



# Reply to: Calcium/Citrate Ratio and Risk of Kidney Stone

Misan Lee<sup>1</sup> Carmen Inés Rodríguez Cuellar<sup>1,2,3</sup> Ravneet Nagra<sup>1</sup> Peter Zhan Tao Wang<sup>4</sup>  
Vipin Bhayana<sup>5</sup> Guido Filler<sup>1,5,6,7</sup>

<sup>1</sup> Division of Paediatric Nephrology, Department of Paediatrics, Children's Hospital, Mexico City, Mexico

<sup>2</sup> Departamento de Nefrología Pediátrica, Instituto Nacional de Pediatría, Mexico City, Mexico

<sup>3</sup> Department of Pediatrics, Universidad Nacional Autónoma de México, Mexico City, Mexico

<sup>4</sup> Departments of Surgery, Division of Nephrology, and Schulich School of Medicine and Dentistry, University of Western Ontario, London, Ontario, Canada

<sup>5</sup> Departments of Pathology and Laboratory Medicine, Schulich School of Medicine and Dentistry, University of Western Ontario, London, Ontario, Canada

<sup>6</sup> Lilibeth Caberto Kidney Clinical Research Unit, London Health Sciences Centre, London, Ontario, Canada

<sup>7</sup> Departments of Medicine, Division of Nephrology, and Schulich School of Medicine and Dentistry, University of Western Ontario, London, Ontario, Canada

**Address for correspondence** Guido Filler, MD, PhD, FRCPC, Medicine and Pathology and Laboratory Medicine, Children's Hospital, London Health Sciences Centre, University of Western Ontario, 800 Commissioners Road East, Rm B1-135, London ON, Canada, N6A 5W9 (e-mail: guido.filler@lhsc.on.ca).

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We recently published our article entitled “Does the Urinary Calcium/Citrate ( $U_{Ca}/U_{Ci}$ ) Ratio Add to the Diagnostic Workup of Children at Risk of Kidney Stones?” in your prestigious journal.<sup>1</sup> We have received a letter to the editor by Beuy Joob and Viroj Wiwanikit. In that letter, the authors acknowledge that our findings are in accordance with the literature, especially the study by DeFoor et al.<sup>2</sup> However, they also highlight that there is sexual variation for urine citrate.<sup>3</sup> In adults and older adolescents, there clearly is a higher urinary citrate excretion in women as compared with that in men.<sup>3</sup> Sex differences of the urinary citrate/creatinine ratio have since then been confirmed in adolescents.<sup>4</sup> These sex differences start with the onset of puberty and may explain the higher prevalence of kidney stones in men.<sup>4</sup> Interestingly, the substantial increase of nephrolithiasis in children and adolescents, however, is among adolescent girls.<sup>5,6</sup>

Our study by Lee M et al<sup>1</sup> involved 56 males with a median (25th, 75th percentile) age of 8 (3, 15) years and 41 females with a median age of 10 (6.8, 15) years, which was not statistically different ( $p = 0.2720$ , Mann Whitney U test). The details of the patients are listed in ► **Table 1**. This means that most of the patients were prepubertal. As pointed out, the

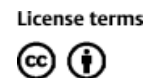
sex differences begin with the onset of puberty.<sup>4</sup> The proposed cutoff for assessing the stone risk therefore holds in our patient cohort and the main conclusion that “ $U_{Ca}/U_{Ci}$  rather than  $U_{Ci}/U_{Cr}$  may be more predictive in the clinical setting when evaluating for nephrolithiasis” remains adequate as we did not observe any sex differences for the urinary citrate/creatinine ratio (► **Fig. 1**). Unfortunately, our cohort of patients was too small to perform a subanalysis of adolescents, and we did not routinely obtain the Tanner stage to precisely determine the onset of puberty. Therefore, we do acknowledge that more work is needed to assess the utility of the urinary  $U_{Ca}/U_{Ci}$  as a predictor for nephrolithiasis or urolithiasis in pubertal adolescents. We agree with the conclusion in Joob and Wiwanikit's letter to the editor that the sex variation should be kept in mind in interpreting  $U_{Ca}/U_{Ci}$  in adolescents. We do see many adolescent girls with kidney stones who have normal  $U_{Ci}/U_{Cr}$  but abnormal  $U_{Ca}/U_{Ci}$ . The reasons for the substantial increase of kidney stones in adolescent girls remain a main question for our ongoing research.

**Conflict of Interest**  
None declared.

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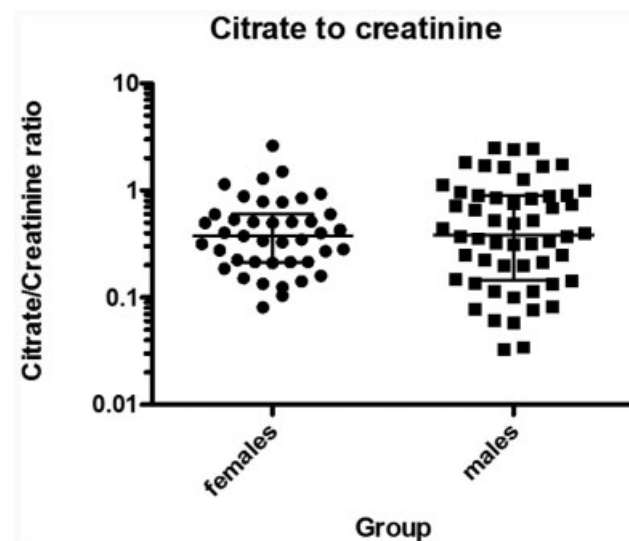


**Table 1** Patient characteristics and comparison of parameters

Group	SF	NSF	Comparison	Test
Number of patients	51	46		
Age (years, median and IQR)	8 (3,15)	10 (6.8, 15)	0.1755	Mann Whitney
Female (%)	19 (37.3%)	22 (47.8%)	0.3074	Fisher's exact test
Urinary citrate (mmol/L, median and IQR)	1.55 (0.95, 2.32)	1.675 (0.79, 3.13)	0.7743	Mann Whitney
Urinary calcium (mmol/L, median and IQR)	1.87 (1.21, 4.29)	1.0 (0.26, 2.3)	<b>0.0021</b>	Mann Whitney
Urinary sodium (mmol/L, median and IQR)	77 (30, 121)	107 (48, 154)	0.0963	Mann Whitney
Urinary potassium (mmol/L, median and IQWR)	42 (28, 101)	48 (19, 80)	0.9895	Mann Whitney
Urinary creatinine ( $\mu$ mol/L, median and IQR)	3.4 (1.5, 6.8)	4.6 (1.9, 9.0)	0.3878	Mann Whitney
Urinary oxalate ( $\mu$ mol/L, median and IQR)	189 (111, 291)	134 (38, 290)	0.1438	Mann Whitney
Urinary urate ( $\mu$ mol/L, median and IQR)	1.9 (1, 5.7)	2.3 (1, 12)	0.2544	Mann Whitney
Urinary pH (mean $\pm$ SD)	6.6 $\pm$ 0.91	6.5 $\pm$ 0.98	0.7366	t-test
Urinary specific gravity (median and IQR)	1.010 (1.005, 1.020)	1.015 (1.005, 1.020)	0.1842	Mann Whitney
Urinary citrate/creatinine (mmol/mmol, median and IQR)	0.48 (0.21, 0.90)	0.38 (0.21, 0.86)	0.8784	Mann Whitney
Urinary calcium/creatinine (mmol/mmol, median and IQR)	0.67 (0.31, 1.37)	0.24 (0.11, 0.73)	<b>0.0029</b>	Mann Whitney
Urinary calcium/citrate (mmol/mmol, median and IQR)	1.30 (0.73, 2.78)	0.68 (0.29, 1.83)	<b>0.0114</b>	Mann Whitney
Urinary sodium/potassium (mmol/mmol, mean $\pm$ SD)	2.08 $\pm$ 1.92	2.50 $\pm$ 1.36	0.3185	t-test

Abbreviations: IQR, interquartile range (25th and 75th percentiles); NSF, non-stone formers; SD, standard deviation, SF, stone formers.

Note: Statistically significant differences are in boldface. The comparison column represents the *p*-value, and in the test column, the test that was used is listed (based on the distribution and data type).



**Fig. 1** Comparison of urinary citrate/creatinine ratio in the aforementioned study.<sup>1</sup> There was no significant difference between both sexes.

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