215[e]	1.29 (1.15/1.46)	1.32 (1.15/1.52)

[a] About 1 SD in men and women combined
[b] Calculated by exponentiation of logistic regression coefficient
[c] With control for gender, age, body mass index, parental history of USD, urinary excretion of urea, sodium, and potassium
[d] $P = 0.005$; [e] $P \leq 0.001$ compared to persons without USD by gender-controlled analysis of variance (ANOVA); urinary calcium excretion can be converted to mg/hour with use of the multiplier 0.04; urinary calcium concentration can be converted to mg/L with use of the multiplier 40

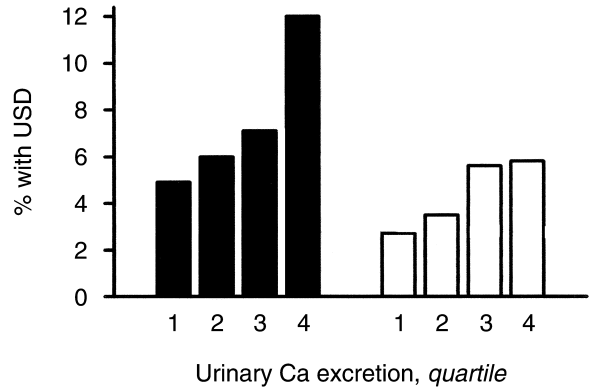

Fig. 2. Percent with urinary stone disease (USD) by quartile of urinary calcium (Ca) excretion at baseline. Number of persons per quartile (1 to 4): men (■) = 364, 366, 367, and 361; women (□) = 447, 454, 450, and 448; urinary calcium excretion (μmol/hour, minimum-maximum): men = 4–115, 116–177, 178–252, and 253–599, women = 4–101, 102–149, 150–219, and 220–598. $P < 0.001$ in men and = 0.009 in women for linear trend by chi-square analysis.

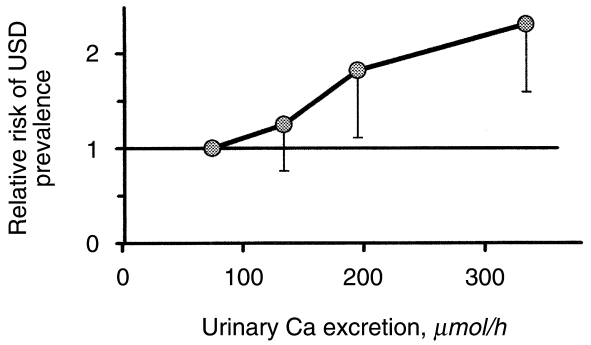

Fig. 3. Relative risk with lower limit of 95% CI for urinary stone disease (USD) prevalence over mean urinary calcium (Ca) excretion in quartiles 2 to 4 of baseline urinary calcium excretion in comparison to risk for USD prevalence in quartile 1 (risk = 1). Analyses were done in men and women combined with control for gender, age, body mass index, parental history of USD, urinary excretion of urea, sodium, and potassium. Risk was significantly increased in quartiles 3 and 4. *P* for linear trend in relative risk = 0.021.

Logistic analyses. Regression coefficients of urinary calcium excretion to USD incidence were positive for all strata of age in analyses for men and women combined with control for gender and other variables (not shown). Table 3 shows for age stratum and for the entire cohort the differences in relative risk of USD incidence calculated for a difference of 100 μmol/hour in urinary calcium excretion in models with control only for gender and in models with control for gender and other variables. Findings for urinary calcium excretion were similar in the two sets of models. Significant or borderline significant relationships to USD incidence were found for gender (women vs. men, relative risk = 0.54, 95% CI = 0.37/0.81, $P = 0.003$), parental history of USD (yes vs. no, relative risk = 1.72, 95% CI = 0.96/3.08, $P = 0.073$), and body mass index (difference of +4 kg/m^2, relative risk = 1.18, 95% CI = 0.98/1.42, $P = 0.087$). Findings were similar with control for other variables or with use of log-transformed urinary calcium excretion (not shown).

In models analyzed separately in the two genders and controlled for age, logistic coefficients of urinary Ca excretion to USD incidence were similarly positive in men and women (+0.00143 and +0.00194, respectively). With exponentiation of these coefficients, a difference of 100 μmol/hour in urinary calcium excretion related to a difference in USD incidence of 1.15 in analyses for men (95% CI = 0.95/1.39) and 1.21 for women (95% CI = 0.95/1.55).

Logistic coefficients of urinary calcium concentration to USD incidence in age-controlled models were significant in analyses for men ($P = 0.015$), borderline significant for women ($P = 0.091$), significant for men and

Table 3. Baseline urinary calcium excretion and incidence of urinary stone disease (USD), men and women combined by baseline age: Mean of baseline urinary calcium excretion in persons without and with incident USD, and difference in relative risk of USD incidence associated with a difference of 100 μmol/hour in baseline urinary calcium excretion[a]

Age	Number	With USD		Urinary calcium excretion *μmol/hour*		Difference in relative risk[b] 95% CI	
		Number	%	Without USD	With USD	Gender-controlled models	Multivariate models[c]
25–34	584	11	1.9	155	210[d]	1.48 (0.97/2.28)	1.70 (0.97/2.96)
35–44	616	35	5.7	178	205	1.23 (0.93/1.63)	1.24 (0.86/1.79)
45–54	731	30	4.1	199	217	1.13 (0.84/1.51)	1.21 (0.85/1.72)
55–64	660	34	5.2	187	190	1.03 (0.74/1.42)	1.10 (0.74/1.65)
65–74	479	11	2.3	177	198	1.19 (0.71/1.97)	1.29 (0.69/2.42)
25–74	3070	121	3.9	181	202[e]	1.17 (1.02/1.36)	1.21 (1.01/1.45)

[a] About one SD in men and women combined
[b] Calculated by exponentiation of logistic regression coefficient
[c] With control for gender, age, duration of interval from baseline to follow-up, body mass index, parental history of USD, urinary excretion of urea, sodium, and potassium
[d] $P = 0.063$; [e] $P = 0.034$ compared to persons without USD by gender-controlled analysis of variance (ANOVA); urinary calcium excretion can be converted to mg/hour with use of the multiplier 0.04; urinary calcium concentration can be converted to mg/L with use of the multiplier 40

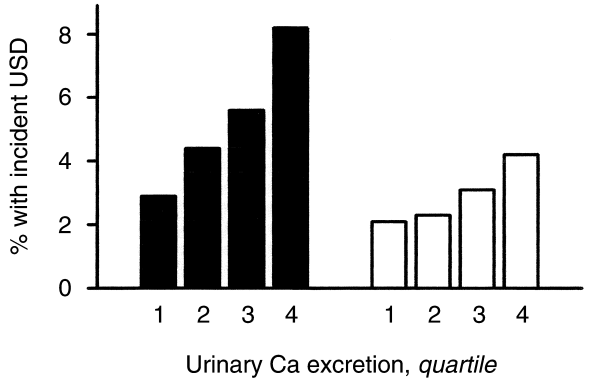

Fig. 4. Percent with urinary stone disease (USD) incidence by quartile of baseline urinary calcium (Ca) excretion. Number of persons per quartile (1 to 4): men (■) = 346, 344, 341, and 319; women (□) = 435, 438, 425, and 422; urinary calcium excretion (μmol/hour, minimum-maximum): men = 4–115, 116–177, 178–252, and 253–599; women = 4–101, 102–149, 150–219, and 220–598. $P = 0.001$ in men and 0.044 in women for linear trend by chi-square analysis.

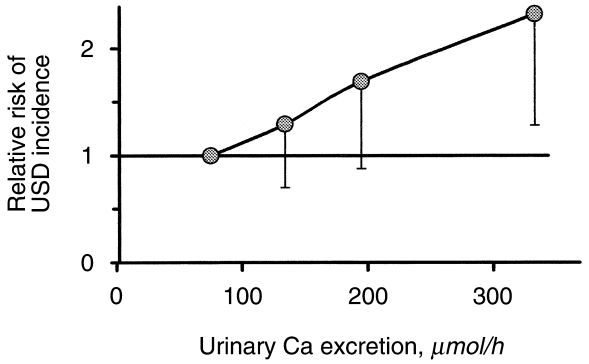

Fig. 5. Relative risk with lower limit of 95% CI for urinary stone disease (USD) incidence over mean urinary calcium excretion in quartiles 2 to 4 of baseline urinary calcium excretion in comparison to risk for USD incidence in quartile 1 (risk = 1). Analyses were done in men and women combined with control for gender, age, body mass index, parental history of USD, urinary excretion of urea, sodium, and potassium. Risk was significantly increased in quartile 4. *P* for linear trend in relative risk = 0.003.

women combined with control also for gender ($P = 0.004$). With exponentiation of these coefficients, a difference of 2 mmol/L in urinary calcium concentration (about 1 SD in men and women) related to a difference in USD incidence of 1.27 for men (95% CI = 1.05/1.54), 1.21 for women (95% CI = 0.99/1.47), and 1.25 for men and women combined (95% CI 1.07/1.45). Findings were similar with control for other variables also (not shown).

Quartile analyses. Figure 4 shows the significant linear trend for USD incidence by quartile of baseline urinary calcium excretion in men and women. In Figure 5, risk of incident USD is plotted over the mean of urinary calcium excretion in quartiles 2 to 4 compared to quartile 1 with control for gender and other variables. The increase in relative risk was significant for quartile 4. Findings were similar in analyses by gender (not shown).

DISCUSSION

The study reports the first prospective and population-based data on the relation between urinary calcium and USD. Data show that urinary calcium excretion and concentration are risk factors for USD. These variables measured at baseline were positively related not only to prevalence but also to incidence of USD. Moreover, persons with history of USD at baseline or with later incidence of USD had at baseline higher urinary calcium excretion and higher urinary calcium concentration compared to persons without USD. Present data for urinary calcium and other variables should be extrapolated cautiously to persons with recurrent USD who represent only a minority of persons with USD in the population.

Criteria for USD diagnosis were chosen to exclude false positive cases with pain or hematuria due to causes

other than USD. Data for annual incidence of USD in the Gubbio cohort were similar to rates reported for Europe [24–26] and higher than rates reported for the United States [1, 27, 28]. This might reflect the average trend toward lower urinary calcium excretion and higher urine volume for the United States in comparison to Italy as reported by an international study on urinary variables in 52 population samples from 32 countries [29]. The real incidence of USD in the Gubbio population might be somewhat higher due to asymptomatic USD. This bias could affect present results only if asymptomatic USD were highly frequent in persons with urinary calcium excretion in the low-normal range. No data support this possibility.

The study was done with use of overnight urine collections. Data from different laboratories suggest that the misclassification due to lack of 24-hour urine collection had played only a minor role since overnight urinary calcium precisely predicts 24-hour urinary calcium of the same day [19, 20]. Data for a subgroup of the Gubbio cohort show similar findings for urine of different days: 24-hour urinary calcium predicted with use of overnight urine collections and 24-hour urinary calcium measured in another day were similar (mean difference $<6\%$) and correlated. The power of analyses was $\geq 95\%$ for detecting differences ≥ 0.58 mmol between measured 24-hour urinary calcium and 24-hour urinary calcium predicted with use of overnight urine. Thus, if a difference were present, this was likely in the order of 0.5 mmol/24 hours or less. The low correlation coefficient between overnight and 24-hour urinary calcium of different days indicates that the use of a single urine sample certainly caused misclassification of some individuals due to day-to-day intraindividual variance in urine composition of free-living individuals [20]. This bias is responsible for regression dilution [23], hence, for a likely underestimate of the relation between urinary calcium and USD. Another limitation of the study is the lack of data on other factors putatively associated with USD, such as urinary oxalate and citrate. The lack of population-based and prospective data for these other factors does not allow estimates about their role in USD. Nevertheless, the possibility exists that the real determinant of USD is one (or more) of these factors and that the association of urinary calcium excretion with USD is due to the relation of urinary calcium excretion with such factor(s). The protective effects against USD of thiazide diuretics reducing urinary calcium excretion support a direct role of urinary calcium excretion in USD [17, 18]. Moreover, these other factors could explain cases of USD in persons with low urinary calcium excretion, hence, increasing the strength of the relation between urinary calcium excretion and USD.

As far as urinary calcium, study results indicate that concentration is a correlate of USD as strong as excretion. A difference of 1 SD in baseline urinary calcium excretion or concentration related to similar differences in the risk of later onset of USD. Thus, for practical scopes, the simple measure of urinary calcium concentration appears a tool for estimate of USD risk as valid as the measure of timed urinary calcium excretion. Also, the study gives new information about the shape of the relation between urinary calcium and USD. In cross-sectional and prospective analyses, USD risk increased almost linearly over urinary calcium excretion. At least in terms of USD risk, the observation of a graded and linear relationship does not support the use of the common thresholds for definition of hypercalciuria [30].

For other variables in the study, data confirm that male gender is a risk factor for USD. The relation of urinary calcium excretion to USD was similar in men and women. However, the excess of USD in men was not explained by their higher urinary calcium since gender related to USD was independent of urinary calcium excretion. Age was important in the relation between urinary calcium excretion and USD. The association of urinary calcium excretion with USD,both cross-sectionally and longitudinally, was progressively less strong with increasing the age of persons. Thus, data suggest that factors other than urinary calcium excretion become important for USD in the elderly. Parental history of USD was a predictor of USD risk independent of several variables as in the study of Curhan et al [31]. Findings for body mass index, an index of calorie balance, were not consistent and borderline significant only in prospective analyses. Urinary excretion of urea, sodium, and potassium were not related to USD and did not affect the relation of urinary calcium to USD. In previous studies, findings on the possible association with USD of dietary protein, sodium, and potassium, as measured by questionnaire or urinary markers, were conflicting [27, 28, 32]. Altogether, data indicate that the role in USD of these urinary parameters is, if any, less important than urinary calcium excretion and detectable only in studies with high statistical power.

CONCLUSION

This study reports the first prospective data on the relation of urinary calcium to USD in the population and shows, with use of overnight urine, a continuous and graded relationship of urinary calcium excretion to USD risk. Urinary calcium concentration was also a predictor of USD supporting the idea that calcium concentration is pivotal in the process of urine stone formation. The study has three practical implications. First, urinary calcium excretion can be used as marker of USD risk within the population. Second, the simple measure of urinary calcium concentration is a marker of USD risk as good as urinary calcium excretion. Third, the thresholds defining high urinary calcium should be reevaluated at least for definition of USD risk.

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