Nephrolithiasis

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Disclosure

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- Educational reasons: small educational grants for nephrology rounds speakers, teaching tool and students (no influence from the company)
  - Atrazeneca
  - Amgen
  - Ortho Janssen
  - Otsuka
  - Boehring Ingelheim

Objectives

- Review the prevalence of nephrolithiasis
- Describe the different types of nephrolithiasis
- List the risk factors for stone formation
- Depict the medical and surgical management of nephrolithiasis
- Summarize the nutritional modification necessary

Prevalence of Nephrolithiasis

- General population prevalence of kidney stone formation is 10–12 % of men and 5–6 % of women
- CKD population has a 2 fold higher risk of calcium stone formation

- a retrospective case-control study based on data from the Rochester Epidemiology Project found stone formers to have a 51 % to 68 % increased risk for a sustained elevation in serum creatinine (SCr) and for a clinical diagnosis of CKD compared with non-stone formers

- a report based on the Third National Health and Nutrition Examination Survey (NHANES III), obese stone formers had a modest decrease in estimated glomerular filtration rate (eGFR) compared with non-stone formers

Different type of nephrolithiasis

- Calcium phosphate
- Calcium oxalate
- Uric acid
- Struvite
- Cystine

Risk factors for nephrolithiasis

- Uric acid stone: hypertension, diabetes mellitus, obesity, metabolic syndrome, and vascular disease
- Hyperparathyroidism, hyperthyroidism, Rheumatoid arthritis
- Males with higher prevalence and incidence of stones than females
- Females more likely to be younger to have kidney stone, calcium phosphate
- Higher body weight, older age, white race associated with stone formation
- Family history
- Critical jobs: truck drivers and pilots
- Hypercalciuria
- hypocitraturia

History and physical examination

History:

- **Stone history: number, side, pain, interventions**
- **Medical history: gout, DM2, obesity, malabsorption syndrome, distal rta, sarcoidosis, IBD, MSK**
- **Hyperparathyroidism, thyroid**
- **Primary hyperoxaluria**
- **Surgical history: bariatric surgery, short bowel**
- **Dietary history**
- **Family history**
- **Drug history**

Physical:

- **Volume status**
- **CVA tenderness**
- **Evidence of autoimmune disease or gout**

24 hour urine

- Calcium
- Oxalate
- Citrate
- Uric acid
- Ph
- Volume
- Creatinine
- Sodium
- Potassium (use of k citrate)

chloride

magnesium

phosphorus

urea

sulphate (protein intake)

ammonium

osmolarity

Investigations

- Urine
- Urinalysis
- Urine c and s
- Stone analysis

- Kidney imaging
- Ctscan
- Ultrasound
- Xray

- Use of houndsfield units to help identify stones

Medical management

- Acute renal stone
  - Size of stone
  - Presence of hydronephrosis
  - Volume resuscitation
  - Tamsulosin
  - Rule out infection
- Chronic nephrolithiasis
  - Volume status
  - Stone burden
  - Urine osmolality
  - Urine pH
  - Urine chemistry of how to prevent

Approach to calcium based vs uric acid based stone

- Calcium based
  - Check for the amount of calcium in urine, if elevated use thiazide diuretic
  - Normal calcium diet
  - Assess for hyperparathyroidism and hyperoxaluria, hypocitraturia
- Uric acid based
  - Serum Uric acid and history of gout
  - Urine uric acid amount
  - Low purine diet, alkalinize urine and use of medication to lower serum uric acid level

Targeted treatment

- High sodium in the urine
- High urea in urine
- Hypocitraturia
- Hypercalciuria
- Concentrated urine
- High oxalate in urine
- hyperuricemia

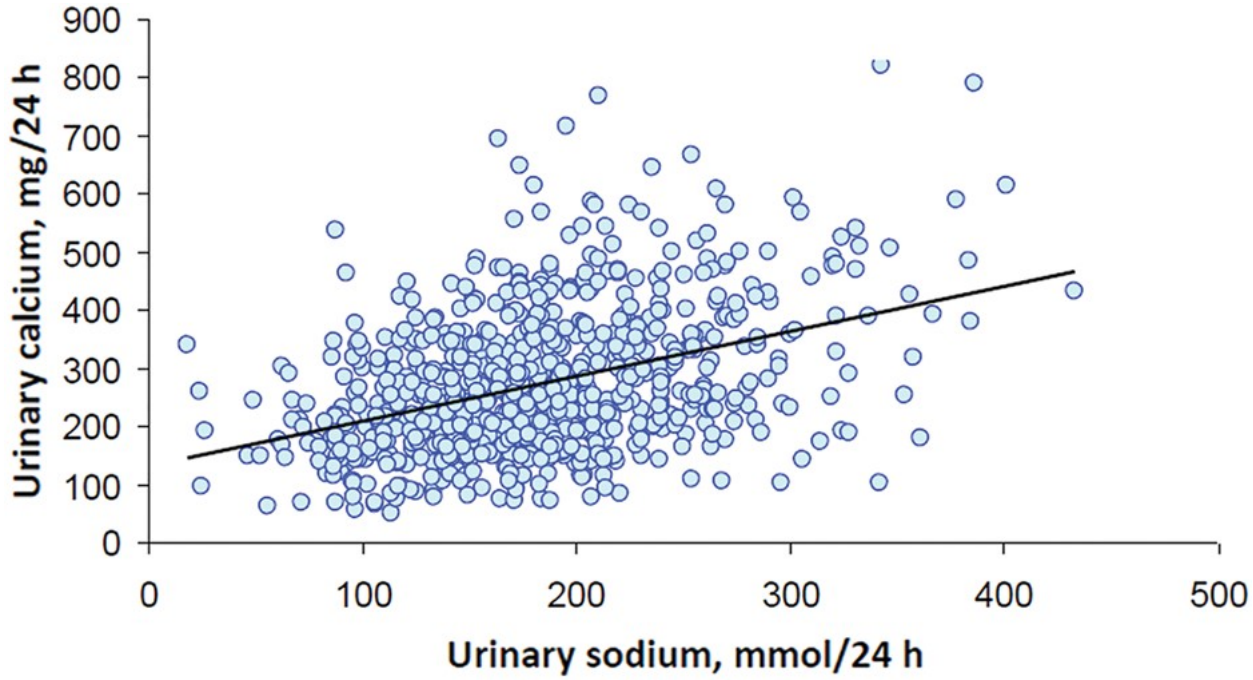
- Lower sodium in diet
- Lower protein in diet
- Replace with k citrate
- Lower calcium in urine: thiazide
- Increase fluid intake
- Adequate calcium intake
- Low purine diet, add allopurinol

Surgical management

Remove stone by

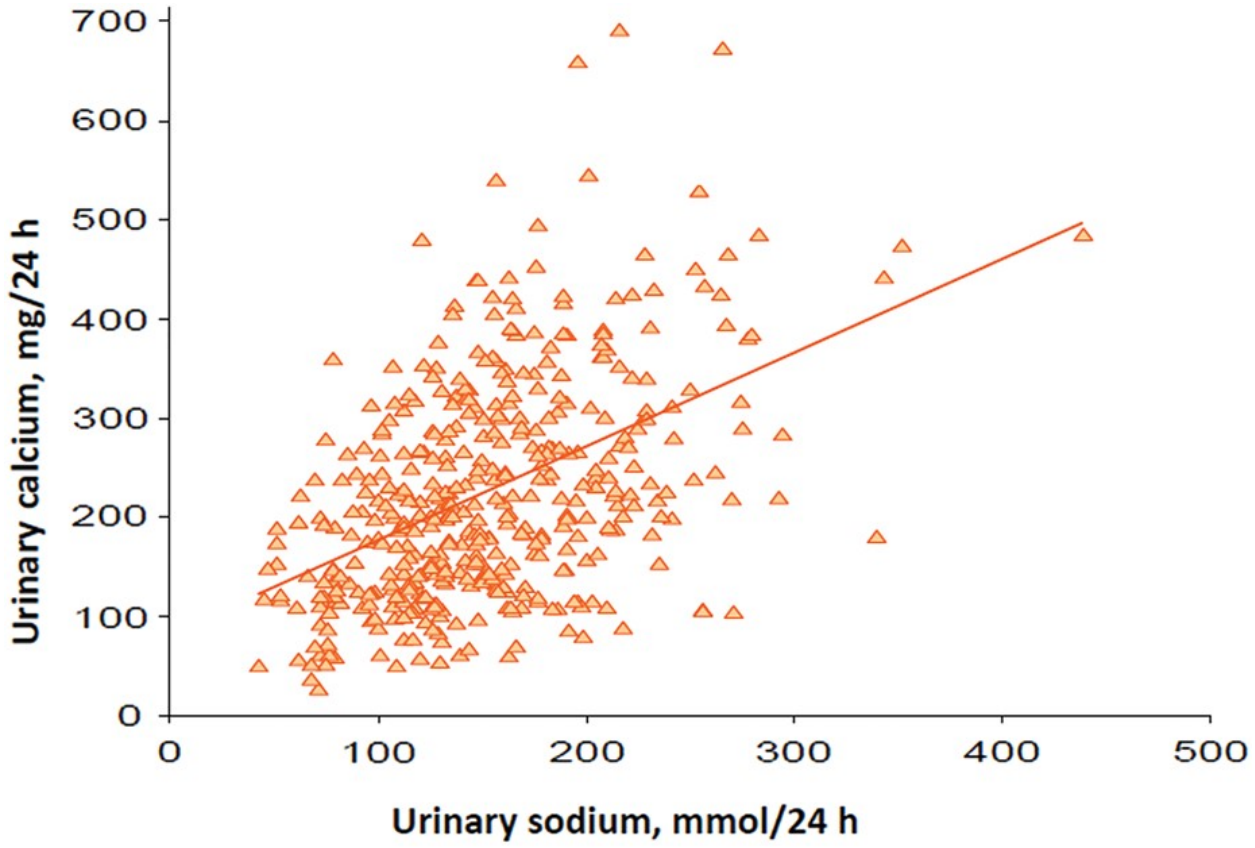
- Laser Lithotripsy
- Percutaneous nephrolithotomy
- Ureteroscopy with Ureteric stenting

FIGURE 1: Correlation of calciuria–sodiuria in a case series of 1192 males from Parma Kidney Stone Clinic, 1986–2011.



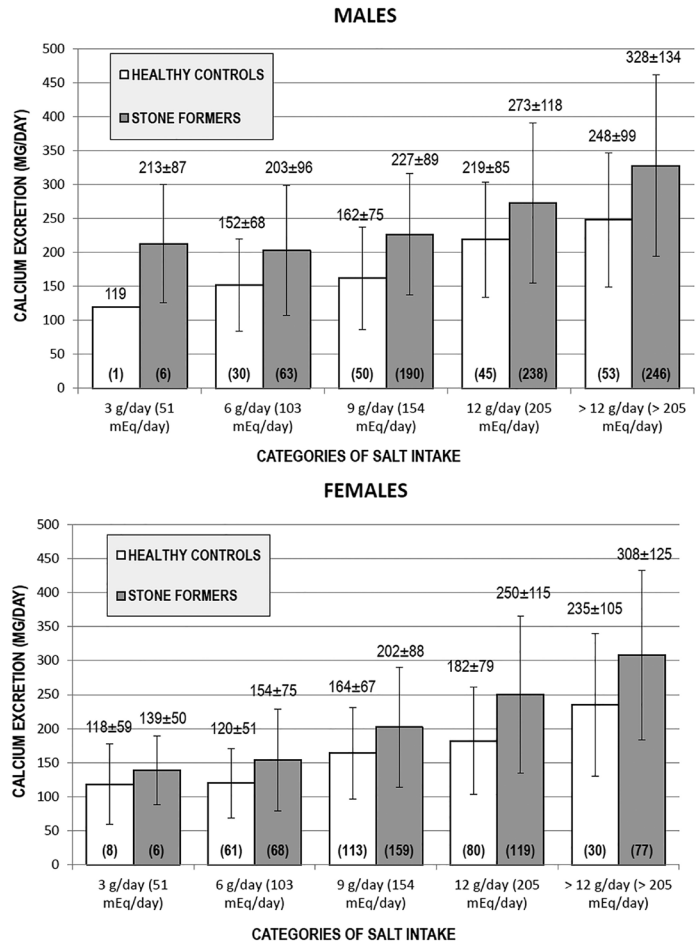
Nephrol Dial Transplant, Volume 31, Issue 1, January 2016, Pages 39–45, https://doi.org/10.1093/ndt/gfu243

FIGURE 2: Correlation of calciuria–sodiuria in a case series of 760 females from Parma Kidney Stone Clinic, 1986–2011.



Nephrol Dial Transplant, Volume 31, Issue 1, January 2016, Pages 39–45, https://doi.org/10.1093/ndt/gfu243

FIGURE 3: Comparison of calcium excretion in male and female stone formers versus male and female healthy controls, ...



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Diet in nephrolithiasis

• Reduced sodium	• < 50 mEq– 100mEq/day
• Reduced protein	• < 52 g/day or 1.2g/kg/day
• Normal calcium	• 750-1200mg/day
• Reduced glycemic index/fructose	
• High potassium	• >120mEq/day (egfr normal)
• (low oxalate: debated)	• < 200mEq/day
• Low purine diet	• 75mg /day
• Low acid load	
• Fluid intake	• 2-3 l/day

Fink, H. A., Akornor, J. W., Garimella, P. S., MacDonald, R., Cutting, A., Rutks, I. R., Monga, M., & Wilt, T. J. (2009). Diet, Fluid, or Supplements for Secondary Prevention of Nephrolithiasis: A Systematic Review and Meta-Analysis of Randomized Trials. *European Urology*, *56*(1), 72-80.

Alkali diet: potential renal acid load index

- Acid forming foods to avoid
  - Meats
  - Fish
  - Coffee
  - Alcohol
  - High salt foods
  - preservatives
- Alkali
  - Vegetable and fruit based diet
  - Low protein diet
  - Vegan even better

Glycemic index

- Glycemic load can be calculated for foods
- **Glycemic Load = (Quantity of carbohydrate content x GI) / 100.**
- Glycemic Load Chart - Glycemic Index (glycemic-index.org)
- Less than 100 in total in a day

POTASSIUM

- HIGH
  - POTATOES UNBOILED/CHIPS
  - POTATOE/TOMATOE/VEGETABLE SOUPS
  - MILK (LIMIT TO ½ CUP A DAY)
  - BRAN
  - DRIED FRUIT
  - RAISANS
  - COFFEE/CHOCOLATE/OVALTINE/
  - FUDGE/CAKES
  - YEAST
  - PEANUT BUTTER/NUTS/CAKES
  - Tomato, banana, coconut, avocado, kiwi, dried fruits, apricot, grapes, black currants, fresh plums, rhubarb
  - Parnips, onions, celery, fresh peas, mushrooms, sprouts, spinach, beans, beetroot, coleslaw
- LOW
- PASTA/RICE/BOILED POTATOES
- CEREALS WITHOUT BRAN
- MEAT
- TEA/LEMONADE/DILUTED FRUIT SQUASHES
- PLAIN BISCUITS/CUSTARDS/CREAMS/
- BOILED SWEETS
- APPLE/PEAR/ONE SLICE PINEAPPLE, 2 THIN SLICES OF MANGO, ONE SLICE OF MELON, 15-20 BLACKBERRIES, 15-20 RASPBERRIES, 8-10 STRAWBERRIES
- BOIL VEGETABLES: frozen peas, mixed veg
- Cabbage, broccoli, cauliflower, carrots, turnip, green beans, sweet corn, green and red pepper

Hypertension and Nephrolithiasis

- Increase odds of nephrolithiasis among those with hypertension
- Odds ratio range of 1.31-1.96

Shang, W., Li, Y., Ren, Y. *et al.* Nephrolithiasis and risk of hypertension: a meta-analysis of observational studies. *BMC Nephrol* **18,** 344 (2017). https://doi.org/10.1186/s12882-017-0762-8

- Mechanisms
  - Predisposed factors: obesity, hyperuricemia, diet, essential hypertension, other genetic disorders such as primary hyperoxaluria
  - Endocrine: hyperparathyroidism, hyperthyroidism/hypothyroidism, hypercortisolism, primary hyperaldosteronism
  - Normal calcium handling
  - Hypercalciuria: endocrine, drugs, genetics

Primary hyperparathyroidism

- Presentation usually with hypercalcemia and hypophosphatemia
- Other signs acute kidney injury, bone pain and pruritus

- Neck ultrasound/ctscan
- Parathyroid sestimibi

- Treatment
  - Calcium mimetic drugs
  - Surgical removal of parathyroid adenoma

Vitamin D deficiency (secondary hyperparathyroidism)

- Highly prevalent (80%)
- Aging population, geographical reasons, diet, comorbidity such as IBD, celiac disease or short bowel syndrome
- Secondary hyperparathyroidism

- Replace low dose
- Avoid additional calcium intake, will increase hypercalciuria

- Elkoushy MA, Sabbagh R, Unikowsky B, Andonian S. Prevalence and metabolic abnormalities of vitamin D-inadequate patients presenting with urolithiasis to a tertiary stone clinic. Urology. 2012 Apr;79(4):781-5. doi:

Proposed mechanisms of CKD in stone disease

- Renal stones can lead to tubular atrophy, interstitial fibrosis and glomerulosclerosis
- inflammation and fibrosis leading to severe kidney damage
- Recurrent infection and scarring
- Recurrent interventions for stone removal, worsens the scarring
- Recurrent stone formation due to renal tubular acidosis
- Certain drugs worsen stone formation, diuretics furosemide and spironolactone

- Alberta Kidney Disease Network database and evaluated the association of kidney stones with ESRD in a large cohort from the general population

(n = 3 089 194)

- Nephrolithiasis cases (only 0.8% of the sample) were identified by diagnostic codes as well as physician claims.
- They showed that any kidney stone episode during up to 11 years of follow-up was associated with an increased risk of subsequent ESRD (hazard ratio 2.16), CKD (hazard ratio 1.74), or doubling of serum creatinine (hazard ratio 1.94) (Fig. 1).
- they also observed a significant modification by sex such that among women, nephrolithiasis had a stronger association with ESRD among women than among men. The strength of the association of nephrolithiasis with ESRD was consistent with other studies, and the predisposition of women to nephrolithiasis-associated ESRD reproduced findings of prior studies [18,21].

In our ckd clinic

- About 10.2% have nephrolithiasis
- Associated with lower phosphate in serum, higher serum uric acid level and higher tsh level

- In review J Nephrol Urol, THE ROLE OF THYROID-STIMULATING HORMONE IN NEPHROLITHIASIS ASSOCIATED WITH CHRONIC KIDNEY DISEASE, Sameena Iqbal[1], Sero Andonian[1], Davine Yang[2], Celena Scheede-Bergdahl[2], and Khashayar Rafat Zand[1]

In ESRD

- The incidence of de novo nephrolithiasis in ESRD patients on HD was 10.5%.

- Increased serum uric acid, decreased serum magnesium and ionized calcium, and absence of hypertension were associated with increased stone-formation in ESRD patients on HD.

- Hesswani, C., Iqbal, S., Rafat Zand, K., Sun, S., Unikowsky, B., Reinhold, C., & Andonian, S. (2019). Identifying risk factors for development of nephrolithiasis in endstage renal disease patients. *Canadian Urological Association Journal*, *14*(5), E185-90.

New agents under review

- Hydroxycitrate
- Renavive: phillantus niruri
- Phtate (Inositol hexaphosphate): Prevents calcium salt formation

- Heilberg IP, Goldfarb DS. Optimum nutrition for kidney stone disease. Adv Chronic Kidney Dis. 2013 Mar;20(2):165-74.

- Prezioso D, Strazzullo P, Lotti T, Bianchi G, Borghi L, Caione P, Carini M, Caudarella R, Ferraro M, Gambaro G, Gelosa M, Guttilla A, Illiano E, Martino M, Meschi T, Messa P, Miano R, Napodano G, Nouvenne A, Rendina D, Rocco F, Rosa M, Sanseverino R, Salerno A, Spatafora S, Tasca A, Ticinesi A, Travaglini F, Trinchieri A, Vespasiani G, Zattoni F; CLU Working Group. Dietary treatment of urinary risk factors for renal stone formation. A review of CLU Working Group. Arch Ital Urol Androl. 2015 Jul 7;87(2):105-20.

Summary

- Nephrolithiasis
  - Clinical examination
  - Work up
  - Medical vs surgical intervention
  - Hormonal interventions
- Complications

Hypertension

Chronic kidney disease/ESRD

infections

Public health concern: it is important to move the rocks