Nephrolithiasis and systemic Disease

Rahele Hamedanian

Nephrologist

Isfahan university of medical sciences

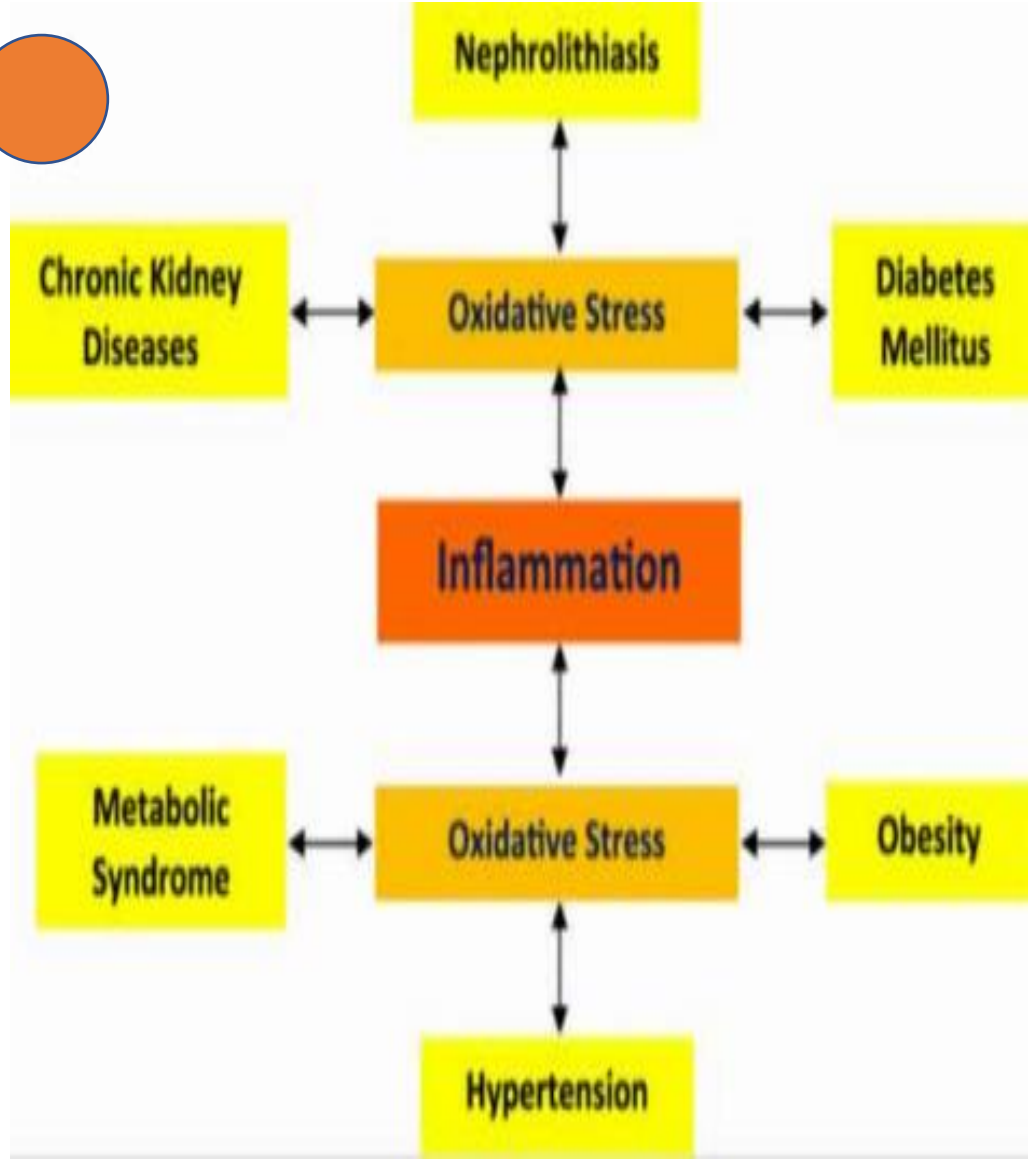
1404/3/9

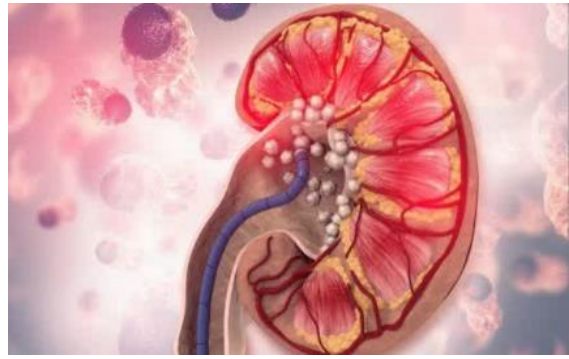
Nephrolithiasis and systemic Disease

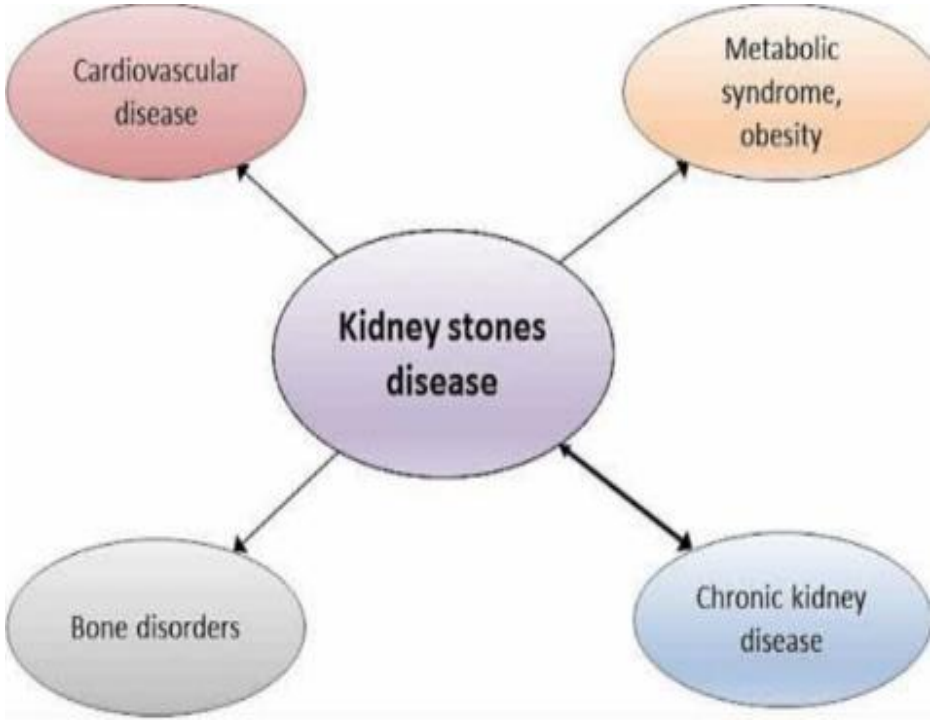
- Diabet
- heart disease
- Hypertension
- Microbiome
- kidney function
- OSTEOPOROSIS
- Obesity
- Cancer
- kidney transplantation

Systemic conditions associated with nephrolithiasis

Coronary artery disease
Chronic kidney disease and end-stage kidney disease
Bone disorders and fractures
Aortic calcification
Hypertension
Type 2 diabetes mellitus
Gout
Metabolic syndrome
Sarcoidosis
Renal tubular acidosis
Bowel disease and intestinal surgery
Renal and bladder anatomic anomalies
Medications
Genetic abnormalities







- Uric acid stones is more prevalent in patients with T2DM than in nondiabetic stone formers and more in obese than in nonobese stone formers.

- Higher **BMI and T2DM** are shown to be **independent** risk factors for uric acid nephrolithiasis.


Does DIABETES
increase risk of developing
KIDNEY STONES?

Diabetic Severity and Risk of Kidney Stone Disease

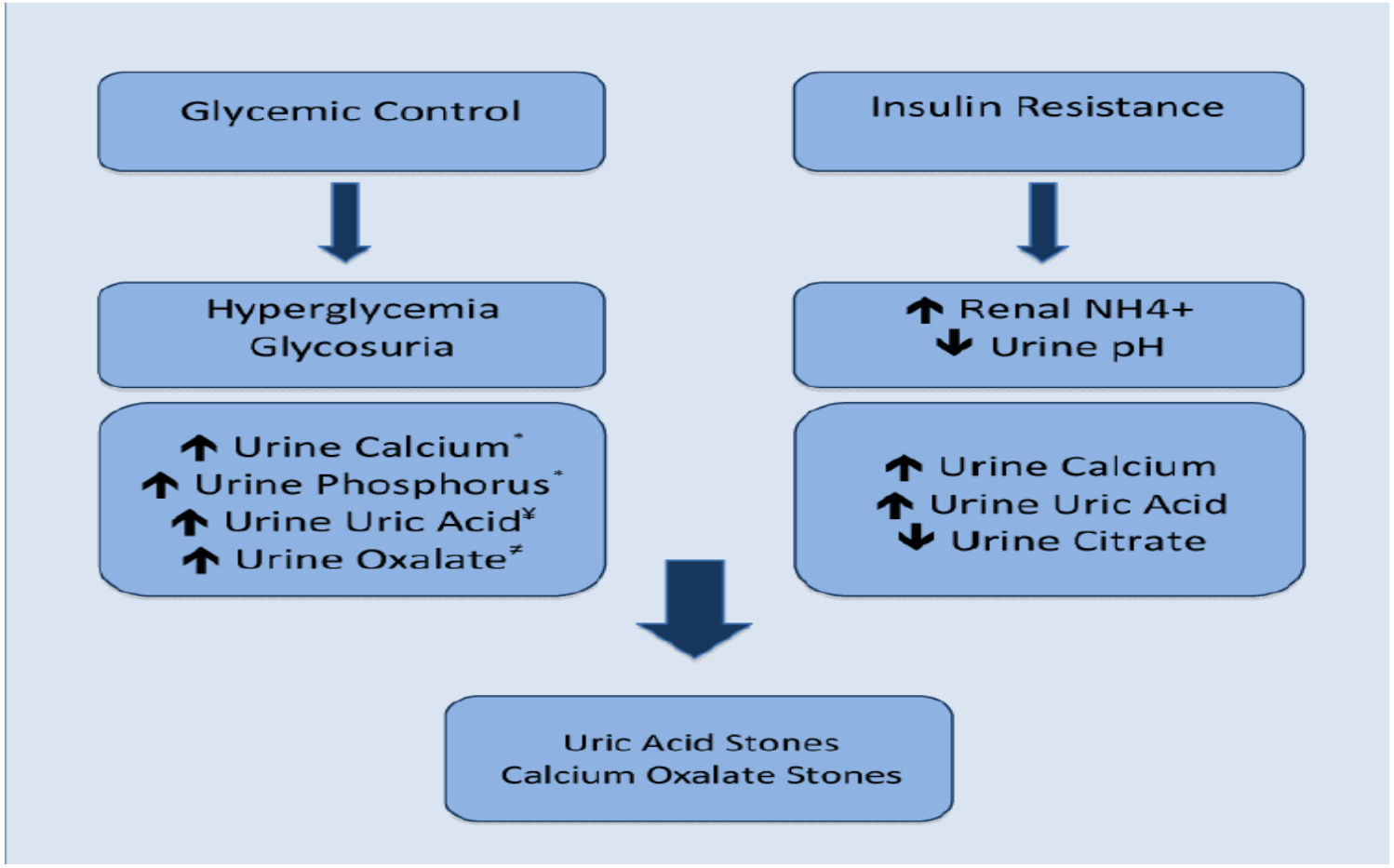
- Patients with type 2 diabetes are at **1.3–1.7 times the risk of nephrolithiasis** compared with the general population . This association is highlighted for **uric acid stones** in that UA stones are prevalent as **35.7%** of all stones in type 2 diabetes, whereas only 11.3% of those in nondiabetic patients.

- The link between **UA stones and type 2 diabetes** is thought to be driven by excess undissolved urinary UAs in relation to insulin resistance and unduly acidic urine.

- Insulin resistance is also associated with prolithogenic urinary profiles for **calcium stones such as hypocitraturia, hyperoxaluria, and/or hypercalciuria.**

Diabetes mellitus and the risk of nephrolithiasis. Kidney international. 2005;

Diabetic Severity and Risk of Kidney Stone Disease



Diabetes mellitus and the risk of nephrolithiasis. Kidney international. 2005;

Diabetic Severity and Risk of Kidney Stone Disease

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Eur Urol. 2014 January ; 65(1): . doi:10.1016/j.eururo.2013.03.026.

Diabetic Severity and Risk of Kidney Stone Disease

Aviva E. Weinberg, MD[a], **Chirag J. Patel, PhD**[b], **Glenn M. Chertow, MD, MPH**[c], and **John T. Leppert, MD, MS**[a]

[a]Department of Urology, Stanford University School of Medicine, Stanford, California, USA

[b]Stanford Center for Prevention Research, Department of Medicine, Stanford University School of Medicine, Stanford, California, USA

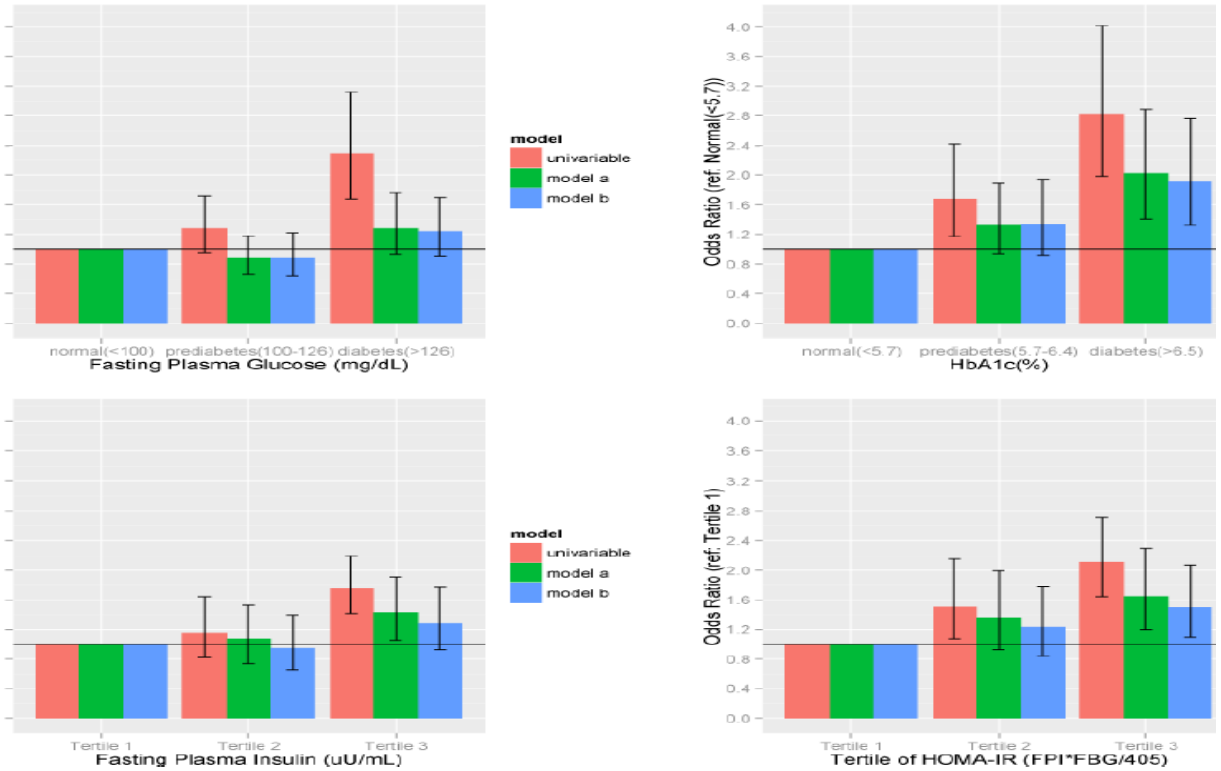


Figure 1.
Odds ratios of kidney stone disease by biochemical measures of T2DM severity

- glycemic control is also associated with the pathogenesis of stone disease.
- **HbA1c** bore the strongest association with the odds of kidney stone disease.

Eur Urol. 2014 January ;

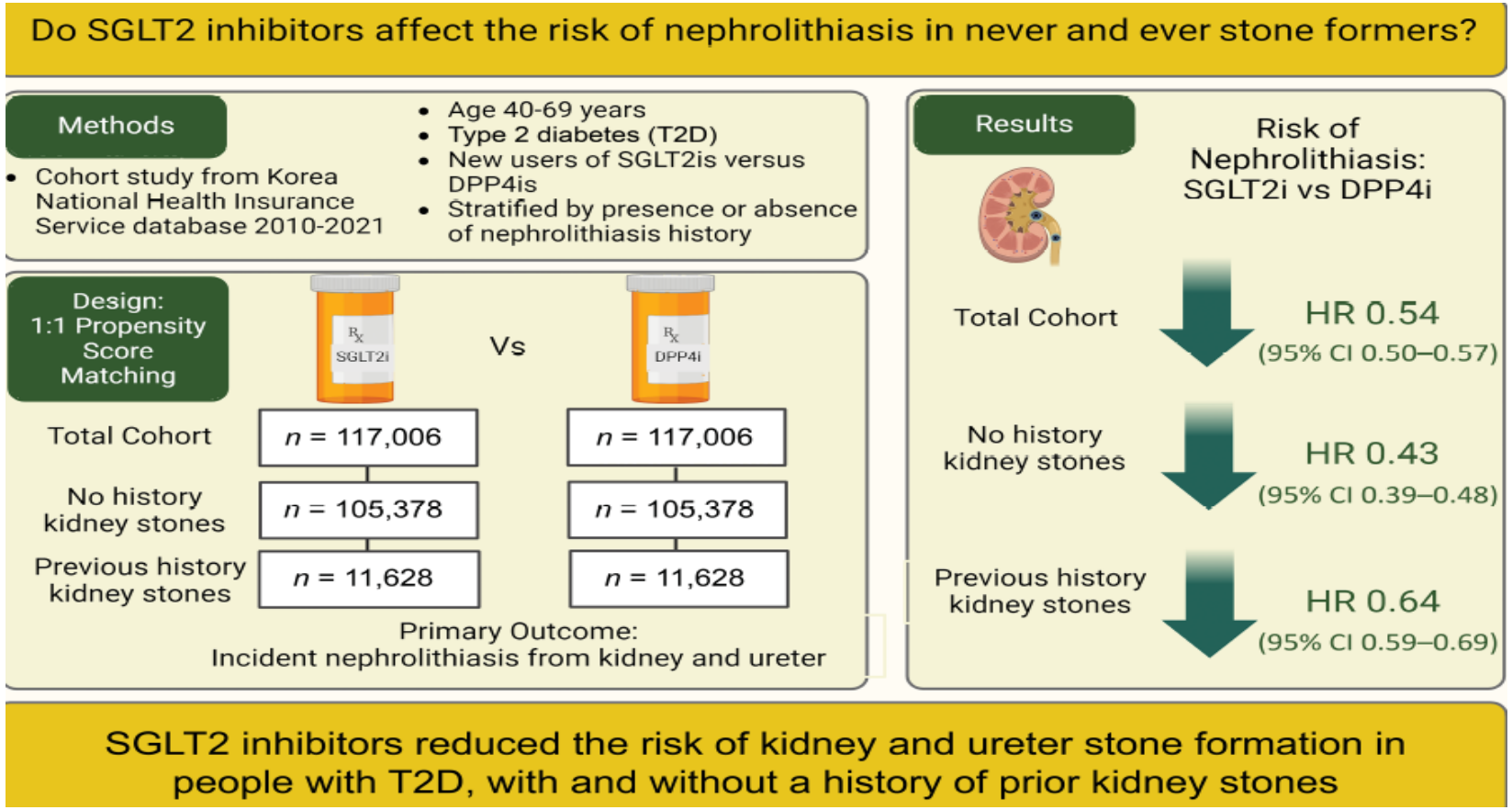
Nephrolithiasis With SGLT2 Inhibitors

Diabetes Care
American Diabetes Association

Risk of Nephrolithiasis Associated With SGLT2 Inhibitors Versus DPP4 Inhibitors Among Patients With Type 2 Diabetes: A Target Trial Emulation Study

Anna Shin, Ju-Young Shin, and Eun Ha Kang

Diabetes Care 2025;48(2):193–201 | https://doi.org/10.2337/dc24-1652



Nephrolithiasis With SGLT2 Inhibitors

- results are in line with a recent meta-analysis pooled from 27 RCT on SGLT2is that showed :.

A **36%** reduced of nephrolithiasis compared with placebo and also with a **26%** risk reduction compared with DPP4i

increased urinary flow → reduced inflammation → higher citrate excretion → mechanisms underlying stone prevention by SGLT2is

Nephrolithiasis With SGLT2 and DPP4 Inhibitors , Diabetes Care 2025;48:193–201

Pioglitazone and nephrolithiasis

- pioglitazone not only improved the metabolic syndrome, reduce the incidence of nephrolithiasis in patients with type 2 diabetes.

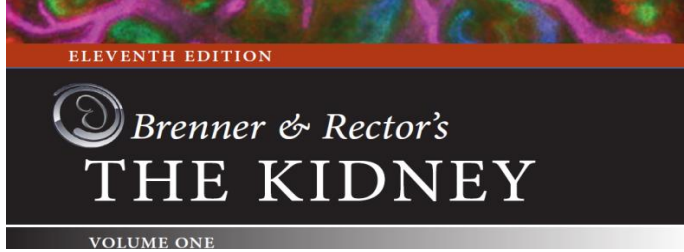
Table 1 | Risk of new-onset nephrolithiasis in the pioglitazone and nonpioglitazone users with type 2 diabetes

Group	Cases, *n* (%)	Per 1000 person-year	Crude HR (95% CI)	*P* value	Adjusted HR (95% CI)	*P* value
Nonpiogliazone users	1167 (6.65)	15.36	Ref.		Ref.	
Piogliazone users	289 (4.94)	11.36	0.74 (0.65–0.84)	<0.001	0.74 (0.65–0.84)	<0.001
Cumulative DDD						
<78	133 (6.87)	17.39	1.13 (0.94–1.35)	0.196	1.14 (0.95–1.37)	0.149
78–241	94 (4.74)	10.94	0.71 (0.58–0.88)	0.002	0.72 (0.58–0.88)	0.002
≥242	62 (3.21)	6.73	0.44 (0.34–0.57)	<0.001	0.43 (0.33–0.56)	<0.001

CI, confidence interval; DDD, defined daily dose (see Niu *et al.*[2]); HR, hazard ratio; Ref, reference.

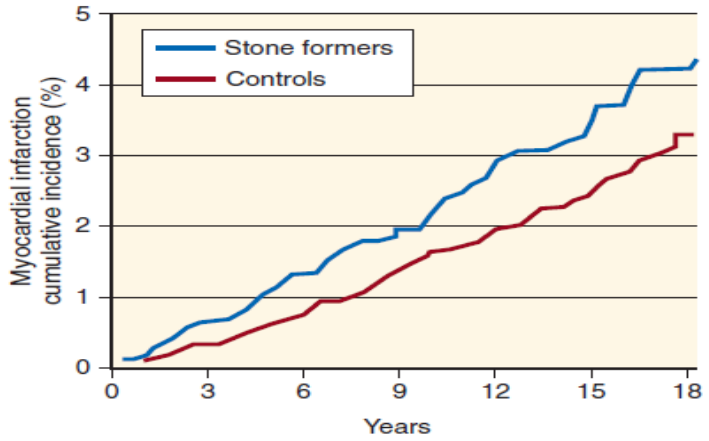
Kidney International (2019) 96, 517–524

NEPHROLITHIASIS, CARDIOVASCULAR DISEASE, AND HYPERTENSION



- the prevalence of nephrolithiasis increasing from 1% in those with the lowest blood pressure compared with 13% in those with the highest blood pressure.

- In a Canadian study of 25,000 subjects compared with people without kidney stones, kidney stone had a higher risk of subsequent myocardial infarction and stroke.

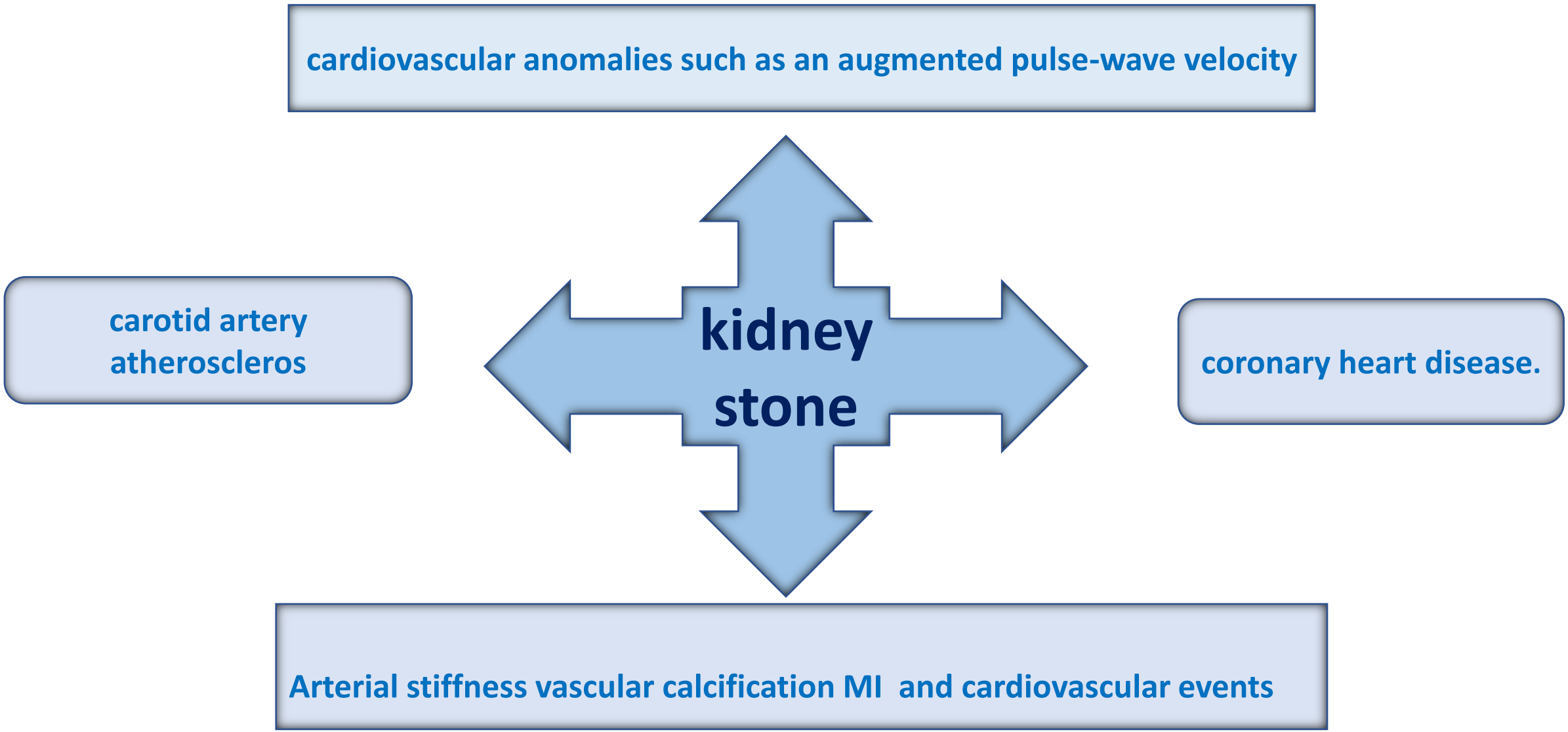


Incidence (no. at risk)

Control	0 (10,860)	0.8 (6,689)	2 (3,184)	4.2 (1,010)
Stone formers	0 (4,564)	1.3 (2,686)	3 (1,276)	5.2 (404)

Fig. 38.27 Increased risk for myocardial infarction in stone formers. Data collected from Olmsted County, Minnesota, residents. (Modified from Rule AD, Roger VL, Melton LJ 3rd, et al. Kidney stones associate with increased risk for myocardial infarction. *J Am Soc Nephrol.* 2010; 21[10]:1641–1644.)

kidney stone and heart disease



Shang et al. BMC Nephrology (2017)

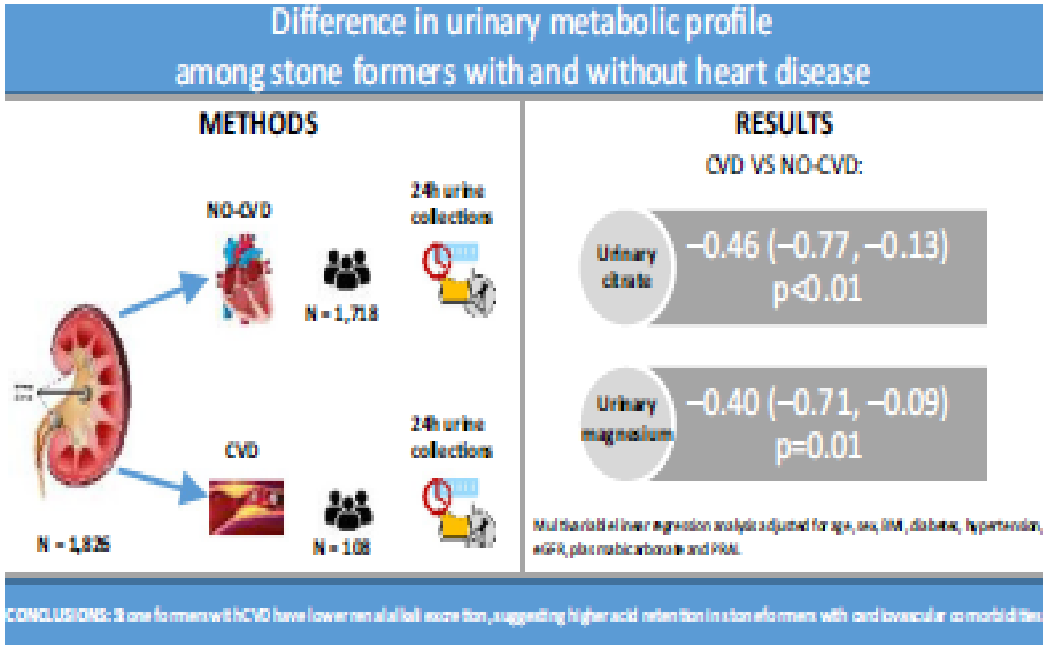
NEPHROLITHIASIS, CARDIOVASCULAR DISEASE

Journal of Nephrology (2022) 35:851–857
https://doi.org/10.1007/s40620-021-01096-w

ORIGINAL ARTICLE

Urinary metabolic profile and stone composition in kidney stone formers with and without heart disease

Matteo Bargagli[1] · Shabbir Moochhala[2] · William G. Robertson[2,3] · Giovanni Gambaro[4] · Gianmarco Lombardi[4] · Robert J. Unwin[2] · Pietro Manuel Ferraro[1,5]



- That stone-formers affected by heart disease have a multifactorial 24-h urine pattern characterized by lower urinary excretions of both citrate and magnesium, this might indicate a shared underlying pathogenesis.

Does Kidney Stone

Cause High Blood Pressure ?

Shang et al. BMC Nephrology (2017) 18:344
DOI 10.1186/s12882-017-0762-8

BMC Nephrology

RESEARCH ARTICLE Open Access

Nephrolithiasis and risk of hypertension

Nephrolithiasis and risk of hypertension: a meta-analysis of observational studies

Weifeng Shang[1], Yuanyuan Li[2], Yali Ren[3], Yi Yang[4], Hua Li[1] and Junwu Dong[1*]

- Since the association between arterial hypertension and nephrolithiasiswas described in **1965** for the first time.
- Data from several observational studies suggested a risk of hypertension in nephrolithiasis patients of 1.24–1.96 compared to the general population.

Nephrolithiasis and risk of hypertension

Shang et al. BMC Nephrology (2017) 18:344
DOI 10.1186/s12882-017-0762-8

BMC Nephrology

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- several potential reasons which mayexplain the observed associations:

First: calcium metabolism

Second: metabolic syndrome and insulin resistance

Third :CKD

Finally, inflammation and oxidative stress [

Shang et al. BMC Nephrology (2017)

High Blood Pressure & Cardiovascular Prevention (2023) 30:343–350
https://doi.org/10.1007/s40292-023-00587-0

ORIGINAL ARTICLE

Low Potassium Intake: A Common Risk Factor for Nephrolithiasis in Patients with High Blood Pressure

Veronica Abate[1] · Anita Vergatti[1] · Antonella Fiore[1] · Angelo Forte[1] · Alessia Attanasio[1] · Nadia Altavilla[1] · Gianpaolo De Filippo[2] · Domenico Rendina[1] · Lanfranco D'Elia[1]

Received: 21 March 2023 / Accepted: 29 May 2023 / Published online: 17 June 2023

- **The potassium 24-h urinary levels in SF-Hs were significantly lowe compared to nSF-Hs.**

- in conclusion, a higher potassium urinary excretion in 24-h is a protective factor against NL in patients affected by Htn and dietary interventions can be considered for kidney protection.

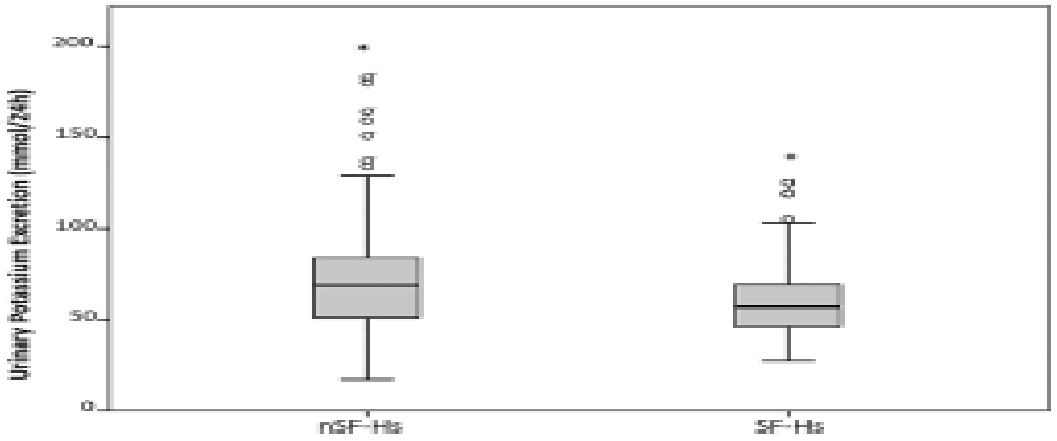

Fig. 1 Urinary Potassium Excretion in patients affected by Hypertension and Nephrolithiasis (SF-Hs) and in patients affected by Hypertension but not by Nephrolithiasis (nSF-Hs). Black line in the boxes represents the median value for each group. Grey squares indicate the standard deviation. *$p < 0.001$

The role of the microbiome in kidney stone formation

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.journal-surgery.net

Review

The role of the microbiome in kidney stone formation

Mansi Mehta [a], David S. Goldfarb [a, b], Lama Nazzal [a, *]

[a] Nephrology Division, NYU School of Medicine, New York, NY, USA
[b] New York Harbor VA Healthcare System, New York, NY, USA

- **Oxalobacter formigenes (Oxf),** in **1985** has attracted considerable attention regarding its involvement in **calcium oxalate stone disease** .
- It is unique in that it requires oxalate both as a carbon source and for ATP generation and could degrade ingested oxalate and reduce intestinal absorption, and stimulate oxalate secretion from the colon, offering protection from hyperoxaluria..
- Clinical findings have suggested that there is a direct correlation between the **organism's absence and hyperoxaluria and oxalate stone formation.**

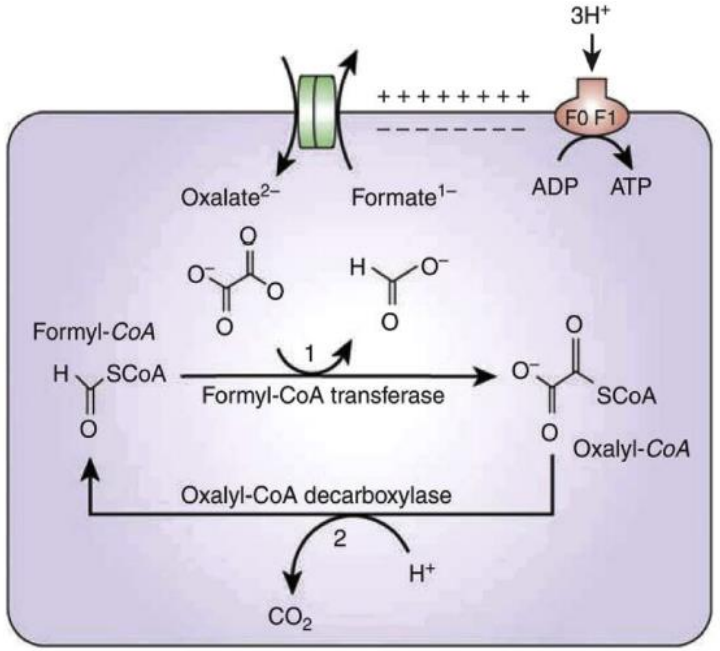

Fig. 1. Metabolism of oxalate by *Oxf* [6]. Reproduced with permission.

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- **A case control study found a strong invers association between colonization with Oxf and recurrent calcium oxalate stones with a 70% risk reduction.**

Reported Oxf colonization rates in various adult populations

Country	Population	Number of subjects	% colonization
India	Normal	48	56
	Inflammatory Bowel Disease	48	10
USA	Normal	26	62
	Inflammatory Bowel Disease	16	9
USA	Normal	259	38
	Recurrent CaOx Stone formers	247	17
Germany	Normal	61	69
	CaOx Stone formers	145	43
Korea	Normal	233	77
	CaOx Stone formers	103	46

❖ Antibiotic effect on O. formigenes in humans

Antibiotic use could be responsible for the decrease in the prevalence of Oxf in adults .
Oxf strains are susceptible to multiple antibiotics including quinolones, macrolides, tetracyclines and metronidazole.

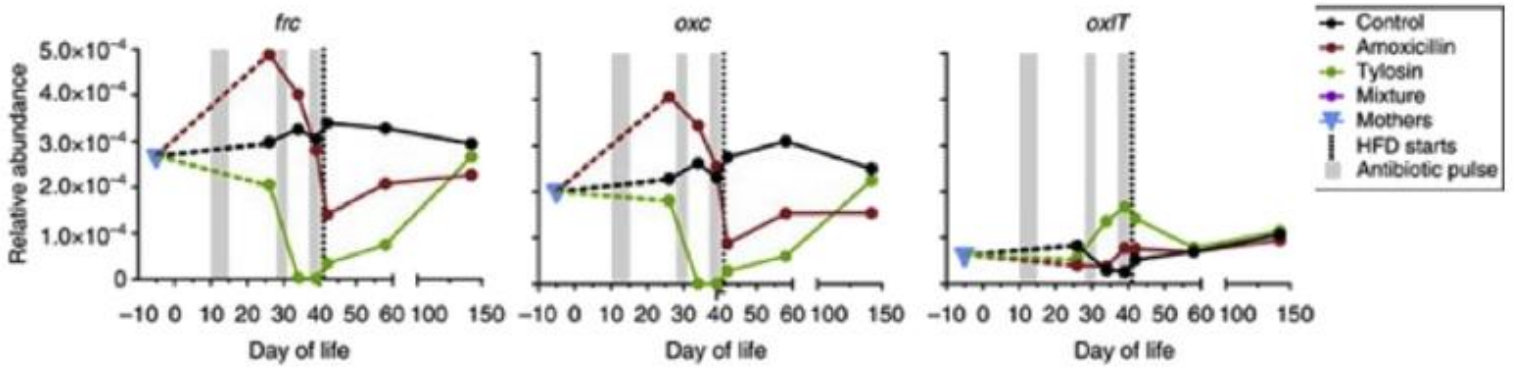
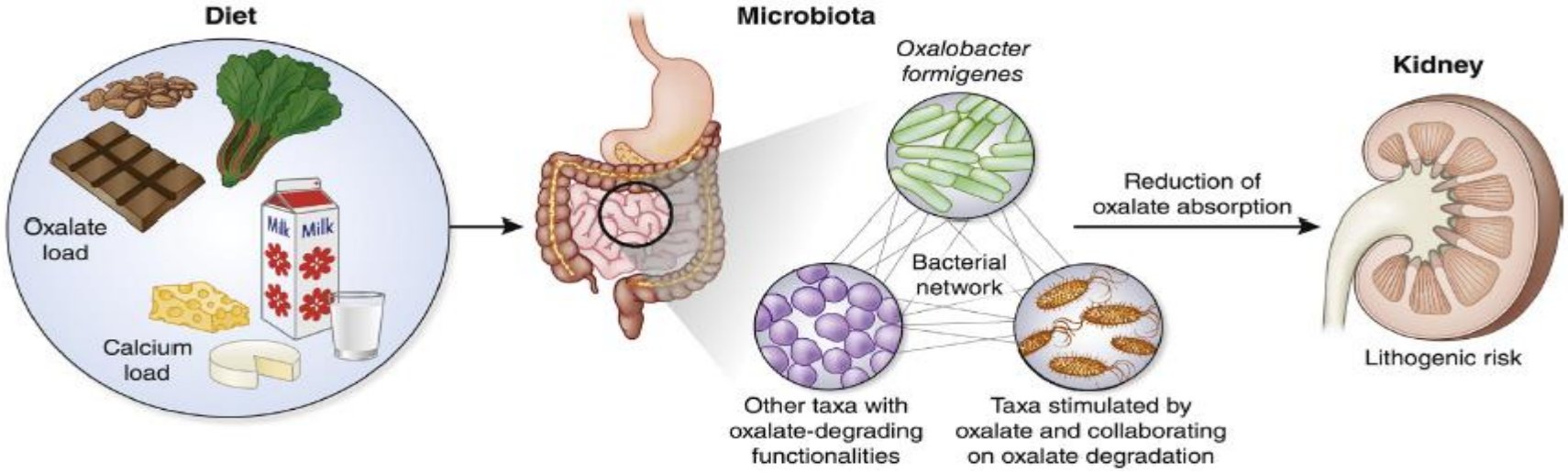


Fig. 2. Changes in the relative abundance of gene expression of *oxc*, *frc*, and *oxlT* during development with pulsed antibiotic treatment [24] (HFD: high fat diet reproduced with permission.

. Mehta et al. / International Journal of Surgery 36 (2016) 21

The role of the microbiome in kidney stone formation

- These **oral probiotic preparations** include Oxf alone, or different combinations of Lactobacillus, Bifidobacterium, and other oxalate degraders.
- Attempts to introduce oxalate-degrading microbes though **oral probiotic formulations** into the human gut have resulted in **a decrease in urinary oxalate excretion**



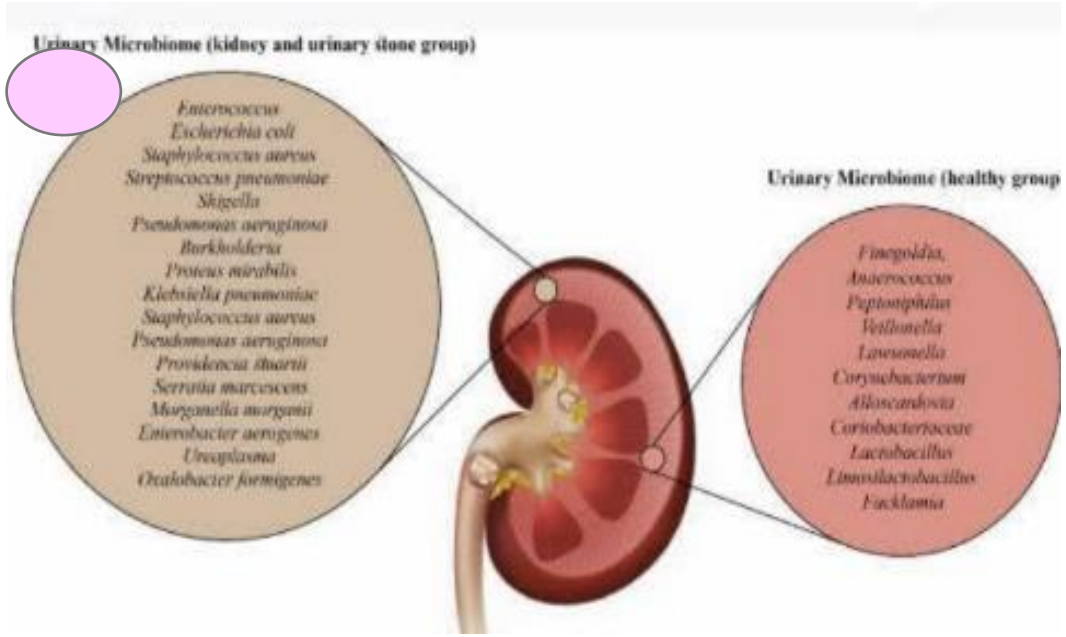
Kidney International (2019) 96, 25–27

Gut microbiome and kidney stone disease: not just an *Oxalobacter* story

Andrea Ticinesi[1,2], Antonio Nouvenne[1,2] and Tiziana Meschi[1,2,3]

- In fact, Oxalobacter may be flanked by a **large number of other bacteria,** with an overall higher representation in the microbiome and exhibiting a certain degree of oxalate-degrading capacity.

- Moreover, the average relative abundance of some specific taxa including Sutterella, Veillonella, and Peptococcus, was significantly correlated with urinary oxalate excretion.



- **Gut dysbiosis** with selective depletion of these microbial populations, may thus promote oxalate absorption, hyperoxaluria, and kidney stone formation

Kidney International (2019) 96, 25–27

Yuan et al. BMC Microbiology (2023) 23:143
https://doi.org/10.1186/s12866-023-02891-0

BMC Microbiology

RESEARCH Open Access

The role of the microbiome in kidney stone formatior

Gut microbiota in patients with kidney stones: a systematic review and meta-analysis

Tianhui Yuan[1†], Yuqi Xia[1†], Bojun Li[1†], Weimin Yu[1], Ting Rao[1], Zehua Ye[1], Xinzhou Yan[1], Baofeng Song[1], Lei Li[1], Fangyou Lin[1*] and Fan Cheng[1*]

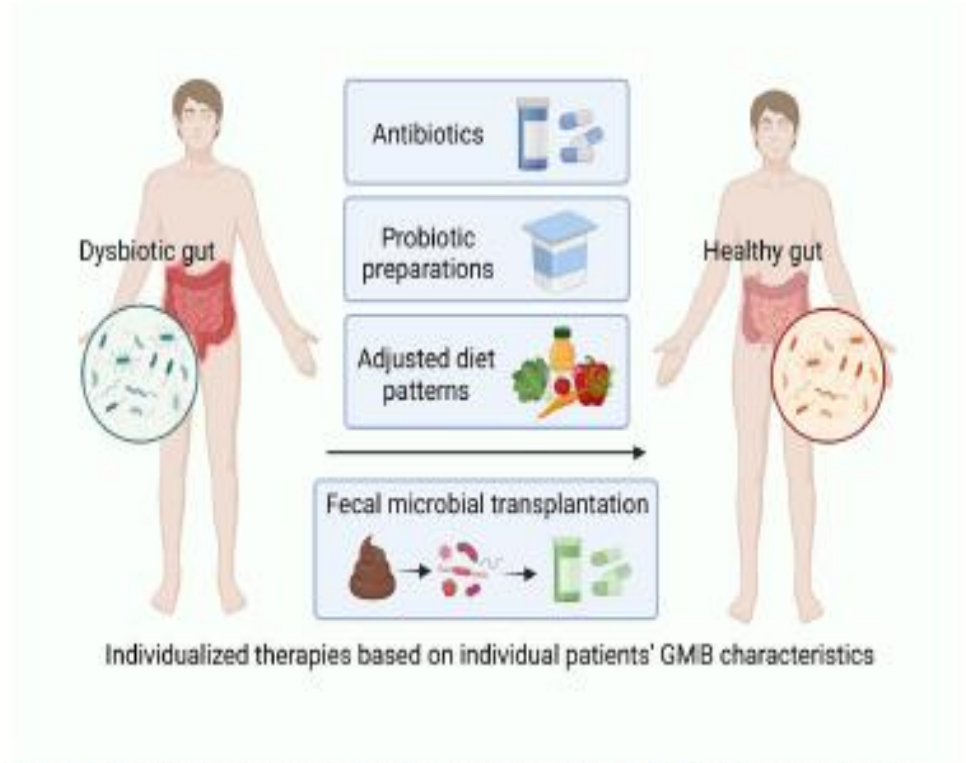
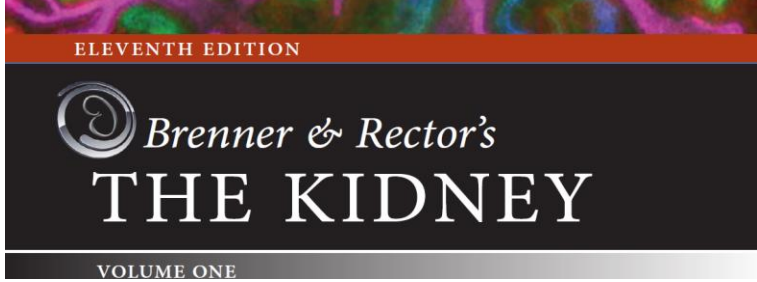


Fig. 5 Various methods for restoration of gut microbial dysbiosis to prevent occurrence and recurrence of kidney stones

- There is a characteristic gut **microbiota dysbiosis** in kidney stone patients.
- Individualized therapies like:
  - **Microbial supplementation**
  - **probiotic**
  - **adjusted diet patterns**

KIDNEY STONE DISEASE AND CHRONIC KIDNEY DISEASE



- Kidney stone disease and CKD can potentially be causally related because of **recurrent obstruction and infection, repeated shock wave therapy**.

- A study has shown that symptomatic kidney stone with followed over 9 years were at **increased risk of developing ESKD.**

- The association between kidney stones and risk of ESKD was found to be increased in those **with urologic abnormalities, hydronephrosis, recurrent uti, single kidney, neurologic bladder.**

Nephrolithiasis and loss of kidney function

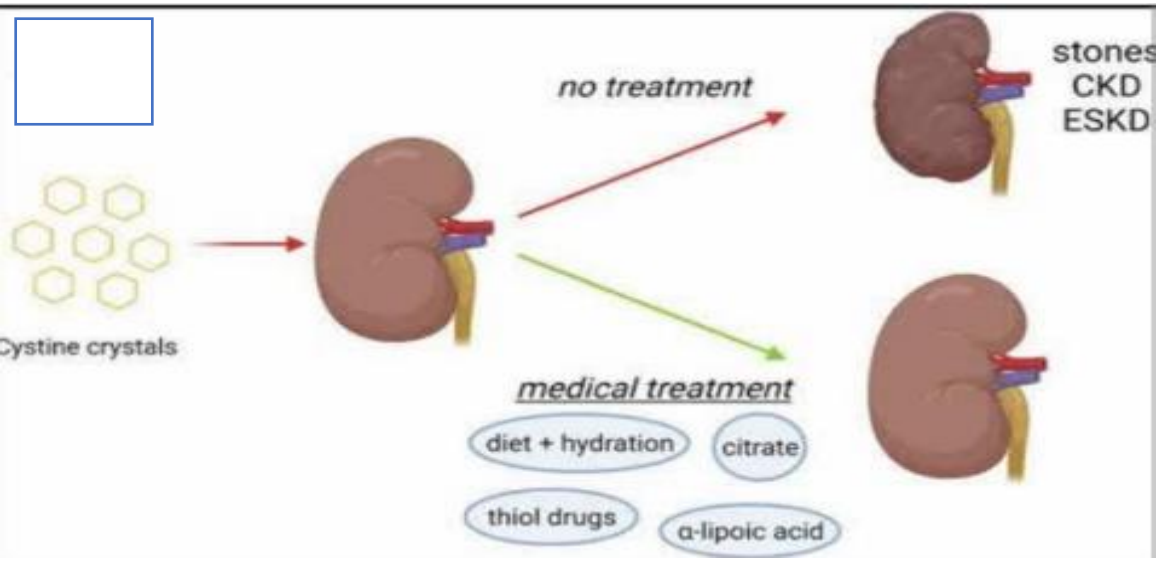
NIH Public Access
Author Manuscript
Curr Opin Nephrol Hypertens. Author manuscript; available in PMC 2014 July 01.

Published in final edited form as:
Curr Opin Nephrol Hypertens. 2013 July ; 22(4): 390–396. doi:10.1097/MNH.0b013e32836214b9.

Nephrolithiasis and loss of kidney function

Mira T. Keddis and **Andrew D. Rule**
Department of Medicine, Division of Nephrology and Hypertension, Mayo Clinic, Rochester, Minnesota, USA

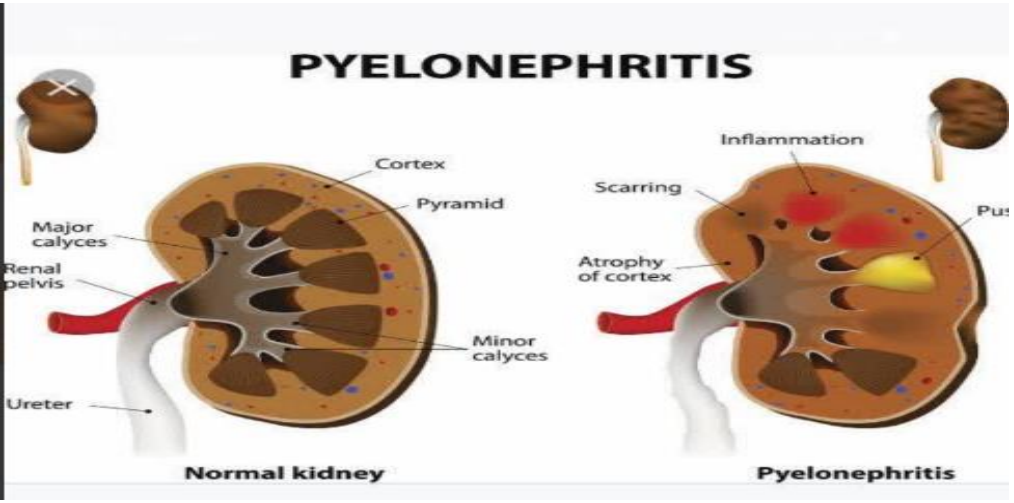
- Across several studies, patients with nephrolithiasis had about a **two-fold higher risk for decreased renal function or need for renal replacement therapy**.



MECHANISMS OF NEPHROLITHIASIS-ASSOCIATED KIDNEY DAMAGE

- **pyelonephritis complicates** the stone episode, **acute kidney injury** may occur.are potential pathways for subsequent CKD.

- **chronic pyelonephritis** due to an infected stone predisposes to **tubulointerstitial inflammation and renal scarring**



- **complicated by infection or obstruction may indeed lead to more permanent renal damage and CKD.**

Curr Opin Nephrol Hypertens. 2013 July

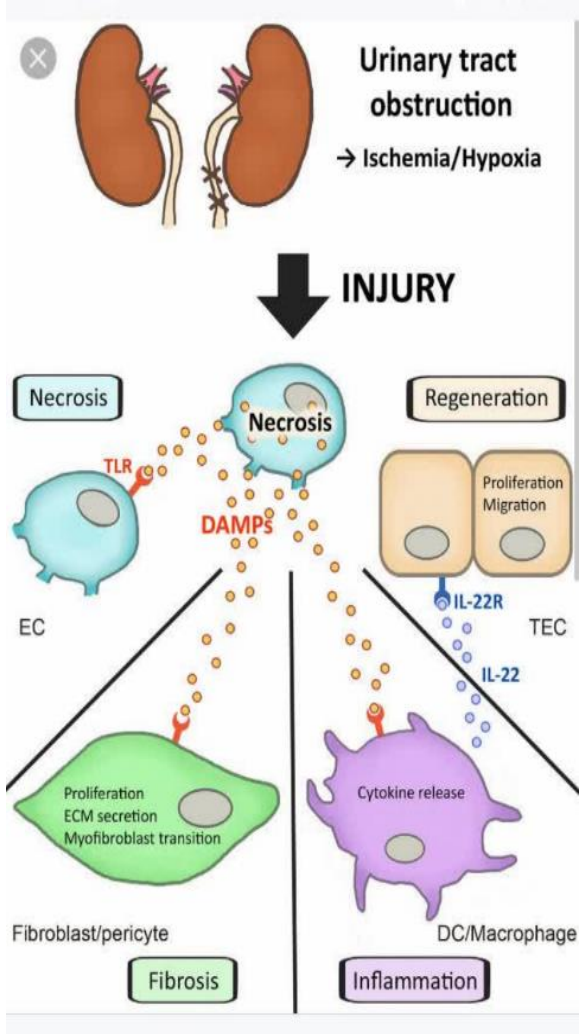
MECHANISMS OF NEPHROLITHIASIS-ASSOCIATED KIDNEY DAMAGE

unilateral ureteral obstruction (UUO) → increased intratubular pressure → renal vasoconstriction

↓

decline in GFR and renal bloodflow partially

UUO prolonged → TGF-β and TNF-α → increased interstitial volume, matrix deposition, monocyte infiltration, and fibroblast differentiation → tubulointerstitial inflammation and fibrosis and glomerulosclerosis

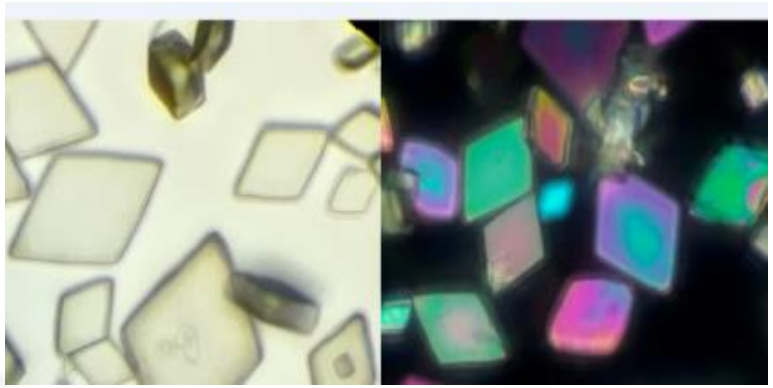


Curr Opin Nephrol Hypertens. 2013 July

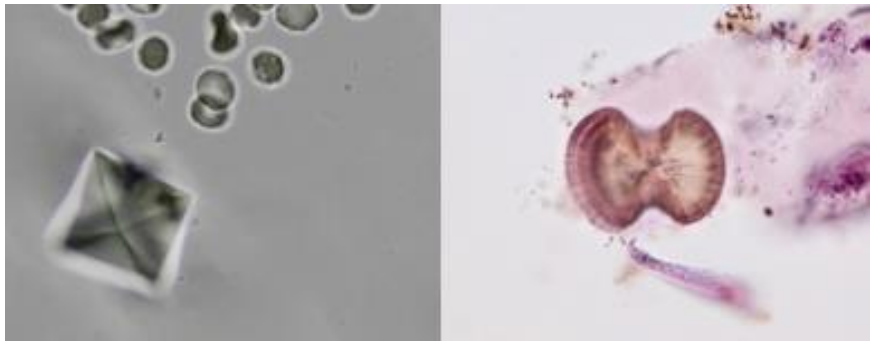
Nephrolithiasis and loss of kidney function

- **In a retrospective analysis of stone composition and urine chemistries:**

GFR be low 60 ml/min/1.73 m2 → **lower urine pH and uric acid struvite stones.**

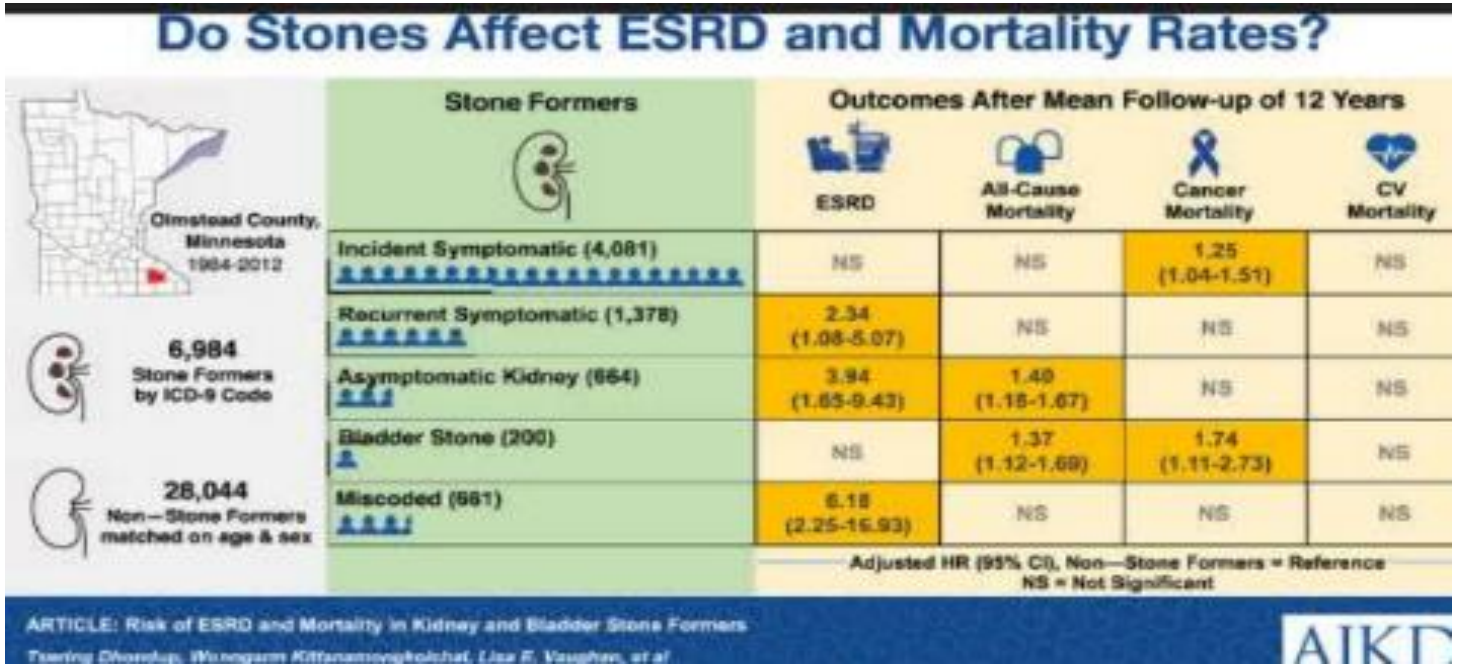


GFR at least 60 ml/min/1.73 m2. → **calcium phosphate stones**



Curr Opin Nephrol Hypertens. 2013 July

Nephrolithiasis and loss of kidney function



❖struvite and calcium were the most common stone compositions of those that developed ESRD,

OSTEOPOROSIS AND KIDNEY STONES

- recent systematic review and comparative meta-analysis in 24 case-control studies has shown that a **lower BMD involves all skeletal sites and that the risk of osteoporosis in patients with nephrolithiasis is four times more than in healthy controls**

- Several epidemiologic studies have established an **association between a history of kidney stones and a higher prevalence of fractures**

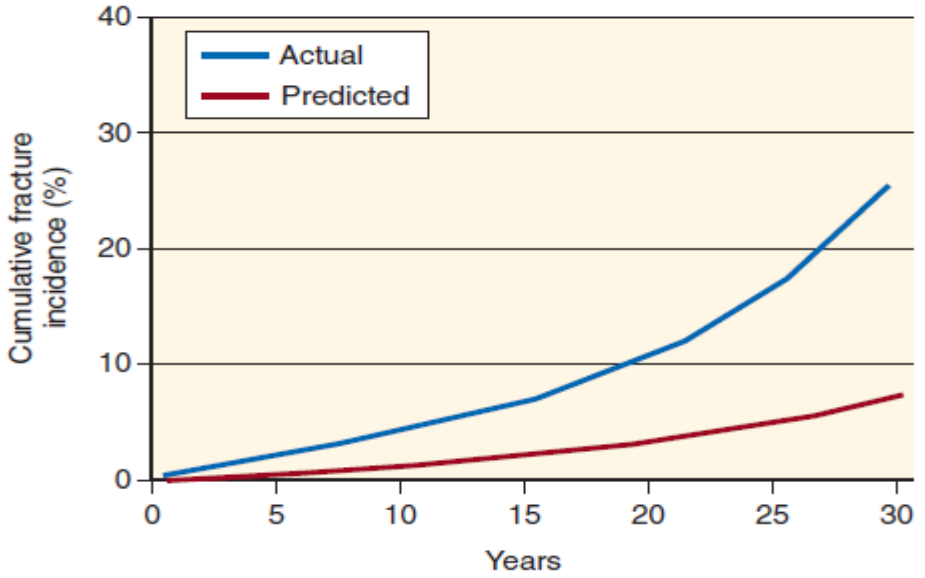
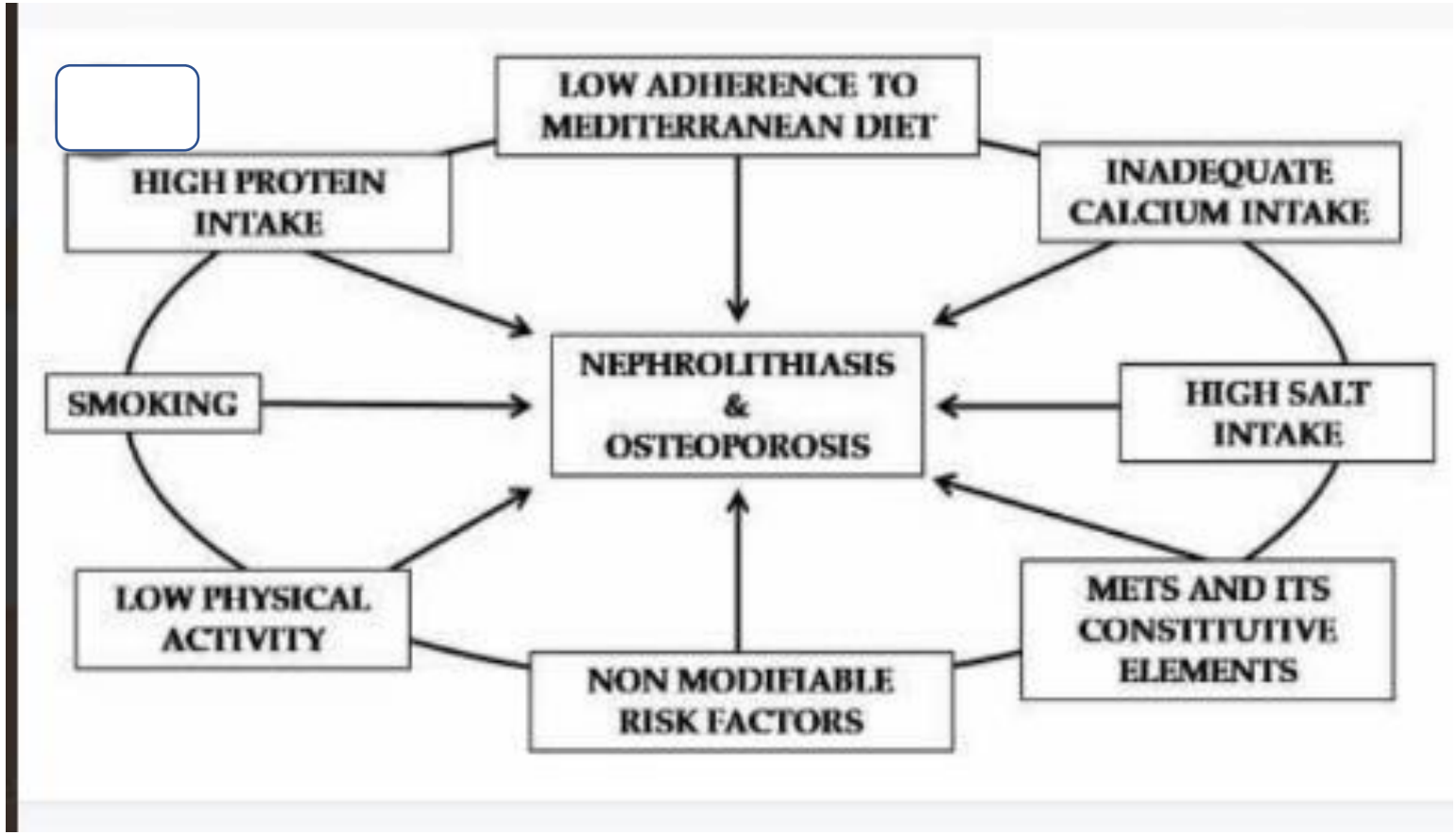


Fig. 38.28 Cumulative incidence of vertebral fractures in stone formers; data from Rochester, Minnesota, residents following an initial episode of symptomatic nephrolithiasis. The elevated fracture risk was vertebral and was present in both genders. (Modified from Melton LJ 3rd, Crowson CS, Khosla S, et al. Fracture risk among patients with urolithiasis: a population-based cohort study. *Kidney Int.* 1998;53[2]:459–464.)

PATHOPHYSIOLOGIC MECHANISMS LINKING OSTEOPOROSIS AND KIDNEY STONES

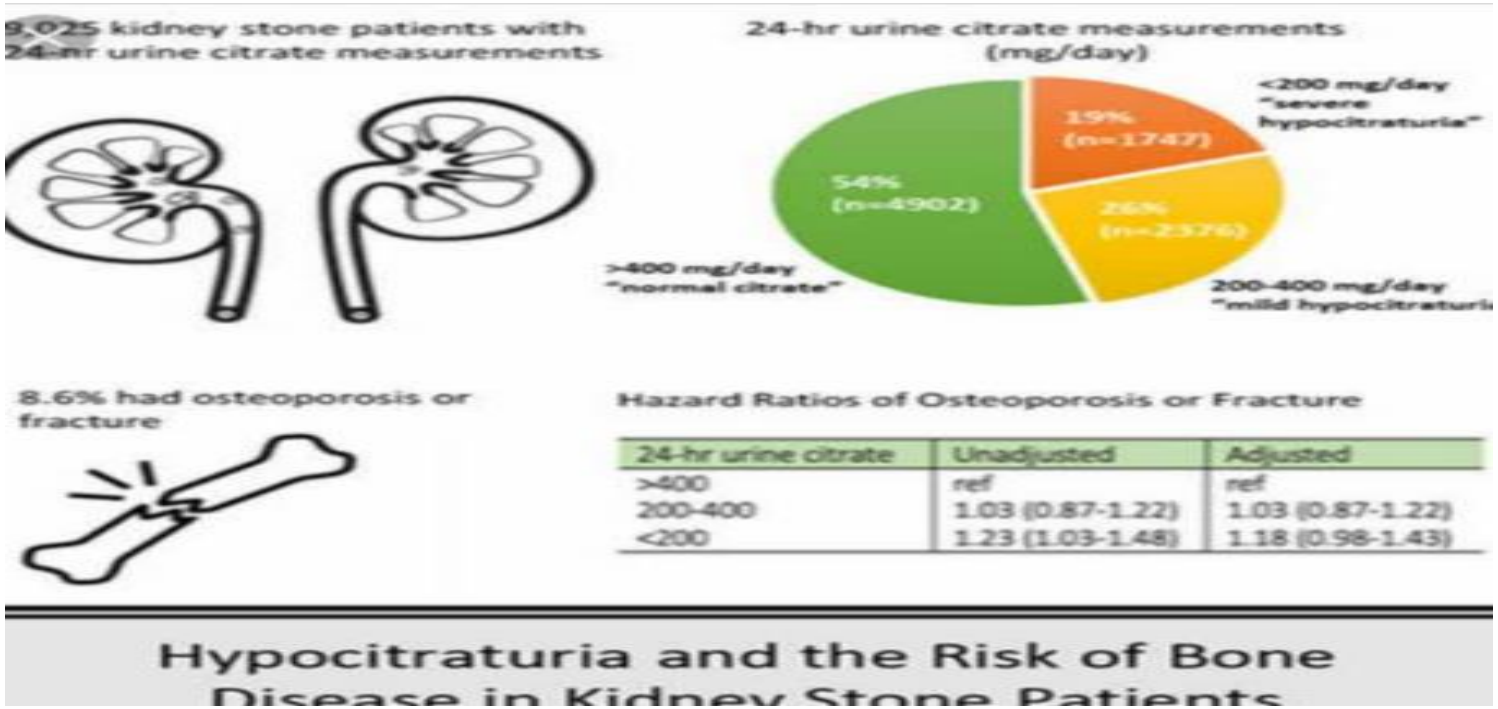


JBMR PLUS Open Access ASBMR

Hypocitraturia and Risk of Bone Disease in Patients With Kidney Stone Disease

Calyani Ganesan,[1] I-Chun Thomas,[2] Maria E Montez-Rath,[1] Glenn M Chertow,[1] John T Leppert,[1,2,3] and Alan C Pao[1,2,3]

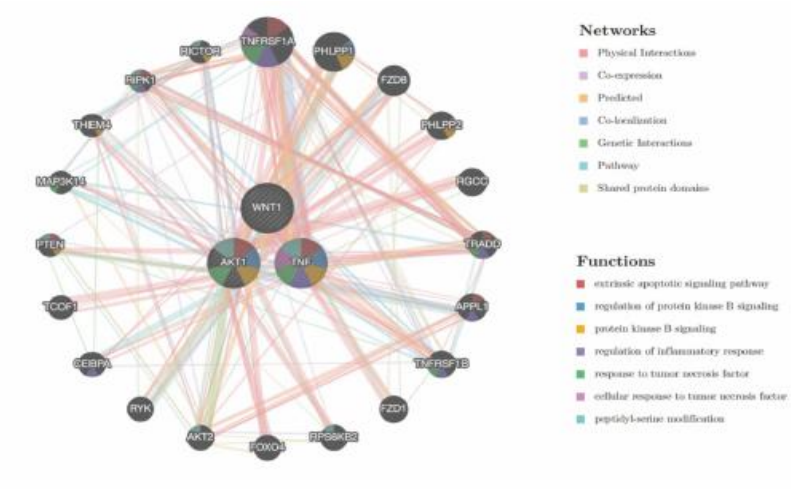
[1]Department of Medicine, Division of Nephrology, Stanford University, Palo Alto, CA, USA
[2]Division of Nephrology and Department of Urology, Veterans Affairs Palo Alto Health Care System, Palo Alto, CA, USA
[3]Department of Urology, Stanford University, Palo Alto, CA, USA

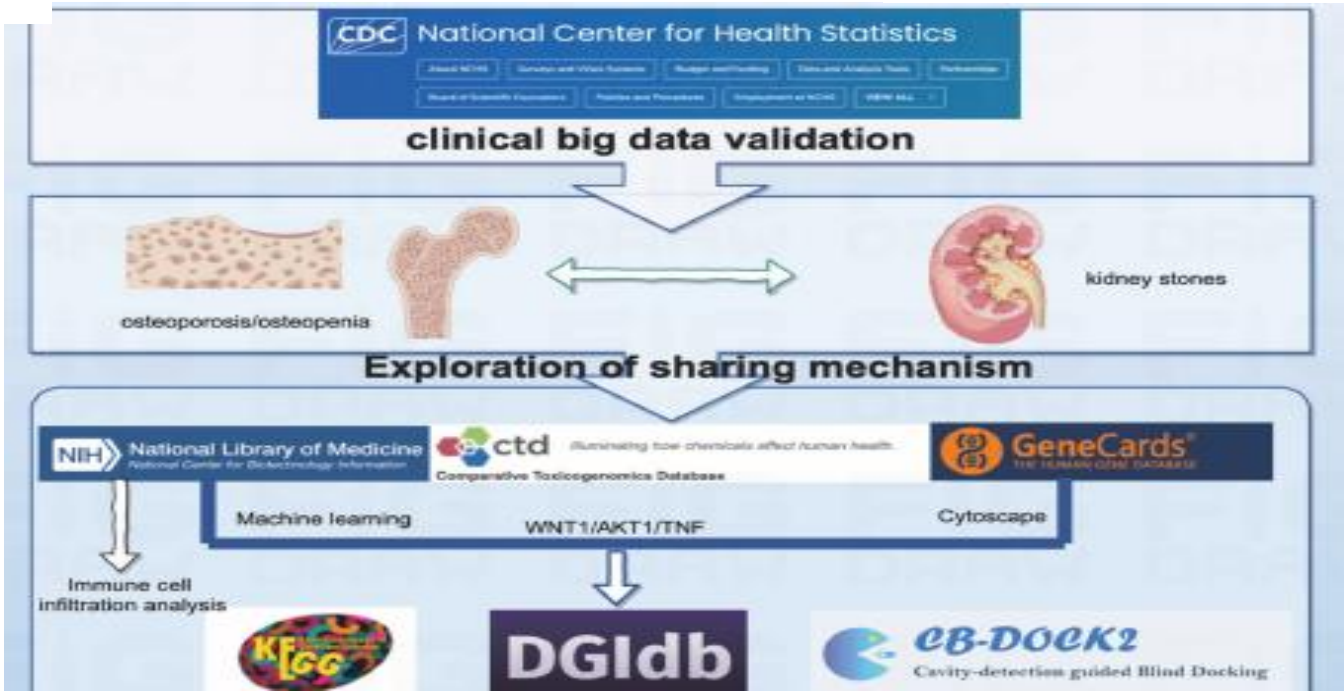


RESEARCH Open Access

Exploring the association between osteoporosis and kidney stones: a clinical to mechanistic translational study based on big data and bioinformatics

Di Luo[1], Linguo Xie[1], Jingdong Zhang[1] and Chunyu Liu[1*]





- **Bone loss is associated with an increased risk of kidneystones. Targeting the mTOR signaling pathway may offera potential therapeutic approach for treating both osteoporosis and kidney stones**

Effect of bisphosphonates on the crystallization of stone-forming salts in synthetic urine

Innovations in Urology
Investig Clin Urol 2020;61:310-315.
https://doi.org/10.4111/icu.2020.61.3.310
pISSN 2466-0493 • eISSN 2466-054X

INVESTIGATIVE AND CLINICAL UROLOGY
ICUROLOGY

Effect of bisphosphonates on the crystallization of stone-forming salts in synthetic urine

Larisa Kovacevic[1], Hong Lu[1], Natalija Kovacevic[1,2], Yegappan Lakshmanan[1]
[1]Department of Pediatric Urology, Children's Hospital of Michigan, Detroit, MI, [2]Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI, USA

Table 1. Range of effective doses of various bisphosphonates that resulted in inhibition of crystallization of COM, CaP, and MAP in synthetic urine (expressed as IA)

Medication	Range of effective dose (mg/mL)	Type of crystal	Range of IA (%)
Etidronate	0.004–0.3	COM	36–65
	0.021–0.3	CaP	29–68
	0.004–0.3	MAP	42–71
Alendronate	0.001–0.625	COM	8–73
	0.001–0.039	CaP	10–63
	0.039–0.625	MAP	39–94
Risedronate	0.001–2.5	COM	18–67
	0.001–0.625	CaP	37–97
	0.002–2.5	MAP	30–98
Ibandronate	0.0012–1.25	COM	24–77
	0.0012–0.078	CaP	17–69
	0.005–1.25	MAP	11–91

COM, calcium oxalate monohydrate; CaP, calcium phosphate; MAP, magnesium ammonium phosphate; IA, inhibitory activity.

- At the lowest dose of 0.001 mg/mL, risedronate induced the highest IA of 37% on CaP, whereas ibandronate had the strongest IA on COM (24%).
- To initiate the inhibition of MAP crystallization, **risedronate required a two-fold higher concentration (0.002 mg/mL) to reach 30% IA,** whereas **etidronate required a four-fold higher concentration (0.004 mg/mL) to reach 42% IA.**

Investig Clin Urol 2020;61:310-315.

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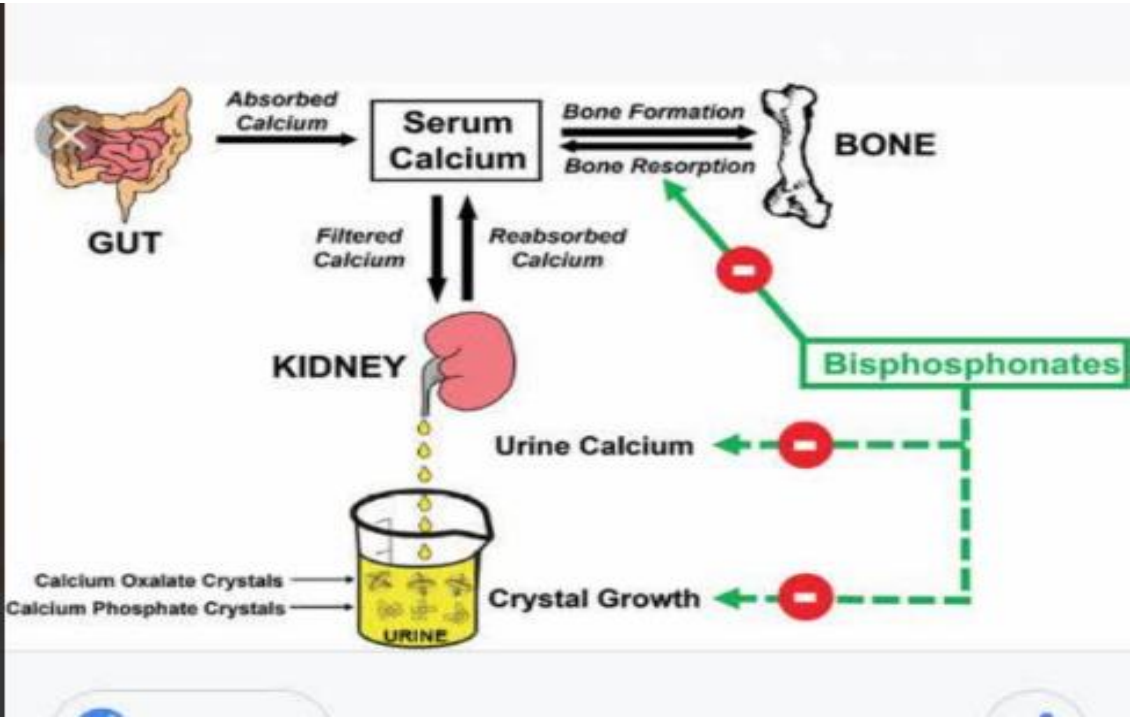

- BPs are good inhibitors of crystallization in synthetic urine, with risedronate and ibandronate being the most potent.
- At a **low clinically acceptable dose**, their highest inhibitory action was on **CaP and COM** crystals. **Higher doses** were needed to prevent **MAP crystallization**.

Effect of bisphosphonates on the crystallization of stone-forming salts in synthetic urine

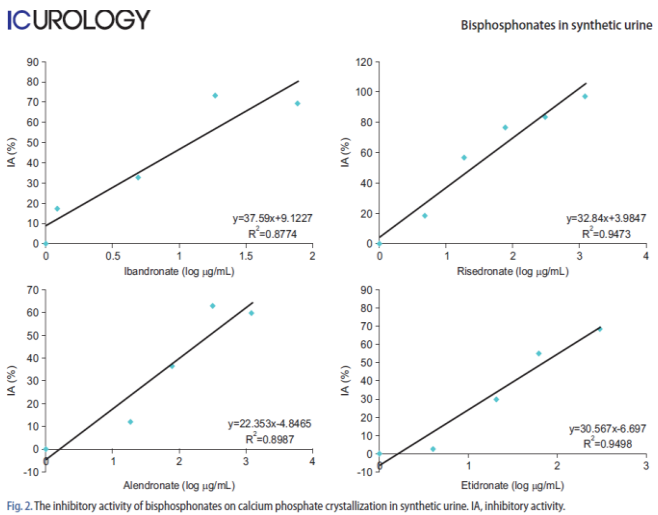

Fig. 2. The inhibitory activity of bisphosphonates on calcium phosphate crystallization in synthetic urine. IA, inhibitory activity.

cap

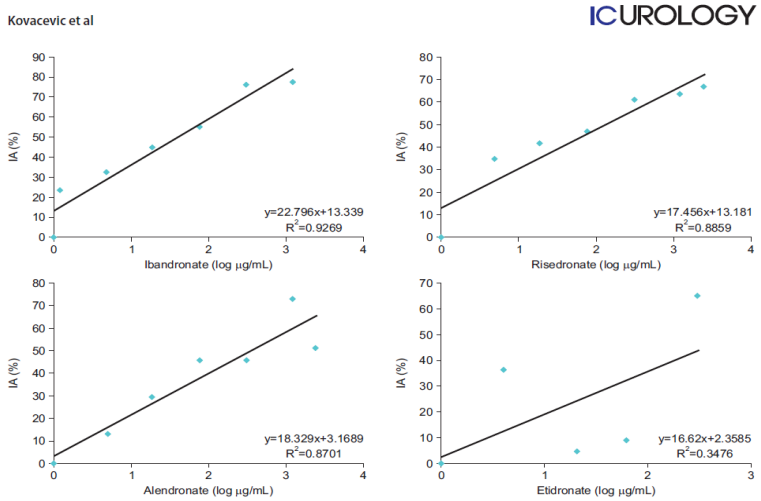

Fig. 1. The inhibitory activity of bisphosphonates on calcium oxalate crystallization in synthetic urine. IA, inhibitory activity.

COM

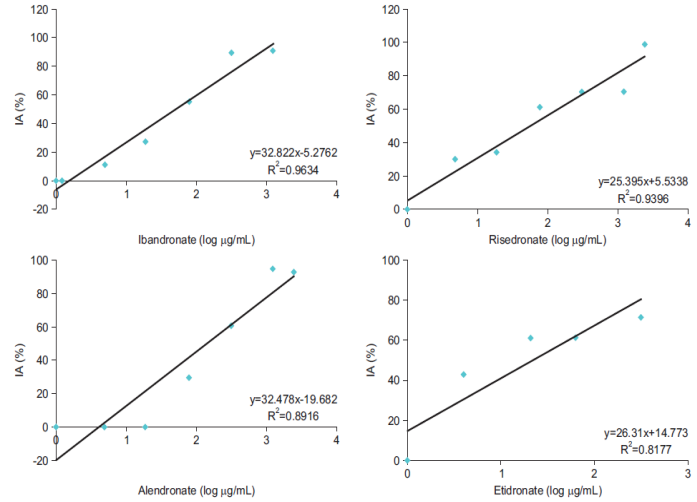

Fig. 3. The inhibitory activity of bisphosphonates on magnesium ammonium phosphate crystallization in synthetic urine. IA, inhibitory activity.

MAP

- BPs are good inhibitors of crystallization in synthetic urine . Overall, BPs showed the best inhibitory effect on **CaP and COM crystallization** at clinically acceptable **low doses.**
- **Higher doses** of BPs were needed to prevent **MAP crystallization.** The difference in the IA of BPs on these three types of crystals is likely **due to their high affinity for calcium**

Investig Clin Urol 2020;61:310-315.

Obesity and kidney stone disease

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Online version at http://www.minervamedica.it

Minerva Urologica e Nefrologica 2018 August;70(4):393-400
DOI: 10.23736/S0393-2249.18.03113-2

REVIEW

Obesity and kidney stone disease: a systematic review

Antonio CARBONE [1, 2], Yazan AL SALHI [1], Andrea TASCA [3],
Giovanni PALLESCHI [1, 2], Andrea FUSCHI [1], Cosimo DE NUNZIO [4], Giorgio BOZZINI [5],
Sandro MAZZAFERRO [6], Antonio L. PASTORE [1, 2] *

- the percentage of stones raised with BMI in the male population, from 7.1% in normal BMI to 11.3% in overweight and 28.7% in obese patients.

- Hypercalciuria, gouty diathesis, hypocitraturia and a low urinary volume were found in more than 50% of obese patients included in a nephrolithiasis database. Other reported metabolic defects included hyperoxaluria and high urinary excretion of sulfate

TABLE I.—*Prevalence of patients presenting metabolic risk factors.*[4]

	% Obese group	% Non-obese group
Gouty diathesis	54	18
Hyperuricosuria	43	20
Hypercalciuria	59	48
Hypocitraturia	54	63
Hyperoxaluria	31	10
High urine sulfate	70	24
Low urine volume	58	70

Bariatric Surgery and Risk of Urolithiasis


Article

Bariatric Surgery and Risk of Urolithiasis: A Review

Authors: Maliza Persaud,[1] *Satyendra Persaud,[2] Chantal Gosine,[1] Kristy Sadho,[1] Dilip Dan[2]

1. San Fernando General Hospital, San Fernando, Trinidad and Tobago
2. Division of Clinical Surgical Sciences, University of the West Indies, St. Augustine, Trinidad and Tobago

- **DASH-style** diet has been shown to decrease kidney ston incidence due to the high vegetable and fruit, moderate low-fat dairy, and low animal protein intake.[37] These favourable effects seen with the DASH diet are a result of increases in urine volume, pH, and urinary excretion of citrate, potassium, magnesium

- **bariatric surgery** may also adversely affect stone risk. Restrictive procedures appear to have the lowest risk, whereas malabsorptive procedures are associated with the highest risks of stone formation.

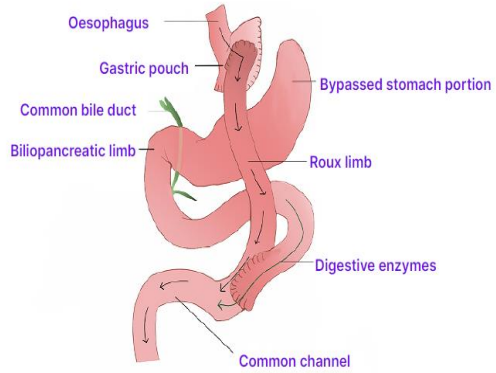
BARIATRIC PROCEDURES AND RISK OF NEPHROLITHIASIS

- Each type of surgery is accompanied by varying levels of stone risk.

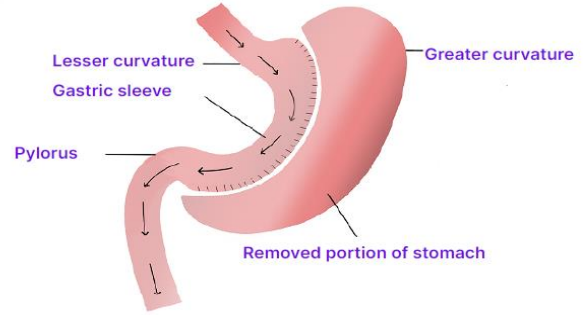
Table 1: Risk of urolithiasis following bariatric surgery.[30,39,43,44]

Type of procedure	Associated risk of urolithiasis
Obese non-operative controls	5–7%
Restrictive (LAGB, LSG)	Low (1.3–1.5%)
RYGB	Intermediate (7.65–13.00%)
Malabsorptive procedures (JIB)	High (22.0–28.7%)

: Roux-en-Y gastric bypass.



Vertical sleeve gastrectomy



Bariatric Surgery and Riskof Urolithiasis: A Review .EMJ Urol. 2022;

- There are various complex underlying pathophysiologic mechanisms associated with nephrolithiasis following bariatric surgery, including:

❖low urine volume → A decreased urine volume due to restricted gastric volumes

❖Aciduria → Acidic urine (pH: <4.6) has been demonstrated in several series of patients following RYGB, leading to uric acid stones

❖Hyperoxaluria →
- ❖ fat malabsorption and altered gut microflora
- ❖ RYGB are at higher risk for nephrolithiasis. An even greater concern was the occurrence of oxalate nephropathy and renal failure

❖Hypocitraturia → patients who have had RYGB have higher lower urinary citrate levels when compared to gastric banding patients.

MANAGEMENT OF STONE RISK IN PATIENTS OF POST-BARIATRIC

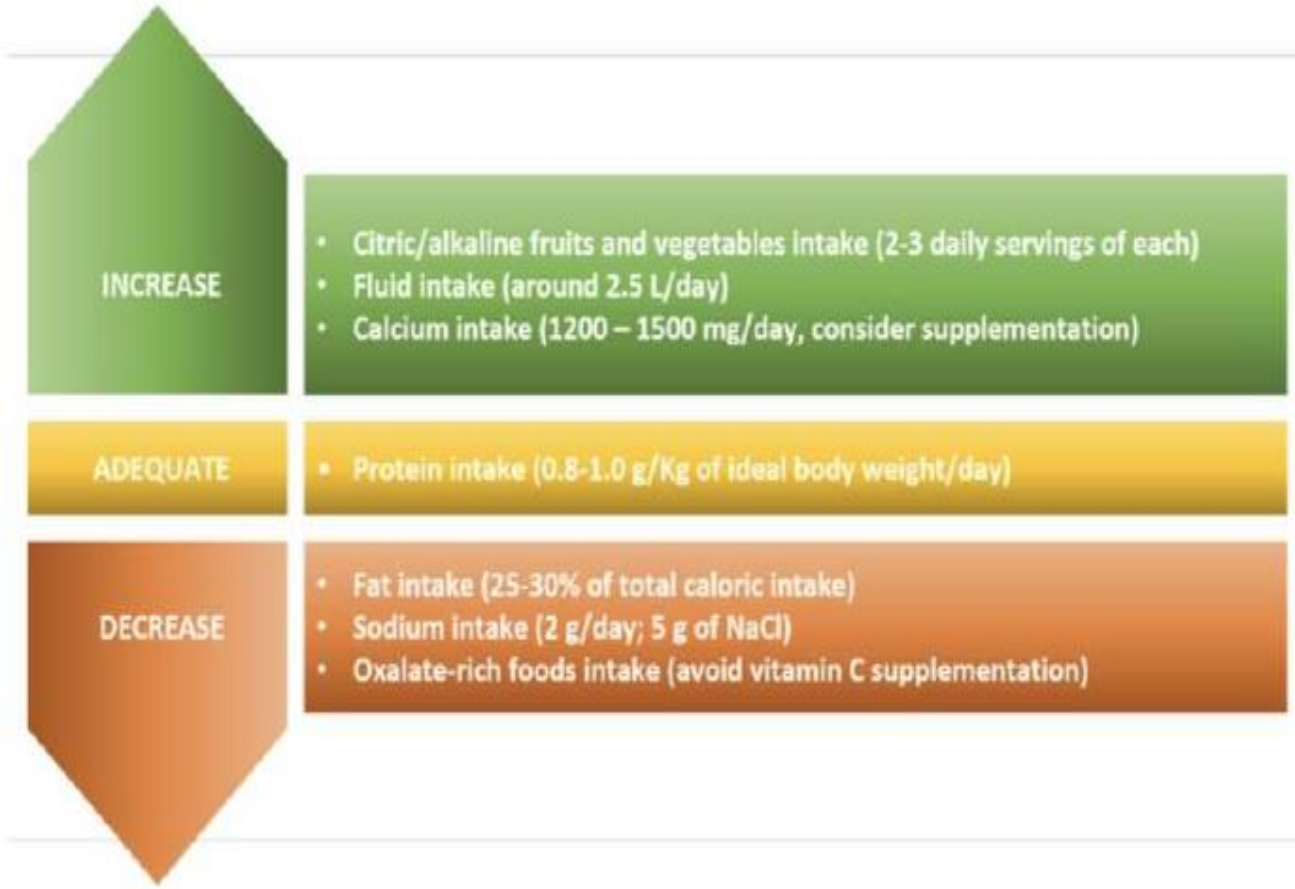


Figure 2. Dietary recommendations for BS patients to prevent the risk of stone formation and to reduce recurrence for those who already had stones before the surgery.

❑a purely **restrictive procedure** such as gastric banding is associated with a much **lower stone forming rate** than malabsorptive procedures.

❑The oral administration of O**. formigenes or its oxalate degrading enzymes**

Bariatric Surgery and Riskof Urolithiasis, EMJ Urol. 2022

Review Article

Kidney360

Risk Factors for Kidney Stone Formation following Bariatric Surgery

Megan Prochaska and Elaine Worcester

- **RYGB** is also associated with **higher risk of kidney stones** and bone disease after surgery. **Three years after surgery**, new kidney stone incidence is **8%** , and this continues to rise to **14% 10 years after surgery**.

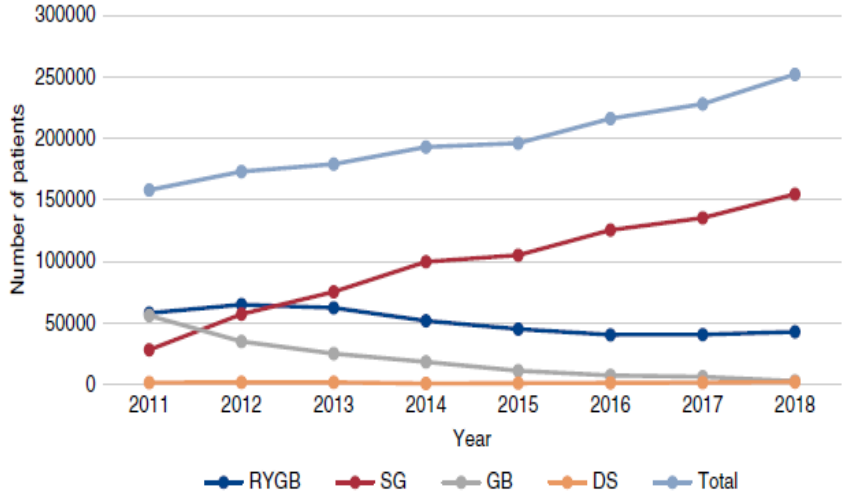


Figure 1. | Trend in more overall bariatric surgery procedures and more sleeve gastrectomies over time in the United States. DS, duodenal switch; GB gastric band; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy. Data from https://asmbs.org/resources/estimate-of-bariatric-surgery-numbers.

EXPLAINING THE DIFFERENCES BETWEEN KIDNEY STONES VS. KIDNEY CANCER

❖ Kidney stones and the risk of renal cell carcinoma and upper tract urothelial Carcinoma

BJC British Journal of Cancer www.nature.com/bjc

ARTICLE
Epidemiology

Kidney stones and the risk of renal cell carcinoma and upper tract urothelial carcinoma: the Netherlands Cohort Study

Jeroen A. A. van de Pol[1], Piet A. van den Brandt[1,2] and Leo J. Schouten[1]

- ❑ kidney stones were associated with an increased risk of **papillary RCC but not clear-cell RCC.**
- ❑ UTUC risk was increased for participants with kidney stones **No heterogeneity of associations was found for UTUC in the ureter and renal pelvis.**
- ❑ this is the first prospective study to examine the relationship between kidney stones and RCC and UTUC risk and the first study to **show heterogeneity of associations between pRCC and ccRCC..**

Shared mechanisms between kidney stones and urologic malignancies

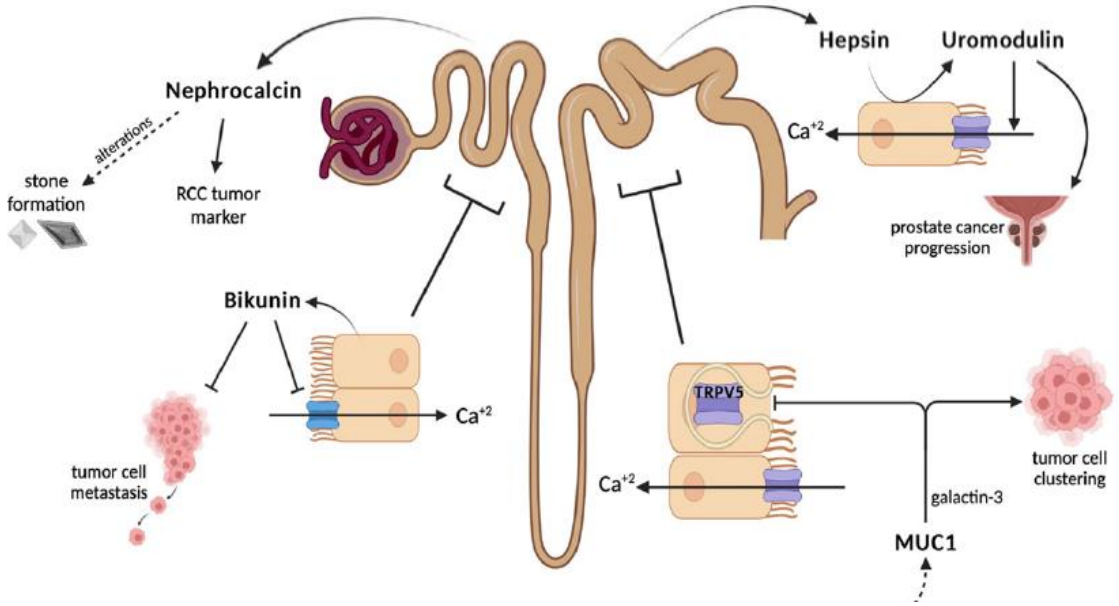
Am J Clin Exp Urol 2022;10(5):277-298
www.ajceu.us /ISSN:2330-1910/AJCEU0144941

Review Article

Understanding the link between kidney stones and cancers of the upper urinary tract and bladder

Meredith Mihalopoulos[1], Alan Yaghoubian[1*], Shirin Razdan[1*], Johnathan A Khusid[1*], Reza Mehrazin[1,2], Ketan K Badani[1,2], John P Sfakianos[1,2], William M Atallah[1], Ashutosh K Tewari[1,2], Peter Wiklund[1,2], Mantu Gupta[1], Natasha Kyprianou[1,2,3,4]

- **Contributors to stone formation and cancer development and progression: shared cellular pathways :**
- The inflammatory reaction caused by irritation of calcul and any superimposed infection drives hyperplasia in t renal epithelia. These cellular changes can progress int frank carcinoma or become dysplastic.



AmkJ Clin Exp Urol 2022;10(5):277-298

Shared contributors to renal stone formation and risk of urinary tract cancer

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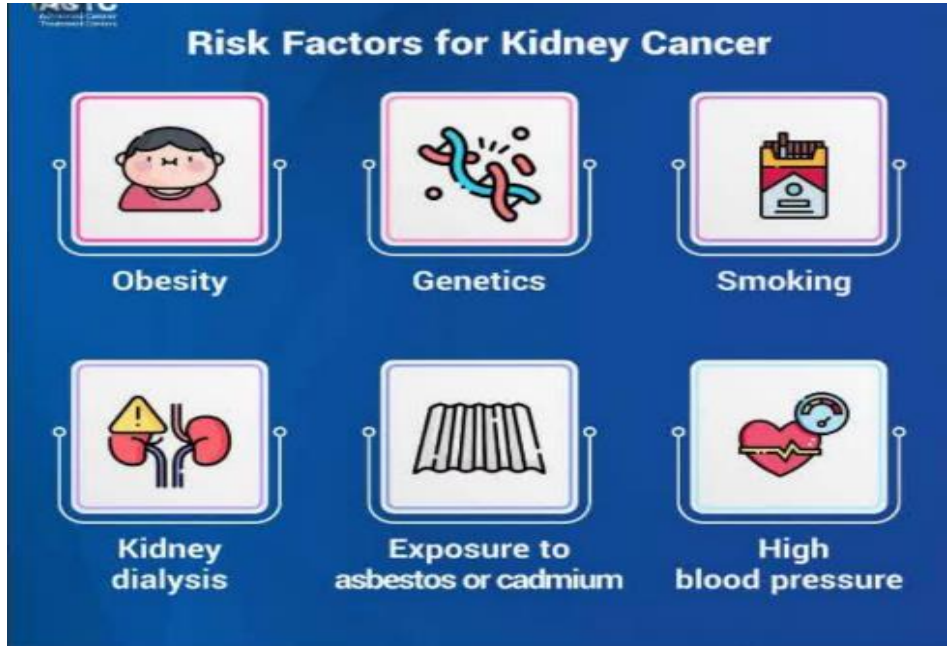
Shared mechanisms between kidney stones and urologic malignancies

Table 1. Shared contributors to renal stone formation and risk of urinary tract cancer

Type	Contributor	Stone Risk	Cancer Risk
Genetic	*Combined Heritability*	Heritability of stone formation 46% for women, 57% for men [112]	Kidney Cancer SIR 1.04 (95% CI 0.89-1.20) for those with family history of urolithiasis [119]
Genetic	*Gender*	Prevalence of stones in males 10.6% vs. 7.1% in females [2]	In males, RCC twice as common [4], TCC three times as common [179]
Comorbidity	*Obesity*	Incidence increase 20% to 42% with increasing BMI [185]	RR 1.77 for developing RCC in obese patients compared to non-obese patients [144]
Comorbidity	*Diabetes*	OR 6.9 (95% CI 5.5-8.8) for uric acid stone formation in patients with type 2 diabetes [186]	1.5 increase in incidence of diabetes in patients with RCC versus non-RCC patients [145]
Comorbidity	*Hypertension*	Incidence of stone formation 14% in patients with HTN vs. 3% in those with normal blood pressures [149]	10-22% increase risk in kidney cancer with each 10-mmHg increase in systolic or diastolic blood pressure [155]
Environmental	*Smoking*	OR 1.66 (95% CI 1.11-2.50) for calcium urolithiasis in patients who smoke [168]	52% increased risk developing RCC in current smokers and 25% in former smokers [162]
Environmental	*Alcohol**	HR 0.79 (95% CI 0.72-0.87) for risk of nephrolithiasis in those who drank > 1 drink per day compared to non-alcohol consumers [175]	28% reduction in risk of RCC in those who drink > 1 drink per day [172]

SIR: Standard Interval Ratio; CI: Confidence Interval; RR: Relative Risk; OR: Odds Ratio; HR: Hazard Ratio; RCC: Renal Cell Carcinoma; TCC: Transitional Cell Carcinoma; HTN: Hypertension. *These studies demonstrate that higher alcohol consumption lowers the risk of both stone formation and renal cancer risk; however, the evidence has been contradicted in other studies, and this relationship must be further explored.



International Journal of Surgery Case Reports 110 (2023) 108678

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.elsevier.com/locate/ijscr

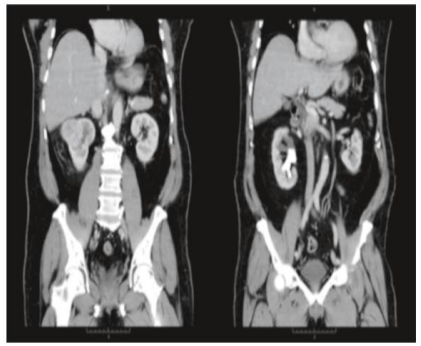
Case report

Renal cell carcinoma in a patient with staghorn stones: A case report

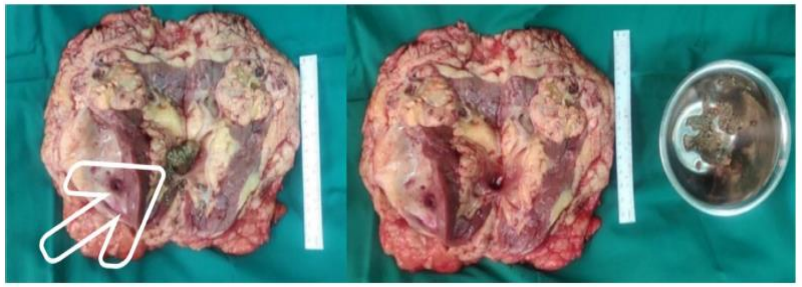
Handaru Satwikananda [a], Made Adi Wiratama [a], Karinda Triharyu Caesari Putri [b], Doddy Moesbadianto Soebadi [a,*]

[a] Department of Urology, Faculty of Medicine, Universitas Airlangga/Dr. Soetomo General-Academic Hospital, Surabaya, East Java, Indonesia
[b] Department of Urology, Faculty of Medicine, Jenderal Soedirman University/Prof. Dr. Margono Soekarjo Hospital, Purwokerto, Central Java, Indonesia

- The presence of kidney stones in renal malignancy is rare. Kidney stones can be a risk factor for renal cell malignancy, and renal cell malignancies can cause urinary stasis, making it a risk factor for kidney stones.



1. Abdominal CT scan with contrast showing staghorn stones and an inhomogeneous solid mass with contrast enhancement at the upper pole of the right kidney.



2. Gross examination of radical nephrectomy showing enlarged kidney sized 18 × 12 × 9 cm and staghorn stone (white arrow) inside the renal pelvic.

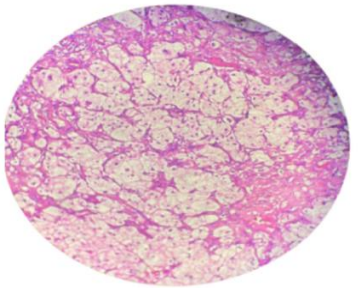


Fig. 3. Histologic examination specimen showing the histology of clear cell RCC.

Renal pelvis, and caliceal wall biopsy should be considered in chronic and large renal stone, especially staghorn stone in patient that did not have any signs of malignancy on CT scan.

de novo nephrolithiasis after kidney transplantation

Clinical Kidney Journal, 2024, vol. 17, no. 2, sfae023
https://doi.org/10.1093/ckj/sfae023
Advance Access Publication Date: 6 February 2024
CKJ Review

CKJ REVIEW

Management of *de novo* nephrolithiasis after kidney transplantation: a comprehensive review from the European Renal Association CKD-MBD working group

Mehmet Kanbay[1], Sidar Copur[2], Cicek N. Bakir[2], Alper Hatipoglu[2], Smeeta Sinha[3] and Mathias Haarhaus[4]; on behalf of the European Renal Association CKD-MBD Working Group

- ***De novo* nephrolithiasis after kidney transplantation can potentially threaten kidney graft function and survival..**

- **risk factors for nephrolithiasis in the transplanted:**
  - Female gender
  - history of kidney stone disease before transplantation
  - gout
  - hypertension
  - a longer pretransplant dialysis
  - urinary tract infections

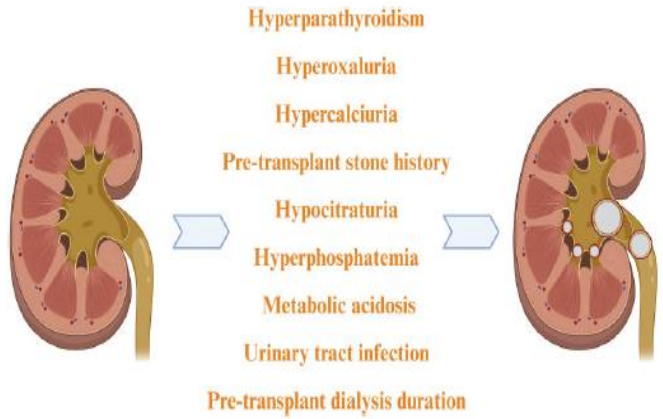


Figure 1: Possible risk factors for post-transplant nephrolithiasis.

Clinical Kidney Journal , 2024

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de novo nephrolithiasis after kidney transplantation

- ✓ prevalence of kidney stone disease of **1.7% within 3 years after transplantation**
- ✓ prevalence of nephrolithiasis among kidney transplant recipients is approximately **1%–2%**
- ✓ The mean age at diagnosis was **44years.**
- ✓ the mean time interval from trans- plant to nephrolithiasis was **28 months.**

Clinical Kidney Journal , 2024

de novo nephrolithiasis after kidney transplantation Clinical presentation

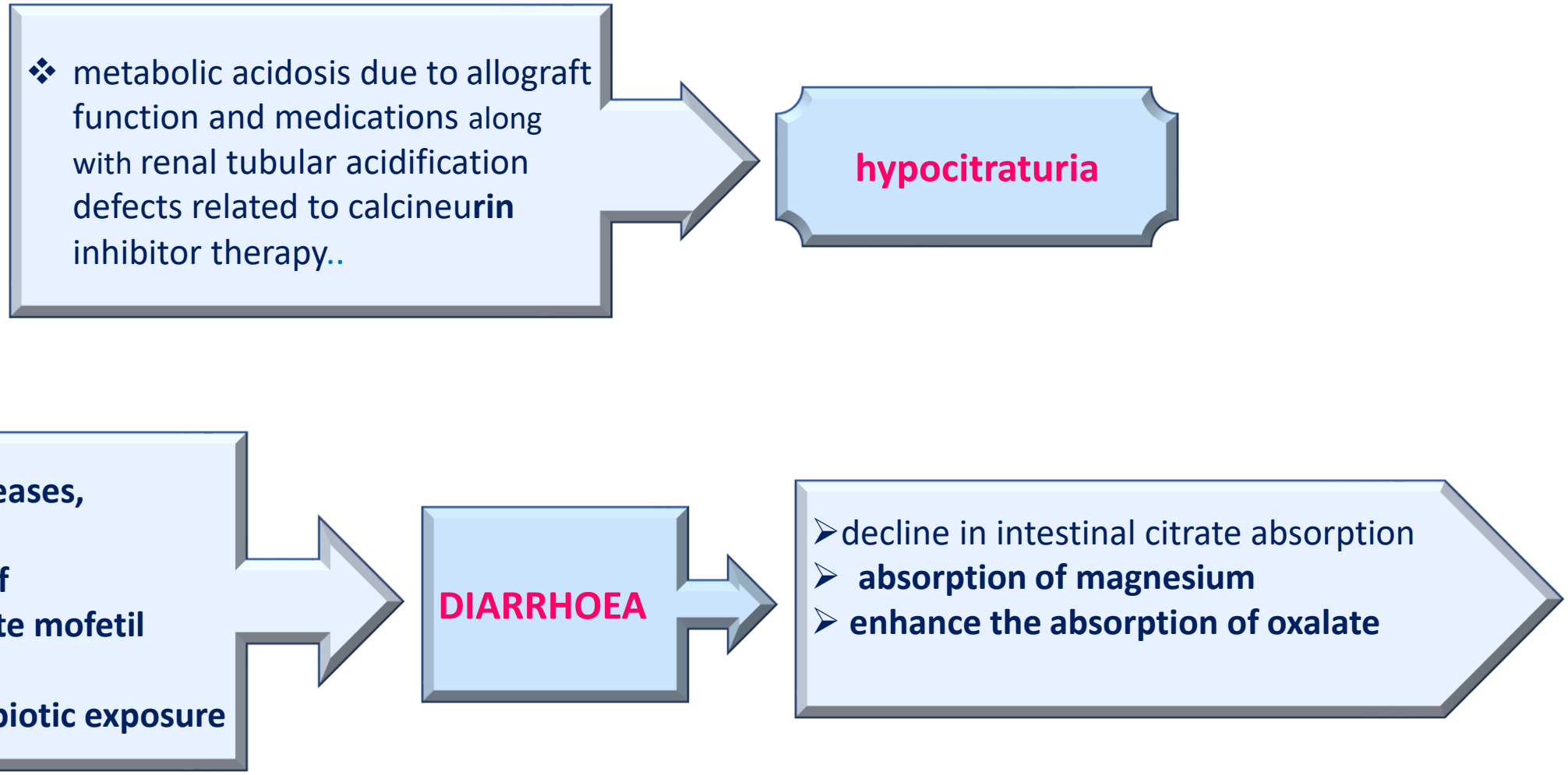
- renal transplant recipients require frequent monitoring, including imaging of the renal graft

→ asymptomatic kidney stones may be more frequently detected than in the general population.

- pain may be less prevalent because of denervation of the transplanted kidney

→ later diagnosis and more frequent complications, such as hydronephrosis and AKI

hypocitraturia and hyperoxaluria are even more prominent in renal transplant recipients.



Management *de novo* nephrolithiasis after kidney transplantation

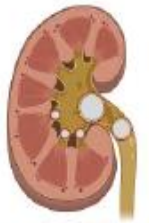
Prevention of stone formation in transplanted kidney

Life-style arragements

- Increased fluid uptake
- Controlled diuretic use
- Maintaining normal body-mass index
- Probiotic intake
- Balanced Diet
  - Controlled oxalate intake
  - Controlled calcium intke
  - Controlled sodium intake
  - Controlled citrate intake
  - Controlled animal protein intake

Medical supporting

- Citrate supplementation
- Regular kidney surveilence
- Thiazide diuretic use



Treatment of kidney stone in transplanted kidney

Non-invasive methods

- Extracorporeal shock wave lithotripsy (SWL)
- Medication
  - Thiazide diuretics
- Urinary alkalization
- Increased hydration

Invasive methods

- Semi-rigid ureteroscopy (URS)
- Retrograde intrarenal surgery (RIRS)
- Percutaneous nephrolithotomy (PNL)
- Endoscopic combined intrarenal surgery (ECIRS)
- Open-Laparoscopic and Robotic Surgery
- Ex-vivo Allograft Stone Treatment

Figure 3: Diverse treatment modalities for post-transplant nephrolithiasis.

Clinical Kidney Journal , 2024, vol. 17, no. 2, sfae023

Computational and Structural Biotechnology Journal 21 (2023) 3854–3864

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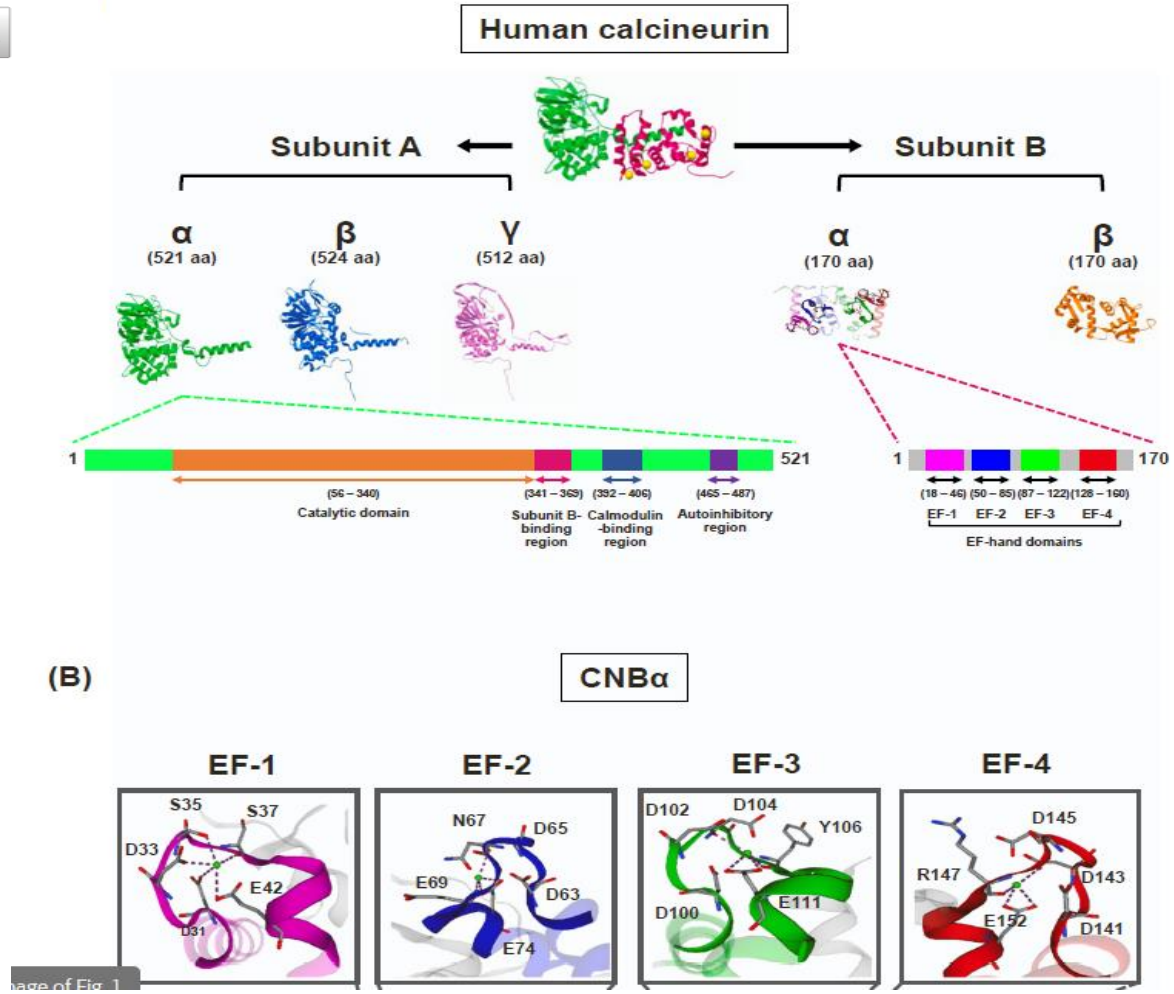
Calcineurin B inhibits calcium oxalate crystallization, growth and aggregation via its high calcium-affinity property

Sudarat Hadpech, Sakdithep Chaiyarit, Visith Thongboonkerd *

Medical Proteomics Unit, Research Department, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

- CNB dramatically inhibited COM crystal formation, growth and aggregation. At an equal amount, degrees of its inhibition against crystallization and crystal growth were slightly inferior to that of TUPs from healthy subjects that are known to strongly inhibit COM stone formation.



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Calcineurin B inhibits calcium oxalate crystallization, growth and aggregation via its high calcium-affinity property

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Medical Proteomics Unit, Research Department, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

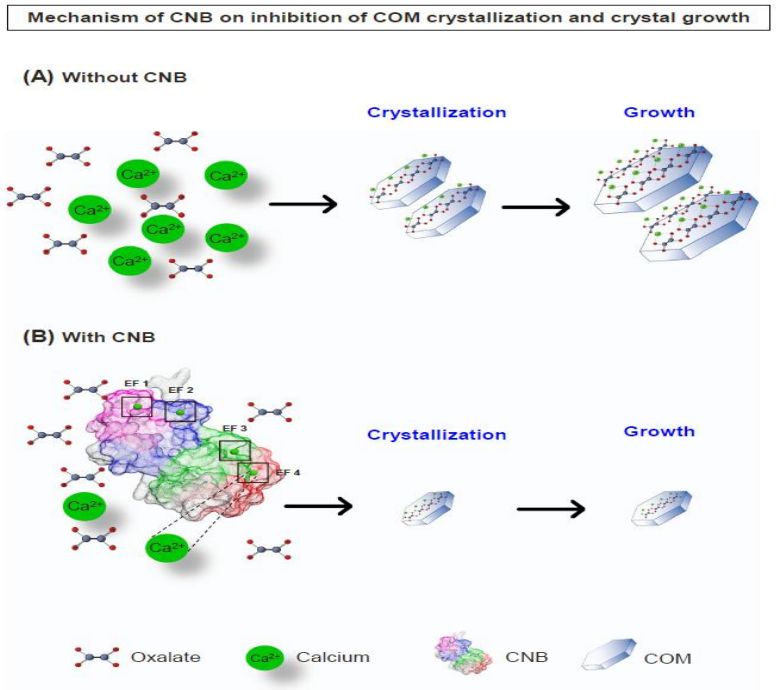

Fig. 7. Mechanism of CNB on inhibition of COM crystallization and crystal growth. (A): COM crystals are formed by Ca^{2+} and oxalate ions in the supersaturated urine or renal tubular fluid. After crystallization, the free Ca^{2+} and oxalate ions can add onto crystalline surfaces, leading to crystal growth. (B): In the presence of CNB in the urine, the free Ca^{2+} ions are captured by EF-hand (Ca^{2+}-binding) domains in the CNB molecules, leading significant decrease in free Ca^{2+} ions, which are crucial for COM crystal formation and growth, leading to inhibition of COM crystallization and crystal growth.

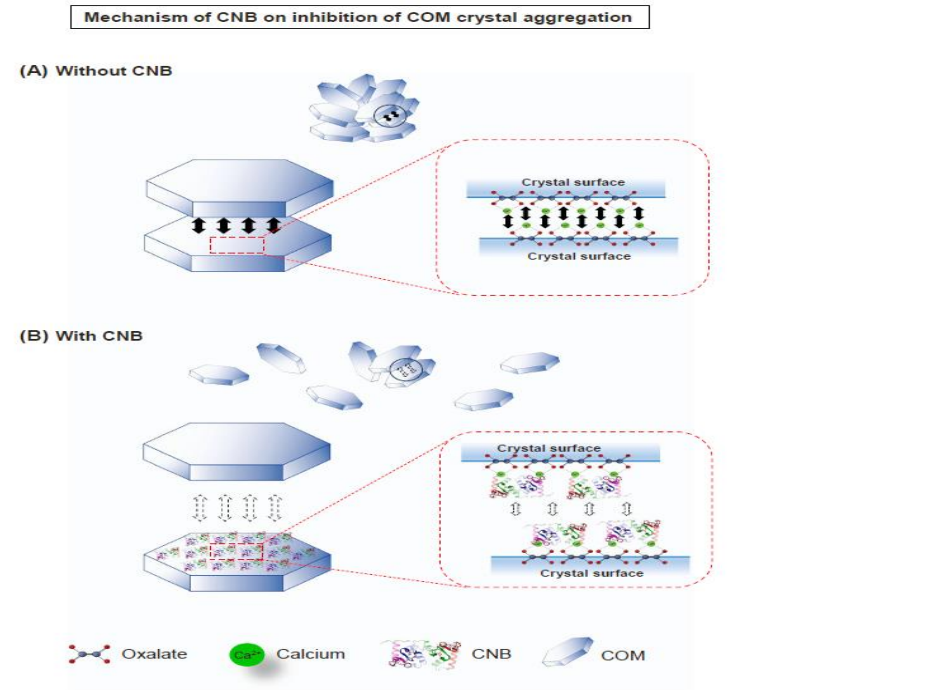

Fig. 8. Mechanism of CNB on inhibition of COM crystal aggregation. (A): COM crystals generally have a high adhesive capability that can bind to various surfaces, including the crystal surfaces themselves, leading to crystal self-aggregation. (B): In the presence of CNB in the urine, CNB can bind to the crystal surfaces rich with Ca^{2+} molecules via EF-hand (Ca^{2+}-binding) domains, thereby reducing adhesive force on the crystal surfaces, leading to inhibition of crystal aggregation.

Systemic conditions associated with nephrolithiasis

Coronary artery disease
Chronic kidney disease and end-stage kidney disease
Bone disorders and fractures
Aortic calcification
Hypertension
Type 2 diabetes mellitus
Gout
Metabolic syndrome
Sarcoidosis
Renal tubular acidosis
Bowel disease and intestinal surgery
Renal and bladder anatomic anomalies
Medications
Genetic abnormalities

- Nephrolithiasis is now recognized as a marker for **systemic disease** and a predictor of **metabolic and cardiovascular complications**
- kidney stone disease is best addressed by a **team led by nephrologists and urologists** with input from multiple other health professionals including dietitians, endocrinologists,interventional radiologists, and endocrine surgeons.