Dietary treatment of urinary risk factors for renal stone formation. A review of CLU Working Group

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HYPERCALCIURIA

Author	Type	N°	Design	Results	Comments & evaluation
26: Ortiz A. Omega-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid in the management of hyperciuric stone former. Urology. 2012;79: 282-6.	Uncontrol and longitudinal study; retrospective	29 hypercalciuric patients treated for urolithiasis	24-hour urinalysis during/after empiric dietary reccomendation and fish oil supplementation	Decrease in urinary calcium, oxalate and calcium oxalate supersaturation; increase in urinary citrate	Very low quality
41: Nouvenne A, Meschi T, Prati B, et al. Effects of low-salt diet on idiopathic hypercalciuria in calcium-oxalate stone formers: a 3-mo randomized controlled trial. Am J Clin Nutr. 2010; 91:565-70.	Uncontrol and longitudinal study; retrospective	210 patients affected by idiopathic calcium stone disease and hypercalciuria	2 groups: 1) 102 control diet 2) 108 low salt diet for 3 months, valueted with 2 non consecutive 24-hour urinalysis	Low sodium group shows lower urinary sodium, calcium and lower oxalate excretion	Good quality
70: Pak CY, Odvina CV, Pearle MS, et al. Effect of dietary modification on urinary stone risk factors. Kidney Int. 2005; 68: 2264-73.	Uncontrolled longitudinal study; retrospective	951 patients with calcareous stone	24-hour urine samples were collected during ramdom diet and after dietary modification (restriction of calcium, oxalate, sodium and meat products).	Secondary rise in urinary oxalate occurring from calcium restriction can be avoided by concurrent dietary oxalate restrction	Very low quality
105: Borghi. Comparison of two diets for the prevention of recurrent stones in idiopathic hypercalciuria. N Engl J Med. 2002; 346:77-84.	RCT	Two diets in 120 men with recurrent calcium oxalate stone and hypercalciuria	60 men with diet normal calcium but recuced protein and salt; 60 men traditional low calcium diet	At five years, 12 patients of normal calcium had a relapse against 23 of low calcium that show an increase in xalate escretion	RCT control group at very high risk
112 Yasui T, Tanaka H, Fujita K, et al. Effects of eicosapentaenoic acid on urinary calcium excretion in calcium stone formers. Eur Urol. 2001; 39:580-5.	Uncontrolled longitudinal study; prospective	88 pt with urinary stone	Administration of highly purified preparation (EPA) (1800 mg/day) for 3 months and 18 months	Urinary calcium was significantly reduced in hypercalciuric but not in normocalciuric	Very low quality

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No conflict of interest declared.

128 Liatsikos EN, Barbalias GA. The influence of a low protein diet in idiopathic hypercalciuria. Int Urol Nephrol. 1999; 31:271-6.	Uncontrolled longitudinal study; prospective	42 hypecalciuric pt with recurrent stone disease	Normocalcium (900-1000 mg/d) and moderate low protein diet (0.8 g/Kg BW) per 10 days Blood exam and 24 h urine	Statistically significant variation in 24 h urine calcium, oxalate, sodium, urate and hydroxiproline	Very low quality
137: Giannini. Acute effects of moderate dietary protein restriction in patients with idiopathic hypercalciuria and calcium nephrolithiasis	Uncontrolled longitudinal study; prospective	18 patients with idiopathic hypercalciuria and calculi	Before and after 15 days of protein restriction diet the patients were evaluated serum and urinary measures	Decrease in urinary calcium and oxalate	Very low quality
152: Messa. Different dietary calcium intake and relative supersaturation of calcium oxalate in the urine of patients forming renal stone	Uncontrolled longitudinal study; prospective	34 stone forming patients	Assenssing supersaturation of urinary calcium oxalate with free choice diet and after 30 days of low calcium (440 mg/d) diet	Dietary calcium restriction has potentially deleterious effets on lithogenesis by increasing the relative supersaturation of calcium oxalate	Very low quality
188: Rothwell. Does fish oil benefits stone formers? J Urol. 1993; 150:1391-4.		18 hypercalciuric recurrent stone patients		Decreasing in calcium excretion	Full text non available
231: Tizzani A, Casetta G, Piana P, Vercelli D. Wheat bran in the selective therapy of absorptive hypercalciuria: a study performed on 18 lithiasic patients. J Urol. 1989; 142:1018-20.	Uncontrolled longitudinal study; prospective	18 pt with diagnosis of absorbitive hypercalciuria	Supplement diet of 14 gm wheat bran at the 2 princpal meal for 90 days. Assessment of mineral metabolism at 45 and 90 days	Significant decrease in calciuria	Very low quality
251. Strohmaier WL, Kalchthaler M, Bichler KH. Calcium metabolism in normal and in hypercalciuric patients on Farnolith, a dietary fibre preparation. Urol Res. 1988; 16:437-40.	Uncontrolled longitudinal study; prospective	6 pt normal and 6 pt with absorbitive hypercalciuria type 1	Administration of farnolith (granular powder of different dietary fiber) 30 g/day for 18 months	Significant reduction of calciuria and oxaluria	Very low quality
294: Jaeger Ph. Influence of the calcium of the diet on the incidence of mild hyperoxaluria in idiopathic renal stone formers. Am J Nephrol. 1985; 5:40-4.	Uncontrolled longitudinal study; prospective	110 men idiopathic calcium stone former (38 normocalciuric; 63 hypercalciuric)	Considered 3 dietary conditions (free-choice, Ca-enriched and low-Ca diet)	Mild hyperoxaluria can be encountered in each group of patients; its incidence is influenced by the calcium content of diet (increase in low calcium diet	Full text non available

HYPEROXALURIA

Author	Type	N°	Design	Results	Comments & evaluation High = High M = Medium L = Low VL = Very Low
1. Noori 2014	RCT	29+28 recurrent RSF with hyperoxaluria (urine oxalate > 40 mg/d)	24-hour urinary composition Calorie-controlled Dietary Approaches to Stop Hypertension (DASH)-style diet (high in fruit, vegetables, whole grains, and low-fat dairy products and low in saturated fat, total fat, cholesterol, refined grains, sweets, and meat) (29 pts) Vs Low-oxalate diet (28 pts) 8 weeks	Increase of urinary oxalate excretion in the DASH versus the low-oxalate group (point estimate of difference, 9.0mg/d; 95% CI, -1.1 to 19.1mg/d; P=0.08). Trend for calcium oxalate supersaturation to decrease in the DASH versus the low-oxalate group (point estimate of difference, -1.24; 95% CI, -2.80 to 0.32; P=0.08)	H
2. Siener 2013	Experimental non controlled	20 healthy subjects	24-hour urine specimens diet normal in oxalate (6 weeks)	Urinary oxalate excretion increased significantly from 0.354 ± 0.097 at baseline to 0.542 ± 0.163 mmol/24 h under the oxalate-rich diet and remained elevated until the end of treatment,	M

			oxalate-rich diet (1 week) oxalate-rich diet + 2.6 g/day of a lactic acid bacteria preparation (5 weeks) diet normal in oxalate 4 weeks after treatment	as did relative supersaturation of calcium oxalate. Four weeks after treatment, urinary oxalate excretion and relative supersaturation of calcium oxalate fell to reach initial values.	
Schwen 2013	Retrospective	149 idiopathic RSF with hyperoxaluria	24-hour urine collections dietary management	Urine oxalate and supersaturation of calcium oxalate were significantly (P < .001) reduced by 8.9 ± 19.2 mg/d and 1.7 ± 4.3, respectively. Women lowered urine oxalate nearly twice as much as men (12.7 ± 2.0 mg/d vs 6.7 ± 2.2 mg/d, P = .022) and body mass index (BMI) negatively correlated with oxalate reduction (Pearson's r = -0.213).	L
3. Kıraç 2013	Experimental non controlled	108 idiopathic recurrent calcium oxalate RSF	24-hour urinalysis specialized diets for their 24-hour urine abnormalities	Hyperoxaluria, was found in 84 (77%), The differences between the oxalate before and after the dietary intervention were significant (p < 0.05).	M
4. Eisner 2012	Retrospective	311 RSF	24 hour urine	On multivariate analysis, an increasing quintile of urine magnesium was associated with decreasing hyperoxaluria (β = -0.37, 95% confidence interval -0.6 to -0.14, P < .05 for trend).	L
5. Ortiz-Alvarado 2011	Experimental non controlled	95 RSF with idiopathic hyperoxaluria	24-hour urine collection Dietary measures by registered dietician (urine volume > 2 L per day, sodium restriction, protein moderation, increased calcium intake with meals and low oxalate diet combined with oral pyridoxine 50- 200 mg daily)	Significant decrease in urinary oxalate excretion (58.26 ± 27.05 to 40.61 ± 15.04, P < .0001).	M
6. Lieske 2010	RCT	40 RSF with mild hyperoxaluria on a controlled diet .	Placebo (14) vs probiotic (14) vs synbiotic preparation (12)	Urinary oxalate fell as did CaOx and brushite supersaturation (SS) on the controlled diet compared with baseline on a free-choice diet Neither study preparation reduced urinary oxalate excretion nor calcium oxalate supersaturation	H
7. Ferraz 2009	Experimental non controlled	14 RSF patients	oxalate restriction period (1 week) oxalate-rich diet (2 weeks) (200 mg/day) oxalate-rich diet + lyophilized Lactobacillus casei and Bifidobacterium breve (2 weeks).	Urinary oxalate excretion was significantly higher after oxalate-rich diet versus baseline (27 +/- 8 vs. 35 +/- 11 mg/24 h) No difference between oxalate-rich diet and oxalate-rich diet plus LC and (35 +/- 11 vs. 33 +/- 10 mg/24 h	M
8. Nouvenne 2009	Observational cohort study	56 RSF	Free diet with a normal-calcium, low-animal protein, low-salt diet for a 3-month period Idiopathic calcium oxalate RSF with mild hyperoxaluria (> 40 mg/d) versus Historical control group of 20 hyperoxaluric patients treated with a low-oxalate diet	Mean oxaluria level decreased from 50.2 to 35.5 mg/d with the normal-calcium, low-animal protein, low-salt diet and from 45.9 to 40.2 mg/d with the traditional diet	L
9. Penniston 2009	Experimental non controlled	22 RSF with hyperoxaluria	Dietary changes alone (diet group, n = 10) Dietary changes + calcium citrate with meals Mean follow-up 317 and 266 days, respectively	Urinary oxalate excretion decreased from 56 to 43 mg/d in the diet group and from 60 to 46 mg/d in the diet +supplement group Calcium oxalate supersaturation decreased from 3.48 to 1.83 in the diet group and from 2.37 to 1.52 in the diet + supplement group	M
10. Goldfarb 2007	RCT	20 calcium RSF with idiopathic hyperoxaluria (>40 mg/d)	Placebo Vs Lactic acid bacteria preparation 28 days	Urinary oxalate was 73.9 mg at baseline and 72.7 mg after placebo treatment 59.1 mg at baseline and 55.4 mg after Oxadrop	H
11. Zimmermann 2005	Experimental non controlled	25 healthy volunteers	First phase [13C2]oxalate absorption test	First phase Oxalate absorption on low-oxalate diet was 7.9 +/- 4.0%.	M

			low-oxalate (63 mg) for 2 days vs high-oxalate (600 mg) for 2 days Second phase (4 subjects) Absorption test on high-oxalate diet for 6 weeks Wash out for 4 weeks with individual normal diet and absorption test on high-oxalate diet	On high-oxalate diet absorption almost doubled (13.7 +/- 6.3%) Second phase Oxalate absorption after 6 weeks of high-oxalate diet significantly decreased (8.2 +/- 1.7%) After the wash-out phase, the absorption was again high (14.1 +/- 2.2%) on the 600 mg oxalate challenge.	
12. Massey 2005	Experimental Non controlled	29 Stone formers 19 age- and gender-matched non-stone formers	Low oxalate diet with supplementation of 1000 mg ofascorbic acid twice each day for 6 d versus no supplementation for 6 d in random order. On 6th day evaluation of oxaluria, intestinal absorption of oxalic acid (13C2 oxalic acid) and Tiselius Index	19/48 (12 RSF + 7 non SF) showed an increase of oxaluria > 10% after ascorbic acid supplementation because of a 31% increase in the percentage of oxalate absorption (10.5 +/- 3.2% vs 8.0 +/- 2.4%) and a 39% increase in endogenous oxalate(544 +/- 131 vs 391 +/- 71 micromol/d) This group had a greater 24-h Tiselius Risk Index (TRI) with ascorbic acid supplementation (1.10 +/- 0.66 vs 0.76 +/- 0.42) The increase of oxaluria was greater in normoxaluric both RSF or not	M
13. Siener 2005	Experimental non controlled	76 men and 31 women with idiopathic calcium oxalate stone disease	24-hour urine self-selected diet vs balanced standardized diet	After a balanced diet significant increase in urinary volume, pH and citrate excretion and significant decrease in urinary calcium and uric acid excretion. No change occurred in urinary oxalate and magnesium excretion.	M
14. von Unruh 2004	Experimental non controlled .	8 healthy subjects 3 F and 5 M	Measurement of intestinal absorption of oxalate by [(13)C(2)]oxalate with different calcium intakes from 5 mmol (200 mg) to 45 mmol (1800 mg) of calcium.	Within the range of 200 to 1200 mg calcium per day, oxalate absorption depended linearly on the calcium intake from a mean absorption of 17% +/- 8.3% with 200 mg calcium per day to 2.6% +/- 1.5% with 1200 mg calcium per day, Beyond 1200 mg/d calcium intake reduced oxalate absorption only one-tenth as effectively. With 1800 mg calcium per day, the mean absorption was 1.7% +/- 0.9%.	M
15. Peña de la Vega 2004	Experimental non controlled .	13 non stone subjects receiving home total parenteral nutrition (TPN)	Two different IV doses of vitamin C (100 and 200 mg)	Urinary oxalate excretion increased on the 200-mg vitamin C dose, from 0.34 +/- 0.13 to 0.44 +/- 0.17 mmol/d (mean increase = 0.10 mmol/d; p = .04; 95% confidence interval 0.004 to 0.19 mmol/d).	M
16. Meschi 2004	Experimental non controlled	12 normal adults 26 idiopathic calcium stone formers characterized by hypocitraturia	Normal subjects: two-week period of fruit and vegetable elimination Idiopathic calcium stone formers: supplementation of the diet with a fair quantity of low-oxalate fruits and vegetables	Normal subjects decreased urinary excretion of potassium, magnesium, citrate and oxalate and increased that of calcium and ammonium. The relative saturation for calcium oxalate and calcium phosphate increased from 6.33 to 8.24 and from 0.68 to 1.58 respectively. Idiopathic calcium stone formers: Increased urinary volume, pH, potassium, magnesium and citrate while it decreased the excretion of ammonium. The relative saturation for calcium oxalate and uric acid fell from 10.17 to 4.96 and from 2.78 to 1.12 respectively.	M
17. Oehlschläger 2003	Retrospective	22 calcium RSF	Plasma values and urine excretion of creatinine, calcium, oxalate, magnesium, and citrate before and on days 1 and 2 after ESWL under conditions of a standardized diet	After ESWL, hyperoxaluria was noted in 10 patients compared with 2 before ESWL. Oxalate/creatinine was significantly increased after ESWL.	L

				The AP(CaOx) index EQ(s) and the CaOx risk index were significantly increased after ESWL	
18. Siener 2003	Observational Retrospective	93 + 93 calcium oxalate stone formers with hyperoxaluria (>or= 0.5 mmol/day) or with normal oxalate excretion (<0.4 mmol/day), .	24-hour weighed dietary record. 24-hour urine during the completion of the food record.	The mean daily intakes of energy, total protein, fat and carbohydrates were similar in both groups. The mean daily intakes of water (in food and beverages), magnesium, potassium, dietary fiber and ascorbic acid were greater in patients with hyperoxaluria In hyperoxaluric patients the mean daily intake of oxalate and calcium were 130 mg/day and 812 mg/day as compared to 101 mg/day of oxalate and 845 mg/day of calcium among patients without hyperoxaluria Multiple logistic regression analysis revealed that urinary oxalate excretion was significantly associated with dietary ascorbate and fluid intake, and inversely related to	L
19. de O G Mendonça 2003	Retrospective and experimental controlled	70 calcium RSF and 41 healthy subjects (HS) 58 calcium RSF randomly selected to receive milk (N = 28) or dark (N = 30) chocolate as an oxalate load.for 3 days.	24-hour urine sample and 3-day dietary record Milk chocolate (94 mg Ox + 430 mg Ca) Dark chocolate (94 mg Ox + 26 mg Ca)	RSF presented mean Ox intake of 98 +/- 137 mg/d, similar to that of HS (108 +/- 139 mg/d). Mean Ox and vitamin C intake was directly correlated with Ox excretion only in CSF Dark chocolate induced a significant increase in mean urinary Ox (36 +/- 14 versus 30 +/- 10 mg/24 hr) not observed in the milk chocolate group	M
20. von Unruh 2003	Experimental non controlled	120 healthy volunte(60 F, 60 M)	13C2 Oxalate absorption Standard diet at a fixed 800 mg calcium daily	Absorption 2.2% to 18.5% (mean +/- SD 7.9% +/- 4.0%). Mean intra-individual SD was 3.39% +/- 1.68%.	M
21. Siener 2002	Experimental non controlled	10 healthy male volunteers	Risk of calcium oxalate crystallisation, calculated as relative supersaturation (EQUIL2) from urine Self-selected diet (SD) for 14 days Western-type diet (WD) for 5 days Normal mixed diet (ND) for 5 days Ovo-lacto-vegetarian diet (VD) for 5 days	Risk of calcium oxalate crystallisation was highest during ingestion of diets SD and WD. ND resulted in a significant decrease in relative supersaturation with calcium oxalate by 58% compared with diet WD (decline in urinary calcium and uric acid excretion and increase in urinary volume, pH-value and citrate excretion) No decrease in the risk of calcium oxalate crystallisation was observed on VD (increase in urinary pH, citrate and magnesium excretion and decline in calcium excretion, but increase in urinary oxalate by 30%).	M
22. Borghi 2002	RCT	60+60 RSF	24 hour collection A. Low calcium diet (<10 mmol) (n= 60) B. Low protein (<93 g) and low sodium (50 mmol) diet (n=60)	Decrease of oxalate urinary excretion on low- protein low-sodium diet 411+/-132 vs 344 +/-92 [p<0.001] Decrease of calcium oxalate product and calcium oxalate supersaturation on low- protein low-sodium diet 1.82 (1.26) vs 0.70 (0.48) mol -6/L [p<0.01] 9.6 (4.2) vs 5.1 (2.5) [p<0.01]	H
23. Nguyen 2001	Experimental non controlled	12/8 idiopathic calcium RSF with/without mild metabolic hyperoxaluria 13 healthy males	24-hour urinary excretion of oxalate , 4-pyridoxic acid and markers of protein intake (urea, phosphate, uric acid, and sulfate) moderate protein diet (MPD; 160 g meat/fish daily) for 5 days vs high meat protein diet (HPD; 700 g meat/fish daily) for 5 days	Switching from MPD to HPD Increased urinary excretion rates of all markers of protein intake Increased mean urinary excretion of oxalate increased in ICSFs but not in controls.	M

			During both diets oxalate-rich nutrients were avoided, as well as sweeteners and vitamin C-containing medicines.		
24. Kočvara, 1999	RCT	242 first calcium RSF Multicentric	Specific dietary regimen adjusted according to metabolic evaluation (n=113) General dietary measures (n=94) 3 year follow up	On tailored diet urinary oxalate was unchanged 351+/156) vs 334+/-138)	L
25. Giannini 1999	Experimental non controlled	18 RSF with idiopathic hypercalciuria	diet with 0.8 g protein x kg x d and 955 mg Ca for 15 day	uric acid ($P < 0.005$) and oxalate ($P < 0.01$) decreased after protein restriction	M
26. Trinchieri 1998	Retrospective	476 idiopathic RSF (286 M, 190 F)	24-hour urine sample and dietary diary for a 3-day period on their customary diets.	Daily urinary oxalate excretion was significantly ($p < 0.001$) related to urinary volume ($R = 0.24$), vitamin C intake ($R = 0.33$) and body mass index ($R = 0.37$) and inversely related to calcium intake ($R = -0.35$).	L
27. Nomura 1995	Experimental non randomized	66 RSF	Dietary counseling in accordance to Recommended Dietary Allowance for Japanese with reduction of intakes of total protein, animal protein, fat, and carbohydrates	Reduction of excretion of oxalate owing to the diet counseling program	
28. Massey 1993	Experimental non controlled	13 hyperoxaluric calcium RSF	Low calcium diet Vs Low oxalate diet plus dairy Vs High oxalate plus dairy	Highest levels of urinary oxalate higher after high oxalate diet, lowest after low oxalate plus dairy diet	M
29. Mahe 1993	Observational cross-sectional	84 calcium RSF	Dietary evaluation	Hyperoxaluric patients showed higher lipid intake, lower glucidic and calcium intake;	VL
30. Laminski 1991	Experimental non controlled	207 RSF 40 (19%) with mild hyperoxaluria	Dietary oxalate restriction in hyperoxaluric patients	18 (45%) responded to dietary oxalate restriction by normalising their urinary oxalate.	
31. Gleeson MJ, et al. Urology. 1990; 35:231-4.	RCT	17 hypercalciuric RSF	low-calcium, low-oxalate diets with (p pts) or without (8 pts) the addition of 30 g of dietary fiber as unprocessed wheat bran	Oxaluria was decreased 21.4 % by diet alone compared with 3.9 % in the diet and fiber treatment group. Diet alone resulted in a 5.6 % decrease in calciuria compared with a 23.5 % decrease with the addition of the fiber.	M
32. Marangella M, et al. Br J Urol. 1989; 63:348-51.	Experimental non controlled	41 + 40 non RSF 20 calcium RSF	41 practising vegetarians 40 healthy subjects on a free, mixed, "mediterranean" diet. 20 idiopathic calcium RSF on low calcium, low oxalate diet with high or restricted animal protein content	Vegetarians higher urinary oxalate levels than controls, calcium levels markedly lower, and urinary saturation with calcium/oxalate significantly higher. Calcium RSF on low animal protein intake showed a decrease in calcium excretion but no variation in urinary oxalate. Decrease in calcium oxalate saturation was only marginal	L
33. Nakada 1988	Experimental non controlled	85 idiopathic RSF	Intake of high-calcium diet for 5-6 days Administration of 60 mg/day of pyridoxal phosphate for 3 months	Reduction of urinary oxalate excretion after high-calcium diet and after pyridoxal administration	M
34. Mitwalli 1988	Experimental non controlled	12 recurrent calcium oxalate RSF with idiopathic hyperoxaluria	Pyridoxine in oral doses of 250-500 mg daily	Urinary oxalate excretion significantly decreased	M
35. Brown 1987	Experimental non controlled	22 recurrent calcium RSF	Administration of an hospital diet containing 1000 mg calcium per day	Urinary oxalate excretion fell significantly	L
36. Griffith HM, 1986	Observationa cross-sectional	88 RSF 88 age and sex matched controls	dietary history using a standardised questionnaire.	Cases with a high urinary oxalate had a significantly higher intake of vitamin C than controls.	L
37. Jaeger 1985	Experimental non controlled	101 male idiopathic calcium RSF	free-choice vs Ca-enriched vs low-Ca diet	On low-Ca diet mean oxalate excretion increased significantly in hypercalciurics but not in normocalciurics	M
38. Bataille P. 1983	Experimental non	Idiopathic calcium	oxalate load (200 g of spinach) on a calcium	Increase in oxalate excretion after oxalate load	M

	controlled	RSF with normocalciuria, dietary hypercalciuria and idiopathic hypercalciuria	unrestricted vs calcium restricted diet	significantly greater on calcium restricted than on calcium unrestricted diets in all groups of patients	
39. Butz 1980	Experimental non controlled	Healthy and oxalate RSF	sodium oxalate at two doses (130 and 400 mg daily) ascorbic acid (1-6 g daily) glycine (4.5 g daily) protein (50 g daily, 50% animal protein) had any effect on serum or urinary oxalate.	The high dose of oxalate induced significant hyperoxaluria Serum oxalate but not urinary oxalate increased upon ingestion of ascorbic acid Glycine (4.5 g daily) or protein (50 g daily, 50% animal protein) administration had any effect on serum or urinary oxalate.	M
40. Rose GA, 1975.	Observational	regional variations in diet	Dietary evaluation	high intake of fruit and vegetables may protect against renal calculi	VL
HYPERURICOSURIA					
Author	**Type**	**N°**	**Design**	**Results**	**Comments & evaluation**
Pais, 2007	RCT	65 CaOx RSF vs 61 controls	Administration for 3 days of a standardized formula diet (Ensure adjusted for caloric needs as determined by the Ohio Weight Loss Planner)	mean uric acid excretion lower in the stone-forming group (337+/-64 vs 379+/-76 mg/g of Cr)	H
Siener, 2005	Experimental non controlled	109 RSF 78 M 31 F	hyperuricosuria in 41.3% on self-selected diet balanced standardized diet	significant decrease in uric acid excretion	M
Kočvara, 1999	RCT	11 Vs 94 RSF	Tailored diet vs General diet	Urinary uric acid Baseline vs 6 months follow up 3.74 (1.18) mmol (SD) vs 3.62 (1.34) mmol (SD)	M
Hiatt, 1996	RCT	50 Vs 49 RSF	Low animal protein and high fiber diet (animal protein 56-64 gm/day, purine containing foods 75 mg/day, increase of fruits, vegetables, and whole grains + 1/4 cup bran/day) Vs fluid intake and adequate calcium intake	Urinary uric acid Baseline vs 6 months follow up Mean mmol (SD): A (n=43) 4.36 (0.22) B (n=37) 4.40 (0.29) Mean mmol (SD): A (n=32) 3.8 B (n=28) 4.2	H
Mateos Antón, 1984	Experimental non controlled	9 RSF with hyperuricosuria on a self-selected diet.	purine-free diet	normalized uric acid excretion in 4 of these 9 patients.	L
Breslau, 1983	Experimental non controlled	11 normal subjects	diet containing 10 mEq. sodium per day for 10 days vs 240 mEq. sodium daily for another 10 days.	uric acid clearance increased from 5.9 plus or minus 0.4 to 7.1 plus or minus 0.6 ml. per minute (p less than 0.01). serum uric acid decreased from 6.4 plus or minus 0.4 to 5.5 plus or minus 0.3 mg./dl. (p less than 0.001) total urinary excretion of uric acid did not change (533 plus or minus 24 to 535 plus or minus 26 mg. per day).	M

HYPOCITRATURIA					
Author	**Type**	**N°**	**Design**	**Results**	**Comments & evaluation**
Barcelo P ,et al. J Urol. 1993; 150:1761-4		57 RSF with hypocitraturia	randomly group taking 30 to 60 mEq. potassium citrate daily group receiving placebo 3 years	- Potassium citrate therapy caused a significant increase in urinary citrate, pH and potassium 18 patients receiving potassium citrate for 3 years - stone formation significantly declined after treatment from 1.2 +/- 0.6 to 0.1 +/- 0.2 per patient year (p < 0.0001) - 13 patients (72%) disease remission 20 patients taking placebo - no significant change in stone formation rate (1.1 +/- 0.4 to 1.1 +/- 0.3 per patient year) - 4 patients (20%) in remission. Adverse reactions to potassium citrate were mild	H
Ettinger B, et al. J Urol. 1997; 158:2069-73.	RCT	64 RSF	placebo versus potassium-magnesium citrate (42 mEq. potassium, 21 mEq. magnesium, and 63 mEq. citrate) daily for up to 3 years.	Placebo New calculi formed in 63.6% Potassium-magnesium citrate 12.9% of subjects receiving potassium-magnesium citrate.	H
Domrongkitchaiporn, et al. Am J Kidney Dis. 2006; 48:546-54.	Experimental non controlled & observational	83 RSF 44 M 39 F	One month of oral potassium chloride supplementation in a subgroup of 58 RSF	Hypocitraturia is independently associated to urinary potassium level, net gastrointestinal alkaline absorption, calcium level, and titratable acid. Hypocitraturic subjects had lower fruit intake Potassium chloride supplementation resulted - significant increase in urinary citrate excretion - no alteration in fractional excretion of citrate	M
Hess B, et al. Nephrol Dial Transplant. 1994; 9:642-9.	Observational	34 male calcium RSF 23 normal urinarycitrate 6 low urinary citrate 5 hypo-citraturia < 1.70 mmol/day	24 hour urine 3-day NH4Cl loading test (0.95 mEq/kg BW daily in 3 doses)	Urinary citrate correlated with - urine volume - vegetable fibre intake - gastrointestinal alkali absorption Urinary volume, dietary fibre and alkali are lower RSF with low-/hypo-cit. On a plot of urine pH versus serum bicarbonate, 10 of 11 RCSF with low-/hypo-cit, but only six of 23 with normo-cit (P = 0.0004) fell off the normal range, indicating incomplete RTA.	L
Siener R, et al. J Urol. 2005; 173:1601-5.	Experimental non controlled	108 calcium RSF 76 M 31 F	self-selected diets vs balanced standardized diet	increase in - urinary volume, pH and citrate decrease - urinary calcium and uric acid excretion. - no change in urinary oxalate and magnesium excretion.	M
Trinchieri A, et al. Urol Res. 2006; 34:1-7.	187 calcium RSF 114 M 73 F		24-h dietary record and 24-h urine sample	Significantly negative correlation between daily PRAL and daily urinary citrate Daily urinary citrate was related to the intakes of copper riboflavin and piridoxine	L

Trinchieri A, et al. Eur J Clin Nutr. 2013; 67:1077-80.	Observational Case-control study.	123 calcium RSF 123 age- and sex-matched controls.	Dietary history by 24-h Recall	Increased risk of renal stone formation for the highest quartile of PRAL Significant protection against stone formation for a high consumption of vegetables (two or more servings/day)	M
Meschi T, et al. Kidney Int. 2004; 66:2402-10.	Experimental non controlled	12 normal adults 26 idiopathic calcium stone formers characterized by hypocitraturia	Normal subjects: two-week period of fruit and vegetable elimination Idiopathic calcium stone formers: supplementation of the diet with a fair quantity of low-oxalate fruits and vegetables	Normal subjects decreased urinary excretion of potassium, magnesium, citrate and oxalate and increased that of calcium and ammonium. The relative saturation for calcium oxalate and calcium phosphate increased from 6.33 to 8.24 and from 0.68 to 1.58 respectively. Idiopathic calcium stone formers: Increased urinary volume, pH, potassium, magnesium and citrate while it decreased the excretion of ammonium. The relative saturation for calcium oxalate and uric acid fell from 10.17 to 4.96 and from 2.78 to 1.12 respectively.	M
Haleblian GE, et al. J Endourol. 2008; 22:1359–1366			Citrate concentrations measured using 1H NMR.	- grapefruit juice (64.7 mmol/L) - lemon juice (47.66 mmol/L) - orange juice (47.36 mmol/L) - pineapple juice (41.57 mmol/L) - reconstituted lemonade (38.65 mmol/L) lemonade flavored Crystal Light (38.39 mmol/L) ready to consume not from concentrate lemonade (38.24 mmol/L) cranberry juice (19.87 mmol/L) lemon-flavored Gatorade (19.82 mmol/L) homemade lemonade (17.42 mmol/L) - Mountain Dew (8.84 mmol/L) - Diet 7Up (7.98 mmol/L)	Not evaluated
Seltzer MA, Low RK, McDonald M, et al. J Urol. 1996; 156:907-9.	Experimental non controlled	12 RSF	- 4 ounces of reconstituted lemon juice (5.9 gm. citric acid) mixed with tap water to a total volume of 2 l. and consumed at uniform intervals throughout the day.	- increased urinary citrate levels during lemonade therapy from 142 mg. daily (range less than 10 to 293) at baseline to 346 mg. daily (range 89 to 814) after treatment ($p < 0.001$) - urinary calcium excretion decreased an average of 39 mg. daily, while oxalate excretion was unchanged - the lemonade mixture was well tolerated.	L
Aras B, et al. Urol Res. 2008; 36:313-7	Experimental controlled non randomized	30 calcium RSF with hypocitraturia	Basal vs 3-month follow up in 3 groups - Fresh lemon juice 60 mEq/day (approximately 85 cc/day) - Potassium citrate (60 mEq/day) - Dietary recommendation	2.5-, 3.5- and 0.8-fold increase in urinary citrate level in the 3 groups Decreased urinary calcium in lemon juice and potassium citrate groups no significant difference of urinary oxalate levels decrease in urinary uric acid levels in all groups	M
Kang, DE, et al. J Urol. 2007; 177:1358-1362	Observational age- sex-matched	11+11 hypocitraturic RSF L	Patients on lemonade therapy for a mean of 44.4 months Age and sex matched control group of patients treated with oral slow release potassium citrate for a mean of 42,5 months	Lemonade - increased urinary citrate levels (mean increase +383 mg per day, $p < 0.05$). Potassium citrate - increased in urinary citrate (mean increase +482 mg per day, $p < 0.0001$). Mean pretreatment and posttreatment stone burden in the lemonade group was 37.2 and 30.4 mm(2), respectively ($p > 0.05$). and stone formation rate decreased from 1.00 to 0.13 stones per patient per year ($p > 0.05$).	L
Koff, et al. Urology. 2007; 69:1013–1016	Experimental cross over	21 RSF	Patients were treated with lemonade therapy and potassium citrate supplementation in a prospective cross-over trial	Potassium citrate, but not lemonade, improved citrate levels and urinary ph to a significant degree.	M

Odvina CV. Clin J Am Soc Nephrol. 2006; 1:1269-1274	Experimental crossover study	9 healthy subjects 4 RSF	Distilled water, orange juice, or lemonade while on constant metabolic diet.	Orange juice vs lemonade - higher net gastrointestinal alkali absorption - higher urinary pH and citrate compared with control - not significantly different urinary calcium - higher urinary oxalate – lower supersaturation of calcium oxalate compared with control - lower calculated undissociated uric acid compared with both control and lemonade phases - higher calculated supersaturation of brushite compared with both control and lemonade phases.	M
Penniston KL, et al. Urology. 2007; 70:856-860	Observational Retrospective	Calcium oxalate RSF	Lemonade therapy (group 1, n = 63) versus potassium citrate plus lemonade (group 2, n = 37)	Urinary citrate increased maximally by 203 and 346 mg/day for groups 1 and 2, respectively. The change from baseline to the last visit was significant (P = 0.008) only in group 2.	L
Wabner CL. & Pak CY. J Urol. 1993; 149:1405-1408.	Experimental	8 healthy men and 3 men hypocitraturic RSF	Placebo phase and 2 treatment phases with 1.2 l. orange juice (containing 60 mEq. potassium and 190 mEq. citrate per day) with meals or potassium citrate tablets (60 mEq. per day) with water and meals	Orange juice compared to potassium citrate : - delivered an equivalent alkali load - caused a similar increase in urinary pH and urinary citrate - decreased urinary undissociated uric acid levels - increased the inhibitor activity (formation product) of brushite (calcium phosphate) - increased urinary oxalate and did not alter calcium excretion, whereas potassium citrate decreased urinary calcium without altering urinary oxalate	H
Goldfarb DS, et al. J Urol. 20011; 166:263-7.	Experimental non controlled	10 healthy subjects	- 240 ml. of tap water at least 3 times daily for 7 days during the control period. - 7 days experimental period 240 ml. of grapefruit juice 3 times daily	- increase oxalate excretion - increase citrate excretion - no net change in the supersaturation or upper limit of metastability of calcium oxalate, calcium phosphate or uric acid. Crystal aggregation and growth inhibition by urinary macromolecules was not affected by grapefruit juice ingestion.	L
Tosukhowong, et al. Urol Res. 2008; 36:149-55.	Experimental non controlled	RSF	3 month periods with - solution containing lime powder (Group 1, n=13), - potassium citrate (Group 2, n=11) - lactose as placebo regimen (Group 3, n=7). Lime powder and potassium citrate contained equal amounts of potassium (21 mEq) and citrate (63 mEq).	- increase in urinary pH, potassium and citrate in Group 1 and 2. – Increase plasma potassium and red blood cell glutathione (R-GSH) and decrease urinary malondialdehyde in Group 1, but not in Group 2.	L
Gettman MT, et al. J Urol. 2005 ; 174:590-4	Experimental non controlled	12 normal subjects and 12 calcium RSF	7-day periods 1 l of cranberry juice daily vs 1 l of deionized water	Cranberry juice Increased - urinary calcium, urinary oxalate and urinary saturation of calcium oxalate Not changed - urinary citrate Slightly increased - urinary magnesium increased Decreased - urinary pH Increased - urinary ammonium - titratable acidity - net acid excretion Decreased - urinary uric acid Decreased - urinary saturation of brushite and monosodium urate Increased undissociated uric acid	L
McHarg T, Rodgers A, Charlton K. BJU Int. 2003 ; 92:765-8	Experimental study with crossover	20 healthy subjects	10 subjects drank 500 mL of cranberry juice diluted with 1500 mL tap water for 2 weeks 10 subjects drank 2000 mL of tap water for the same period. 2-week 'washout' period before the two groups crossed over.	- oxalate and phosphate excretion decreased - citrate excretion increased. - decrease in the relative supersaturation of calcium oxalate	M

Kessler T, Jansen B, Hesse A. Eur J Clin Nutr. 2002; 56:1020-3	Experimental		3 loading phases -in each loading phase a neutral mineral water was substituted for 330 ml of the particular juice.	Cranberry juice: - decreased urinary pH, - increased oxalic acid - increased relative supersaturation for uric acid Blackcurrant juice: - increased the urinary pH - increased urinary citric acid - increased oxalic acid Plum juice - no significant effect on the urinary composition	L
Baia Lda C, et al. J Endourol. 2012; 26:1221-6.	Experimental non controlled	30 hypocitraturic RSF	2-hour urine samples - fast - 2, 4, and 6 hours after the consumption of 385 mL (13 oz) of - freshly squeezed orange juice (n=10) - freshly blended melon juice (n=10) - freshly squeezed lime juice (n=10).	Comparable increases of urinary citrate in all groups urinary potassium, pH, and net gastrointestinal absorption (NGIA) increased only after consumption of melon and orange juices. The pH of melon juice was higher and the PRAL value was more negative compared with orange juice	L
Goodman JW, et al. Urol Res. 2009; 37:41-6.	experimental	19 healthy subjects	Two sports drinks in 9 and 10 subjects : Performance (Shaklee Corp., Pleasanton, CA, USA) and Gatorade (Gatorade, Chicago, IL, USA) Performance: pH 4.3, 21 mmol/L sodium, 5.3 mmol/L potassium, 0.8 mmol/L calcium, 19.5 mmol/L of citrate. Gatorade: pH 2.9 to 3.2, 20 mmol/L sodium, 3.2 mmol/L potassium, negligible calcium, 13.9 mmol/L citrate 946 ml (32 oz) of tap water daily for 3 days 946 ml (32 oz) of sports drink daily for 3 days	Performance - increased citrate excretion by 170 mg/day - increased urine pH by 0.31 Gatorade: - no change of urinary citrate excretion or pH. Both: - no significant differences in the excretion of sodium and calcium or any supersaturation value.	L
Passman CM, et al. J Endourol. 2009; 23:347-50.	experimental	6 healthy subjects	5-day periods. 2-day washout between each sequence Le Bleu water caffeine-free Diet Coke Fresca (citrate containing).	- urinary volumes higher and supersaturation of calcium oxalate lower compared with a self-selected dietary regimen - decreased uric acid in the Fresca cohort - no statistically significant differences for any of the urinary parameters	L

ELDERLY

Title	Type	N° pts	Design	Results	Comments & evaluation
1.Torpy JM, Lynm C, Glass RM. JAMA patient page. Frailty in older adults. JAMA 2006; 296:2280					
2.Purser JL, Kuchibhatla MN, Fillenbaum GG, et al. Identifying frailty in hospitalized older adults with significant coronary artery disease. J Am Geriatr Soc. 2006; 54:1674-1681.					
3.Usui Y, Matsuzaki S, Matsushita K, et al. Urolithiasisin geriatric patients. J Exp Clin Med. 2003; 28: 81.					
4.Gentle DL, Stoller ML, Bruce JE, Leslie SW. Geriatric urolithiasis. J Urol. 1997; 158:2221-4.	Observational	6000 pz	standardized questionnaires, serum biochemical profiles and 24-hour urinalyses	Hypocitraturia alone (29%)was the most common abnormal urinary value in the geriatric stone population. Uric acid stones occurred less fre- quently (5%)in the younger group compared to the geriatric stone formers.	Grade M

5.Asper R.: Epidemiology and socioeconomic aspects of urolithais. Urol Res. 1984; 12:1					
6.Hiatt RA, Dales LG, Friedman GD, et al. Frequency of urolithiasis in prepaid medical care program. Amer J Epidemiol. 1982; 115 255.					
7.Moesch C, Charmes JP, Gaches F, et al. Crystalluria prevalence in the elderly. Eur J Med. 1993; 2 512.					
8. Knoll T, Schubert AB, Fahlenkamp D, et al. Urolithiasis through the ages: data on more than 200,000 urinary stone analyses. J Urol. 2011; 185:1304-11	Prospective	224,085 pz	Urinary stone analyses were evaluated to determine the incidence of stone composition and identify age and gender distributions	uric acid stones tended to become more common at ages 60 to 79 years	Grade L
9.Krambeck AE, Lieske JC, Li X, et al. Effect of age on the clinical presentation of incident symptomatic urolithiasis in the general population. J Urol. 2013; 189:158-64	Observational	1,590 pz	data on individuals diagnosed with stone disease were obtained he the Rochester Epidemiology Project	uric acid and atypical stones were associated with older age	Grade L
10.Stoller ML. Gout and stones or stones and gout? J Urol. 1995; 154:1670.					
11.Riese RJ, Sakhaee J. Uric acid nephrolithiasis: Dathogenesis and treatment. J Urol. 1992; 148:7657.					
12.Yagisawa T, Hayashi T, Yoshida A, et al. Metabolic characteristics of the elderly with recurrent calcium oxalate stones. BJU Int. 1999; 83:924-8.	Prospective	88 pz	70 pz <60 years 18 pz >60 years. All recurrent stone formers were evaluated metabolically	Hyperossaluria was the most common abnormaliy in elderly patients	Grade L
13.Freitas Junior CH, Mazzucchi E, Danilovic A, et al. Metabolic assessment of elderly men with urolithiasis. Clinics (Sao Paulo). 2012; 67:457-61.	Case-control study	51 pz men older than 60 years of age (II) who had a first episode of renal colic (lumbar or flank pain) or an incidental diagnosis of renal stones after age 60.control arm were selected from a database of men with benign prostate hyperplasia (BPH).	Urinary metabolic assessment	Hypocitraturia in 56.0% of the case arm patients and 15.4% of the control arm patients (p = 0.002). Hypernatriuria was detected in 64.0% of the case arm patients and in 30.8% of the controls (p = 0.017).	Grade L
14.Fardellone P, Sebert JL, Garabedian M, et al. Prevalence and biological consequences of vitamin D deficiency in elderly institutionalized subjects. Rev Rheum. 1995; 62:576.					
15.Komar L., Nieves J, Cosman F, et al. Calcium homeostasis of an elderly population upon admission to a nursing home. J Amer Ger Soc. 1993; 41:1057.					
16.Taylor EN, Curhan GC. Body size and 24-hour urine composition. Am J Kidney Dis. 2006; 48:905-15.	Observational	3,273 pz Stone-forming and non-stone-forming patients.	Age range 25-75 years. 24-hour urine samples from participants with a history of kidney stones and randomly selected controls were collected	Participants with greater BMIs excreted more urinary oxalate (P for trend < 0.04), uric acid (P < 0.001), sodium (P < 0.001), and phosphate (P < 0.001) than participants with lower BMIs	Grade L
17.Ettinger B, Pak CY, Citron JT, et al. Potassium-magnesium citrate is an effective prophylaxis against recurrent calcium oxalate nephrolithiasis. J Urol. 1997; 158:2069-73.	RCT	64 patients	All subjects were instructed in a diet that recommended restricting salt, refined sugar, foods rich in oxalate and animal protein but allowed up to 2 servings of dairy foods per day. Subjects were further instructed to take 2 tablets of the study drug 3 times daily. This provided a daily dose of 42 mEq. potassium, 21 mEq.	New calculous events occurred in 63.6% of the placebo group and in 12.9% of the potassium-magnesium citrate group. Compared with placebo, risk of treatment failure using potassium magnesium citrate was 0.16 (95% confidence interval 0.05 to 0.46)	Grade L