

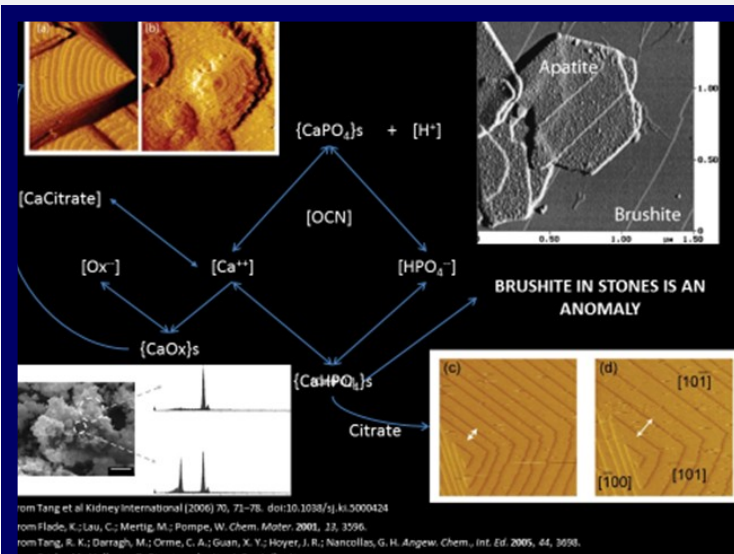
HIGHLIGHTS



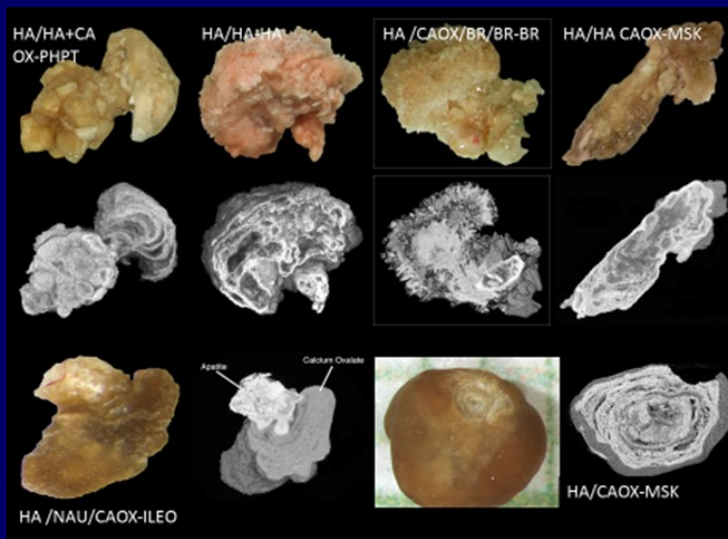
Fredric Coe
University of Chicago
Medicine
Department of
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Chicago, USA

Calcium kidney stones: different phenotypes

Prof. Coen from Chicago presented very recent data on the phenotyping of calcium kidney stones. Calcium oxalate, Brushite, hydroxyapatite. These are three main phenotypes that calcium kidney stones are divided into. Their formation observes well defined physical laws and is based on the phenomenon of "Supersaturation" that takes place in the urine. Hence, in the presence of "supersaturated" urine the calcium molecules combine with those of the monophosphate to form brushite molecules which in turn combine with hydrogen ions to form the hydroxyapatite molecules. Finally, the calcium molecules combine with those of the calcium oxalate. The supersaturation condition is in turn



responsible for the crystallisation of said molecules. These are the main phenotypes of calcium kidney stones. At this point Prof. Coen described how, by starting from these three main situations, it is possible to delineate different phenotypic levels: the genetic level, the disease level and the syndrome level. Based on these different levels we are able to make diagnoses, decide on treatment, hypothesise the prognostic outcomes, and conduct different genomic studies.



What are the main mechanisms involved in these phenomena? What are the main formation procedures of kidney stones? Are they always located at the level of particular loci defined as plaques?



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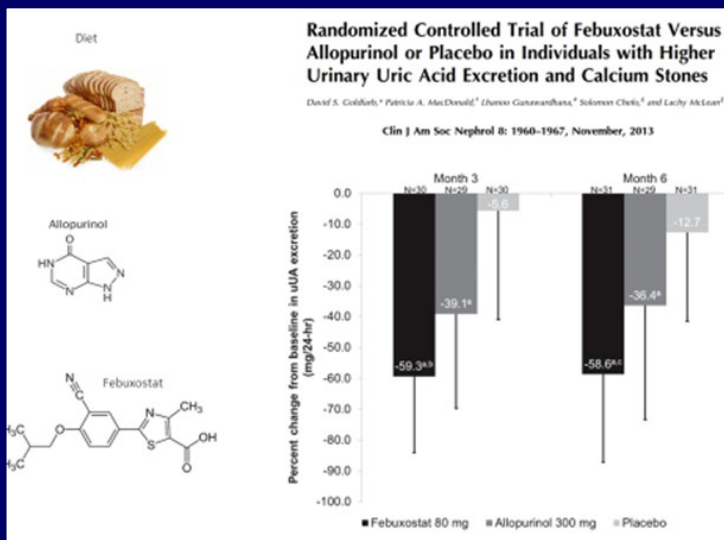
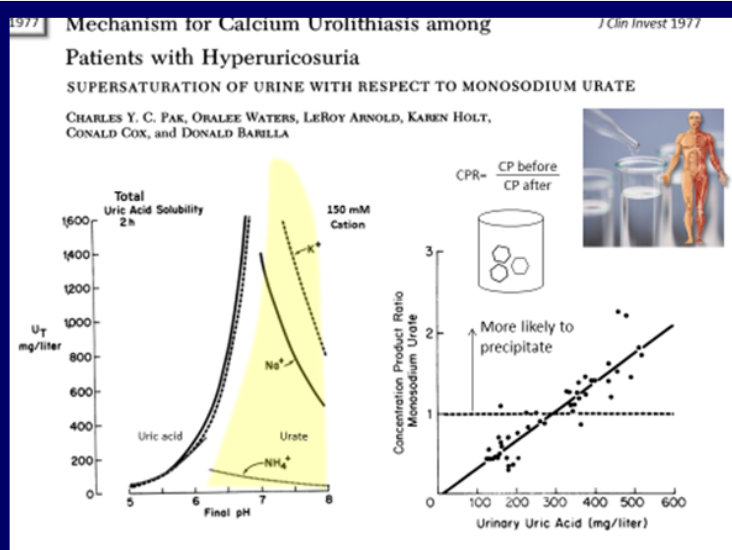


Orson Moe

University of Texas
Southwestern
Medical Center
Department of
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Dallas, USA

What are the main interactions between calcium kidney stones and hyperuricosuria?

Patients suffering from different urinary levels of uric acid are also prone to developing urolithiasis. This issue was addressed by Prof. Moe from Dallas. We are mainly dealing with subjects with hyperuricosuria, mixed calcium oxalate and urate kidney stones, and other risk factors such as hypercalciuria. The presence of high concentrations of monosodium urate in the urine favours the precipitation of the calcium salts. This phenomenon is further reinforced by the colloidal condition of the urate molecules that in turn



determine the inhibition block of the formation process of the calcium oxalate molecules thus encouraging the formation. In order for these complexes to complete the transformation process into calcium oxalate crystals, another passage is fundamental, defined as salting-out and deriving from the high saline concentration in the urine. Prof. Moe addressed the issue regarding these patients by presenting data on treatment with allopurinol and febuxostat.

Are all hyperuricosuric patients exposed to the risk of developing urolithiasis to the same extent? Does this pathological condition expose patient to other risks of disease?



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David Bushinsky

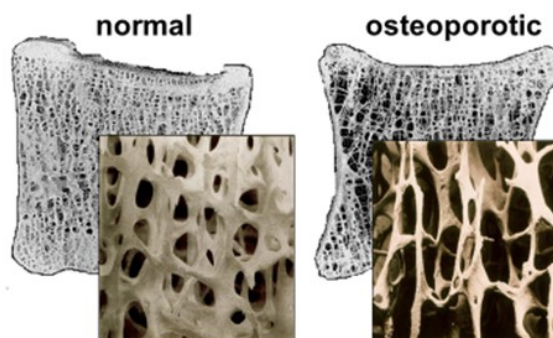
University of
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Rochester, USA

Which patients with hypercalciuria are at the risk of Osteoporosis?

The main calcium deposit in our body is found in the bone tissue; on the other hand, calcaemia is an indicator that must never undergo significant variations in its values. As a result, all the control mechanisms present in our organism are designed to maintain stable blood calcium levels, to the detriment of the tissue storage, especially the bone tissue. Starting from this assumption, Prof. Bushinsky from Rochester posed the following question: are all patients suffering from hypercalciuria at the risk of osteoporosis ? The answer to this question is unequivocal: yes, patients with hypercalciuria are all at the risk of osteoporosis, but

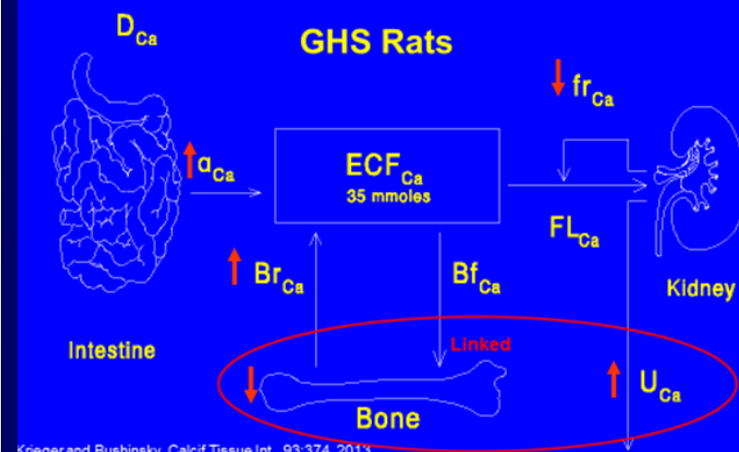
hypercalciuria at the risk of osteoporosis ? The answer to this question is unequivocal: yes, patients with hypercalciuria are all at the risk of osteoporosis, but

Vertebral body



Calcium

GHS Rats



which are the mechanisms at the metabolic bone level underlying this disease? In other words, we find ourselves facing hyper bone reabsorption phenomena, is this problem linked to a multitude of factors that arise during our lifetime? To find a convincing answer to this question Prof. Bushinsky presented data produced from studies on so-called kidney-stone forming rats subjected to well controlled diets. But which pharmacological treatments are available? In fact, not all drugs that act on the bones have superimposable mechanisms, and based on the effects that we want to achieve, it is possible to choose one specific drug instead of another one.

We still need to answer the aforementioned questions: what are the metabolic mechanisms which determine osteoporosis in patients with hypercalciuria? Which are the most suitable pharmacological treatments?



HIGHLIGHTS



Elaine Worcester

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Department of
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Chicago, USA

Nephrolithiasis: a disease associated with different systemic causes: how can we assess these?

Prof. Worcester from Chicago, addressed this topic by explaining that a common denominator exists in all these conditions: the state of supersaturation of the urine, is an essential condition for the onset of nephrolithiasis. At the basis of this phenomenon there may be a whole series of mechanisms, both genetic and acquired, that must be identified also using recent family genetic-based screening methods. There is therefore a wide range of genetic diseases that determine the state of “stone former”, and which must be treated as they expose patients to the risk of developing kidney failure. There are also the so-called acquired forms, such as primitive hyperparathyroidism for example, as well as Sarcoidosis, nutritional disorders, intestinal resection

surgery, all conditions that facilitate the onset of kidney failure. The basic diagnostic tools are very easy to use and quite economical. A simple dipstick for uricosuria and a blood specimen for the dosage of creatinine, uric acid, calcium, sodium potassium and a blood count. The patients selected in this way can then be subjected to additional tests.

Genetic Stone Diseases	Specific Rx	Organ sequelae	Family screening	Genes
Cystinuria	Yes	CKD	Yes	2
APRT (2,8-DHA)	Yes	CKD	Yes	1
Dent disease 1,2	No	CKD	Yes	2
Primary HO 1,2,3	Yes	CKD	Yes	3
HNL/OP (NHERF)	No	Bone	Yes	1
Sodium-phosphate transporter disorders	No	Bone	Yes	2
CYP24A1	Yes	CKD	Yes	1
Claudin disorders	No	CKD	Yes	2
Bartter's syndromes 1-5 (and ADH)	Yes		Yes	4
Xanthinuria	Yes			(3)
Uric acid metabolism disorders		CKD	Yes	3
Distal RTA	Yes	CKD, bone	Yes	4

Are there any specific therapeutic protocols per single disease? What are the systemic diseases with the highest prevalence of nephrolithiasis?



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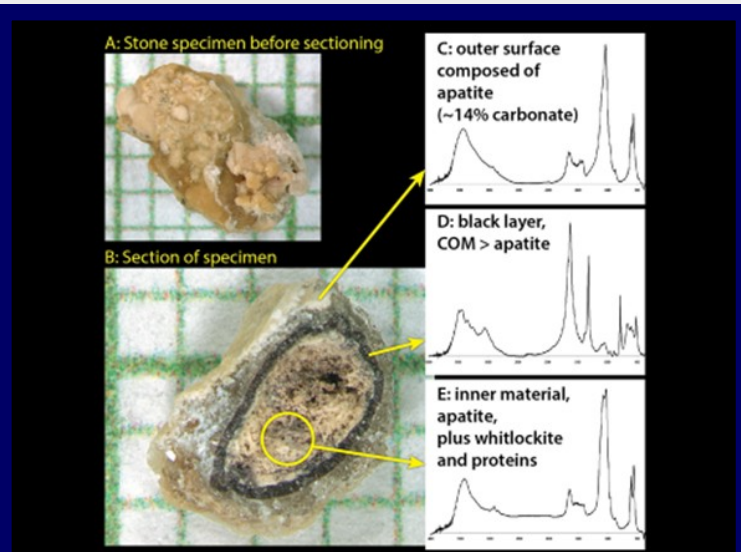


James Williams
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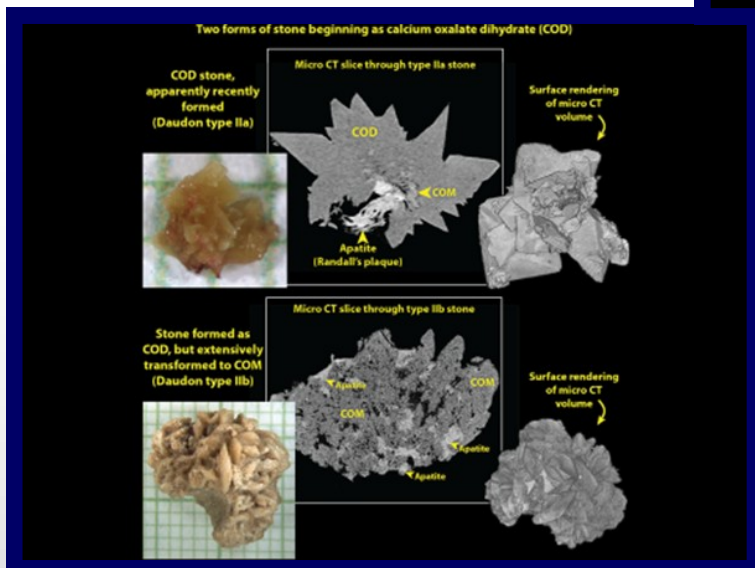
How important is it to analyse kidney stones?

Prof. Williams from Indianapolis spoke about the diagnosis applied to the analysis of kidney stones. Firstly, not all available methods are reliable, in terms either of the results or the intrinsic complexity of the method. The only reliable methods are the infrared spectroscopy and the diffraction X-ray, both of which must be integrated with dissection of the stone using the stereo microscope. Why should we dissect the stone? Because experimental data have demonstrated that over 90% of kidney stones contain

more than one component. It is also important in clinical terms to study the chemistry of the individual stones, as the morphology of a stone



is often linked to specific diseases. Renal tubular acidosis, some rare diseases, and chronic hypercalciuria are all diseases linked to specific morphological characteristics of kidney stones. For these reasons, but not only, the analysis of the stone becomes crucial in order to be able to correctly manage the patient. Prof. Williams stressed how this method has not been sufficiently developed worldwide, above all when compared with other diagnostic methods applied in different clinical conditions.



Several open queries: in clinical terms is it preference to know the chemical composition of the stone that initially formed, or the one arising from following transformations? Also, is it possible to identify the chemical composition of the stone with in vivo diagnostic methods?



HIGHLIGHTS



Emanuele Croppi
A.S.L. 10 Florence
Florence, Italy

Cooperation between Urologists and Nephrologists: what are the advantages?

Prof. Croppi from Florence, addressed this delicate and at the same time, very important topic. Even though it is to be hoped for, the interaction between these two specialists is still not very widespread. The urologist is the one who surgically treats the patient, thus intervening during the acute phase of the disease, whereas the nephrologist steps in afterwards, especially when

the kidney is involved in clinical terms. The latter therefore intervenes during the chronic stage of the disease. Collaboration between these two specialists becomes fundamental for a whole variety of aspects typical of the evolution, diagnosis, complications and treatment of



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NEPHROLITHIASIS AND ITS SYSTEMIC MANIFESTATIONS

Despite this

nowadays the relationship between
urologist and nephrologist :



- Receives little attention from the literature
- Is not ruled by guidelines
- Is often "alternative" rather than "complementary"



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NEPHROLITHIASIS AND ITS SYSTEMIC MANIFESTATIONS



Summarizing ...

*Many overlap areas where it is necessary to
work together*

this disease. To give a few examples: in case of renal failure which therapeutic protocol should be applied, interventional or conservative? How should the analysis of the kidney stone be carried out? What indications can this analysis give in therapeutic terms? Are there alternatives to surgical treatment?

What actions should be undertaken to make this collaboration more efficacious? How should patients be managed in case of recurrent episodes? Do any common guidelines exist that involve both specialists?



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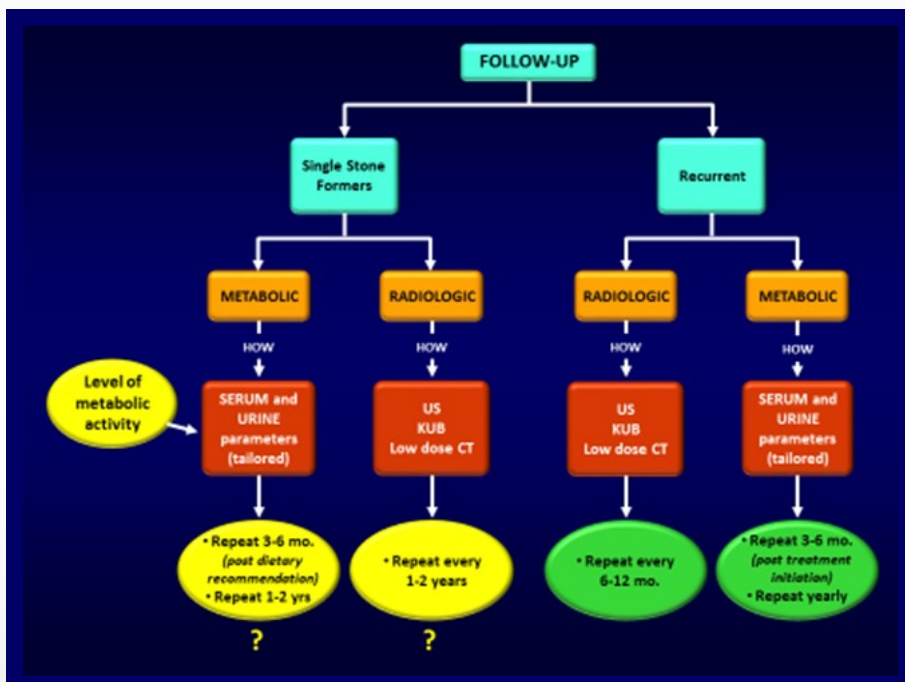
Ita P. Heilberg

Sao Paulo University
Department of Nephrology
Sao Paulo, Brazil

How to manage the follow-up of patients suffering from nephrolithiasis?

Prof. Heilberg from San Paolo in Brazil spoke about the follow-up strategies to be applied to these patients. They can be divided into two broad categories: metabolic and radiological. In fact, these patients are in any case at the risk of developing renal failure over time that lead to the terminal stage. In other words, after renal cancer, nephrolithiasis is one of the main causes of nephrectomy. In patients suffering from relapses, there are rather definite rules regarding the exams to be implemented and how often. In-

stead, the problem arises with the so-called “single stone formers” who are those patients who develop nephrolithiasis maybe only once in their lives but still present the same metabolic and genetic traits typical of the disease, despite the fact that the symptoms only manifest in a single episode. These patients are equally at the risk of renal failure as the ones who have recurrent episodes. In order to be able to act on these patients especially, the indications that can be drawn from randomised clinical trials are not sufficiently clear or homogeneous. Above all, there is no evidence that the therapeutic strategies used are predictive for the intermediate outcomes, such as the prevention of relapses or even the final outcomes such as long-term health conditions.



Which metabolic and radiological exams should be implemented? How often should patients be recalled for a check-up?



HIGHLIGHTS



José M. Reis Santos
Catholic University of
Portugal, Department
of Urology
Lisbon, Portugal

Urological treatment of kidney stones: a situation in continuous evolution

Prof. Santos from Lisbona addressed this topic by starting off with one of Hippocrates' adages: "I will never use the knife (read scalpel here), not even on patients suffering from kidney stones". It is indeed rare that a statement in medicine holds the pace for more than a thousand years.... this is perhaps the exception to the rule! To date open surgery for treating nephrolithiasis has only been carried in very few select cases and not more than 4% in all case studies.

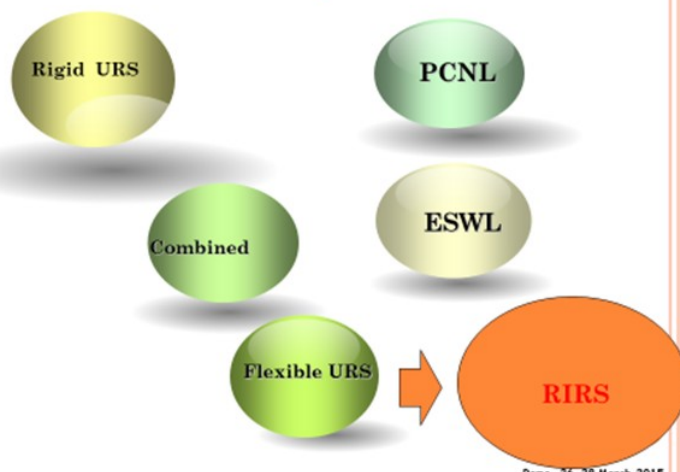
Over time, a series of decidedly less invasive techniques have been perfected, such as URS (Ureterorenoscopy), PCNL (Percutaneous Nephrolithotomy), a combined technique known as a ESWL (Extracorporeal

FACTS: FUTURE ADVANCES IN URS



Rome, 26-28 March 2015

Less invasive techniques



Rome, 26-28 March 2015

shock wave lithotripsy), up to the very recent RIRS (endoscopic surgery of the upper urinary tract). Of all these methods, the one most used is ESWL, seeing that it is the least invasive, nevertheless it is associated with a higher incidence of relapses compared to URS. The interesting aspect is that these methods are in constant evolution, and even arrive at the use of robotic assistance which today allows for operating in better conditions with evident benefits from all points of view, for the patient and the operator, by reducing the intervention times, in the training of new operators and also by cutting costs.

What are the advantages and disadvantages of each of these methods?
Which should be applied to the different types of patient? How do robotics intervene in managing these patients?



HIGHLIGHTS



Giovanni Gambaro
Catholic University of
the Sacred Heart
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Department of Ne-
phrology and Dialysis
Rome, Italy

Are all the so-called “stone former” patients at the risk of renal failure?

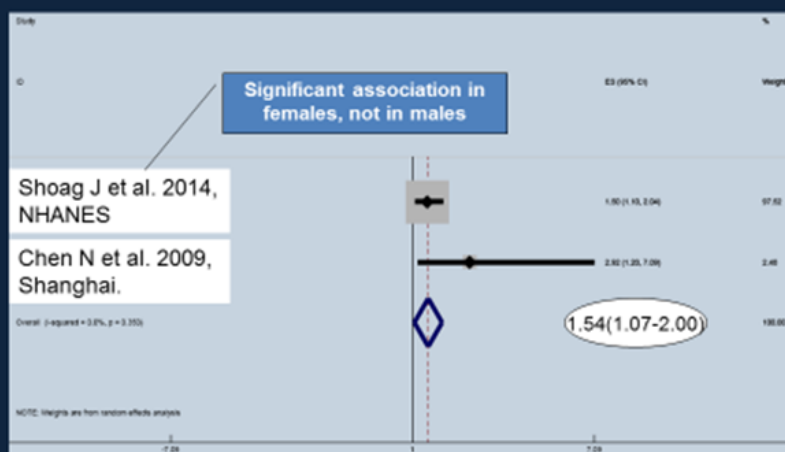
Prof. Giovanni Gambaro from Rome addressed this delicate issue. Are patients who during their lifetime suffer one or more episodes of kidney stones subject to a greater prevalence of renal failure compared to the population not affected by this disease?

From an analysis of literature Prof. Gambaro provided some very interesting results: first and foremost, there is a significant

difference between genders as women have a stronger correlation for the risk of developing renal failure than men. Not only, but their risk increases even more if these patients are also suffering from hypertension, diabetes, dyslipidaemia, obesity or gout.

Kidney stones and CKD

2 cross sectional studies allow the estimation of the associated risk CKD-renal stones



But what effect does surgical treatment of renal lithiasis have on the functioning of the kidneys?

Finally, the Congress consisted of the presentation of a whole series of recommendations advanced by 9 work groups led by experts, regarding the main themes that still need in-depth analysis and precise regulations by the main international societies in this sector, with the drafting of updated guidelines. In order to examine this last section of the congress and view the other talks given, please visit the website of the Fondazione Internazionale Menarini which contains the integral versions of all the congress works. Visit the link: www.fondazione-menarini.it/... and after having logged in, access the multimedia material.



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