

13th International Symposium on Urolithiasis

LECTURE

L-01

Extracorporeal shock wave lithotripsy (ESWL)

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Despite the successful achievements with SWL there is presently a trend towards the preferred use of invasive endoscopic procedures rather than a non-invasive approach by means of SWL. This development is an effect of a considerable discrepancy in SWL results. Literature data name stone-free rates for renal and ureteral stones in the range of 32–90 % and 43–98 %, respectively, and a similar variation in terms of successful stone disintegration. Proper use of the lithotripsy system and correct application of shock waves are crucial aspects for the SWL outcome regarding efficacy and safety.

Before asking for technical improvement it needs to be pointed out that a significant fraction of patients with inferior SWL results could have been better treated if the SWL technique had been used in an appropriate way. Lack of interest in SWL and the false assumption that it is the lithotripter rather than the operator that is responsible for the treatment result are a bad prerequisite for success.

All users should be aware, that SWL is a complex technology with potential risks and that they must have basic knowledge of the underlying physics as well as of characteristics and features of the used lithotripsy system. Sufficient analgesia, fixation of the patient, proper coupling of the shock wave system and a slow shock wave administration rate are important measures to ensure a good stone disintegration. Patient adapted selection of shock wave parameters, pretreatment with low shock wave energy and renoprotective drugs like calcium channel blockers or antioxidants seem to be beneficial for a reduction of tissue traumatization. Stonefree rate after SWL can be improved with supporting measures like physical therapy (percussion, diuresis, inversion) and short term medical therapy (medical expulsive therapy) with α 1-receptor blockers or calcium channel blockers.

In spite of all newly arisen discussion SWL still remains the only non-invasive treatment modality for urolithiasis besides conservative stone management and it plays a major role in stone therapy due to its efficacy, low rate side effects and comfortable application, without the need of general anaesthesia and—last but not least—patients' acceptance.

COI: No.

L-02

Residual fragments: definition, evaluation and management

Kemal Sarica

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The number of patients undergoing active minimal invasive stone removal procedures is steadily increasing. Depending on this fact again, concern of the residual stone material is being encountered in a significant proportion of the patients treated in this manner. Although the residual fragments (RF) are commonly seen after ESWL, but they may also remain in the renal collecting system following PNL and RIRS. Currently, a consensus that symptomatic residuals need to be eliminated has been established while studies did show that in up to 42 % of the of these patients additional stones may form at a follow-up of 5 years. Again, long-term studies did show that recurrent stone formation may be seen in as many as 70–80 % of the patients after 10–20 years. Regarding the definition of RF; asymptomatic, non obstructive as well as non-infection related stone particles sizing less than 4 mm after certain types of treatment are being accepted as RF. The risks involved with RF are new stone formation, recurrent UTI and obstruction-pain due to positional change. Some types of calculi including infection, uric acid and cystine stones have the most likelihood of growth over time. On the other hand, for calcium containing stones the presence or absence of metabolic risk-factors are highly important for re-growth and new stone formation. Available data showed that secondary procedures are needed in symptomatic patients with urinary obstruction and UTI as well as in special cases as pilots and kidney recipients. Although stone type, size and location seem to be important for future changes in residual fragments; extensive invasive methods, do not seem to be necessary in a majority of these patients, where SWL will be the first choice. However removal of all remaining fragments is paramount importance in patients with non-calcium contain in stones. Last but not least, while calcium stone residual fragments usually do not require aggressive re-treatment with the aim of removing every little fragment from the kidney; they require a meticulous metabolic evaluation and recurrence preventive measures.

COI: No.

L-03

Urinary risk factors for urolithiasis

William G. Robertson

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Objectives: Three systems are compared for assessing the biochemical risk of forming urinary stones based on the composition of 24-h urine.

Methods: The relative supersaturation of urine (RSS), the Tiselius Indices (TI) and the Robertson Risk Factor Algorithms ($P_{s,t}$) are compared in the 24-h urine samples from 460 consecutive calcium and/or uric acid stone-formers in terms of the numbers of variables required to be measured, the ease of use of the system and the relative cost of the analyses concerned.

Results: The calculation of RSS (SUPERSAT) requires 12 analyses in every urine sample but provides RSS data on calcium oxalate

(CaOx), calcium phosphate (CaP), uric acid (UA) and magnesium ammonium phosphate (MAP). TI and P_{sf} each require only 7 analyses. TI yields information on the crystallisation potentials of CaOx and CaP; P_{sf} provides information on the crystallisation potentials of CaOx, CaP and UA. All three procedures identify the urinary abnormalities that lead to the abnormal crystallisation potential of the urine concerned. Comparison of the three indices in the 24-h urines from 460 consecutive stone-formers shows (a) that there are good correlations between RSS, TI and P_{sf} as measures of the risk of forming CaOx- and CaP-containing stones and (b) that there is also a good correlation between RSS and P_{sf} for the risk of forming UA-containing stones. There is currently no TI procedure for measuring the risk of forming UA-containing stones.

Conclusions: Measuring RSS in urine is work-intensive and expensive to run making it unsuitable for the routine screening of patients. TI and P_{sf} are equally as good as RSS at predicting the risk of a patient forming further calcium-containing stones and P_{sf} is as good as RSS for predicting the risk of a patient forming further UA-containing stones. Since TI and P_{sf} only require 7 analytes to be measured, it is suggested that these are the methods of choice for the routine screening of patients attending a Stone Clinic. P_{sf} has a slight advantage over TI since it also measures the risk of forming UA-containing stones.

COI: No.

L-04

Overview of endourology

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The term “endourology” has been coined by Arthur Smith to describe closed, controlled manipulation in the genitourinary tract. With respect to urolithiasis endourology comprises percutaneous nephrolithotomy (PCNL), laparoscopic pyelolithotomy and ureterolithotomy, and ureterorenoscopy (URS). Although these techniques have been introduced already 40 years ago, there was a push in the worldwide acceptance and dissemination during the last decade. This is mainly due to technical improvements of the instruments used for endourologic procedures therefore enabling higher stone free rates combined with less morbidity. Although extracorporeal shock wave lithotripsy (ESWL) is still a widespread treatment modality for renal and ureteral stones, its administration is decreasing for several years whereas the use of endourology is increasing. Today, all urinary stones are amenable by endourologic procedures with higher success and similar complication rates when compared to ESWL.

For therapy of renal stones different types of PCNL (conventional, mini, ultra-mini, micro-PCNL) are available. Especially smaller renal stones can be managed also by retrograde intrarenal surgery (RIRS) using flexible ureterorenoscopes. In a few, selected cases laparoscopic stone removal can be an alternative approach.

For therapy of ureteral stones different types of ureteroscopes (semirigid, flexible) are available. In rare special situations laparoscopic surgery may be indicated.

The differential indication of the appropriate treatment modality is dependent on the location, size and composition of the stone and anatomical factors.

For stone disintegration several systems (laser, ultrasound, pneumatic) are available. The holmium laser may be regarded as the gold standard as it is very effective and can be used also with flexible instruments.

In this overview lecture all these techniques mentioned above will be discussed in detail especially with its indications, results and complications for the different stone situations in the upper urinary tract.

COI: No.

L-05

Cystinuria: genomic characteristics in Japan

Tomohiko Ichikawa, Shinichi Sakamoto

Department of Urology, Graduate School of Medicine, Chiba University, Japan

Introduction: Cystinuria is caused by a defect in the cystine transporter rBAT(SLC3A1)/BAT1(SLC7A9). We have previously identified the unique mutation, P482L that is responsible for Japanese patients with cystinuria. Since P482L mutation has not been found in European countries, Japanese patients seem to possess unique genomic characteristics that are quite different from European patients. Although cystinuria is known to be an autosomal recessive disorder, a heterozygous P482L mutation causes cystinuria in a number of Japanese patients. Based on those unique characteristics, we have analyzed a correlation between genotype and phenotype of cystinuria patients in Japan.

Materials and Methods: DNA was extracted from blood samples of patients at Chiba University Hospital and a collaborative hospital in Japan. Mutations in rBAT/BAT1 were examined by direct sequencing. Cystine concentrations in urine were assessed by 24-h acidic urine collection. Written informed consent was obtained from each patient.

Results: Mutations in rBAT were found in 24 % of patients examined. The P482L mutation was found in 72 % of the patients. A half of those patients possessed a homozygous P482L mutation and the other possessed a heterozygous P482L mutation. When these patients were grouped based on a genotype classification proposed by Dello et al., 62 % of patients were classified into either Type A (two rBAT mutation), Type B (two BAT1 mutation), or Type AB (one rBAT and one BAT1 mutation). However, the other patients were unclassified in those three categories. Therefore, two more categories, Type a (one rBAT mutation) and Type b (one BAT1 mutation) were added. Nearly 90 % of unclassified patients were classified as Type b and the other were classified as Type a. Type b showed a clinically significant increase in the average cystine concentration as observed in Type B and AB. Moreover, the highest concentration was observed in the P482L homozygous mutation.

Conclusion: Cystinuria has been recognized as an autosomal recessive disorder; however, in cases with a P482L mutation, half of the patients were heterozygous. Because their genotype is quite different from that of patients in western countries, a new classification may be needed for Japanese patients with cystinuria.

COI: No.

L-06

Transporter and urolithiasis

Yoshikatsu Kanai

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The genetic defect or functional alteration of renal tubular transporters has been related to urolithiasis. Among them, one of the most prominent examples is the cystinuria caused by the loss-of-function

mutations of renal cystine transporter. The cystine transporter is the heterodimeric protein composed of a catalytic subunit $b^{0,+}AT$ (SLC7A9) and an auxiliary subunit rBAT (SLC3A1). The mutation of either subunit causes urinary loss of cystine as well as dibasic amino acids leading to urolithiasis. The mutation of $b^{0,+}AT$ shows interesting ethnic difference: among more than 80 % of Japanese cystinuria cases, we found P482L mutation of $b^{0,+}AT$ that is quite unique to Japanese or Asian population. One of the unsolved issues regarding the cystinuria and renal cystine transport has been the presence of the second cystine transporter whose genetic defect is proposed to be involved in a type of cystinuria distinct from that caused by the mutations of the $b^{0,+}AT/rBAT$. In fact, there is a remarkable discrepancy in the tubular localization of rBAT and $b^{0,+}AT$: rBAT is highly expressed in the late proximal tubules, whereas $b^{0,+}AT$ expression is the highest in the early proximal tubules. We have found that SLC7A13 is the partner of rBAT in the late proximal tubules and comprises the cystine transporter. We proposed that SLC7A13 is the long-postulated second cystine transporter and a possible candidate involved in isolated cystinuria. Another unsolved problem on cystinuria-related transporters has been the cause of the functional loss of P482L mutation that affects C-terminus end of the transporter protein. To solve this issue, we have generated P482L knock-in mouse. The knock-in mouse exhibited urine phenotype similar to cystinuria patients. P482L protein was properly located in vivo as wild-type $b^{0,+}AT$. It is noted that P482L transporter in the brush border membrane preserved the similar substrate binding ability to that of the wild-type, although it lost cystine transport activity, suggesting that disturbing the conformational changes after substrate binding leads the dysfunction of transporters. We propose that the pathogenic protein–protein interaction is involved in this process, which can be removed by appropriate treatment to ameliorate the disease phenotype.

COI: No.

L-07

Animal models for study of calcium oxalate nephrolithiasis: lessons learned

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Number of animal models of CaOx nephrolithiasis have been developed using animals such as rats, mice, pigs and drosophila. Hyperoxaluria is induced by administration of oxalate as sodium or potassium oxalate, or oxalate precursors such as ethylene glycol or hydroxyl-L-proline which leads to CaOx nephrolithiasis. Epithelial exposure to high oxalate and CaOx crystals results in production of reactive oxygen species and biomineralization regulating macromolecules (MM). Results indicate that there are two types of MMs, one is inducible and another non inducible. Genes encoding for fibronectin, CD 44, fetuin B, osteopontin, and matrix-gla protein, are up-regulated while those encoding for heavy chains of inter-alpha-inhibitor 1, 3 and 4, calgranulin B, prothrombin, and Tamm-Horsfall protein are down-regulated. Epithelial cells are injured and cellular degradation products (CDP) are released into urine. The MMs and CDPs become incorporated into growing crystalline deposits as organic matrix. CaOx nephrolithiasis also induces osteogenic changes in the kidneys consistent with dedifferentiation of epithelial cells into osteogenic phenotype. Genes for runt related transcription factors (RUNX1 and 2), zinc finger protein Osterix, bone morphogenetic

proteins-2 and 7, bone morphogenetic protein receptor-2, collagen, osteocalcin, osteonectin, osteoprotegerin, cadherins, fibronectin and vimentin are upregulated. Anti-inflammatory and anti-oxidative treatments to hyperoxaluric rats are associated with reduction and in some cases complete inhibition of renal CaOx crystal deposition.

There are two basic pathways to stone formation. Some develop attached to sub-epithelial plaques on renal papillary surfaces. These plaques consist of calcium phosphate, begin deep inside the renal interstitium and are called Randall's plaques. None of the animal models have so far been able to imitate development of Randall's plaques. Other types of stones grow on crystals plugging the openings of the ducts of Bellini. Most animal model studies appear to imitate the production of plugs. Apparently, urine becomes supersaturated with respect to CaOx leading to crystal formation. Crystal growth, aggregation and their retention within the tubules initiate their blockage. Such a blockage of the ducts of Bellini and their openings into the pelvic urine lead to the formation of plugs, which become nidus for future development of the kidney stones.

COI: No.

L-08

The role of fluid intake in the recurrence prevention of urinary stones

Roswitha Siener

University Stone Centre, Department of Urology, University of Bonn, Germany

A low urine volume is one of the most important risk factors for urinary stone formation. An adequate fluid intake, to achieve a urine volume of at least 2.0 l/24 h, is the most important dietary measure for the prevention of recurrent urinary stone formation, irrespective of stone composition. The type of beverages should be carefully selected. Although mineral water has been suggested to be a suitable beverage for urine dilution, the water composition has to be taken into account. The bicarbonate content of mineral water can replace alkalization therapy with potassium citrate and contribute to urine inhibitory power by increasing urinary pH and citrate excretion. The effect of fruit juices on urine composition is mainly determined by the presence of citrate. Citrus juices are rich sources of citrate. However, RCTs are lacking and data from interventional and cohort studies on the effect of different types of fruit juices on the risk of urinary stone formation are conflicting. Coffeinated coffee, black and green teas are less suitable for urine dilution. Alcoholic beverages and soft drinks are unsuitable for recurrence prevention of urolithiasis.

COI: No

L-09

Role of race, ethnicity and environmental factors

Allen L. Rodgers

University of Cape Town, South Africa

The potential existence of a relationship between race, ethnicity, environmental factors and urolithiasis has been investigated for decades. Race refers to groups who share biologically or genetically transmitted physical traits while ethnicity refers to groups who are linked culturally. The literature abounds with observations of apparent differences in stone occurrence between cognate groups of

different race and ethnicity. The motivation behind these studies has been, and continues to be, the hope that one or more crucial clinical or epidemiological factors will be identified which accounts for the relatively high occurrence of stones in one group, or the relatively low occurrence in another. The number and variety of groups which have been compared is substantial. These include intra- and inter-regional group comparisons. Within groups, several different sub-groups have been compared including males and females, urbanized and semi-urbanized, and stone-formers and non stone-formers. Retrospective and prospective approaches have been adopted. Well-established surveys and hospital databases from many sources have been scrutinized. In these studies, a wide variety of determinants has been interrogated in attempts to account for reported differences in stone occurrence between groups. These include anthropometrics, radiological data, stone composition, stone size, stone location, diet, urine composition, blood metabolic risk factors, co-morbidities, genetics, sex hormones, demographics, environment and socio-economics. Consideration of these studies indicates that race, ethnicity and environment do indeed play a role in urolithiasis, but precise details of this role are unclear. A difference in one or more urinary components is the most widely promulgated notion which purportedly accounts for racial differences in stone occurrence. However, consistent evidence in support of this is lacking. In some cases, no significant differences in urinary lithogenic factors were found, while in others counterintuitive differences were observed. It is apparent that traditional urinary physicochemical factors cannot convincingly account for racial and ethnic differences in stone occurrence. Identification of other risk factors in this regard remains a challenge for the future. This challenge is no different to that of identifying risk factors (urinary or otherwise) which universally discriminate between stone-forming and non stone-forming individuals in general.

COI: No.

L-10

Randall's plaques versus ductal plugs as sites of the earliest growth of kidney stones

James C. Williams

Indiana University School of Medicine, USA

There are two renal pathologies described by which stones can be retained within the renal calyx during early growth: attachment to Randall's plaques, and growth onto ductal mineral plugs. Randall's plaques are depositions of calcium phosphate within the interstitial tissue of the renal papilla. When the epithelium overlying Randall's plaque is damaged, calcium oxalate (CaOx) from the calyceal urine can deposit on the plaque, forming a nascent stone. In a completely different mechanism, mineral can be deposited in the lumens of collecting ducts; such deposits of mineral are called ductal plugs. When the tip of a ductal plug extends into the calyceal urine, it can also be a site for growth of a nascent stone.

Study of surgically removed stones using micro computed tomographic imaging (micro CT) shows that stones growing on Randall's plaque all had a plaque region composed of apatite, with the plaque regions on average 350 μm wide and 310 μm long (i.e., depth of interstitium pulled out with the stone). These stones showed luminal spaces (from tubules or capillaries trapped in the plaque) in over 80 % of the cases, confirming the identification of interstitial plaque. The calyceal mineral growing on Randall's plaque was composed exclusively of CaOx or CaOx mixed with apatite. Ductal plug regions on stones were all cylindrical in shape and composed of apatite, on average 550 μm wide and 1200 μm long. Calyceal mineral growing

on ductal plugs was composed of CaOx, CaOx with apatite, or mixtures including brushite.

It is not yet known what proportion of stone formers create new stones solely by the mechanism of growth on Randall's plaque, rather than on ductal plugs. Nor is it known how many stone formers may have both of these early growth mechanisms operating to form new stones. However, micro CT is a powerful technique for understanding the genesis of stones within the kidney, and its extension into studies of different types of stone formers will certainly yield new insights into stone formation.

COI: No.

L-11

The primordial protein: macromolecules, minerals and renal stones

Rosemary L. Ryall

Flinders University, Australia

Organisms throughout the natural world fabricate a huge variety of minerals essential for healthy life. Such biominerals are essential components of structures designed to fulfil functions ranging from scaffolding and defence, to navigation, balance, armoury and attack. Without exception, their manufacture compulsorily involves the activity of specific macromolecules, primarily proteins, which control the initiation of the mineralization process and direct the accumulation and assembly of the crystal products.

As with healthy biominerals, proteins are obligatory components of human kidney stones. However, while the commanding roles of proteins in healthy biomineralization have long been recognised, their inclusion in renal calculi along with their roles, if any, in their formation are less well understood.

In this presentation I will review recent studies designed to enlighten our understanding of the possible involvement of proteins in the development of human renal stones, with particular reference to information gleaned from salubrious biomineralization systems and other scientific disciplines.

COI: No.

L-12

A probiotic treatment for kidney stone disease

Marguerite Hatch

University of Florida, USA

We have examined the promotion of active intestinal elimination and luminal degradation of oxalate by probiotics as a way of managing two different clinical entities having in common an increased urinary excretion of oxalate leading to kidney stone formation. (1) In the genetic disease of Primary Hyperoxaluria Type 1 (PH1), an increased endogenous production of oxalate, due to a deficiency of the liver enzyme alanine-glyoxylate aminotransferase (AGT), results in hyperoxaluria, oxalate stone formation and tissue deposition of oxalate (oxalosis) in addition to renal failure and death unless early aggressive clinical management is instigated. (2) A new population of hyperoxaluric patients who have undergone bariatric surgery for obesity has been steadily emerging and the increased incidence of kidney stone formation in this group is significant. In addition to the population of patients with PH1 and bariatric surgery, the potential impact of this therapeutic approach, if effective, will extend to a much

larger population of idiopathic calcium oxalate stone formers. We have shown that the substrate/oxalate-specific microorganism, *Oxalobacter sp.*, which resides in the large intestine, can significantly lower urinary oxalate excretion by altering the direction of colonic oxalate transport from absorption to active secretion/excretion and we are currently addressing the transport mechanisms involved.

Other bacteria including *Lactobacillus sp.* and *Bifidobacterium sp.* that are “generalists” in terms of their oxalate-degrading activity have been demonstrated to significantly reduce urinary oxalate excretion in humans and in rats; however, *Bifidobacterium sp.* does not appear to influence enteric oxalate movements. Regardless of the mechanisms involved, perhaps it is possible to exploit the activities of these intestinal bacteria, either individually or together, in order to reduce the oxalate burden in PH1. Now that we have an animal model of PH1 as well as a rat model for bariatric surgery, we have a unique opportunity to directly address these questions and obtain information regarding a treatment for hyperoxaluria. The results from these studies should reveal a novel direction leading to the development of a probiotic system based upon bacteria/bacterial products that promote both enteric oxalate excretion and degradation thereby normalizing urinary oxalate excretion.

COI: No.

L-13

Future prospects for herbal remedies in the management of urolithiasis

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Background: Alternative medicine such as herbal remedies are gaining popularity as more information regarding its contents and efficacies are being documented in several studies. To treat kidney stones, anti-lithic herbs/phytotherapeutic concoctions have been used to aid their passing and to guard against any further deposits. *Herniaria hirsuta* has been widely used in Morocco as a diuretic, *Phyllanthus niruri* is used in Brazilian folk medicine, *Kampo* mixture is well researched and used in Japan and China as anti-lithic medicine and *Pashanbhedha* ayurvedic drugs are used widely in India and the sub-continent. Many such studies are done in vitro or in animals. There are very few clinical studies on human subjects. However, with advancing knowledge in the herbal medicines with regards to their origins, preparations, toxicities, chemical content and pharmacological effects, there are some promising herbal drugs that can be recommended alongside western medicine approach. Traditional Chinese medicine usage in Hong Kong and China reaches over 80 % once diagnosis of renal stone is confirmed by western methods.

Methods: In our clinical trials with Shi wei (pyrrosia powder), 50 patients were recruited for a randomized, double-blinded, placebo-controlled studies. The test group received 1500 mg of Shi Wei and the placebo group received 1500 mg of starch in the form of 3 × 500 mg capsules daily for 7-days. Early morning urine was collected before and after the study.

Results: This study confirmed our earlier pilot studies, (1) there were increases in urination, magnesium and citrate, (2) decrease in specific gravity of urine and (3) there were no changes with regards to calcium, oxalate, sodium, potassium, chloride and phosphates.

Conclusion: Indirect benefit was seen in those patients with increased urination to expel crystals and stone fragments following ESWL or PCNL. No side-effects was reported.

COI: No.

GUIDELINE

G-01

The 2016 EAU Guideline on Urolithiasis

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The EAU Guideline on Urolithiasis covers the whole field of urolithiasis: From diagnosis, conservative therapy, intervention to follow-up and stone prevention. It is updated annually by an expert panel and cross-reviewed by external experts. Updates are based on structured evidence research and own systematic reviews are performed on controversial topics. It therefore offers the most comprehensive available clinical guideline world-wide.

COI: No.

G-02

AUA Surgical Stone Management Guidelines

Bodo E. Knudsen

The Ohio State University Wexner Medical Center, USA

The American Urological Association currently has guidelines published on the Management of Ureteral Calculi and on the management of Staghorn Calculi. The lecture will review these guidelines. Furthermore the lecture will discuss the ongoing evolution of the surgical management and how we have adopted the Guidelines into our practice the Ohio State University Wexner Medical Center.

COI: No.

SYMPOSIUM

S-01

Radiographic diagnosis and treatment of urolithiasis

Coordinators: Isao Hara¹, Noor Buchholz²

Chairs: Isao Hara¹, Noor Buchholz²

¹Department of Urology, Wakayama Medical University, Japan;

²U-merge London & SVMC Dubai, United Arab Emirates

Diagnosis and treatment for stone disease requires imaging every step of the way. This symposium will try to outline the crucial role of between imaging in the decision making for stone diagnosis, stone treatments, and in the follow up of stone formers. It will look at the various radiological techniques available and outline when to use what safely.

Three state-of-the-art presentations will outline

1. The role of imaging in the diagnostic clinical work up to stone surgery: Imaging before stone surgery.
2. The role of imaging in the clinical follow up of stone patients to establish treatment success, efficient prevention of recurrence, and meaningful follow up: Imaging after stone surgery what why when
3. The possible role of imaging in establishing a correct diagnosis from detailed CT anatomy of the stone bearing kidney: CT attenuation value of renal papilla: a novel predictor for stone recurrence. This is a new approach aiming at refining clinical diagnosis if eventually implemented in clinical practice.

COI: No.

S-01-1**Imaging before stone surgery**

Anthony Cf. Ng

SH Ho Urology Centre, The Chinese University of Hong Kong, Hong Kong

Imaging is an important instrument in stone management, from the point of diagnosis to the long-term management and monitoring of stone recurrence. The use of non-contrast CT scan has become the gold standard in diagnosing renal/ureteric stone. The assessment of renal function by isotope scan and the assessment of stone fragility would greatly affect the choice of treatment for our patients. When a patient is subjected to PCNL, the use of imaging will be important to help the planning of suitable tracks to maximize stone clearance. Therefore, urologists are obligated to understand the principle and application of these imaging during stone management.

COI: No.

S-01-2**Imaging after stone surgery what why when**

M Hammad Ather

Aga Khan University, Pakistan

Imaging following stone surgery is pivotal in providing information about the treatment outcome. Surveillance for complications (steinstrasse, hemorrhage, infections, ureteral injury and stricture) stone clearance, and resolution of obstruction are main concerns. Extracorporeal shock wave lithotripsy (ESWL), percutaneous nephrolithotomy (PCNL) and ureteroscopy (URS) currently represent the mainstay treatment options for the vast majority of patients with urolithiasis. Routine imaging following ureteroscopy for treatment of kidney and ureteral calculi continues to be a topic of debate. A recent study suggests that fragment size >4 mm following ureteroscopy is associated with significantly higher rates of stone growth, complications, and need for re-intervention. It is therefore important to define the residual stone size accurately following intervention. However, with the increasing focus on healthcare costs and quality, judicious use of diagnostic imaging to optimize outcomes while minimizing resource utilization is a priority. The post-ureteroscopy imaging practices among experienced urologists vary. Currently outside trails the most commonly used imaging post endourological interventions for urolithiasis is plain x-ray KUB with or without ultrasound. Multidetector CT allows confident assessment of stone-free status and post procedural complications. However, not only it is associated with increased radiation, but also much higher cost. A plain X-ray is associated with 0.5–1 mSv, whereas an IVU 1.5–3.5 mSv, and a regular dose CT about 4.5–5 mSv of radiation exposure. There is significant literature available to indicate that the use of low dose CT significantly reduces the radiation without compromising the diagnostic value of CT. low dose CT decrease radiation exposure to less than half from regular CT (1–2 mSv). The judicious and tailored use of imaging is recommended for post interventional imaging.

COI: No.

S-01-3**CT attenuation value of renal papilla: a novel predictor for stone recurrence**Yasuo Kohjimoto¹, Takashi Iguchi¹, Shimpei Yamashita¹, Akinori Iba¹, Hideaki Ogura², Isao Hara¹¹Wakayama Medical University, Japan; ²Koyo Hospital, Japan

Introduction and Objectives: In idiopathic calcium stone formers (ICSFs), most stones are known to grow attached to Randall's plaque, which can be identified by measuring computed tomography (CT) attenuation value of renal papilla. The purpose of the present study was to test the hypothesis that CT attenuation value of renal papilla can predict the severity and recurrence of the stone disease.

Methods: We retrospectively reviewed the charts of ICSFs who underwent non-contrast CT scan from February 2005 to May 2012. Two observers independently measured the Hounsfield unit (HU) of the renal papilla from the upper pole, middle region and lower pole in both kidneys. Patients were classified into high- and low-HU value groups based on the mean HU values of all papillae. The median value was used for differentiation. Proportions of patients with severe disease (recurrent and/or multiple stones), urine chemistries and recurrence rates were compared between the groups.

Results: A total of 134 patients, 89 men and 45 women, with at least 1-year follow-up, were included in the analysis. Median HU value of all papillae was 49.3. The proportion of patients with recurrent and/or multiple stones was significantly higher in high-HU group compared to low-HU group (94.0 vs. 76.1 %, $p < 0.01$). AP (CaOx) index in high-HU group was higher than that in low-HU group, although the difference was marginally significant ($p = 0.06$). Recurrence rate in high-HU value group (0.62 person-year) was significantly higher than that of low-HU value group (0.09 person-year, $p < 0.01$). Multivariate analysis revealed that high-HU value was an independent predictor of stone recurrence (OR 8.48, 95 % CI 3.45–22.88, Table).

Conclusions These results demonstrated that the HU value of renal papilla was correlated with disease severity, AP (CaOx) index and recurrence in ICSFs. This may allow us to identify patients with a higher risk of recurrent stone formations and change the clinical management of these patients if necessary.

COI: No.

Table. Multivariate analysis of stone recurrence

	Odds ratio	95% confidence interval	p=
Age	0.95	0.90-0.98	<0.01
Male	1.76	0.68-4.70	0.24
Multiple stones	1.35	0.48-3.87	0.56
Recurrent stone former	0.88	0.31-2.39	0.81
Medication	3.98	1.51-11.07	<0.01
High-HU (≥ 49.3)	8.48	3.45-22.88	<0.01

S-02**Dietary habit and risk of urolithiasis**

Coordinator: David S. Goldfarb

Chair: David S. Goldfarb

NYU School of Medicine, NYU Langone Medical Center, USA

This symposium will review recent information regarding the relationship between diet and kidney stones.

Information about diet and its effects on stone risk can be derived from 24 h urine collections.

Recommendations regarding diet and beverage use will be surveyed. Proposals regarding randomized controlled trials, both past and future, will be presented.

COI: No.

S-02-1**Use of urine chemistries to assess dietary habits**

John R. Asplin^{1,2}

¹*Litholink Corporation, USA*; ²*University of Chicago, USA*

Dietary intervention is a standard component of therapy for patients with urolithiasis. Dietary treatments include increased fluid intake, increased dietary alkali, and reduced intake of sodium, protein and purines. Clinicians may not have the time and/or training to take an adequate dietary history. For many clinicians and patients, there is not easy access to dietitians to aid in evaluation and management of patients. Urine chemistries can be used as an adjunct to the diet history to identify the risk factors that contributed to stone formation and to monitor patient adherence to recommended dietary modifications.

Sodium, potassium, protein and water are nearly completely absorbed from the GI tract; when the patient is in steady state, urine excretion is a good marker of their dietary intake. 24 h urine volume provides an assessment of the adequacy of fluid intake. Sodium intake is difficult to assess via diet history or food frequency questionnaire, but the measurement of urine sodium excretion is a useful tool to guide diet advice for the patient. Urine urea and sulfate excretions are both good markers of diet protein intake. There is no direct marker of diet purine intake, but most purine rich foods are also high in protein, so the protein markers can be used as a rough guide of purine intake. Urine potassium excretion can serve as a marker of dietary alkali content, because much of the alkali in human diets is accompanied by the cation potassium. For a more accurate assessment, one could calculate net GI alkali absorption from commonly measured urine chemistries. Unfortunately, carbohydrate and fat intake do not leave a signal in the urine chemistries, so urine testing is not useful to monitor caloric intake. Also, peculiarities of diet might be recognized via urine chemistries. For example, a low urine magnesium, phosphorus, sodium and/or potassium in a patient without bowel disease may help diagnose a patient with an eating disorder or laxative abuse.

In this presentation, the use of urine chemistries to define dietary intake in clinical practice will be reviewed. The limitations and potential problems of urine testing will also be described.

COI: Yes.

COI Relation: I am employed by Litholink Corporation, a subsidiary of LabCorp. Litholink performs metabolic testing for patients with kidney stones.

S-02-2**Evidence-based dietary recommendations for stone formers**

Roswitha Siener

University Stone Centre, Department of Urology, University of Bonn, Germany

Prevalence and incidence of urolithiasis in industrialized countries have markedly increased over the past decades. The appropriate diet is playing a crucial role in the recurrence prevention of urolithiasis. Different dietary factors can alter composition and supersaturation of urine, which can affect the process of stone formation. Specific dietary recommendations should be tailored to the metabolic risk factors according to the type of stone. Calcium oxalate is the major component of about 75 % of renal calculi. Urinary risk factors are a low urine volume, an increased excretion of oxalate, calcium and urate and a decreased excretion of citrate. An adequate fluid intake to achieve a daily urine volume of at least 2 L is the most important measure for recurrence prevention of urinary stones. Increased dietary protein intake favours increased urinary excretion of calcium as well as decreased excretion of citrate. A diet high in fruit and vegetables provides an alkali load and reduces stone risk by increasing urinary citrate and volume. For patients at risk for recurrent calcium oxalate stone formation it is important to exclude foods with high oxalate content. A daily calcium intake of 1000–1200 mg is recommended, corresponding to a normal calcium diet, satisfying daily calcium requirements. Moderate dietary salt restriction is useful in limiting urinary calcium excretion. A high dietary purine intake is associated with an enhanced endogenous production and urinary excretion of uric acid and should therefore be reduced.

COI: No.

S-02-3**Prospects for dietary therapy of urolithiasis**

David S. Goldfarb

NYU Langone Medical Center, USA

Diet, of course, influences urine chemistry. Yet only one randomized controlled trial has demonstrated that a change in diet led to reduction in stone recurrence. I will review some of the deficiencies in the current scientific dietary literature and suggest how these deficiencies could be addressed. Highlights will include comparisons of diet with pharmacologic therapy, how prescribing dietary patterns, rather than individual nutrients, might be a preferable way to address therapy, and the possible effect of the microbiome on how diet influences urinary chemistry.

COI: No.

S-03**Epidemiology and recent advances in pathophysiology of uric acid nephrolithiasis**

Coordinators: Alberto Trinchieri¹, Khashayar Sakhaee²

Chairs: Alberto Trinchieri¹, Khashayar Sakhaee²

¹*Urology Unit, Manzoni Hospital, Lecco, Italy*; ²*Department of Internal Medicine, Division of Mineral Metabolism, Charles and Jane Pak Center for Mineral Metabolism and Clinical Research, University of Texas Southwestern Medical Center, Dallas, USA*

Obesity and metabolic syndrome have been a major burden on human quality of life and economy worldwide. Globally, there are wide variations in the prevalence of uric acid stones. The incidence and prevalence of uric acid stones are escalating with epidemic of obesity and metabolic syndrome worldwide. Furthermore, there is a wide geographical heterogeneity in the prevalence of uric acid nephrolithiasis worldwide. Whether this heterogeneity reflects environmental differences in addition to genetic predisposition has not been yet fully explored. The more invariable factor the development of uric acid stones is unduly acidic urine. Over the past decades, extensive effort has been made in the defining the pathophysiologic mechanisms of uric acid stone formation and its link to obesity and the metabolic syndrome. Numerous human animal and cell culture studies have shown that unduly acidic urine originates from defective ammoniogenesis as well as increased acid production and consequently increased acid excretion. The defective ammoniogenesis has been proposed to be due to sustained fat delivery to the kidneys as it occurs more prevalently with Western diet leading to renal fat accumulation, consequently in renal tubular proximal damage (renal lipotoxicity) the main site of renal ammonia production. Supporting evidence originates from short-term placebo controlled treatment of these patients with thiazolidinediones known to redistribute fat from organs to adipocytes showing reversal urine pH commensurate with increased in urinary ammonium excretion. Alternatively, with an increased supply of the fatty acids in conjunction with an increased level of plasma free fatty acids, there is potential for the substitution of glutamine, the major substrate for ammoniogenesis, with fatty acids (substrate switch) resulting in lower ammonium excretion. Moreover, increased acid production may be a “second hitting” mechanism in elaborating very acidic urine. At present time, the origin and nature of these putative organic anions have not been fully explored. However, preliminary studies have shown the potential role of intestinal microbiota in the pathogenesis of increased acid production.
COI: No.

S-03-1

Epidemiology of uric acid nephrolithiasis

Alberto Trinchieri

Urology Unit Manzoni Hospital Lecco, Italy

Urate stones makes up about 10 % of all urinary stones, although this rate tends to be higher in the elderly and in the obese. Urate stones may be pure uric acid, sodium urate or ammonium urate. Uric acid are formed as a result of an high urinary excretion of uric acid and/or undue acidity of urine. In fact, uric acid tends to precipitate when the urinary pH is lower than the ionization constant of uric acid ($pK_a < 5.5$). Monosodium urate and ammonium urate stones are rare (<1 %).

Uric acid (or other purine metabolites) can be caused by inborn defects of the metabolism of uric acid (hereditary hyperuricemias) or other purine (2,8-dihydroxyadeninuria, xanthinuria) that result, in addition to stone formation, in crystal deposition in the renal parenchyma. These cases occur in childhood and have a high tendency to recur.

In the adult uric acid can be associated with specific diseases that cause an excessive urinary excretion of uric acid as psoriasis, myeloproliferative disorders and other malignancies receiving chemotherapy.

Idiopathic uric acid stone disease can be caused by a high urinary excretion of uric acid and/or a unduly low urinary pH. A high urinary excretion of uric acid may be caused by a diet rich in proteins and purines. Hyperuricosuric patients often form mixed calcium oxalate/uric acid stones as the high protein intake can also result in a modification of the risk factors for calcium stones.

Uric acid stones are also formed for an undue urinary acidity with a normal excretion of uric acid. The excessive acidity of urine is associated with an increased net acid excretion and a reduced urinary

excretion of ammonium which normally acts as a buffer for urinary acidity. Mechanisms of increased urinary acidity are not fully elucidated. The treatment of uric stones is based on dietary measures, administration of drugs reducing urinary excretion of uric acid and urinary alkalization. Proper treatment allows the dissolution of kidney stones and prevention of the formation of new stones.

COI: No.

S-03-2

Recent advances in pathophysiology of uric acid nephrolithiasis (UA)

Khashayar Sakhaee

University of Texas Southwestern Medical Center, USA

Multiple etiologic mechanisms including congenital, acquired, and idiopathic are known to participate in the development UA stone formation. Idiopathic UA nephrolithiasis (IUAN) a pathogenically distinct entity with features of metabolic syndrome has been increasingly recognized as the most common cause of UA stone formation. With the epidemic of obesity worldwide, the prevalence of IUAN has progressively escalated over the past three decades. The most invariant feature in this population is overly acid urine that increases the propensity for uric acid precipitation. Over the past two decades major efforts have been made in elucidating the underlying mechanisms of unduly acidic urine in this population. One mechanism has attributed defective urine acidification to defective urinary ammonium (NH_4^+) excretion. A study in normal subjects using dual energy X-ray absorptiometry (DXA) have shown that total body and truncal fat (visceral) are more significantly associated with lower urinary NH_4^+ and acid urine pH than leg fat mass. Additional studies including magnetic resonance spectroscopy (MRS) and magnetic resonance imaging (MRI) are being performed in IUAN to directly correlate renal cortical fat content (a principle site of renal NH_4^+ synthesis and transport) accumulation to the defective urinary NH_4^+ excretion. The defective renal ammoniogenesis has been proposed to be due to sustained fat delivery to the kidney as it occurs most prevalently with Western diet leading to renal tubular proximal injury (renal lipotoxicity). Furthermore, increased fatty acid supply by “substrate competition” may substitute glutamine, as a major source of energy and consequently impair ammoniogenesis. A second and mutually important underlying pathophysiologic mechanism in the development of abnormally acidic urine in IUAN has been demonstrated to be due to increased endogenous acid production. This “second hit” mechanism is potentially due to increased endogenous organic acid production. A supportive evidence originated a preliminary study under fixed metabolic diet demonstrated increased production of the some key bacterial metabolites including 3-Hydroxy-3-methylglutarate, Pyruvate and 4-Hydroxyphenylacetate IUAN stone formers more than non-stone formers.

COI: No.

S-03-3

Uric acid urolithiasis as a feature of the metabolic syndrome: a multi-hit model

Orson Moe¹, Khashayar Sakhaee², Naim M. Maalouf¹, Ion Alexandru Bobulescu¹

¹UT Southwestern Medical Center, USA; ²Department of Internal Medicine, Division of Mineral Metabolism, Charles and Jane Pak Center for Mineral Metabolism and Clinical Research, University of Texas Southwestern Medical Center, Dallas, USA

The pivotal urinary abnormality in idiopathic uric acid urolithiasis is unduly low urinary pH promoting uric acid crystallization. The underlying pathophysiology is complex involving multiple organs, and consists of integral aspects of the metabolic syndrome. We postulate a three organ model where the root of the lithogenicity commences at organic acid production gut microbiome, that bypasses a steatotic liver presenting as an excess acid load to the kidney. Due to renal lipotoxicity from steatosis and alternative substrate use, renal ammoniogenesis and excretion is impaired leaving protons free to titrate the other abundant urinary buffers including urate. We propose that uric acid urolithiasis is the final manifestation that captures medical attention but is a consequence of a broad systemic disorder of metabolism.

COI: No.

S-04

Ureteroscopy (URS)

Coordinators: Kemal Sarica¹, Takashi Arakawa²

Chairs: Kemal Sarica¹, Petrisor Geavlete³

¹Department of Urology, Dr. Lutfi KIRDAR Research and Training Hospital, Turkey; ²International University of Health and Welfare Mita Hospital, Japan; ³Saint John Emergency Clinical Hospital, Romania

During the past 20 years URS has dramatically changed the management of ureteral calculi with a great impact on active stone removal. Among the major technical advancements, miniaturization of the endoscopes, enhanced optical quality and tools as well as introduction of disposables could be mentioned. Currently in addition to fine semi-rigid instruments, scopes with smaller outer diameter, larger working channel, active deflection and better fibre optics are now available. Additionally, with digital imaging and high definition television, the image quality has improved and the digital chip is now incorporated in the tip of the newer f-URS. As a result of all these achievements, the latest flexible endoscopes have also made it possible to visualize the entire collecting system almost in all kidneys where the durability of the latest generation of flexible scopes has been improved by stiffer shaft construction. On the other hand as a breakthrough advancement, clinical introduction of holmium: YAG laser have made f-URS a valuable alternative to ESWL and PCNL for treating renal calculi. Today, with rapid absorption of its energy in water (3 mm), and minimal tissue penetration (0.4 mm) with negligible thermal damage Ho-YAG laser improved the safety of the procedures and made it “Gold standart” for stone management. With all these technical advances and increasing experience, ureteroscopy is now trying to offer the low morbidity of ESWL. FURS has some certain advantages where the SFR’s are approaching to those of PCNL for small to moderate-sized renal calculi and also it is applicable in cases with stone density (higher than 1000 HU), high BMI values and under anti-coagulant therapy. Additionally, fURS is the treatment of choice in patients with SWL failure, calyceal diverticulum stones, horseshoe kidneys and lower-pole stones. Improvement in optics and ancillary equipment will allow access and treatment in all cases even those with anomalous or reconstructed urinary tract anatomy. Last but not least, despite its established application; classical f-URS may have deficiencies in ergonomics. As a new technology in this field, robotic-assisted f-URS using the Avicenna Roboflex™ seems to provide a suitable and safe platform with significant improvement of ergonomics.

COI: No.

S-04-1

Management of ureteral stones with semirigid ureteroscopy: tips and tricks for a successful and complication free procedure

Sven Lahme

Center for minimally-invasive Therapy-robotic-assisted Surgery, Siloah St. Trudpert Hospital, Pforzheim, Germany

Semirigid ureterorenoscopy allows to treat ureteral stones of the lower, mid and upper part of the ureter. Today there are ureteroscopes with a small instrument diameter available, that allow an easy and atraumatic access to the ureter. In order to know the morphology of the upper urinary tract it is recommended first to perform a retrograde pyelography. After that a guidewire should be inserted in the ureter. This allows to insert a DJ-stent or to manage difficulties at any time during the procedure. It is recommended to pass the ureteral orifice next to the guidewire. During the advancement of the ureterorenoscope an irrigation flow is needed. The mucosa of the ureter should always slide over the instrument (“sliding mucosa”). After the stone had been reached, smaller stones can be taken out by different stone baskets. In case of large stones lithotripsy is needed. A lot of different lithotripsy techniques are available, such as ultrasound, ballistic lithotripsy and holmium laser lithotripsy. After removal of the stone the insertion of a DJ-stent is often needed. During the whole procedure fluoroscopy should be available in order to have a maximum security. The presentation gives tips and tricks to reach a maximum success of the procedure and to avoid or manage any complication.

COI: No.

S-04-2

Management of renal stones with flexible ureteroscopy: tips and tricks for a successful and complication free procedure

Olivier Traxer

Department of Urology, Tenon Hospital Paris, France

Not available at time of print.

S-04-3

Robotic assisted flexible ureterorenoscopic (Robotic fURS) management of renal calculi

Kemal Sarica

Department of Urology, Dr. Lutfi KIRDAR Research and Training Hospital, Turkey

Flexible ureteroscopy (FURS), facilitated by retrograde intrarenal surgery, evolved rapidly over the last decade based on significant improvements in the armamentarium and has become a viable alternative to ESWL and PCNL, even for larger renal calculi. However, FURS represents a technically challenging procedure that requires specific endourologic skills. Despite progress in the design of ureterorenoscopes and accessories, FURS cannot be performed as solo surgery. The endourologist needs assistance to insert and advance laser fibres or baskets and to start and maintain irrigation while holding the endoscope and focusing on the target. Digital endoscopes with “tip at the chip” technology may lead to difficulties orienting the renal collecting system in comparison to standard systems with a pendulum camera attached to

the eyepiece. During FURS, the surgeon has to activate several devices by foot pedal, such as those for digital fluoroscopy, laser lithotripsy, or irrigation. Most surgeons accomplish this in a standing position, a suboptimal ergonomic posture that may result in orthopaedic complaints. It may have also a negative impact on performance of FURS, particularly in cases of larger stones requiring longer operative times, and may contribute to higher rates of secondary treatment when compared with mini-PCNL.

Like other fluoroscopically guided procedures, FURS is associated with radiation exposure of the operator in the range of 1.7–56 mSv. Robot-assisted surgery has dramatically influenced minimally invasive surgery with the introduction of console-based manipulators, such as the da Vinci robot (Intuitive Surgical, Sunnyvale, CA, USA) or the Hansen device (Hansen Medical, Mountain View, CA, USA). Desai and colleagues used the Hansen device, designed for cardiovascular interventions, to perform robot-assisted flexible ureterorenoscopy; however, this project has been discontinued. Since 2012, ELMED (Ankara, Turkey) has been working on a robot specifically designed for FURS.

In conclusion, despite its increased application, FURS may represent a challenging technique, particularly in complicated cases. Roboflex Avicenna provides a suitable and safe platform for robotic FURS, with significant improvement of ergonomics.

Future studies must evaluate the impact of the device on clinical outcomes of FURS (IDEAL stage 3) to determine the role of robotic FURS.

COI: No.

S-05

Advances in percutaneous nephrolithotomy (PNL)

Coordinators: Madhu S. Agrawal¹, Olivier Traxer²

Chairs: Madhu S. Agrawal¹, Olivier Traxer²

¹Global Rainbow Healthcare, India; ²Department of Urology, Tenon Hospital Paris, France

[Symposium Outline]

1. How to get the right access in PCNL—Junichi Matsuzaki (15 min).
2. Minimally-invasive PCNL (MIP) and other advances—Madhu Agrawal (15 min).
3. MIP vs flexible Ureteroscopy: what is the evidence—Olivier Traxer (15 min).
4. Panel discussion: Challenging cases (15 min).

COI: No.

S-05-1

How to get the right access in PCNL and Endoscopic combined intrarenal surgery

Junichi Matsuzaki

Ohguchi Higashi General Hospital, Japan

A suitable percutaneous access is the key point of the success of any PNL, maximizing the effectiveness of the procedure in terms of stone-free status and minimizing the risk of complications. The selection of the best calyx of entry should be preoperatively planned, to define the better strategy for a definite patient with a given urolithiasis.

The selection of the best calyx of entry should be preoperatively planned on the base of CT and other imaging studies, able to define

the better strategy for a definite patient with a given urolithiasis according to the modern principles of tailored therapies and personalized medicine. The ideal puncture should maximize the effectiveness of the procedure in terms of stone-free status and minimize the risk of complications, particularly bleeding and visceral damage.

The puncture of the collecting system is usually performed from the skin to the collecting system, exploiting different guidance methods. None of them can be considered the best one alone, but their combined use exploiting the respective advantages may supply a valid support. Presently the optimal guidance for renal puncture is still to be sought out.

(1) Fluoroscopy Guidance

(2) Ultrasound Guidance

(3) Endoscopic Guidance

(4) CT Guidance

(5) Other Guidance Methods (“all-seeing” needle, etc.)

Endoscopic combined intrarenal surgery (ECIRS) using retrograde fURS and PNL was developed as a single-step treatment for removal of renal calculi to avoid multiple access points and the related morbidity while achieving a high stone-free rate.

ECIRS is one of the appropriate methods to get the right access.

COI: No.

S-05-2

Minimally-invasive PNL

Madhu S. Agrawal

Global Rainbow Healthcare, Agra, India

It has been well established by now that Percutaneous nephrolithotripsy (PCNL) can achieve a higher stone-free rate over a shorter treatment period in most patients as compared to other modalities. However, the biggest limitation of PCNL is its relatively higher morbidity, including complications like bleeding and renal injury. Since there is now enough evidence suggesting that decreasing the tract size for PCNL could decrease bleeding and morbidity, recent efforts to decrease the complications of PCNL have focused on reducing access size, leading to the development of several ‘Minimally-invasive’ percutaneous approaches.

‘Minimally-invasive PCNL’ or simply (‘MIP’), also referred to as ‘Mini-PCNL’, essentially signifies use of nephroscope and Amplatz sheaths of smaller caliber as compared to the conventional PCNL where nephroscopes of 19–26 F are used with Amplatz sheaths of 24–30 F sizes.

The popularity of Mini-PCNL started with the nephroscope of 12 F size with Amplatz sheath size being reduced to 15–18 F. Reducing the sheath size from 30 F to 15 F effectively reduces the cross-sectional surface area of the tract to one-fourth, thereby significantly reducing the tissue trauma as well as the risk of bleeding-related complications.

Compared with ESWL and RIRS, Minimally-invasive PCNL (MIP) approach offers higher stone-free rates with low complication rates. This is possibly the only procedure for kidney stone where the patient can leave the hospital completely stone-free and tube-free within 24 h after treatment, something which cannot be claimed after any other minimally invasive options like ESWL or RIRS on a routine basis. Prospective randomized trials are ongoing to compare these modalities in the management of small and medium sized renal lithiasis.

COI: No.

S-05-3**MIP vs flexible ureteroscopy: what is the evidence**

Olivier Traxer

Department of Urology, Tenon Hospital, Paris, France

Not available at time of print.

S-06**What we know and what we can do to prevent stone recurrence?**Coordinator: José M. Reis Santos¹Chairs: José M. Reis Santos¹, Kemal Sarica²¹*Uroclínica-Centro Clínico de Urologia, Lda., Portugal;*²*Department of Urology, Dr. Lutfi KIRDAR Research and Training Hospital, Turkey***Introduction:** Stone recurrence in the urinary stone patient is very high with or without prophylaxis.

Everywhere we look there is affirmation that recurrence is more than 50 % at 5 years.

Therefore, these patients should be studied, treated and protected from this risk.

When analyzing the possible medical attitudes available, recognized as potential prophylactics, we can conclude that credible scientific arguments are missing if we want to meet the criteria for evidence based medicine (EBM),

Put simply, diet, increase in water intake, privation of fizzy drinks or specific medication (citrate, allopurinol, thiazides, etc.) do not show sufficient scientific support for doctors to make judicious and conscious decisions and advise patients on treatment “for life” based on EBM.

This obliges us to review our clinical practice and make the necessary changes to be able to acquire this data.

In this symposium experts will present new data to help understand better recurrence in stone patients and how to implement this data using criteria based on EBM.

1. Reasons for failure of recurrence prevention

Prof. Bernhard Hess (Internist/Nephrologist Internal Medicine & Nephrology, Kidney Stone Center Zurich, Klinik Im Park, Zurich) 15 min

2. How to prevent renal stone disease recurrence: a review from my practice

Prof. Guohua Zeng (The First Affiliated Hospital of Guangzhou Medical University, Guangzhou) 15 min

3. Can endoscopic study of the papilla with new tools help fight recurrence?

Prof. James C. Williams (Indiana University School of Medicine) 15 min

4. Discussion 10 min

5. Final message to take home

Prof. Reis Santos 5 min

COI: No.**S-06-1****Reasons for failure of recurrence prevention**

Bernhard Hess

Internal Medicine and Nephrology, Kidney Stone Center Zurich, Klinik Im Park, Zurich, Switzerland

Only small and not always well-controlled studies have addressed the question of the optimum management for preventing recurrent kidney

stones. A thorough meta-analysis included 28 randomized trials on preventive treatments of recurrent kidney stone formers with outcome data (*Ann Intern Med* 158: 535–543, 2013). With various levels of evidence, the following treatments were found to significantly *reduce stone recurrence rate*:

- increased fluid intake (urine volume at least 2.0–2.5 L/day)
- reduced soft-drink consumption
- extensive biochemical evaluation *plus* tailored diet (vs. limited evaluation and empiric diet)
- multicomponent diet plus normal to high calcium intake
- Thiazides for calcium stones
- Citrate for calcium stones
- Allopurinol for hyperuricemic/hyperuricosuric calcium stone formers

Based on many years of personal experience as well as from published data, *reasons for failure of preventive strategies* are as follows:

- The burden of disease is “too low” for certain patients such as the “common variety” calcium stone former
- Residual stones are not removed/treated
- Recommendations are “too general”, i.e. not based on a reliable stone analysis and/or a careful metabolic work-up
- Physicians fail to clearly explain the underlying pathophysiology of stone formation whereby the rationale for a specific treatment remains obscure to the patient
- Wrong treatments strategies are recommended by physicians (i.a. low calcium diet)
- Recommended changes in lifestyle/diet are not accepted by patients
- Low adherence to prescribed medication due to adverse effects, especially in patients receiving either thiazides or citrate.

COI: No.**S-06-2****How to prevent renal stone disease recurrence: a review from my practice**

Guohua Zeng, Wen Zhong, Tao Zhang

Department of Urology, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China

Nephrolithiasis represents a common disease. It has been reported that the lifetime prevalence of nephrolithiasis is increasing, and its incidence depends on geographical, climatic, ethnic, dietary and genetic factors. Renal stone disease has a great tendency to recur if left untreated with a reported 28–52 % recurrence rate following 10 years after the first stone formation. Prompt metabolic evaluation followed by appropriate medical management is of paramount importance for preventing disease recurrence. Apart of the medical or surgical management of urolithiasis, prevention has an equal role in the overall management of the disease. We encourage complete metabolic evaluation in all high-risk stone formers consisting of stone analysis, 24 h urine analysis and serum biochemistry. Based on the findings, there are several pharmacological options (Thiazides, Allopurinol, Potassium citrate, etc.) for disease prevention. In addition, in our practice, we encourage remove all stones as much as possible during the surgery using endourological treatment which can reduce the stone recurrence, and surgical treatment for urinary tract anatomic deformity is also fundamental to prevent stone recurrence. But can laser destruction of the Randall’s plaque, during surgery, prevent stone recurrence is still a problem that needs to be resolved.

COI: No.

S-06-3**Can endoscopic study of the papilla with new tools help fight recurrence?**

James C. Williams

Indiana University School of Medicine, USA

Recent work using endoscopic observation of stone patients has revealed that calcium stone formers do not all have the same papillary pathologies. Specifically, those calcium oxalate (CaOx) stone formers who grow their stones solely on Randall's (interstitial) plaque show only the mineralization of Randall's plaque in their papillae, with no sign of crystal binding within the collecting ducts. In contrast, apatite and brushite stone formers have significant deposits of mineral in papillary collecting ducts. These two different pathologies are relatively easy to recognize by endoscopic observation. Can recognition of these pathologies aid in treatment for recurrent stone formers? Perhaps. It is known, for example, that the presence of Randall's plaque correlates with hypercalciuria; thus, any patient with significant Randall's plaque should be suspected of this, and carefully studied with 24-h urines. In contrast, the deposition of apatite into collecting ducts in other calcium stone patients points to more serious issues of crystallization within the renal tubules and the consequent micro-obstruction that will result. Future work will reveal whether endoscopic observations and diagnosis of papillary pathology allow better treatment of stone formers by identifying different disease types.

COI: No.

S-07**Oxalate**

Coordinators: Ross Holmes¹, Dawn S. Milliner²
 Chairs: Dawn S. Milliner², Ross Holmes¹

¹University of Alabama at Birmingham, USA; ²Mayo Clinic, Division of Nephrology, Mayo Clinic Hyperoxaluria Center, Rare Kidney Stone Consortium, USA

The oxalate load on the kidney produced by glomerular filtration and the secretion of oxalate by the proximal tubule can contribute to kidney disease. If this load is excessive it may result in calcium oxalate stone formation, deposition of calcium oxalate crystals in the renal parenchyma, and ultimately renal failure. Critical determinants of the oxalate load are the amount of oxalate absorbed from the intestine and that synthesized in the body. This symposium will examine the current state of knowledge of the factors that influence these steps and identify ways they can be modified. Topics that will be covered include dietary sources of oxalate, the fate of this oxalate in the intestine, its absorption, and synthetic pathways in the body. The important ways normal processes are modified by intestinal disease, intestinal surgery and inherited traits will also be discussed. Emerging novel approaches to treatment will be considered.

COI: No.

S-07-1**Endogenous and dietary sources of oxalate**

Ross P. Holmes

University of Alabama at Birmingham, USA

Oxalate in urine is derived from both dietary and endogenous sources. On average, equal amounts are obtained from these sources, but the

contribution of dietary oxalate can vary more substantially due to wide variations in calcium and oxalate intake. Assessing the dietary oxalate intake of individuals is difficult due to inadequate tables of the oxalate content of food due to natural variabilities in food oxalate content and complexities in measuring food oxalate. Important sources of endogenous oxalate synthesis are hydroxyproline, derived from collagen turnover and the diet, and ascorbic acid. There are possibly other sources that remain to be identified and could include glyoxal, a peroxidation product. Endogenous synthesis of oxalate is substantially increased in individuals with the rare inherited disease Primary Hyperoxaluria. Recent studies suggest that therapies using siRNA to reduce the activities of glycolate oxidase and hydroxyproline dehydrogenase can decrease oxalate production in hyperoxaluric animal models. This novel therapeutic strategy may be helpful in treating both Primary Hyperoxaluria and idiopathic calcium oxalate stone disease.

COI: No.

S-07-2**Stone disease: idiopathic and secondary hyperoxaluria**

Roswitha Siener

University Stone Centre, Department of Urology, University of Bonn, Germany

Idiopathic and secondary hyperoxaluria, resulting from high dietary intake, intestinal hyperabsorption of oxalate, other dietary constituents as well as the lack of oxalate-degrading bacteria, is a major risk factor for calcium oxalate stone formation. Intestinal hyperabsorption of oxalate can considerably contribute to urinary oxalate, even in the absence of gastrointestinal diseases. The proportion of oxalate absorbed from an oral load, as measured by [¹³C₂]oxalate ingestion, is significantly higher in calcium oxalate stone formers (10.2 %) than healthy controls (8.0 %). An increased intestinal absorption greater than 10 % was found in 46 % of patients with idiopathic calcium oxalate stone disease. Intestinal absorption of oxalate is highly dependent on dietary calcium intake, because calcium in the diet binds with oxalate in the intestinal lumen, thus reducing oxalate absorption and excretion. Magnesium may reduce oxalate absorption and urinary excretion nearly as effective as calcium by binding oxalate in the gut. Certain microorganisms in the colon, such as *Oxalobacter formigenes* contain enzymes that can metabolize oxalate, reducing luminal concentrations and thus oxalate absorption and excretion. Moreover, an increased phospholipid arachidonic acid level may induce hyperoxaluria by activating the anion carrier and consequently the intestinal and renal transport of oxalate. It is suggested, that n-3 fatty acid supplementation might decrease urinary oxalate excretion and reduce the risk of calcium oxalate stone formation.

COI: No.

S-07-3**Kidney disease: primary and enteric hyperoxaluria**

Dawn S. Milliner

Mayo Clinic, Division of Nephrology, Mayo Clinic Hyperoxaluria Center, Rare Kidney Stone Consortium, USA

High concentrations of oxalate in the urine pose risk not only for calcium oxalate urolithiasis, but also for kidney disease caused by deposition of calcium oxalate crystals in renal tubules and interstitium of the kidney. Crystal induced Inflammation, which can be

characterized by multinucleated giant cell formation, and subsequent fibrosis can cause chronic progressive, or acute loss of kidney function.

Primary hyperoxaluria due to autosomal recessive deficiency of liver enzymes important in glyoxylate disposition results in some of the highest urine oxalate excretion observed in human disease. It is notable that the hyperoxaluria is present lifelong and Kidney failure is frequent. Three types of primary hyperoxaluria have been recognized, caused by mutations of the *AGXT*, *GRHPR*, or *HOGA1* genes. They differ in the severity of hyperoxaluria and stone disease, and in the frequency of chronic kidney disease. Patients with any form of enteric hyperoxaluria demonstrate more variable degrees of urine oxalate excretion, but it may be severe. With increasing numbers of gastric bypass procedures performed in many parts of the world for management of obesity, the number of patients with enteric hyperoxaluria is increasing. Kidney stones and kidney failure are increasingly recognized. Mechanisms of kidney injury, treatments available and under investigation, and clinical management of patients with advanced oxalate related kidney disease will be discussed.

COI: No.

S-08

Inflammation and formation of kidney stones

Coordinators: Saeed R. Khan¹, Takahiro Yasui²
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Two major pathways lead to kidney stone formation. One pathway involves overgrowth on interstitial apatite plaques (Randall's plaques), and the other involves the formation of intratubular crystal plugs in the duct of Bellini. Mechanisms underlying the formation and growth are poorly understood. Renal tubular cell injury affects the initial process of renal calcium crystallization through an unknown mechanism. Inflammation and intracellular morphological changes via oxidative stress (OS) are considered essential to renal calcium crystallization. Studies have hypothesized that stone formation is a form of pathological biomineralization or ectopic calcification. Pathological calcification and plaque formation in the body are triggered by reactive oxygen species (ROS) and OS. Under normal conditions, the production of ROS is tightly controlled, increasing when and where needed. Results of clinical and experimental studies have shown that renal epithelial exposure to high oxalate levels and crystals of calcium oxalate or calcium phosphate generates excess ROS, causing injury and inflammation. Antioxidant treatments reduce crystal- and oxalate-induced injury in vitro and in animal models. ROS are produced through the involvement of both mitochondria and nicotinamide adenine dinucleotide phosphate oxidase; however, the intracellular mechanism is complicated. ROS regulate crystal formation, growth, and retention through the timely production of crystallization modulators. To be able to prevent stones, we need to clarify the mechanisms underlying inflammation and formation of kidney stones.

In this session, three speakers will address three key aspects of inflammation and formation of kidney stones. Dr. Hari K. Koul, a molecular biologist from LSU Health Sciences Center, USA, will discuss the expression of signature genes in human renal epithelial cells involved in oxalate-induced inflammation. Dr. Atsushi Okada, a

urologist from Nagoya City University, Japan, will discuss about the relation between macrophages and inflammation in stone formation, and proinflammatory adipocytokines in metabolic syndrome. Dr. Chanchai Boonla, a medical technologist and biochemist from Chulalongkorn University, Thailand, will present how inflammation mediates the formation of kidney stones, from the aspects of intrarenal inflammation and presence of inflammatory proteins in urine.

COI: No.

S-08-1

Gene expression signature of human renal epithelial cells involved in oxalate-induced inflammation

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Introduction: Elevated urinary oxalate and calcium levels have independently been associated with sub-sets of idiopathic stone formers. However, precise mechanisms of interplay between elevated oxalate levels and renal tubular inflammation is not fully understood.

Materials and Methods: Renal epithelial cell lines (HK2 cells) were used in culture to evaluate the effects of oxalate and COM crystals. We utilized microarray analysis using Affymetrix HG_U133_plus2 gene chip. Data analysis was performed using Data Mining Tool (DMT 3.1, Affymetrix) and GeneSpring 7.2 (Silicon Genetics). Cell Intensity files were processed into expression values for all the 55,000 probe sets (transcripts) on each array and following the respective normalization step. Differentially expressed genes were classified according to the Gene Ontology functional category (GenMAPP v2) and functional significance of differentially expressed genes was determined using Ingenuity Pathways Analysis Software (Ingenuity® Systems, <http://www.ingenuity.com>). Cluster and Heatmap images were generated using BRB-Array tools30. Changes in gene expression were further validated by relative quantitative RTPCR. Protein expression was monitored by Western Blot analysis, immune-histochemical and immunofluorescence methods.

Results and Discussion: In previous studies from our laboratory, over last two decades have demonstrated that oxalate exposure to the renal epithelial cells results in a program of events including cell damage, re-initiation of DNA synthesis as well as cell death, activation of p38 MAP/stress kinase and NF-KB transcription factor. We are the first group to have identified expression of IL2b receptor in renal epithelial cells in response to oxalate. We have obtained new evidence that suggests oxalate and COM crystals engage TLR4 a member of the pattern recognition receptor system. Given the roles played by IL-6, IL1B receptor and TLR4, we hypothesize that elevated levels of oxalate promote renal tubular inflammation. In this talk we will discuss the gene expression of signatures in human renal epithelial cells involved in oxalate-induced inflammation. These studies provide mechanistic links as to how exposure to the elevated levels of oxalate may promote renal epithelial cell inflammation and remodeling to promote calcification.

COI: No.

S-08-2**Intrarenal inflammation and presence of inflammatory proteins in urine and stone matrix of urolithiasis patients: do these evidences give us a clue of how inflammation mediates the formation of urinary stones?**

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Inflammation and oxidative stress are known to mediate many chronic pathological conditions. Our studies in urolithiasis patients and cell culture model demonstrate that oxidative stress, inflammation and fibrosis are involved in the pathogenesis of kidney stone. Overall, the kidney function of kidney stone patients is significantly reduced compared with healthy controls. Increased oxidative stress, inflammation and fibrosis are found in the stone-forming kidneys of the patients. Urinary excretion of oxidative DNA lesion, 8-hydroxydeoxyguanosine (8-OHdG), is found to increase in the patients compared with the healthy controls, indicating an increase in oxidative stress. Additionally, exposure of renal tubular cells to calcium oxalate monohydrate crystals causes increase in 8-OHdG lesion. Infiltration of leukocytes, especially CD68-positive cells (monocytes/macrophages), is commonly found in the nephrolithiatic renal sections. Intrarenal transcript expressions of monocyte chemoattractant protein-1 and interleukin-6 are associated with increased intrarenal inflammation, decreased renal function and increased renal tubular injury. Degree of intrarenal inflammation is correlated with renal fibrosis, and increased renal fibrosis is correlated with decreased renal function. Renal tubular epithelial-mesenchymal transition (EMT), which is possibly induced by transforming growth factor-beta 1, is evident in the stone-containing kidneys, suggesting that EMT, at least in part, contributes to the stone-induced renal fibrosis. Proteomic data show that inflammatory and fibrotic proteins are abundant in stone matrix and nephrolithiatic urine. S100A8 (calgranulin A) and fibronectin, as representatives of inflammatory and fibrotic proteins, are detected in nephrolithiatic urine and stone matrix, but not in healthy urine. Furthermore, S100A8 and fibronectin are verified to up-regulate in the nephrolithiatic renal tissues. Based on our findings, we do believe that oxidative stress and inflammation are critically involved in the development of kidney stone, and renal fibrosis is an inevitable consequence. We hypothesize that lithogenic crystals formed in the supersaturated urine induce the generation of reactive oxygen species (ROS) causing oxidative stress and damage. Subsequently, ROS up-regulates the expression of inflammatory cytokines/chemokines to initiate the inflammatory response. The provoked inflammatory reaction in turn creates a vicious cycle to exaggerate the oxidative and inflammatory damage, and therefore accelerate the formation and growth of calculi.

COI: No.

S-08-3**Macrophage-derived cytokines and chemokines may be new markers for calcium oxalate stone formation risk in humans**

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We previously demonstrated the involvement of macrophages (M ϕ s) in the calcium oxalate (CaOx) kidney stone formation process by basic studies using a mouse model. And it was concluded that the activity balance of inflammatory M ϕ s (M1) and anti-inflammatory M ϕ s (M2) related to promotion and suppression of the kidney stone formation, respectively. However, in human, the correlations between stone formation risk and M ϕ activity have not been examined. The aim of the present study was to analyze the characteristics of CaOx stone formation factors and detect the urinary M ϕ -related factors specific to stone formation. Using 2 spot urine of stone formers (SFs) and non-stone formers (NSFs), we determined the concentration of 18 urinary candidate proteins using multiplex (MP) analysis on a Mag-Pix[®] system. We found no significant differences in the background data or urine biochemistry between SFs and NSFs. The two-stage MP analyses demonstrated eight factors with significant differences between the two groups. By logistic regression analyses and the validation analyses, several M2-related factors in SFs showed significantly lower values than NSFs group regardless of first time or recurrence. From the results, in CaOx SFs, decreased function of M2, including phagocytosis and processing of CaOx crystals, may play a more important role in the stone formation process than urinary biochemical abnormalities.

COI: No.

S-09**Review of the role of small molecules and macromolecules as inhibitors or promoters of kidney stone formation**

Coordinators: Neil S. Mandel¹, Jeffrey A. Wesson^{2,3}

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Growth inhibition of urolithiasis encompasses a broad range of chemical species and processes, which have been a major focus of stone research for many years. Processes include both shifting chemical equilibria to limit crystal formation by controlling urine composition (supersaturation) and direct, kinetic inhibition of crystal formation. The chemical species (inhibitors) involved range from small mineral or organic ions to macromolecules (principally proteins and glucosaminoglycans) to epithelial cell or basement membrane surfaces. The chemical equilibria involved in crystal formation are probably most completely understood, as the effects of most small ions contributing to urine supersaturation can be reliably estimated by various speciation programs. Consequently, control of the small ion composition of urine remains the cornerstone of current medical therapy, though these interventions are only incompletely effective at reducing stone formation. Kinetic inhibition of crystal formation (stone formation) likely plays an important role, since small ion components known to contribute to crystal formation vary widely in individuals, and these variations far exceed the differences in average

small ion composition observed between stone forming and healthy adults. Thus, supersaturation is insufficient to explain stone formation, and kinetic inhibition or promotion differences between individuals likely distinguish stone formers from healthy adults. In this session, three speakers will address three key aspects of inhibitor functions in urolithiasis. Dr. Jeffrey Wesson, a nephrologist and physical chemist from the Department of Veterans Affairs and Medical College of Wisconsin, USA, will discuss characterization of crystal inhibition by urinary proteins and other macromolecules and how inhibitors can become promoters through macromolecular aggregate formation. Dr. Takahiro Yasui, a urologist from Nagoya City University, Japan, will discuss evidence suggesting that osteopontin, a urinary protein long thought to be an inhibitor of urolithiasis, may actually be a promoter of stone formation and how anti-oxidants or adiponectin may be protective. Dr. Allen Rodgers, a physical chemist from the University of Cape Town, Republic of South Africa, will present an overview of micro- and macro-molecular inhibitors and speculate on their clinical importance.

COI: No.

S-09-1

The inhibitor/promoter paradox in kidney stone disease: contributions of proteins and other macromolecules to calcium oxalate crystallization

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All kidney stones form as aggregates of crystals with a bio-organic material layer that is primarily protein coating each crystal surface, though the role of proteins in stone formation is poorly understood. On the other hand, crystal formation and its connection to supersaturation have been extensively studied for all stone types, and supersaturation reduction forms the basis of stone prevention therapies. Unfortunately, supersaturation data are poorly correlated with stone risk in calcium oxalate stone formers. Consequently, considerable attention has been given to the organic matrix, particularly urinary proteins that are found in calcium oxalate stone matrix. While many of these proteins have been identified and studied extensively over several decades for their putative role in stone formation, no consistent picture has emerged regarding the identity of a single protein determinant of stone formation or its mechanism of action. Most proteins thought to be important to stone formation contain a large number of acidic amino acids (aspartic acid or glutamic acid) or posttranslational sites (phosphorylation or glycosylation). Most of these proteins studied individually in *in vitro* solution experiments inhibit the various crystallization processes (nucleation, growth, aggregation and cell attachment) that must comprise the stone forming process. On the other hand, many proteins, including osteopontin, are consistently identified in stone matrix and are correlated with increased risk for stone formation in some living system models. In this presentation, a series of experiments that probe the nature of protein or polymer interactions with pre-existing or growing calcium oxalate crystal surfaces at a near molecular level will be summarized. By correlating these data with studies of bulk crystallization effects on growth and aggregation rates, the effects polymer structure on crystal surface interactions can be isolated. These experiments suggest that similar crystal surface interactions are likely common to both inhibitors and promoters of stone formation, which appear to be dominated by the presence of

anionic side chains on the macromolecules and involve very local interactions (single amino acid). Conversely, differentiation between inhibition and promotion of stone forming processes appears to be dependent on polymer–polymer (protein–protein) interactions (i.e., solution phase behavior).

COI: No.

S-09-2

The role of osteopontin in stone formation

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Several organic compounds in calcium kidney stone matrices play an important role in stone formation. We identified osteopontin (OPN) as a major organic component of kidney stones. Studies on hyperoxaluric rat models have shown that an oxalate stimulus activates OPN expression in the epithelial cells of distal tubules. The possible role of OPN in kidney stone formation admit of discussion. The urinary form of OPN inhibited calcium oxalate (CaOx) monohydrate nucleation and reduced the growth and aggregation of CaOx crystals. OPN was thought to be an inhibitor of urolithiasis.

However, OPN is a multi-functional phosphorylated glycoprotein, which has an RGD (arginine-glycine-aspartate) amino acid sequence functioning as an adhesion motif and a series of aspartic acid domains with high affinity to hydroxyapatite. By inhibiting OPN in renal epithelial cells, the association of CaOx crystals was inhibited. Therefore, OPN is considered to play a role in the adhesion and growth of CaOx crystals on the surface of renal tubular cells during stone formation. We have reported a method to induce CaOx crystal deposition in normal mouse kidneys. We estimated OPN function in early morphological changes of CaOx crystals by using OPN-knockout (OPN-KO) mice with the method of glyoxylate-induced kidney crystal deposition. Kidney crystal depositions were clearly detected in both genotypes; however, OPN-KO mice had significantly fewer crystals than did WT mice. Morphological observation by polarized light optical microphotography and scanning electron microphotography showed large flower-shaped crystals growing in renal tubules in WT mice, and small and uniform crystals in KO mice. Transgenic mice studies in which calcium-binding sites of OPN (CaX group) and the RGD sequence (RGE group) were deactivated revealed that calcium-binding sites promote the growth of stones and that the RGD sequence promotes the initiation of stone formation. OPN antibody that specifically reacts with the SLAYGLR sequence, which is exposed by thrombin cleavage remarkably inhibits early-stage renal crystal formation by preventing renal tubular cell injury and crystal-cell attachment. These results reveal OPN to be a promoter of stone formation. As an extension of these studies, other studies using mouse models have been conducted. We present recent knowledge regarding this.

COI: No.

S-09-3

Inhibitors of urinary crystallisation processes: what are they and are they clinically important in urolithiasis?

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While clinical and basic studies of small molecule inhibitors such as citrate and magnesium have established their role in calcium urolithiasis, the role of macromolecules such as urinary proteins, remains elusive. Osteopontin (OPN), Tamm Horsfall protein (THP), crystal matrix extract (CME), prothrombin fraction 1 (PTF1) and human serum albumin (HSA) are examples. Many different kinds of studies have investigated their inhibitory potential. These include determination of their concentration in animal and human urines, examination of their inter- and intra-crystal deposition in crystallisation experiments and their effects on *in vitro* calcium crystallisation *per se*. Inorganic, synthetic and real urines have been used with commercially-obtained and urine-derived proteins. Effects on crystallisation mechanisms, crystal-cell attachment processes and crystal degradation and dissolution have been investigated. It has been found that urolithiasis is associated with reduced expression of some proteins (THP) and with structural defects of others (OPN). The degree of phosphorylation or sialylation has been identified as affecting crystal nucleation and growth (OPN) and aggregation (THP) respectively. Protein-crystal interaction is a face-specific process (OPN, THP, PTF1, HSA) which increases crystal growth on some faces and inhibits it on others. Crystal-cell interactions depend on factors such as crystal hydrate and ionic strength. Crystal degradation and dissolution depend on several intra- and extra-cellular factors including intra-crystal concentration and type of protein, type of lysosomal proteins and urinary pH.

These studies have not yielded consistent, robust results. In some cases, proteins have a dual modulatory nature. In other cases findings are counterintuitive and conflicting. Modulatory role depends on multiple factors which often act in concert. In order for urinary proteins to be clinically important, protocols need to be developed which manipulate *in vivo* conditions to optimize their inhibitory effects but minimize their promotory ones. To achieve this, these protocols must be able to alter urinary protein concentrations, ionic strength and pH while simultaneously increasing sialylation and phosphorylation in some of them and reducing self-aggregation in others. Unfortunately, it is very difficult, if not impossible, to control *in vivo* conditions to this extent. As such, urinary protein inhibitors cannot be regarded as being clinically important at this stage.

COI: No.

S-10

Life style-related risk and quality of life in stone formers

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Chairs: Giovanni Gambaro¹, Nestor Schor²

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The symposium will address the effect of stone disease and its complications on the quality of life of patients. This could be a relevant problem in cases with strongly recurrent disease, or of young patients coping with a chronic disorder, or with stones causing renal failure or associated with systemic disorders.

The other way round, the effect of life style (physical activity, smoking, “healthy” nutrition, etc.) on the risk of stone formation will also be discussed.

The session includes 3 presentations:

Quality of life in renal stone formers

Quality of life and pain in patients with MSK

Life style and risk of urolithiasis

COI: No.

S-10-1

Life style-related risk and quality of life in stone formers

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Recent studies have disclosed a significant association between pathologies characterized by painful episodes and symptoms of anxiety and/or depression. However until recently no quantitative methods are available to measure these anecdotal observations. Therefore, it is reasonable to evaluate these conditions in renal stone formers (RSF). It is clear that mental conditions interfere with the quality of life (QoL).

In our Service we evaluated, by using different tools, including the SF-36 questionnaire, socio-demographic data and Self Report Questionnaire in a version of 20-item (SRQ), among others. The SF-36 has been applied in nephrology to End-Stage Renal Disease (ESRD) patients in the USA, the UK and Brazil. We evaluated 64 patients, 32 RSF comparing with 32 controls from de Oftalmologic Clinic. It was used State-Trait Anxiety Inventory—STAI and Beck’s Depression Inventory. Results include higher levels of anxiety-state ($p = 0.001$) and anxiety-trace ($p = 0.005$). Also 18.8 % of RSF had mild depression, 34.4 % moderate depression and 6.2 % severe depression. In the control group mild levels (18.8 %) and moderate level and none severe level ($p = 0.004$) were detected. It was concluded that that anxiety and depression are more frequent in subjects with recurrent renal colic than in controls. In addition, these symptoms are correlated with the number of painful crises. An additional study was performed in 194 subjects (97 RSF/97 controls) evaluating the co-occurrence of painful recurrent renal colic and minor psychiatric morbidity (SRQ instrument and socioeconomic status). In this series RSF presented high level (50.5 %) of psychiatric morbidity (depression) especially in the lower socioeconomic status. In conclusion, it is clear that is necessary to include in the evaluation of RSF a mental status and QoL in order to give a better and more holistic treatment. This study has been supported by FAPESP, CAPES, CNPq and FOR.

COI: No.

S-10-2

Chronic renal pain in medullary sponge kidney (MSK)

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MSK usually occurs with recurrent stones. Much less frequently it is asymptomatic, while very rarely the main manifestation is severe chronic flank pain. Often these pts are accused of seeking pain medications. Because of the rarity of such a presentation it is not know if pain is due to intense lithogenic activity or is independent of it, something like a form of the “loin pain hematuria syndrome”. Three Facebook support groups exist for North American patients with MSK and chronic pain. Their cooperation allowed us to investigate chronic pain in MSK.

An ad hoc questionnaire and the Brief Pain Inventory were administered through a dedicated web site; 92 patients (89 females) participated after verification of the diagnosis of MSK (imaging and diagnosis certified by a nephrologist or urologist).

Mean age of patients was 39.8 years, (range 24–66). Age at onset of manifestations and MSK diagnosis were 23 years (4–47) and 31 years (7–57), respectively. Manifestations at onset were: flank pain (31 %), reno-ureteral colic (RUC) (26 %), hematuria (19 %), cystitis (14 %), pyelonephritis (10 %). 71 % of pts have daily pain, 76.5 % have taken painkillers in the previous week and 69.1 % needed them at the time of questionnaire administration; 58 % take them ≥ 1 time/day. The strong pain (5.4 in a scale from 0 to 10), jeopardizes general activities, mood and sleep. Only 4.6 % of pts have RUC like pain; in 52.9 % it is non-radiating flank pain with manifestations of possible UTI or stone passage (painful micturition, urgency, frequent urination, hematuria, fever); in 42.5 % it is non-radiating lumbar pain without other manifestations (however only in 3 cases the pain was a unilateral flank pain). Pain is frequently associated with stone (67 %) or sand passage (46 %), hydronephrosis (42 %), hematuria (42.4 %). Although the chronic pain that dominates the clinical manifestations of these MSK pts is usually associated with some of the typical symptoms of stone passage, in a fraction of pts this is not the case and pain is not associated with lithogenic activity.

COI: No.

S-10-3

Lifestyle factors and risk of urolithiasis

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Urolithiasis is a common condition, whose prevalence is rising worldwide. It is generally acknowledged that environmental factors play a major role in the risk of developing kidney stones, in particular with regard to dietary factors. Other lifestyle-related risk factors that have been linked with kidney stones include body mass index (BMI), physical activity, smoking, intake of alcohol and use of certain supplements. A high BMI is a well-known risk factor for urolithiasis: longitudinal studies showed that the risk of stones for subjects with a BMI above 30 was up to 109 % higher compared with those with a BMI of 21–23. Published studies regarding physical activity have reported inconsistent results: a longitudinal analysis of data from the Women's Health Initiative showed that those with a high level of physical activity (above 10 metabolic equivalents [METs]/week) had 30 % lower risk of kidney stones. On the other hand, data from three different prospective cohort did not find an association between physical activity and stones. Similarly, data regarding the risk of stones associated with smoking are conflicting. The intake of some alcoholic beverages such as wine and beer has been associated with a 30–40 % lower risk of stones in longitudinal studies. Supplemental intakes of vitamin C, calcium and vitamin D have been suggested to increase the risk of forming calcium stones, whereas vitamin B supplements might play a protective role in certain phenotypes of stone formers.

COI: No.

ORAL

O-01

Symptoms and biochemical status

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Introduction: Metabolic evaluation of patients attending the hospital with suspected stone disease is still discussed widely. Patients are of different categories—those with severe symptoms and those who come for earlier episodes of stone disease. This study was undertaken to identify whether the metabolic changes were related to the presenting symptoms.

Materials and methods: 1200 patients who presented to the stone clinic were on the basis of the temporary risk classified as (1) no symptom at the time of presentation, (2) minor symptoms at the time of presentation, (3) moderate symptoms at the time of presentation, (4) severe symptoms at the time of presentation and (5) unbearable pain or significant haematuria at the time of presentation. The extent of stone disease at the time of presentation, considering the size of the stones, renal involvement and presence of back pressure were also considered in deciding the temporary risk of the patient. The patients in the different categories temporary risk mentioned above were investigated for metabolic assessment by performing the 24 h urine volume, calcium, phosphorus, uric acid, magnesium, creatinine, oxalate, citrate sodium and potassium and serum calcium, phosphorus, uric acid, magnesium and creatinine. The values in the different groups were statistically analysed by analysis of variance using SPSS software program to study the variability in the different grades of temporary risk.

Observation: It was observed that there was no significant variation in any of the 24 h urine or blood parameters in any of the groups of temporary risk factors risk values in the study subjects. This indicates that the metabolic profile of the patient does not decide the immediate provocation to stone crystallisation or growth. The lack of identification of metabolic changes may be due to the fact that the patients are grouped as a whole as stone formers. The mechanism of stone formation may be different in different groups of individuals.

Conclusions: It is concluded from the study that the symptoms of the patient are not influenced by the biochemical changes in the body of the stone patients.

COI: No.

O-02

Is it possible to identify urinary stones in a doctor's office?

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In many rural areas of the world, physicians do not have access to basic lab services. Therefore, diagnosing and treating urinary stones can become very difficult. By finding new uses for existing equipment, we can help physicians better treat patients and increase patients' quality of life. The most helpful way for a physician to treat patients with urolithiasis is to send it to a lab for analysis so that the stone may be categorized by chemical composition and a proper method of treatment may be prescribed. However, in developing countries, access to lab services may be non-existent. A dermoscope is an inexpensive magnifying instrument used by physicians and dermatologists to examine skin lesions. This project developed a methodology to use a dermoscope to examine and identify urinary stones to see if there are any common patterns in the different types of urinary stones and categorized them by physical appearance.

To do this, the stones were examined with the dermoscope. A picture was taken of each stone as well. A description of the appearance of the stone under the dermoscope was done. The lab analysis of the stone composition was compiled and compared to the description and photograph to come up with common predictable patterns of common urinary stone types. Once this step was completed, the chemical

composition of the stone by dermoscopy was predicted before it was sent for infrared spectroscopy analysis. The predicted chemical composition of each stone was compared to the analysis results from the lab. The data was then analyzed for predicted outcomes that were correct.

By finding a few common physical characteristics that can quickly identify what type of stone a patient has, physicians in rural areas can begin the proper treatment for patients as quickly as possible, increasing better patient outcomes for prevention and quality of life. Physicians would only have to purchase a relatively inexpensive dermoscope to examine urinary stones. This study would help physicians who do not have access to a stone analysis lab to still have a viable option for identifying urinary stones and treating their patients.

COI: No.

O-03

Effects of seasonal changes in ureterolithiasis morbidity on the diagnostic relevance in emergency clinical practice

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This study aimed to evaluate the diagnostic importance of seasonal changes in the incidence of colic symptoms caused by ureteral stones. We retrospectively reviewed the medical records of patients aged 15 years and over, who complained of back, flank, or lower abdominal pain, and visited our emergency department (ED) between April 1, 2007, and March 31, 2015. Independent predictors of ureteral stones were identified using a multivariate logistic regression model, including variables showing a univariate association ($P < 0.05$) with ureterolithiasis. The equation for the multivariate logistic regression model was built using a linear regression analysis. The receiver operating characteristic (ROC) with area under the curves (AUC) was used to determine the optimal cut-off value corresponding to the intersection of sensitivity and specificity curves. This study included 491 patients (358 with ureteral stones [mean \pm standard deviation {SD} age = 49.8 ± 14.2 , range = 15–89 years]; 133 with other diseases [mean \pm SD age = 57.3 ± 17.1 , range 18–90 years]) who met our selection criteria. In the multivariate logistic regression, 8 independent variables—age, <60 years; gender, male; <6 h of pain; nausea or vomiting; hydronephrosis; hematuria; history of urinary stone; and summer (July to September in Japan)—achieved statistical significance, and indicated that summer was an independent factor for the differential diagnosis of ureterolithiasis in patients experiencing pain during ED visit. Pain experienced in summer was 9 times more likely than that experienced in other seasons to be associated with ureteral stone attack. The optimal threshold value of estimated probability for ureteral stone was 0.703 at the intersection of the sensitivity and specificity curves, yielding good prediction of ureteral stone (AUC = 0.974, positive negative predictive value = 0.983, negative predictive value = 0.955). Of the 491 patients, 6 patients (acute aortic dissection, ileus, acute bleeding of renal cyst, retroperitoneal fibrosis, colonic diverticulitis, and retroperitoneal tumor) with an estimated probability of >0.703 showed non-stone diseases. Seasonal changes affected the diagnostic performance for ureteral stone.

COI: No.

Results of multivariate logistic regression analysis

Factors	Multivariate logistic regression analysis					
	odds ratio	95%CI		coefficients	SE	P value
Age	< 60 years	3.04	(1.20 – 7.69)	1.1112		0.0189
	≥ 60 years	1.00 (Ref.)				
Sex	male	3.86	(1.49 – 9.98)	1.3508	0.4848	0.0053
	female	1.00 (Ref.)				
Pain location	back					NS
	none					NS
	flank					NS
	none					NS
	lower abdomen					NS
Pain onset	none					NS
	sudden					NS
	not sudden					NS
Duration of pain	< 6 h	10.20	(4.13 – 25.40)	2.3261	0.4634	5.2E-07
	≥ 6 h	1.00 (Ref.)				
Gastrointestinal symptoms	nausea or vomiting	3.26	(1.09 – 9.73)	1.1821	0.5578	0.0340
	none	1.00 (Ref.)				
Clinical examination	hydronephrosis	46.60	(14.60 – 149.00)	3.8423	0.5934	9.5E-11
	none	1.00 (Ref.)				
	gross hematuria or occult blood in urine	39.10	(14.30 – 107.00)	3.6662	0.5133	9.2E-13
	none	1.00 (Ref.)				
Medical history	ureterolithiasis	4.42	(1.32 – 14.80)	1.4855	0.6158	0.016
	none	1.00 (Ref.)				
	hypertension or dyslipidemia					NS
	none					NS
	diabetes mellitus					NS
	none					NS
Transport to ED	ambulance					NS
	none					NS
Visiting time in ED	1:00 AM–8:30 AM					NS
	8:30 AM–1:00 AM					NS
Season at presentation	hot season *	9.02	(3.13 – 26.00)	2.1993	0.5395	0.000046
	other seasons	1.00 (Ref.)				

* Hot season corresponds to summer (July to September) in Japan. NS: not significant, SE: standard error, Ref.: reference value, ED: emergency department, E: exponential

O-04

Economics of stone metaphylaxis in the diagnosis related groups (DRG) calculation system in Germany

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Urolithiasis is a considerable economic burden for health care systems in industrialized countries where the incidence of stone disease increased during the last decades and probably will further increase for several reasons. For the first time in Germany, some years ago we could obtain actual figures on the cost for stone treatment. In a calculation model, we could show that rational metaphylaxis could lower the cost for stone treatment by 170 Mio Euro (E) per year. Between 2003 and 2009 a new reimbursement system has been introduced in Germany. This system is based on diagnosis related groups (DRG) and completely different from the previous one which was based on payment for the days of hospital stay. Therefore, we were interested to see whether metaphylaxis can reduce the treatment costs for urolithiasis also under the new conditions of the DRG system.

We analyzed the patients with renal and ureteral stones (ICD 10 N 20.0/20.1) treated in our department in 2011. Considering the diagnosis, the relative weight, the patient clinical complexity level (PCCL) and the state base case value, the treatment costs per patient were calculated. According to epidemiological data, the costs for stone treatment in Germany were assessed. The costs for metabolic evaluation and metaphylaxis were calculated as well. It was assumed that metaphylaxis could lower the recurrence rate by 40 %. Using these figures, the net saving was calculated.

The costs for inpatient therapy/patient in 2011 were 5,195 E. There are about 200,000 recurrent stone patients/year in Germany. Inpatient treatment was required in 80 %. The mean N° of hospital stays/episode was 1.8. Therefore, the total costs/year in Germany are E 831 millions. For outpatient treatment (40,000 patients), the costs are calculated to 7,360,000 E. The total costs for stone treatment are 1,129,993,000 E. Calculating the costs for metabolic evaluation and Metaphylaxis to 114 Mio E, the net saving would be 250 Mio E per year.

With the new DRG reimbursement system in Germany, metaphylaxis (secondary prevention) in urinary stone formers is even more cost effective than with the former reimbursement system.

COI: No.

O-05**Upregulation of osteogenic pathways in a rat model of calcium oxalate nephrolithiasis**

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Hyperoxaluria, increased urinary excretion of oxalate, may lead to disorders ranging from calcium oxalate (CaOx) crystal deposition in the kidneys with associated injury and inflammation to the formation of kidney stones. Many calcium oxalate (CaOx) kidney stones develop attached to Randall's plaque (RP), sub-epithelial deposits of calcium phosphate (CaP) on renal papillary surfaces. Pathogenesis of the plaques is not fully understood. We propose that abnormal urinary environment in stone forming kidneys leads to epithelial cells losing their identity and becoming osteogenic. We tested our hypothesis in male rats made hyperoxaluric by administration of hydroxy-L-proline (HLP). After 28 days, rat kidneys were extracted. We performed genome wide analyses of differentially expressed genes and determined changes consistent with dedifferentiation of epithelial cells into osteogenic phenotype. Selected molecules were further analyzed using quantitative-PCR and immunohistochemistry.

Genes for runt related transcription factors (RUNX1 and 2), zinc finger protein Osterix, bone morphogenetic proteins (BMP2 and 7), bone morphogenetic protein receptor (BMPR2), collagen, osteocalcin, osteonectin, osteopontin (OPN), matrix-gla-protein (MGP), osteoprotegerin (OPG), cadherins, fibronectin (FN) and vimentin (VIM) were up regulated while those for alkaline phosphatase (ALP) and cytokeratins 10 and 18 were down regulated. In conclusion, epithelial cells of hyperoxaluric kidneys acquire a number of osteoblastic features but without CaP deposition, perhaps a result of down regulation of ALP and up regulation of OPN and MGP. Plaque formation may additionally require localized increases in calcium and phosphate and decrease in mineralization inhibitory potential.

COI: No.**O-06****Topography, composition and structure of incipient Randall's plaque at the nanoscale level**Emmanuel Letavernier¹, Cécile Verrier¹, Dominique Bazin^{1,2}, Odile Stephan², Alexandre Gloter², Marie-Christine Verpont¹, Vincent Frochot¹, Jean-Philippe Haymann¹, Isabelle Brocheriou¹, Olivier Traxer¹, Michel Daudon¹¹Université Pierre et Marie Curie-Paris VI Sorbonne Universités, France; ²Laboratoire de Physique des Solides, CNRS UMR 8502, Université Paris Sud XI, Orsay, France

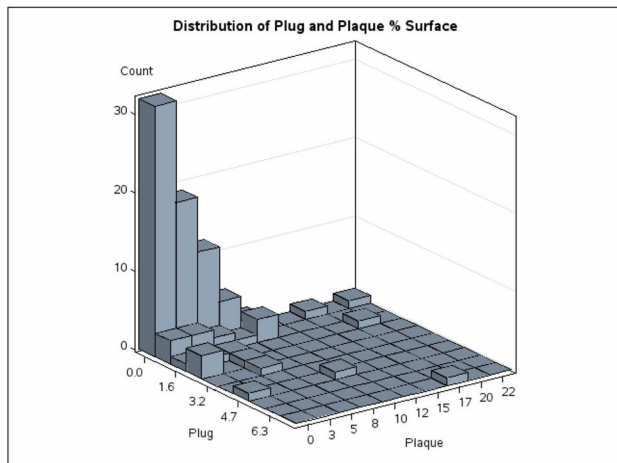
Alexander Randall identified calcium phosphate plaques in renal papillae as the origin of kidney stones. However, little is known about the early steps of Randall's plaque formation, preceding the onset of urolithiasis. Our objectives were to characterize the composition and the initial formation site of incipient Randall's plaque in non-stone formers living patients. Fifty-four healthy papillae from kidneys removed for cancer have been analyzed by immunohistochemistry and Von Kossa staining, Field Emission-Scanning Electron Microscopy with Energy Dispersive X-ray analysis, μ -Fourier Transform Infrared Spectroscopy, Cryo-Transmission Electron Microscopy coupled to Selected-Area Electron Diffraction and Electron Energy Loss Spectroscopy. Incipient Randall's plaque has been observed in 72.7 % of kidneys. Carbonated apatite was as expected the main

component of microcalcifications but amorphous calcium phosphate and whitlockite have been identified in 80 and 40 % of the papillae, respectively. Incipient plaques stood in the deepest part of the papillae, around the loop of Henle tip but also around vasa recta (respectively 62.4 and 37.2 % of microcalcifications) and rarely close to collecting ducts. At the nanoscale level, calcifications were often made of several nanocrystals inside organic material looking like microvesicles. In conclusion, incipient Randall's plaque is frequent and appears at the tip of renal papillae, around the hairpin structure of the loop of Henle and vasa recta as well. Nanoscale analyses suggest a local nucleation process promoting nanocrystal growth in a super-saturated milieu. In addition, plaques contain various calcium and magnesium phosphates and not only carbonated apatite.

COI: No.**O-07****Characterization of inner medullary collecting duct plug formation among idiopathic calcium oxalate stone formers**John C. Lieske¹, Marcelino Rivera¹, Johann Ingimarsson¹, Patrick A. Cockerill¹, Felicity T. Enders¹, Ramila A. Mehta¹, Lisa Vaughan¹, Terri J. Vrtiska¹, Loren P. Herrera Hernandez¹, David R. Holmes¹, Andrew D. Rule¹, James Williams², Amy E. Krambeck¹¹Mayo Clinic, Rochester, USA; ²Indiana University School of Medicine, Indianapolis, USA

Interstitial apatite deposits in the renal papillum have been identified as a possible anchoring site for calcium oxalate (CaOx) stones. However, recent investigations have also commonly demonstrated duct of Bellini plugging in idiopathic CaOx stone formers (SF). Thus in the current study we determined the prevalence of, risk factors for, and renal functional consequences of ductal plug formation in a consecutive cohort of iCaOx SF undergoing percutaneous nephrolithotomy (PCNL) for stone removal. After stone removal, accessible renal papillae were videotaped and quantitatively analyzed to determine the percent surface area (SA) occupied by plaque and ductal plug. A representative papillum was biopsied, and the composition of removed stones determined by micro-CT and infrared spectroscopy. iCaOx SF comprised 96 of 240 enrolled patients between 2009 and 2014. Of these, 41 (43 %) had ductal plugs. There was no significant difference between the low and high % plug groups in mean plaque surface area (2.1 vs 3.4 %, respectively) or secondary stone composition. Further, the amount of plaque and plug did not appear to be closely correlated (Figure), such that patients could have high plaque low plug, low plaque high plug, or any variation of the two features. Over 30 % lacked both endoscopic plaque and plug. Patients with a higher % mean SA plug (>1 %) had a higher urinary pH (mean 6.3 vs 6.0, $p = 0.02$) and elevated urinary hydroxyapatite (HA) SS (mean 4.7 vs 3.4 D.G.; $p = 0.04$). Those with >1 % plugging had more extensive ductal dilation ($p = 0.002$) compared to those with ≤ 1 % plugging. However, estimated glomerular filtration rate (eGFR) was similar between those with ≤ 1 % (75.4 (63.6, 91.0) ml/min/1.73 m²) versus >1 % (74.7 (61.5, 86.9) ml/min/1.73 m²) plugging. Thus within a cohort of iCaOx SF, plaque and ductal plugs often coexist. Intraluminal features known to favor calcium phosphate crystallization, namely higher pH, may play a role in plug formation. However, the pathogenic significance of these plugs in the iCaOx SF population remains to be established. Furthermore, a substantial percentage of iCaOx SF lack macroscopic plaque and plug.

COI: No.

Figure: Distribution of IMCD plug and Plaque % Surface**O-08****Papillary calcifications in uric acid stone formers (UASF): first results**

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For calcium oxalate urolithiasis we could demonstrate that the assessment of renal papillary calcifications by using a calcification index (CI) is a better prognostic parameter to estimate the risk for recurrence than metabolic evaluation. Now we were interested to learn the role and significance of papillary calcifications in UASF.

So far, we studied $n = 30$ patients with UAS. For stone analysis, X-ray diffraction/polarizing microscopy was used. During flexible ureteroscopy and flexible percutaneous nephrolithotomy all the renal papillae were inspected, counted and the severity of calcifications assessed. A calcification index (CI) was calculated: sum of the N° of papillae \times calcification grade (1–3) $\times N^{\circ}$ of calcified/total N° of papillae. Furthermore, the following parameters were examined in all patients: age, sex, BMI, arterial blood pressure, stone episodes, diabetes mellitus; blood: creatinine, glucose, uric acid, calcium, sodium and potassium; urine: pH, volume, calcium, uric acid, citrate, ammonia and urea. Using the statistic programme Prism 5 (Graph-Pad), summary statistics and non-parametric correlations (Spearman) and their significance were calculated.

Contrary to calcium oxalate stone patients (7.7 ± 7.9), the CI was considerably lower in UASF (5.04 ± 4.39), although the number of stone episodes was higher (2.53 ± 1.096 vs. 2.11 ± 1.30). The CI did not correlate significantly ($r = 0.26$; $p = 0.258$) with the recurrence rate and the number stone episodes respectively. Concerning conventional metabolic parameters, blood calcium did positively, and urine pH and volume negatively correlate with the number of stone episodes.

Contrary to calcium oxalate urolithiasis, papillary calcifications play a less important role in the pathway of UAS formation. Accordingly, they seen not to correlate with the recurrence rate and may be no prognostic parameter. However, these preliminary results have to be corroborated in larger series.

COI: No.

O-09**Papillary calcifications: a new prognostic factor in idiopathic calcium oxalate urolithiasis (CaOxU)**

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Metabolic evaluation is not suitable to forecast the course of the disease in idiopathic calcium oxalate stone formation (iCaOxU).

An important pathway in CaOx stone formation is the overgrowth on interstitial apatite papillary plaques. Therefore we studied, whether the extent of such plaques may be used as a prognostic factor in CaOxU.

Prospectively we studied $n = 100$ patients with iCaOxU. For stone analysis, X-ray diffraction/polarizing microscopy was used. During flexible ureteroscopy and flexible percutaneous nephrolithotomy all the renal papillae were inspected, counted and the severity of calcifications assessed. A calcification index (CI) was calculated: sum of the N° of papillae \times calcification grade (1–3) $\times N^{\circ}$ of calcified/total N° of papillae. Furthermore, the following parameters were examined in all patients: age, sex, BMI, arterial blood pressure, stone episodes, diabetes mellitus; blood: creatinine, glucose, uric acid, calcium, sodium and potassium; urine: pH, volume, calcium, uric acid, citrate, ammonia and urea. Using the statistic programme Prism 5 (Graph-Pad), summary statistics and non-parametric correlations (Spearman) and their significance were calculated.

The CI correlated significantly ($r = 0.37$; $p = 0.012$) with the N° of stone episodes. Apart from citrate ($r = 0.51$; $p = 0.002$) none of the conventional metabolic parameters correlated significantly with the N° of stone episodes. Paradoxically, the citrate excretion—although citrate being an inhibitor of CaOx stone formation—positively correlated to the recurrence rate.

The endoscopic assessment of papillary plaques/calcifications and the calculation of the CI is a more suitable prognostic factor in CaOx than conventional metabolic evaluation. Metabolic evaluation is not suitable to forecast the course of the disease in idiopathic calcium oxalate stone formation (iCaOxU).

COI: No.

O-10**Role of serum uric acid in metabolic changes in calculogenesis**

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Introduction: Uric acid stones and uric acid pathology are recognized entities. However, the role of serum uric acid in the formation of calcium oxalate stone disease has not been identified and confirmed properly. The present study was undertaken to assess the role of serum uric acid in relation to the other metabolic parameters of the urinary stone patients presenting to the stone clinic.

Materials and methods: 1469 patients presenting in the urinary stone clinic in the last 5 years were analysed metabolically and were classified into normouricaemic with less than 6 mg% of serum uric acid and hyperuricaemic with more than 6 mg% serum uric acid. 24 h. urine samples of all the patients were collected in thymol and assessed for 24 h. calcium, phosphorus, uric acid, magnesium, creatinine, oxalate, citrate, sodium and potassium. Blood was collected for estimation of serum calcium, phosphorus, uric acid, magnesium and

creatinine. All the differences in means of biochemical values of normouricaemic group and the hyperuricaemic group were compared using student 't' test using the SPSS software program.

Observation: It was observed that 14.2 % of the patients were hyperuricaemic with serum uric acid more than 6 mg%. On analyzing the metabolic data of all the patients, it was seen that the hyperuricaemic patients had significantly higher promoters, namely urine uric acid—473 mg% ($p < 0.001$), higher serum calcium—14.8 mg% ($p < 0.05$) and higher serum phosphorus—3.8 mg % ($p < 0.05$) and significantly lower urinary citrate 769 mgs/day ($p < 0.05$) compared to the normouricaemic group. However the urine potassium level—52.8 mg/day ($p < 0.05$) was significantly higher.

Conclusions: It is concluded that patients with high serum uric acid have increased levels of promoters in the urine and blood and decreased inhibitor like urinary citrate. These make the patient more prone for urinary stone formation. Hence it is surmised that serum uric acid value has a significant bearing to the metabolic process of calcium oxalate stone formation. In the light of the findings, it becomes mandatory for patients with oxalate stone disease to have the uric acid level controlled in the blood by administering appropriate doses of allopurinol.

COI: No.

O-11

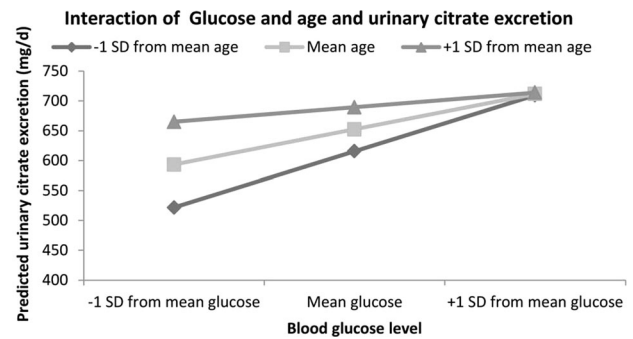
Higher blood glucose is associated with higher urine citrate excretion

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Urinary citrate (Ucit) protects against urinary stone formation. Acid base status and diet influence UCit. However, the effect of demographics, diet, and glucose metabolism on Ucit excretion, urinary pH (U-pH) and net gastrointestinal alkali absorption (NAA) are not known. Twenty-four hour urine samples, blood glucose, creatinine, and cystatin C were obtained from non-Hispanic white sibships in Rochester, MN ($n = 446$; 64.5 ± 9 years; 58 % female). Diet was assessed by a food frequency questionnaire. The impact of blood glucose, demographics and dietary elements on Ucit excretion, U-pH, and NAA were evaluated in bivariate and multivariable models and interaction models that included age, sex, and weight. NAA significantly associated with Ucit and U-pH. In multivariate models UCit increased with age, weight, $eGFR_{Cys}$, and blood glucose, but decreased with loop diuretic and thiazide use. U-pH decreased with serum creatinine, blood glucose, dietary protein but increased with dietary potassium. NAA was higher in males and increased with age, $eGFR_{Cys}$ and dietary potassium. Significant interactions were observed for Ucit excretion with age and blood glucose ($\beta = -0.20$, $p = 0.01$), weight and $eGFR_{Cys}$, ($\beta = 0.07$, $p = 0.01$), and sex and thiazide use ($\beta = -114.22$, $p = 0.04$). Blood glucose had a significant and independent effect on U-pH and also Ucit. This study provides the first evidence that blood glucose could influence urinary stone risk independent of urinary pH, potentially providing new insight into the association of obesity and urinary stone disease. The effect of blood glucose to increase urinary citrate excretion could also contribute to the tendency of patients with diabetes to form uric acid (as opposed to calcium oxalate) stones.

COI: No.



O-12

Association between urine calcium excretion and bone mineral density in calcium stone formers

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Background: Calcium nephrolithiasis is associated with an increased risk of fractures and osteoporosis. Hypercalciuria and negative calcium balance have been assumed to be pathogenic for bone loss in kidney stone formers. Urinary calcium excretion was negatively associated with bone mineral density in small studies. However, this association has not been tested in a larger population of kidney stone formers.

Objectives: To evaluate the association of urine calcium excretion with bone mineral density in a large population of calcium stone formers.

Methods: We have retrospectively studied bone mineral density (BMD) in calcium stone formers in our center. Excluded were patients with hypercalcemia, chronic bowel disease, distal renal tubular acidosis or estimated GFR < 60 ml/min/1.73 m². We assessed the association between bone mineral density and urine calcium (in 24-h urine collected under random and restricted diet, and on fasting and post-oral calcium load). This association was assessed separately in both genders in univariate and multivariate models adjusting for BMI and urine sodium and sulfate. These associations were tested in the entire kidney stone population as well as in the subgroup of hypercalciuric stone formers.

Results: 235 male (mean age 47.4 years, BMI 28.9 kg/m²) and 159 female (mean age 42.7 years, BMI 27.3 kg/m²) were included in this analysis. In the entire population, no significant association was detected between urine calcium (24-hr, fasting or post-calcium load urine) and femoral neck Z-score in either gender ($p > 0.05$ in univariate and multivariate analysis). The association between lumbar spine Z-score and urine calcium was also non-significant in univariate analysis, however it became statistically significant after multivariable adjustment ($p = 0.034$ in men and $p = 0.007$ in women). Among hypercalciuric stone formers ($N = 220$), no significant association was demonstrated between urine calcium and BMD Z-scores.

Conclusions: Unlike previous small studies in calcium stone formers, we found no significant correlation between urine calcium and BMD Z-scores in this large cohort of calcium stone formers. This study suggests that mechanism(s) other than hypercalciuria may explain the higher fracture risk in patients with nephrolithiasis.

COI: No.

O-13**Patients' compliance in the prevention of uric acid urolithiasis**

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An increasing prevalence of urolithiasis and costs of treatment emphasize the importance of effective preventive measures. Uric acid stones are considered to have a high risk of recurrence and require not only general preventive measures, but also specific pharmacological preventive measures. Particularly these types of stones have the best response rates for specific metaphylaxis. Preventive measures could significantly reduce the recurrence rates and the costs of treatment. This message could unfortunately not be conveyed to most of the patients and their GPs and urologists.

To assess the compliance rates among the patients with uric acid urolithiasis, who have been treated in our clinic from 11/2007 till 03/2013 ($n = 165$), we have developed a questionnaire and have sent it to the patients after discharge from the hospital.

25.5 % of questionnaires were sent back and could be evaluated. Most of the patients (90 %) have implemented the general preventive measures, like increasing of fluid intake (76 %), avoiding of excessive intake of animal protein (50 %), reducing weight and sport (21.5 %). Specific pharmacological preventive measures (alkalization of urine with alkaline citrate) were implemented by only half of the patients (50 %). 24 % have done it on a long-term basis. The rest gave up after different periods of time, justifying it with absence of any complaints and recommendation of a doctor.

These results show a relatively high rate of compliance to general preventive measures, but at the same time, low compliance rates to pharmacological preventive measures and implementation of those for only short period of time. The reason of it could be a lacking knowledge of the patients or inadequate counselling. Another reason for the restriction in prescription of alkaline citrate could be that this treatment is not always being taken over by insurance, even though its positive effectiveness has long been proved. To sum up, there are following ways to be paved to achieve better rates in implementation of preventive measures: adequate counselling by discharge from the hospital and in out-patient field and communication with insurance companies to clearly show the immense importance of these measures and to strive for taking over the costs of pharmacological metaphylaxis.

COI: No.

O-14**Synergistic role of calcium and vitamin D in a murine model of kidney stone disease**

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The role of vitamin D in kidney stone formation remains controversial. We analyzed whether long-term exposure of rats to vitamin D

supplementation, with or without calcium-rich diet, would promote kidney stone formation or kidney tissue calcifications.

Four groups of rats received vitamin D alone (100,000 UI/Kg every 3 weeks), a calcium-enriched diet alone (calcium gluconate 2 g/l in drinking water), both vitamin D supplementation and calcium rich diet, or a standard diet (controls) during 6 months. Serum and urine parameters and crystalluria have been monitored during 6 months. Kidney calcifications and stones have been assessed by 3D-micro-computed tomography, μ -Fourier transform infrared spectroscopy, von Kossa staining, and scanning electron microscopy.

Although serum calcium levels were similar in the four groups, rats receiving vitamin D had a progressive increase in urine calcium level over the time, especially those receiving both calcium and vitamin D. Calcium alone did not increase significantly urine calcium levels. Most rats receiving calcium and vitamin D had calcium phosphate and to a lesser extent calcium oxalate crystals in urine. At 6 months, rats exposed to calcium or vitamin D alone had a modest and non significant volume of kidney calcifications (mean volume 0.010 and 0.017 mm³ respectively). By contrast, rats exposed to both calcium and vitamin D supplementation developed significant apatite kidney stones (mean volume 0.121 mm³).

Overall, co-administration of vitamin D and increased calcium intakes exert a synergistic role in kidney stone formation. This original model of murine kidney stone formation raises concerns about the cumulative risk of vitamin D supplementation and high calcium intakes in humans.

COI: No.

O-15**NLRP3 inflammasomes are activated in oxalate nephropathy**

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Hyperoxaluria, increased urinary excretion of oxalate, is caused by increase in oxalate production or absorption of dietary oxalate and may lead to a variety of disorders ranging from kidney stones to calcium oxalate (CaOx) crystal deposition in the kidneys and their injury and inflammation. Such renal changes may eventually result in end-stage renal disease. NLRP3 inflammasomes have been implicated in a number of crystallopathies such as gout and silicosis. NLRP3 null mice fed high oxalate diet demonstrated reduced inflammation and were protected from progressive renal failure and death that occurred in similarly fed wild-type mice.

We investigated genetic changes in the kidneys of rats made hyperoxaluric by administration of hydroxyl-L-proline. Results revealed that genes encoding for PYCARD (ASC: apoptosis-associated speck-like protein containing a CARD), TXNIP (Thioredoxin-interacting protein), NLRP3, Caspase-1, IL-1 β and IL-18 were significantly up regulated. Administration of apocynin, an antioxidant and considered an inhibitor of NADPH oxidase activation caused down regulation of these same genes. Results were verified using quantitative RT PCR with Syber Green assays and immune-histochemical staining of selected molecules.

Data suggest a role for ROS in the activation of inflammasomes and point to novel therapeutic possibilities for crystal induced nephropathies.

COI: No.

O-16

Urinary biomarkers for renal damage in primary hyperoxaluria

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Background: Primary hyperoxalurias are autosomal recessive disorders characterized by overproduction of oxalate. Patients often develop kidney stones and renal failure secondary to oxalosis. Our recent studies demonstrated that higher urinary oxalate excretion and nephrocalcinosis are associated with poorer renal outcome. Thus strategies to reduce oxalate excretion might be beneficial. Furthermore, noninvasive urine markers reflective of active oxalate-related kidney injury, including nephrocalcinosis, could be useful to gauge the effectiveness of ongoing treatments.

Methods: A panel of potential biomarkers that reflect different nephron sites and potential mechanisms of injury were measured in biobanked urine specimens from a cohort of PH patients: retinol binding protein (RBP), clusterin, neutrophil gelatinase-associated lipocalin (NGAL), 8-isoprostane (8IP), monocyte-chemoattractant protein 1(MCP-1), liver-type fatty acid binding protein (L-FABP), heart-type fatty acid binding protein (H-FABP), and osteopontin (OPN). Observations post liver and kidney transplantation were excluded, leaving 114 urine specimens from 30 PH patients over multiple visits. Marker panels were also obtained from 47 healthy controls. Associations between urine biomarkers and 24 h urine oxalate (Uox), calculated CaOx supersaturation (CaOx SS), and calculated proximal tubular oxalate concentration (PTOx = (UOx* serum Cr* 4)/UCr), were assessed. Each biomarker was assessed after natural log transformation to account for skewed distributions.

Results: The mean \pm SD age at first visit was 19.5 \pm 16.6 yrs with an estimated GFR (eGFR) of 68.4 \pm 21.0 ml/min/1.73 m². Concentrations of all biomarkers differed between cases and controls ($P < 0.001$). As shown in Table 1, after adjustment for age, sex and eGFR, higher CaOx supersaturation was associated with higher RBP, 8 IP and MCP-1, and higher PtOx was associated with lower 8 IP.

Conclusion: A panel of renal injury biomarkers systematically differed between PH patients and controls, and specific markers associated with calcium oxalate SS or PTOx. In these patients urinary 8IP excretion might reflect ongoing proximal tubular injury (PtOx) and collecting tubule crystallization (CaOx SS). Increased collecting tubule crystallization (CaOx SS) was also reflected by urinary MCP-1 and RBP excretion. Further studies are warranted to determine whether any of these markers predict long term outcomes or are altered in response to treatment strategies.

COI: No.

Table 1. Association of urine markers with 24 urine oxalate excretion, CaOx supersaturation, and proximal tubular oxalate concentration in age-sex-eGFR adjusted generalized estimating equations.

Natural Log of Urinary Biomarker Concentrations	Age, sex and eGFR adjusted GEE models					
	ln(Urine Oxalate 24hr/1.73m ²)		CaOx (24hr SS)		ln(Pt Ox (Umol/L))	
	β	P	β	P	β	P
Retinol Binding Protein [RBP], ug/L	-0.108	0.42	0.261	<.0001	-0.096	0.57
Clusterin, ng/mL	-0.430	0.13	0.106	0.64	-0.503	0.062
Neutrophil Gelatinase-Associated Lipocalin [NGAL], ng/mL	-0.025	0.93	0.024	0.81	-0.139	0.61
8 isoprostane [8 IP], pg/mL	-0.212	0.067	0.208	<.0001	-0.242	0.023
Monocyte Chemoattractant Protein [MCP1], pg/mL	-0.195	0.59	0.446	0.0002	-0.136	0.68
Liver-type fatty acid binding protein [L-FABP], ng/mL	0.011	0.92	0.053	0.19	0.099	0.37
Osteopontin [OPN], ng/mL	0.253	0.44	0.13	0.27	-0.019	0.95
Heart-type fatty chain binding protein [H-FABP], pg/mL	0.062	0.68	0.149	0.14	0.006	0.97

O-17

Selective protein enrichment in calcium oxalate stone matrix

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Urine proteins are thought to control calcium oxalate (CaOx) stone formation, but more than 100 proteins have been identified in stone matrix providing little insight into their role in stone formation. Proteins that stimulate stone formation are likely to demonstrate increased abundance in stone matrix compared to their urinary abundance, so quantitative proteomic data were acquired for both stone former urine and CaOx stone matrix proteins.

Urine proteins were isolated by ultrafiltration (>10 kDa membrane) from random urine samples from 25 CaOx stone forming patients. CaOx stone matrix proteins were isolated from 3 archival CaOx stone samples (>95 % CaOx content) by dissolution in EDTA/SDS solution followed by ultrafiltration. Proteomic analysis was performed using non-labelled, quantitative mass spectrometry methods. Only proteins with 2 or more peptide matches at >85 % confidence were included, while keratin and redundant proteins were excluded.

Only a small number of urine proteins were strongly enriched in stone matrix compared to urine, suggesting a critical role for these proteins. The 5 most prominently enriched proteins (osteopontin, prothrombin, vitamin K-dependent protein Z, hemoglobin beta chain, and mannan-binding lectin serine protease 2) accounted for about 41 % of matrix protein mass, but only 3.4 % of urine protein mass. Many highly abundant urinary proteins (i.e., albumin and Tamm-Horsfall protein) were present in stone matrix at reduced relative abundance, suggesting that their inclusion was secondary to non-selective interactions with the stone crystals or matrix. The observation that stone matrix was highly enriched in both highly anionic ($pI < 5$, including osteopontin) and highly cationic ($pI > 11$, including histone) proteins was also noteworthy, since mixtures of oppositely charged polymers form aggregates at very low concentrations which could trigger stone formation. Many of these proteins are normally found in intracellular or nuclear compartments.

Relatively few proteins appeared to be critically important to CaOx stone formation, while most abundant urine proteins were likely included non-selectively. The simultaneous presence of highly anionic and highly cationic proteins in matrix suggests that stone formation involves protein aggregation, while a cell injury process is implicated by the presence of many intracellular proteins. These observations present a new paradigm for CaOx stone research.

COI: No.

O-18

Type of stone disease and metabolic derangement

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Introduction: Stone disease involves stone, colic and crystalluria. Metabolic assessment in urinary stone disease has been a controversial subject all over in the world. Even though the biochemical abnormalities are described in many patients, compared to the normal individuals, a definite opinion has not evolved regarding the role of these biochemical alterations in the actual formation and progression

of stone growth. The present study was undertaken to assess the differences between the biochemical presentations of the stone patients, crystalluric patients and colic patients. For this purpose, those who had a definite stone passage or a stone retrieved or radiological evidence of stones were selected. Those with ultrasound reports of stones less than 8 mm diameter and not recognized by X-ray/CT were excluded from the stone group. Crystalluric patients were those who had significant pathological crystalluria in the urine deposit presenting with various symptoms but not having a definite stone in X-ray, ultrasound or CT scan. Colic patients were those with severe pain, but not having proved urinary stone.

Materials and methods: 1600 urinary stone patients were classified into stone, crystalluria and colic groups. 24 h urine was collected in thymol and assessed for 24 h calcium, phosphorus, uric acid, magnesium, creatinine, oxalate, citrate, sodium and potassium. Blood was collected for the estimation of serum calcium, phosphorus, uric acid, magnesium and creatinine.

Observations: It was observed that statistically significant variability was recognized in urine calcium, urine phosphorus and urine uric acid. All these three values were highest in the confirmed stone patients—urine calcium 236 mg/day, urine phosphorus 693 mg/day and urine uric acid 400 mg/day compared to the crystalluria group and colic group even though not statistically significant. Urinary oxalate was highest in the crystalluria group and urinary citrate was lowest in this group. The urinary sodium, serum calcium and serum creatinine were also highest in the colic group even though not statistically significant. The serum uric acid was highest 5.1 mg% in stone group though not statistically significant.

Conclusions: Intricate statistical analysis of data shows that metabolic parameters in the urine may indicate the aggravations of stone formation.

COI: No.

O-19

Demography and symptoms

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Introduction: Urinary stones disease presents with various symptoms mainly pain dysuria, haematuria, lithuria, crystalluria, vomiting and sweating. The urinary stone patients are classified into three groups namely confirmed stone patients, crystalluric patients and colic patients. The symptoms presented by the patients of the three groups vary. In this paper, the presentation of symptoms in the different groups of patients is presented.

Materials and methods: 1616 patients were randomly selected for the study and clinical symptoms present in the patient were recorded. Patients were classified into three groups namely confirmed stone patients, crystalluric patients and colic patients. Patients were studied as those having presence or absence of individual symptoms and findings were recorded.

Observation: The most common symptom was pain in 87.7 % of the patients followed by vomiting (32.6 %), lithuria (22.3 %), haematuria (18.1 %), sweating (13.6 %), crystalluria (3 %) and dysuria (2.7 %). On studying the occurrence of different symptoms, the following were recognized. Pain was present in all colic patients but in 86 % of stone patients and 63 % of crystalluria patients. Patients with history of crystalluria were maximum in the group of crystalluria patients. This indicates that it was the passage of crystals that produces pain.

Dysuria was maximum in crystalluria patients (6.6 %). Haematuria was maximum in stone patients (23 %) followed by crystalluria patients (20 %) and colic patients (15 %). Lithuria was maximum in stone patients (58 %). Sweating was maximum in stone and colic patients (15 % each). Vomiting was maximum in stone patients (40 %) followed by colic patients (33 %).

Conclusions: Symptoms presented by patients varied among the groups namely confirmed stone patients, crystalluric patients and colic patients. Some of the symptoms were related to passage of stones or crystals and associated symptoms like vomiting and haematuria were maximum in patients passing stones.

COI: No.

O-20

Are there seasonal variations of renal colics in calcium oxalate stone formers in Germany?

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In many countries seasonal variations of renal colics have been described during the last decades. There were differences calcium oxalate and other stones. The urine composition also varied according to the season. So far, for Germany, no data were reported in the literature.

We examined n = 1049 consecutive calcium oxalate stone formers presenting with renal colics at our hospital. They were divided in four groups by the quarter of their presentation. The stones were analyzed by x-ray diffraction. The following parameters were measured: age, sex, systolic and diastolic arterial blood pressure (BPs/d), number of stone episodes, diabetes mellitus (DM); serum: creatinine, calcium, sodium, potassium, uric acid, glucose; urine: pH-profiles, citrate, calcium, uric acid, ammonia, urea, and creatinine. For statistical analysis, the Kruskal–Wallis-test was used.

The number of patients per quarter was distributed equally (1. quarter n = 266; 2. quarter n = 257; 3. quarter n = 261; 4. quarter n = 265). There were also no differences in all the parameters examined.

In Germany, obviously there are no seasonal variations of renal colics. The risk factors for urolithiasis also demonstrated no fluctuations. This is in contrast to reports from Spain, the USA, New Zealand, Saudi Arabia, Taiwan and India, but in accordance to reports from the Emirates and Australia. The reasons for the differences are not clear. Temperature fluctuations are no sufficient explanation. Further studies are required to find out the reasons.

COI: No.

O-21

Impact of kidney stones and conventional risk factors on the incidence of chronic kidney disease according to 2 sets of diagnostic criteria in Japanese men

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Introduction and objective: In the present follow-up study, we assessed the impact of kidney stones and conventional risk factors on

the incidence of chronic kidney disease (CKD) according to 2 sets of diagnostic criteria.

Methods: The subjects were 13,205 Japanese men aged 30–69 years who voluntarily underwent medical examinations between April 1995 and March 2001 and did not show CKD at the baseline. CKD onset was defined as an estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73 m² (CKD-1) and eGFR of <60 mL/min/1.73 m² with proteinuria (CKD-2). The hazard ratio (HR) and 95 % confidence interval (CI) for CKD-1/2 onset were calculated according to the history of kidney stones and conventional risk factors, including overweight or obesity, hypertension, diabetes mellitus (DM), gout or hyperuricemia, and dyslipidemia, by using Cox proportional hazards regression models.

Results: Of the total number of the participants, 1333 men (10.1 %) had a history of kidney stones. During the mean follow-up period of 3.7 years, CKD-1 developed in 2583 (19.6 %) men and CKD-2 developed in 122 (0.9 %) men. In a crude model, kidney stones were associated with an increased risk for CKD-1 onset (HR, 1.14; 95 % CI 1.01–1.29); however, kidney stones were not associated with an increased risk for CKD-2 onset (HR 1.60; 95 % CI 0.98–2.61). Although DM was not associated with an increased risk for CKD-1 onset (HR 0.89; 95 % CI 0.74–1.06), DM was associated with an increased risk for CKD-2 onset (HR 2.56; 95 % CI 1.49–4.39). These findings might be attributed to the higher baseline eGFR values in men with DM than in men without DM. After adjustment for multiple variables, including lifestyle, hypertension posed the highest risk for CKD-1 (HR 1.19; 95 % CI 1.08–1.31) and CKD-2 onset (HR 2.47; 95 % CI 1.68–3.63) in the present study.

Conclusions: Hypertension posed the highest risk for CKD. In a rather short-duration follow-up study, hyperfiltration in patients with early-stage DM could attenuate the results.

COI: No.

O-22

Comparison of food intake assessed by food diary and PRODI.6 analysis with 24 h urine excretion in Swiss kidney stone formers

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Kidney stones are highly prevalent in Western countries and are closely related to type and quantity of food intake. Food assessments for one given individual are difficult to obtain and rely mainly on analysis of food diaries or food frequency questionnaires. We evaluated food intake in the Swiss Kidney Stone Cohort and compared it with urine 24 h excretion.

We instructed 27 recurrent Swiss stone formers to fill out a 5 days food diary. During the last 2 days, patients collected 2 × 24 h urine. Food diaries were reviewed together with the patients by a specialized dietician and then analyzed using PRODI.6 software (NutriScience GmbH, Hausach, Germany), allowing micro-nutrient analysis. We compared protein, sodium, potassium, phosphate, calcium, magnesium and liquid intake recorded by this method with 24 h urine excretion of the same metabolites for the same day. Protein was evaluated by 24 h urine urea excretion. Food intake variability was

assessed by comparing 1 day food intake to the mean of the 5-day food intake.

We found that food intake assessed by food diary and PRODI6 correlated with 24 h urine excretion with R² coefficient of 0.41 for the liquids, 0.21 for the protein, 0.24 for potassium, 0.13 for sodium, 0.11 for phosphate, 0.17 for calcium and 0.38 for magnesium. Correlations between 1 day and the mean of the 5-day food diary were: R² 0.76 for the liquid, 0.35 for protein, 0.62 for potassium, 0.33 for sodium, 0.50 for phosphate, 0.49 for calcium and 0.48 for magnesium.

Overall, even if some correlation between intake and output was found for liquid and potassium, food assessment by food diary followed by analysis by PRODI6 performed poorly. Discrepancies might be explained by incomplete indication of food content, only partial reporting of ingredients used and by imprecise quantity assessment. New methodologies should be explored.

COI: No.

O-23

Swiss Kidney Stone Cohort: a prospective cohort of Swiss stone formers

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Kidney stones are one of the most frequent diseases of the urinary tract, cause excruciating pain to the patient and represent a significant burden to the health system. In addition, kidney stones are associated with cardiovascular mortality, renal insufficiency and osteoporosis, conditions that are highly prevalent in the population. The mechanisms leading to stone formation are still poorly understood and new treatment possibilities are needed. The Swiss National Science Foundation launched the Swiss Kidney Stone Cohort in 2014 in order to foster research in this field. We now report on the first patients included in the Swiss Kidney Stone Cohort (SKSC).

Adult patients were recruited in the five University Clinics of Nephrology of Switzerland (Basel, Bern, Geneva, Lausanne and Zurich) if they were recurrent stone formers or had a single episode, but with pre-determined risk factors. Investigations were standardized between the five centers, including 2 × 24 h urine collection, food and activity questionnaires, food diary and cristalluria measurements. Samples of urine, blood and DNA were stored in a biobank. All lab analysis were centralized. Follow-up visits are organized at 3 months and then annually.

Between May 2014 and August 2015, 156 patients were recruited, 48 females and 108 males. Mean age was 46.6 ± 15.1 years. Mean BMI was 26.4 ± 4.7 kg/m². The type of stones was available in 37 % of the cases: 31 mainly whewellite, 11 weddelite, 9 apatite, 2 struvite, 4 uric acid, 1 cystine, 1 other. Mean 24 h urine volume was 1732 ± 812 ml/24 h. Hypercalciuria, defined as urinary calcium >7.5 mmol/24 h in men and >6.5 mmol/24 h in women was present in 30 % of cases. Mean oxaluria was 172 ± 90 μmol/24 h and hyperoxaluria (>400 μmol/24 h) was encountered in 1.5 % of cases. Thirty-five percent had sodium excretion >200 mmol/24 h.

This first description of the Swiss stone formers population will allow further research and open new avenues for intervention.

COI: No.

O-24**Protective role of bergenin in ameliorating mitochondrial dysfunction associated with CaOx induced hyperoxaluria**

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Background: The generation of ROS due to mitochondrial dysfunction is an important deleterious event that occurs during hyperoxaluria induced urolithiasis. A number of reports suggested that Antioxidants exert protective effect against hyperoxaluria induced mitochondrial dysfunction. Bergenin has been found to be a potent antilithiatic metabolite isolated from the rhizome of *Bergenia ligulata*.

Aim: The purpose of the present study was to evaluate the potential of bergenin against hyperoxaluria-induced renal mitochondrial dysfunction in rats.

Methods: Hyperoxaluria was induced in male SD rats by administering 0.75 % ethylene glycol in drinking water for 28 days. Hyperoxaluria accentuated renal oxidative stress in terms of increased ROS production and lipid peroxidation. Mitochondrial dysfunction during stone crystallization was evident by decreased activities of electron transport chain complex I, II and IV, augmented mitochondrial oxidative stress in hyperoxaluric rats. Furthermore, raised mRNA expression of p38 mitogen-activated protein kinases and monocyte chemoattractant protein-1 was observed in the renal tissue of hyperoxaluric rats compared to control.

Results: Bergenin (10 mg/kg/day) administration significantly reduced crystal deposition and improved renal functions in hyperoxaluric rats. Treatment of BRG significantly ($p < 0.05$) restored the enzymatic activities of complex I, II and IV. It was able to protect mitochondria by lowering enhanced LPO and up regulating antioxidant levels considerably ameliorating mitochondrial dysfunction. Down regulation of monocyte chemoattractant protein-1 expression indicated anti-inflammatory potential of bergenin.

Conclusion: The findings of the present study provide evidence that bergenin exert protective effects in hyperoxaluria through mitochondrial protection that involve attenuation of oxidative stress. Hence, it presented itself as a safe and effective remedy in combating urolithiasis.

COI: Yes.

COI Relation: The study has been supported by the research grant from Indian Council of Medical Education and Research, India.

O-25**Medical management of calcium phosphate stone formers-impact of potassium citrate vs citric acid**

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Introduction: Potassium citrate (Kcit) is proven to prevent the recurrence of various types of calcium stones by increasing urine citrate (uCit) and lowering urine calcium (uCa). However, in CaP stone formers (SF), these beneficial effects may be negated by a rise in urine pH (upH) which may worsen CaP crystallization. An alternative medical treatment for CaP stones may be citric acid (CitA), which has the potential to increase uCit without changing upH. The objective of this study was to compare the biochemical effect of KCit and CitA in CaP stone formers.

Methods: Of the 20 non-hypercalciuric CaP SF expected, 13 have so far completed this double-blind, placebo-controlled 3-phase crossover metabolic study. CaP stone disease was defined by stone composition (CaP > 70 % of overall stone components). Exclusion criteria were: hypercalciuria (24-h uCa > 300 mg/day), recurrent urinary tract infections, neurogenic bladder, hyperparathyroidism, eGFR <60 ml/min, or chronic use of diuretics, alkali treatment, or carbonic anhydrase inhibitors. Each subject underwent 3 phases of study, each one week in duration during which they took assigned study medications (Placebo (PBO), CitA (60 mEq/day) or KCit (40 mEq/day)) and consumed a constant metabolic diet. 24-h urine was collected on the final 2 days of each phase for measurement of urine chemistry and calculation of brushite saturation by RSR (calculated by EQUIL2) and Supersaturation Index (SI, calculated by JESS).

Results: 2 men and 11 women have so far been included, with a mean age of 41 years and BMI of 26.7 kg/m². Compared to CitA and PBO, KCit use led to a significant increase in urine pH, potassium and citrate ($p < 0.01$), with a trend for lower urine calcium ($p = 0.062$). Brushite saturation was reduced by KCit when calculated by SI but not by RSR. Urine parameters were not significantly different between the CitA and PBO phases.

Conclusions: These data suggest that CitA has no significant impact on citruria or brushite saturation in CaP SF, while KCit provides a significant alkali load with increases in urine pH and citrate, and reduction in urine calcium. The study is ongoing with additional subjects being recruited.

COI: No.

O-26**Renal stone clinic: how well do patients perceive physician's explanations and recommendations ?**

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Background: Nothing is known about how well results of metabolic work-up and recommended prophylactic measures are perceived by stone formers (SF).

Methods: 2 groups were compared: *Group 1:* 153 consecutive recurrent calcium SF (RCSF, 118 male) referred 1/2011-6/2014. Between 2 and 3 months after a consultation about metabolic evaluation/treatment, RCSF received a questionnaire (6 multiple choice questions) by mail, regarding understanding of stone formation and adherence to therapy (more fluids, Ca, vegetables, salad and fruits; less oxalate, meat and stress; drugs). Response rate was 62 %. *Group 2:* 55 consecutive RCSF (7/2014-6/2015, 38 men) had to answer the same questionnaire while waiting for their 1st consultation after evaluation (forced response rate 100 %). Alkali citrate was prescribed in 47 % in group 1 and 44 % in group 2. Answer sheets were delivered anonymously, and groups were compared by Chi square test.

Results: 67 % in each group indicated >80 % understanding of the given information. Over 80 % adherence to recommendations occurred in 26 % (group 1) and 33 % (group 2, NS). Only 27 % in group 1 and 31 % in group 2 (NS) followed recommendations to 100 % on 6-7 weekdays (perfect adherence). The most frequent change in dietary/lifestyle habits was higher Ca intake (93 vs. 89 %), followed by higher fluid (81 vs. 80 %) and less meat protein (66 vs. 67 %). More vegetables/salad occurred in 72 % in group 1 and 56 % in group 2 ($p < 0.01$). Changes in Ox and fruit intake as well as stress were not different among groups. Perfect adherence (6-7 days/week)

was clearly more frequent for intake of medication than for changing diet/lifestyle in group 1 (84 vs. 27 %, $p < 0.001$) and group 2 (88 vs. 31 %, $p < 0.001$).

Conclusions: (1) Results do not differ whether RCSF are voluntarily participating or forced to answer questionnaires; (2) After a 60-min consultation, pathophysiologic explanations of stone disease are understood to >80 % by 2/3 of RCSF; (3) Perfect adherence to recommended treatment is significantly more frequent with medication than with dietary/lifestyle measures; and (4) Increasing calcium and fluid intake are the most popular dietary measures.

COI: No.

O-27

The change of renal function after treatment with shock wave lithotripsy for urolithiasis; long-term follow-up

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Introduction and objective: Shock wave lithotripsy (SWL) was believed as a minimally invasive treatment for symptomatic renal and proximal ureteral calculi. In fact, indications for SWL have expanded, such that 80–90 % of calculi can be treated successfully with SWL. There was not reported that SWL caused renal dysfunction. A long-term follow-up study reported that patients treated by SWL had an increased incidence of diabetes mellitus and were more likely to develop new-onset hypertension. Animal studies have clearly established that shock waves causes damage to kidney vasculature. However it is still unclear whether SWL injury cause chronic kidney disease (CKD) of at least stage 3 (as defined by an estimated glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m²), which has been shown to be an independent risk factor for cardiovascular disease. Therefore, we investigated the estimated GFR of patients treated by SWL after long-term follow-up.

Methods: Patients with renal calculi (R group) or ureteral calculi (U group) were treated by SWL with MPL-9000 (1994–2002) or Lithotriptor D (2003–2005) (Dornier Medical Systems, Marietta, Georgia) at Osaka City University between 1994 and 2005. They were followed up by consistent laboratory examination even after stone free for more than 5 years. Estimated GFR was calculated by the following formula which was specified for Japanese by Japanese Society of Nephrology in 2008.

Results: 202 patients (R group: 103 patients, U group: 99 patients) were followed for 11.5 ± 4.5 (5–21) years. Although estimated GFR of both group had no difference at SWL, estimated GFR of R group was significantly lower than that of U group after long-term follow-up (59.3 ± 21.1 vs 68.6 ± 21.0, $p < 0.01$). The ratio of CKD stage 3 ≤ is 48 % (R) and 46 % (U), which is approximately 2.5-fold higher than that of standard adult Japanese (19 %).

Conclusions: Our findings suggest that urolithiasis may be a risk factor for CKD and CKD may be a potential long-term adverse effects in SWL for renal calculi.

COI: No.

O-28

Role of alpha adrenergic blockers in uretric stones

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Introduction: Alpha adrenergic blockers have been used recently in treating ureteric stones. The drug is expected to increase peristalsis and dilate the ureter. Even though alpha adrenergic blockers are to be given for a period of 1 week to 10 days, many clinicians prescribe them for longer periods of time, with no benefit for the patient. This study was undertaken to assess the extent of misuse of the drug and the effect of these drugs in the reduction of symptoms and passage of stones.

Materials and methods: 250 patients presenting to the stone clinic with history of intake of alpha adrenergic drugs, alfuzocin and silodocin were studied. The duration of treatment, reduction of symptoms and movement of the stone down the ureter and passage of the stone were assessed retrospectively. Patients on alpha adrenergic blockers for less than 10 days were prospectively followed up till the end of 10 days for changes in clinical pattern, crystalluria level, RBC and PC in urine and movement of stone down the ureter. 57 patients were administered alpha adrenergic blockers alone to assess the effect of drug in reduction of symptoms, clearing urine deposits and in downward passage of stones.

Observations: 77 % of the patient had been taking the drugs before attending the stone clinic. Of these, 22 % had been taking the drug for more than 10 days. Urine deposit and ultrasonogram showed no significant change from the original and were advised to stop the drugs. Only 2 patients out of 250 passed stones. 12 % of patients who had ureteric stones showed movement of stones down the ureter for more than 2 cm during the 10 days course of drug. The size of the stones, which moved down was less than 6 mm in diameter. No movement was observed in 72 % of patients with ureteric stones with 10 days course of alpha adrenergic drugs.

Conclusion: It is concluded that alpha adrenergic drug is not beneficial either in reduction of symptoms of the patients or in reduction of blood cells and crystalluria pattern or movement of stone down the ureter.

COI: No.

O-29

Ureteral stones at Funabashi Clinic: a study of 777 cases based on stone composition

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Objective: To determine the variation in ureteral stone composition in patients undergoing ESWL treatment and its association with sex, age and lifestyle related diseases such as hypertension (HTN), dyslipidemia (DLD), diabetes mellitus (DM) and hyperuricemia (HU).

Methods: We retrospectively reviewed data of patients with ureteral stone treated by ESWL over a 2 year period (2013–2014). Data on patient age, gender, stone composition (stone types, dominant component, and average percentage of each component) and medical treatment for HTN, DLD, DM and HU were collected. To figure out which factors were associated with differences in stone composition, bivariate statistical analysis was carried out.

Result: Among 777 cases, average patient age was 52.42 ± 13.0 years and male- to -female ratio was 2.9:1. Calcium oxalate monohydrate (COM) + calcium oxalate dihydrate (COD) mixed stones were the predominant stone type accounting for 46.7 %

of all stones followed by COM + COD + calcium phosphate (CAP) mixed stones (34.8 %) and COM + CAP mixed stones (5.8 %). The major stone components were COM, COD, and CAP in 53.9, 32.6, and 8.0 % of patients, respectively. Female has higher prevalence of COM + CAP mixed stone type and CAP only stone type than male. Males were more likely to form COM + COD mixed stone type. Effects of aging was seen on COM dominant stones (higher proportion) and COD dominant stones (lower proportion). HTN, DLD, DM, and HU associated with COM + COD mixed stone type (higher proportion) and COM + COD + CAP mixed stone type (lower proportion).

Conclusion: Patient gender, age and certain lifestyle related diseases (HTN, DLD, DM, and HU) were related with ureteral stone composition especially in the COM, COD and CAP content stones. To evaluate which factors are independent and more impact on the stone composition, we should use multivariable analysis as the next step.

COI: No.

O-30

Computational simulation of endoscopic stone surgery: extra- and intra-three-dimensional fly through imaging in upper urinary tract

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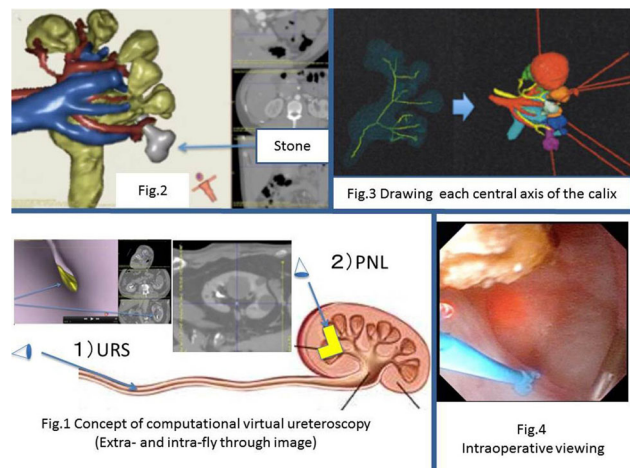
Background: We preliminarily established a new virtual imaging of ureterorenoscopy and laparoscopy using NewVES system which was produced by Nagoya University Information Science Technology Group. An image processing algorithm in computational virtual ureteroscopy combined with nephrostomy was presented (Fig. 1).

Method: Preoperatively, three phases of enhanced abdominal CT images were captured and converted to DICOM data which were divided by every 0.5–1 mm slice. Three-dimensional (3D) images of renal artery, vein and ureter and renal pelvis was obtained and were given the different color each (Fig. 2). Excretory phase of image in upper urinary tract was also captured and fuse together with the arterial and venous phase (Fig. 3). Optimal virtual picture line was draw through each renal calix along the center axis of funnel shaped renal calix. Then virtual puncture line was slightly arranged to avoid the vessel piercing and was projected onto the virtual pneumatic-abdominal wall (Extra fly through image). Three dimensional perspective ureteral images were constructed and a virtual scope eye was moved up- and downward while observing the cranial side. Virtual nephrostomy was made through an intersection point puncture and needle penetration was observed at the pelvic location of the scope eye (Intra fly through image).

Results: Two hours were required to complete the image preparation. Lithotripsy and kidney puncture for 58-year-old male with 2 cm calculi was successfully treated under the preoperative simulation guidance (Fig. 4).

Conclusion: Computational virtual ureteroscopy combined with nephrostomy made by 3D extra- and intra fly through image might predict optimal puncture point, help the preoperative simulation and lead to safer stone surgery.

COI: No.



O-31

Investigation of the ideal position for percutaneous nephrolithotomy: prone position vs. modified Valdivia position

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Background: The prone position (P position) has long been the standard position for percutaneous nephrolithotomy (PCNL). However, recently, the modified Valdivia position (Mod-V position) has been applied, considering the risks of anaesthesia in the P position. Accordingly, to investigate the ideal position for PCNL, this study examined (1) the characteristics of treatment results and (2) the changes in renal anatomy by using computed tomography (CT) for the different positions.

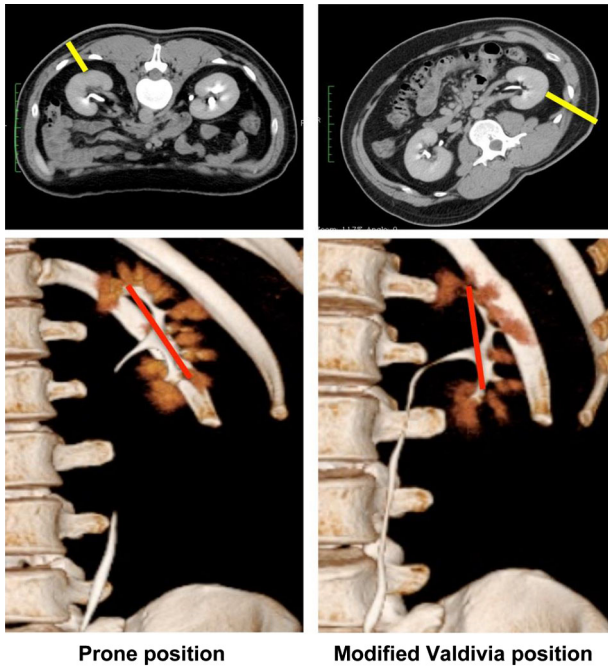
Subjects and methods: (1) The subjects were 89 patients who underwent PCNL between January 2014 and May 2015 at facilities registered for this multicentre study (P position:Mod-V position = 49:40). (2) Contrast-enhanced CT images in the P and Mod-V positions were analysed for each patient. The distance from the skin to the kidney and the tilt of the major renal axes (anterior, lateral) were measured.

Results: (1) The renal punctures in the P position were predominantly executed through the inferior calyces (79.5 %), whereas those in the Mod-V position were primarily performed through the middle calyces (72.5 %). The stone clearance rate 1 day after the surgery did not significantly differ between the positions. Five (10 %) patients in the P-position group and 2 (5 %) patients in the Mod-V-position group showed a fever of >38 °C two or more days after the surgery. (2) The CT images showed that the distance to the kidney was significantly shorter and the tilt of the major renal axis was significantly greater in the anterior direction (21.7°:9.6°; $p < 0.01$) and significantly lesser in the lateral direction (21.5°:32.7°; $p = 0.03$) in the P position than the corresponding values in the Mod-V position (Figure).

Discussion: We consider that the Mod-V position is better suited than the P position is for puncture of the middle calyces but not the lower calyces. Additionally, because the perfusion fluid flows naturally from

the tract in the Mod-V position, the extent of increase in the renal pelvic pressure is lesser than in the P position. Because the surgical results are not altered, flexibility in alteration of the positions depending on the stone position, body type, and infection status will lead to an ideal treatment.

COI: No.



O-32

Dusting vs basketing during ureteroscopic lithotripsy: what is more efficacious? A multi-center prospective trial from the EDGE research consortium

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Introduction: There is controversy and very little evidence as to whether dusting stones is more efficacious than basket extraction of fragments during ureteroscopic lithotripsy. We prospectively followed patients to determine which method resulted in the higher stone free rate.

Methods: IRB approval was obtained across all sites and patients undergoing ureteroscopy for renal stones between 5 and 20 mm were eligible. The Endourology Disease Group for Excellence (EDGE) includes high volume stone centers who had a well established dusting (3 sites) or basketing (5 sites) approach to intrarenal calculi that participated in the study. Laser lithotripsy was utilized and patients were imaged within 3 months following ureteroscopy. The definition of stone-free was no fragments of any size on KUB and ultrasound imaging. All patients were stented postoperatively and given alpha-blocker for 30 days.

Results: 110 patients were enrolled and followed for 3 months (N = 68 Basketing, N = 52 Dusting). The stones were slightly larger in the dusting group and significantly more laser energy was used in the dusting group. There were fragments <2 mm present in 11.8 % in the basketing group compared to 27.3 % in the dusting groups. Only 2.8 % (basketing) and 8.6 % (dusting) of patients in each group became symptomatic from their residual fragments. There was no difference in readmission to ER or hospital between the groups (13.9 %-dusting vs 14.6 %-basketing) or in reintervention rates (9.7 %-basketing vs 4.3 % dusting). There were no differences between the groups in post-operative creatinine or stone analyses. There was a slightly higher risk of complications in the basketing (17 %) vs dusting (13.3 %) cohorts.

Conclusions: Our interim analysis shows that in patients undergoing ureteroscopy for renal stones between 5 and 20 mm that active extraction of all fragments with a basket produces a higher stone-free rate (86.4 %) than dusting the stone (54.3 %). There was no difference in readmission or re-intervention rates and few patients in either group became symptomatic from their residual fragments. Long-term follow-up of these patients will also determine the fate of these fragments.

COI: Yes.

COI Relation: Boston Scientific—Consultant Olympus Surgical—Consultant.

O-33

The urinary kidney stone promoters and inhibitors in various categories of calcium urolithiasis

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Introduction: The study of the differences between the categories of calcium urolithiasis will provide an idea of the severity of disorders on clinical stage of the disease. The results allow to improve prevention of stone recurrence.

Object: To study the condition of urine promoters and inhibitors in pts of So&Sres and Rmo&Rmres categories.

Materials and methods: The first group included 236 (59.60 %) pts of So category and 81 (20.45 %)-Sres. The second group included 53 (13.38 %) pts of Rmo category and 26 (6.57 %)-Rmres. Daily urine volume (UV), urine pH and 24-h excretion (DE) of Ca, Mg, Ox, Cit, Ur, Pi were assessed.

Results: The UV in pts Rmo and Rmres categories was lower than in pts So and Sres categories. The urine pH has not difference among the groups.

The differences in DE of Ca, Ox, Pi and Ur were not found between the groups. However, the concentration of Ca, Ox, Pi and Ur in urine were significantly higher in pts of Rmo&Rmres categories.

The DE of Mg in group Rmo&Rmres was significantly lower than in group So&Sres (3.73 ± 0.22 and 3.05 ± 0.18 mmol/24 h, respectively). The concentration of Mg in the urine in Rmo&Rmres group was also significantly lower than in So&Sres group.

The DE of Cit in pts of Rmo&Rmres group was significantly lower than in group So&Sres (1.09 ± 0.19 and 1.81 ± 0.21 mmol/24 h, respectively). The concentration of Cit in the urine in pts of Rmo&Rmres group was also significantly lower than in group So&Sres.

Discussion: There were found differences between the categories of primary stone formers (So and Sres) and recurrent stone formers (Rmo and Rmres). The UV in pts Rmo&Rmres categories significantly lower than in pts So&Sres categories. Therefore, the increased concentration of the promoters were observed. The urinary Inhibitors Mg and Cit in pts of Rmo&Rmres group were reduced more than in pts of So&Sres.

Conclusion: In the treatment of patients Rmo&Rmres categories, the first step after stimulation of diuresis, must be the correction of magnum and citrate levels in urine.

COI: No.

O-34

Hyaluronan is an accidental risk factor for recurrent calcium oxalate stone formers

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Background: Glycosaminoglycans (GAGs) protect cells from binding of calcium oxalate (CaOx) crystals to prevent CaOx stone formation. Hyaluronan (HA) is a non-sulfated GAG with crystallization-promoting activity during renal stone formation. The excretion of urinary GAGs and HA were measured in stone-formers (SF), post-treated SF, and normal controls to reveal their relationship with renal stone disease.

Methods: Three groups were included—active SF, post-treated SF (SF after extracorporeal shock wave lithotripsy) and normal controls with 40 subjects in each group were recruited. Early morning urine was collected for each subject. The hexuronate content of the GAGs were measured by carbazole reaction and values for GAGs were standardized against creatinine. Individual GAGs extracts were then digested sequentially with *Streptomyces* hyaluronidase and chondroitinase ABC to yield the HA disaccharides for analysis by high performance liquid chromatography.

Results: Hexuronate content of GAGs were in the order of post-treated SF < SF << normal controls. SF had an enhanced urinary excretion of HA with no increase of urinary HA in post-treated SF group. However, both of the SF and post-treated SF groups had increased proportion of HA (of total GAGs) compared to normal controls.

Conclusion: Active-SF and post-treated SF groups had lower total GAGs content but increased proportion of HA than that of the normal controls indicating that urinary GAGs and HA are probably protective/risk factors for the renal stone disease. The higher recurrence rate of renal stone disease may be due to the sub-species of GAGs that may become an accidental participant for renal stone formation.

COI: No.

O-35

Plasma oxalate can be interpreted in relation to GFR to detect the likelihood of primary hyperoxaluria, enteric hyperoxaluria and common urinary stone disease

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Since Plasma oxalate (POx) concentrations increase at lower glomerular filtration rate (GFR) levels, even among those without enteric (EH) or primary hyperoxaluria (PH), the appropriate thresholds for considering a disorder of oxalate metabolism are in general poorly defined. The current study was completed to establish the relationships between POx, GFR, and Urine oxalate excretion (UOx) in cohorts of patients with PH and EH, and routine urinary stone disease (USD).

The most recent POx measurement on all Mayo Clinic patients between 2005 and 2015 were electronically pulled from the Lab

Information System (407 patients), as well as the closest serum creatinine within 14 days and 24 h urine study within 60 days. Records were reviewed for clinical diagnoses to categorize patients as PH, EH, or USD. In all 3 groups POx increased as eGFR fell. For any given eGFR, POx was highest in the PH group, lowest in the USD group, and intermediate in the EH group ($p < 0.0001$). POx was also influenced by UOx excretion. GEE models of POx vs eGFR revealed higher average POx levels in PH compared to either EH or USD, and for EH compared to USD. GEE prediction models were created that use POx or UOx together with age and serum creatinine to estimate the probability of a PH diagnosis. For patients with an eGFR > 45 ml/min/1.73 m² both models using either POx or UOx were more sensitive for PH, while when eGFR was <45 ml/min/1.73 m² both models were more specific for PH. In conclusion, new models were developed for use in clinical practice to help identify PH and EH, even in the presence of reduced GFR. As these models are based on commonly available serum and urine values, they can be routinely used with laboratory results to aid in screening for PH, even when PH was not previously suspected. These models can also be used to estimate the daily oxalate production from the POx value.

COI: No.

O-36

Relevance of urine calcium and metabolism of urinary stone

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Introduction: The process of stone formation has been recognized to be metabolically related to the urine calcium level, which was considered to be a significant parameter in the formation of calcium oxalate stones. However in the recent past, the significance of calcium in blood and urine has been questioned. This study was undertaken to assess the value of urinary calcium in the stone patients in the last 5 years.

Materials and methods: 1469 patients who attended the stone clinic were analysed metabolically and based on the urine calcium level, classified into 2 groups namely those with urine calcium less than 300 mg/day (normocalciuric) and those with urine calcium more than 300 mg/day (hypercalciuric). 24 h. urine samples of all the patients were collected in thymol and assessed for 24 h. calcium, phosphorus, uric acid, magnesium, creatinine, oxalate, citrate, sodium and potassium. Blood was collected for estimation of serum calcium, phosphorus, uric acid, magnesium and creatinine. All the differences in means of biochemical values of normocalciuric group and the hypercalciuric group were compared using student 't' test using the SPSS software program.

Observation: It was observed that 22 % of patients had a urine calcium level of more than 300 mg/day. On comparing the biochemical parameters between the 2 groups—normocalciuric and hypercalciuric, it was found that the hypercalciuric group had significantly higher value of promoters namely urine phosphorus—784 mg/day ($p < 0.001$), urine uric acid—457 mg/day ($p < 0.001$), urinary oxalate 97.1 mg/day ($p < 0.0001$) urinary sodium 305 mg/day ($p < 0.001$) and serum calcium—13.4 mg % ($p < 0.05$). However, the value of the inhibitors of crystallisation namely urinary magnesium 8.4 mg/day ($p < 0.001$), urinary citrate—1033 mg/day ($p < 0.001$) and urinary potassium—62 mg/day ($p < 0.001$) were also higher in the hypercalciuric group. The urinary creatinine—5.4 mg/day ($p < 0.001$) was significantly higher in the hypercalciuric group.

Conclusions: The urine calcium level plays a significant role in the process of formation of calcium oxalate stones. Therefore hypercalciuria should indicate a higher probability of stone formation. Urine calcium should be considered in the prophylaxis of urinary stone disease.

COI: No.

O-37

Renal histopathological features of dent disease, a rare but important cause of calcium stones to recognize

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Background: Dent disease is a rare X-linked disorder characterized by increased low molecular weight proteins (LMWP) and hypercalciuria. Patients often develop nephrocalcinosis, kidney stones, or chronic kidney disease (CKD), but the phenotype of Dent disease is variable which can make diagnosis difficult. Better understanding of the pathological features that suggest Dent disease could be crucial for making an early and correct diagnosis.

Methods: Clinical renal pathology reports and slides (where available) were collected from 30 male patients in eight countries who had previously undergone clinically indicated renal biopsy. Renal histopathological features were characterized and their association with kidney function was assessed.

Results: Median (25th, 75th) age at biopsy was 7.5 (5, 19) years with an estimated glomerular filtration rate (eGFR) of 69 (44, 94) ml/min/1.73 m² and a 24 h urine protein of 2000 (1325, 2936) mg. All patients had increased excretion of LMWP when it was assessed (24/24), and 80 % (20/25) had hypercalciuria. 28 % (8/28) had a history of kidney stones and 14 % (3/21) had rickets. 13 % (4/30) of patients had a repeat biopsy for steroid-resistant proteinuria. Prominent histological findings included focal global glomerulosclerosis in 83 % of patients (25/30) affecting mean \pm SD glomeruli as of 16 % \pm 19 %, mild segmental foot process effacement in 57 % (13/23), focal interstitial fibrosis in 60 % (18/30), interstitial lymphocytic infiltration in 53 % (16/30) and tubular injury in 70 % (21/30). Nephrocalcinosis was reported in 20 % (6/30). Focal segmental glomerulosclerosis (FSGS) was documented in only 7 % (2/30). Lower eGFR at biopsy was associated with a higher percentage of globally sclerotic glomeruli (Figure 1), as well as foot process effacement, and interstitial inflammation (all $P < 0.05$).

Conclusion: Global glomerulosclerosis is commonly seen in Dent disease, well beyond that expected for age, and is associated with reduced kidney function. The association of foot process effacement and kidney function suggests a role for podocyte pathology in disease progression. Given the marked increase in globally sclerotic glomeruli with age, Dent disease must be recognized early in all males that present with unexplained proteinuria and stones so that treatments can be initiated as soon as possible.

COI: No.

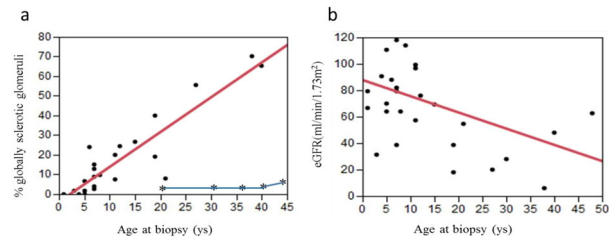


Figure 1. Association of age at biopsy with percentage of globally sclerotic glomeruli and kidney function. (a) A higher percentage of globally sclerotic glomeruli was associated with older age at biopsy (red line, $p < 0.001$). Percentage of globally sclerotic glomeruli appeared higher than the age-matched estimated percentage (blue line), which was generated using the upper limit for percentage of globally sclerotic glomeruli based upon age among living kidney donors. (b) Lower eGFR was associated with older age at biopsy ($p = 0.006$).

O-38

Challenges faced in detecting silent renal stones: lessons learnt from the melamine incident of paediatric stones

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News regarding drinking milk/milk powder products contaminated with melamine has gained considerable coverage. The most affected victims have been infants and children and the most affected organ has been the kidney. There are challenges that lay ahead in detecting renal stones. More pressing, is paediatric assessment of renal stones which is even made more difficult. Paediatric Stone Disease differs considerably in many aspects from that in adults, with a prevalence of 0.5 cases per 1000 (compared to 70 per 1000 in adults). Presentation is mainly haematuria and renal colic, though in young infants and children, the manifestation of pain may be different. Besides infective stones, metabolic cause is the main reason for children getting stones such as hypercalciuria, cystinuria and hyperoxaluria. Diet and nutrition, while important is given less importance and not studied well. Medical Management of children with urolithiasis requires a multi-disciplinary approach. Children do not present typical symptoms as adults, biochemical and imaging assessment needs to be tailored to each individual circumstances and metabolic evaluation is undertaken before the treatment (normally by blasting using lithotripter) and after. Epidemiology studies in the pathogenesis of urolithiasis, nutritional factors play a special role. There are many examples such as incidence of stone disease rising in Japan (4 to 6 %) and in Italy (5 to 7 %). There are many reasons for these, both intrinsic (genetic make-up, sex etc.) and extrinsic (climate, water, diet, occupation, etc.). Whilst it was maintained that renal stones were mainly “adult” disease and most test modalities are designed around adult testing. Paediatric stones were rare and more often related to “infection” type of stones or those with genetic inherited diseases. Two cases of melamine-infected children will be discussed.

COI: No.

O-39

Management of renal stones in older children with SWL: does general anesthesia have any impact on treatment outcomes?

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Aim: To evaluate the possible effects of general anesthesia on the treatment outcomes in children (older than 9 years) after SWL.

Patients and methods: A total of 57 children (aging between 9 and 16 years) treated with SWL for renal stones were included. Depending on the use of general anesthesia children were divided into two groups; (Group-1, n = 25) SWL under general anesthesia and (Group-2, n = 32) SWL without general anesthesia. Patients in both groups were comparatively evaluated with respect to treatment related (mean number of sessions, shock waves applied, success and complication rates) parameters.

Results: Mean overall stone size was 10.37 ± 4.26 mm (5–20). There was no significant difference regarding the stone size ($p = 0.69$), mean number of SWL sessions ($p = 0.29$), complication rates ($p = 0.31$) and the presence as well as size of residual fragments ($p = 0.68$). However, mean number of shock waves applied was significantly higher in patients receiving no anesthesia (Group-2) ($p = 0.002$).

Conclusions: Our findings indicate that SWL for renal stones in children aging older than 9 years is feasible and successful with similar treatment outcome data observed in the same age ranged cases being treated under general anesthesia. We believe that in relatively older and cooperative children “SWL without general anesthesia” can be applied in a safe and successful manner.

COI: No.

O-40

Ureteroscopic management for ureteral stone in pregnancy using ultrasound without fluoroscopic monitoring

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Clinical management of a pregnant urolithiasis patient is complex. Ultrasound (US) is widely used as the diagnostic imaging tool because of its availability and lack of radiation. With the advancements in technology and endourological techniques, ureteroscopy (URS) has become safer with ever improving results as the first line management in ureteral stones in pregnancy. We report on the performance of URS using US without fluoroscopy in a pregnant woman. 31-year-old woman was admitted at 14 weeks of gestation presenting acute abdominal pain. US showed right hydronephrosis and also showed upper urinary tract dilatation with the presence of stone (15 mm) at the level of the upper right ureter. The patient preferred URS to temporizing therapies (ureteral stenting or percutaneous nephrostomy). We performed URS procedure using a small-caliber flexible ureteroscope and a holmium: YAG laser. Real-time US showed dilated ureter and ureteral stone without fetal radiation exposure. Under spinal anesthesia, a guidewire was inserted into right ureter using US, and then the ureteroscope was inserted into the ureter under the guidewire and direct endoscopic guidance without fluoroscopic monitoring. Once the stone was visualized, laser fragmentation could be performed easily. Intraoperative fluoroscopy was not used during URS procedure at all. A 6 Fr ureteral stent was inserted at the end of the procedure, and the stent was removed after 3 days. There were no obstetric or urological complications. Post-URS US showed

improvement of hydronephrosis and no residual ureteral stone. She was normally delivered of a baby at 38 weeks of gestation.

Ureteroscopic approach is both diagnostic and therapeutic in pregnant patients with very low morbidity and the need for only short-term ureteral stenting. URS is a reasonable alternative to avoid long-term stenting/drainage. We recommend that intraoperative imaging should be performed US in pregnant patients to avoid the risk of radiation. We consider that URS in pregnancy could be performed by experienced endourological surgeons using US without fluoroscopic monitoring.

COI: No.

MODERATED POSTER

MP-01

Do stone disease and related parameters have any effect on the physical as well as renal growth of children: results of a long-term follow-up evaluation

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Aim: To evaluate the possible effects of stone disease and disease related parameters on the physical as well as renal growth of the children on a long-term follow-up basis.

Patient and methods: A total of 50 children suffering from stone disease were included into the study program. In addition to a detailed history and physical examination; demographic and stone characteristics of all cases were also evaluated. Moreover, the history of stone disease (first onset, number stone attacks, number of urinary tract infections etc.) and feeding (duration of breastfeeding, additional formulas, additional food etc.), stone related procedures were evaluated and recorded in all cases. In addition to all these parameters, the physical percentiles and renal growth status of each child with stone disease were carefully assessed. The possible relationship with stone disease itself and above mentioned disease related parameters were comparatively evaluated to outline the possible effects of these parameters on the physical growth percentiles and renal growth of these cases.

Results: A total of 50 children with stones were evaluated and mean age for first onset of disease was 2.40 ± 2.65 (0–11.5) years, mean follow-up time was 24.96 ± 15.08 months. Of these cases while the growth percentiles were among normal limits in 35 cases (70 %); physical as well as to some extent renal growth retardation (less than 25 %) for body percentiles) were present in 15 (30 %) cases. Evaluation of the possible effects of stone disease and feeding related parameters on these percentiles did show that the onset of the disease, number of stone as well as infection attacks and the need for stone removal procedures were the main parameters that may be responsible for retardation of physical and renal growth.

Conclusions: Aims of stone management in children should be complete stone clearance, prevention of stone recurrence and regrowth, control of UTI's and most importantly the underlying correction of metabolic disorders. Through these efforts future stone formation and/or growth may be controlled in pediatric population, limiting the morbidity of this disease that may affect the physical as well as renal growth of these cases.

COI: No.

MP-02**Suppression of cellular damage during acute stage of CaOx crystal formation by renal tubular cell autophagy**

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Introduction and objectives: We previously reported renal tubular crystal formation in mice by administration of glyoxylate (GOX). The results of the investigation in these stone model mice indicated that tubular cellular damage induced by oxidative stress facilitated crystal formation. Although recent evidence shows that the damaged cells could induce self-repairing, the so-called autophagy, the association between autophagy and crystal formation remains unclear. Hence, we analyzed the role played by autophagy in renal crystal formation in these stone model mice.

Materials and methods: We induced the formation of renal calcium oxalate (CaOx) crystal deposits in C57BL/6J mice by daily intra-abdominal injection of GOX. Mice kidneys were extracted during the acute phase (3, 6, 12, and 24 h) and during the subacute phase (2, 4, 6, and 8 days). Blood and 24-h urine were collected, and renal dysfunction, oxidative stress, and expression of proinflammatory markers associated with renal cellular damage were evaluated to determine the formation of renal crystal deposits; expression of light-chain 3-B (LC3-B) proteins, which are recognized as autophagy markers; and the ultrastructure of autophagosome and autolysosome.

Results: Polarized light optical microscopy showed renal crystal deposits that appeared 6 h after GOX administration. The number of crystals peaked at day 6. Western blot analysis showed no differences in LC3-B expression among these time points. Transmission electron microscopy showed remarkable accumulation of autolysosomes in slightly damaged proximal renal tubular cells at 12 h after GOX administration. After 24 h of GOX administration, a decrease in the number of renal tubular cells and loss of their foot processes were observed; in addition, excessive accumulation of abnormal lysosomes was observed in renal tubular cells.

Conclusion: Our results indicate activation of autophagy in renal tubular cells during the acute phase of renal crystal formation. The balance between autophagy and cellular damage is important for renal crystal formation.

COI: No.

MP-03**Molecular analysis of the glyoxylate/hydroxypyruvate reductase (GRHPR) gene in Japanese patients with primary hyperoxaluria type 2**

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Objective: Primary hyperoxaluria type 2 (PH2), an inherited autosomal recessive disorder of endogenous oxalate overproduction, is caused by mutations in the *GRHPR* gene encoding the glyoxylate/hydroxypyruvate reductase (*GRHPR*) enzyme. We reviewed the *GRHPR* gene in Japanese patients with PH2.

Methods: We genotyped the *GRHPR* gene in six Japanese patients with PH2 and reviewed clinical features.

Results: We identified a novel mutation, a single nucleotide substitution (c.181G > A) in exon 2 creating a missense mutation (p.Asp61Asn) at codon 61. The c.864_865delITG mutation was the most common with the allelic frequency of 58.3 % (7/12). Also, we found that the c.864_865delITG mutation was associated with the rs35891798 single-nucleotide polymorphism. Only one patient received hemodialysis and the other patients had normal renal function with recurrent urinary stone.

Conclusions: Japanese with PH2 should be screened for the c.864_865delITG mutation.

COI: No.

MP-04***Nnt* gene suppresses kidney stone formation and oxidative stress**

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Introduction: By paying attention to the subtle genetic differences between mice substrains (C57BL/6J(B6J) and C57BL/6N(B6N)) as a new kidney stone candidate gene, we identified nicotinamide nucleotide transhydrogenase (*Nnt*) to elucidate the possibility of inhibiting kidney stone formation. Here we focused on this cellular disorder.

Materials and methods: Eight-week-old male B6J and B6N mice ($n = 15$ in each group) were used in this study. Renal calcium oxalate monohydrate crystal deposition was induced with daily intra-abdominal injection of 80 mg kg⁻¹ glyoxylate for 12 days. Every 6 days, animals were sacrificed and renal specimens were collected. Kidney cross-sections were observed with polarized-light optical microphotography, while crystal regions with strong birefringence were measured and expressed as percentages of the total tissue area of the renal cross-section using NIH Image software. Total RNA was isolated from glyoxylate-treated kidneys and reverse-transcribed into double-stranded cDNA. In another study, renal specimens were fixed with methacarn and reactive oxygen species (ROS) activity was investigated using a Carbonyl Protein Immunostaining kit[®]. In addition, the change in oxidative stress in the kidney using superoxide dismutase-1 (SOD-1) and malondialdehyde (MDA) as markers was compared using immunostaining.

Results: Numerous kidney stones in the renal tubules were detected in both B6J and B6N mice. The number of stones was greatest after 12 days of treatment, and the stone count was 16.2-fold higher in B6J mice than in B6N mice. ROS activity in the kidney revealed strong activity throughout the kidney tissue and a slightly higher tendency in B6J. SOD-1 and MDA expression in the kidney was observed in the renal tubular epithelial cells and did not differ significantly between the B6J and B6N mice.

Conclusion: The decreased expression of *Nnt* observed in B6 J mice is also present in humans. *Nnt* reduces intracellular ROS in the mitochondria. ROS is increased by decreased *Nnt* expression, while kidney stone formation is predicted to be promoted. Although this study's findings showed the same tendency, it was not possible to recognize a clear difference between the sub-systems. To confirm the

effects of *Nnt* on kidney stone formation, attention focusing on the mitochondria was considered necessary.

COI: No.

MP-05

Genome wide gene expression profiling of Randall plaques in calcium oxalate stone formers

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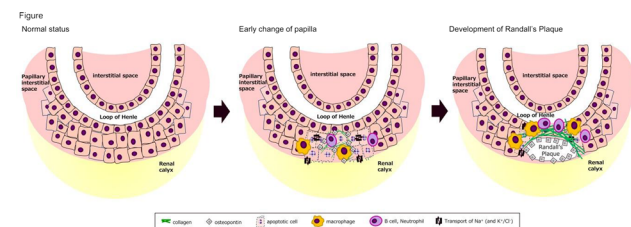
Introduction and objectives: Randall plaque (RP) is the origin of renal calcification on which idiopathic calcium oxalate (CaOx) kidney stones develop; however, its exact role in CaOx crystal formation remains unknown. We previously reported the potential therapeutic roles of osteopontin and macrophage (M ϕ) for CaOx kidney stone formation using transgenic mouse and genome wide analysis. To establish the genomic pathogenesis of RP, we performed a microarray as well as immunohistochemical analysis for comparing the gene expressions among renal papillary RP and normal tissue of 23 CaOx, six calcium phosphate (CaP) stone formers, and normal papillary tissue of seven control patients.

Materials and methods: We obtained the papillary tissue samples by cold cup biopsy during retrograde intrarenal surgery or ureteroscopy. Comparisons were made between: (1) RP of CaOx and CaP stone formers; (2) RP and normal tissue of CaOx stone formers and normal tissue of control patients; and (3) between RP and normal tissue of CaOx stone formers. The analyses were performed using GeneSpring13.1[®] and IPA[®] software. We then validated the results using reverse transcription-PCR and immunohistochemistry.

Results: Genes that expressed more than two-fold higher levels in CaP than in CaOx stone formers included fibrinogen, collagens, P38 mitogen activated protein kinase (MAPK), nuclear factor κ B, and chemokines but decreased expressions of immune-related molecules, such as immunoglobulin, interferon α , and T cell receptor. Papillary tissue both from RP and normal lesions of CaOx stone forming patients expressed activated cellular hyperpolarization, reproductive development, and molecular transport. Compared to normal papillary tissue, RP tissue contained upregulated lipocalin 2, interleukin 11, prostaglandin endoperoxide synthase 1, glutathione peroxidase 3, and monocyte to M ϕ differentiation but downregulation of solute carrier family 12 member 1 and sodium leak channel non selective (either >2.0 or 0.5 fold, $p < 0.01$). Network and toxicity analyses showed that these genes were associated with activated MAPK, the Akt/phosphatidylinositol 3 kinase pathway, and proinflammatory cytokines, which caused renal injury and oxidative stress.

Conclusion: Our results are the first to establish that genes related to renal dysfunction, proinflammation, oxidative stress, and ion transport induce the development of RP in CaOx stone formers (Fig).

COI: No.



MP-06

Effects of atherosclerosis-related factors on renal crystal formation in a mouse model of metabolic syndrome

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Introduction and objective: Kidney stones are considered part of metabolic syndrome (MetS). The mechanism of renal crystal formation is similar to that of the MetS-associated disease atherosclerosis. We previously showed a strong association between the aortic calcification index and kidney stones detected using computed tomography. We also reported increased renal crystal formation in a mouse model of MetS (ob/ob, B6.V-Lep^{ob}) relative to lean mice (wild type, WT). In this study, we focused on cell adhesion as an atherosclerosis-related factor and performed genome-wide expression analysis to investigate the role of cell adhesion in renal crystal formation.

Methods: WT (+/+) and ob/ob mice were administered 50 mg/kg glyoxylate (GOx) daily for 6 days. Animals were sacrificed and their kidneys were extracted on days 0 and 6. We performed gene ontology analysis focused on the molecular function category of adhesion using GeneSpring[®]GX11.0 software and extracted the genes for which expression changed significantly. On the basis of the microarray analysis results, we evaluated the expression levels of *Spp1* (osteopontin, OPN) as a stone-related factor and *Fn1* (fibronectin, FN), *Icam1* (intercellular adhesion molecule 1, ICAM1) and *Col3a1* (collagen III, COL3A1) as atherosclerosis-related factors by quantitative polymerase chain reaction (PCR) and immunohistochemical staining.

Results: There was no stone formation in WT mice, but significant renal crystal formation around the cortico-medullary junction was observed in ob/ob mice on day 6. Gene ontology analysis showed significant inter-group differences, with the highest ratio in the molecular function category of adhesion (68.6 %, $p = 1.25 \times 10^{-9}$). Furthermore, 4 adhesion-related genes, *Spp1*, *Fn1*, *Icam1*, and *Col3a1*, showed significant inter-group differences in expression in the microarray analysis. The expression levels of these 4 genes on day 6 were significantly higher in ob/ob mice than in WT mice ($p < 0.05$) by quantitative PCR. The protein expression levels of these 4 factors were also significantly higher in ob/ob than in WT mice by immunohistochemical staining.

Conclusions: The present study showed that MetS-associated renal crystal formation increased the expression of atherosclerosis-related factors, indicating that cell adhesion plays an important role in renal crystal formation as well as in arteriosclerosis.

COI: No.

MP-07

Uric acid stone components is potential risk factor for renal function deterioration

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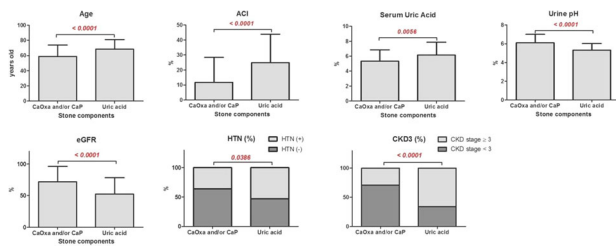
Objective: Although urolithiasis is a potential risk factor for chronic kidney disease (CKD), the impact of uric acid stone components on renal function is unknown. We accessed the significance of uric acid components in urolithiasis patients.

Methods: Between Jan 2010 and Sep 2014, we treated 1793 consecutive patients with urolithiasis in our hospital. Of those, we identified stone components available 473 patients. The patients were divided into two groups according to the stone components, non-uric acid components stone group (calcium oxalate, calcium phosphate, or mixed stone) or uric acid components stone group (uric acid stone with or without calcium oxalate). We compared age, body mass index (BMI), aortic calcification index (ACI), renal function, serum uric acid concentrations (UA), urine pH, presence of diabetes mellitus (DM) and hypertension (HTN) between the groups. We accessed the independent risk factor for impaired renal function by multivariate logistic regression analysis. The renal function was evaluated as estimated glomerular filtration rate (eGFR).

Results: The number of patients in calcium containing and uric acid containing stone group were 350 and 123, respectively. The patients with uric acid components stone group had significantly higher in age), systolic blood pressure, ACI, serum UA, urine pH, positive urine protein, and significantly lower in eGFR compared with non-uric acid components stone group. Multivariate logistic regression analysis showed age older than 62, serum uric acid greater than 7.0 mg/dL and uric acid containing stone former were significant and independent risk for concomitant CKD stage 3.

Conclusion: Uric acid stone components may have a considerable impact on renal function deterioration.

COI: No.



Univariate	Risk factor	P value	OR	95%CI
Age	> 62 years	< 0.001	3.12	2.10-4.62
Gender	Male	0.274	1.25	0.84-1.87
BMI	> 25	0.040	1.48	1.01-2.19
ACI	> 6.6	< 0.001	2.30	1.57-3.38
Type of stone	Uric acid	< 0.001	4.46	2.89-6.88
HTN or DM	Pos	0.008	1.69	1.15-2.50
Urine pH	< 6	< 0.001	2.84	1.93-4.18
serum Uric Acid	> 7	< 0.001	3.60	2.20-5.89
Urine protein	Pos	0.001	2.10	1.36-3.24
Multivariate	Risk factor	P value	OR	95%CI
Age	> 62 years	0.001	2.44	1.48-4.03
Gender	Male	0.217	0.74	0.46-1.19
BMI	> 25	0.372	1.22	0.79-1.89
ACI	> 6.6	0.738	1.09	0.66-1.80
Type of stone	Uric acid	0.008	2.26	1.24-4.12
HTN or DM	Pos	0.181	1.35	0.87-2.11
Urine pH	< 6	0.140	1.47	0.88-2.44
serum Uric Acid	> 7	< 0.001	3.37	1.92-5.94
Urine protein	Pos	0.176	1.41	0.86-2.32

MP-08

Metabolic syndrome increases the risk for calcium oxalate stone formation: results from a Nationwide Survey on Urolithiasis in Japan

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Introduction and objective: Recent epidemiologic studies have shown an increased prevalence of kidney stones in patients with metabolic syndrome (MetS). We have reported that the clustering of MetS traits is associated with greater severity of kidney stone disease (Am J Kidney Dis 61: 923–929, 2013). The aim of the present study is to clarify which stone composition is associated with MetS.

Methods: We retrospectively analyzed detailed clinical data from 30,448 patients with urolithiasis enrolled in the 6th Nationwide Survey on Urolithiasis in Japan conducted in 2005. Patients with lower urinary tract stones, struvite stones, cystine stones, other types of rare stone composition, unknown stone composition, or hyperparathyroidism and those younger than 15 years were excluded. According to the types of stone composition, the severity of kidney stone disease, assessed by the number of existing stones (single/multiple) and number of stone episodes (first time/recurrent), and abnormalities in urine constituents were examined by the number of MetS traits (obesity, hypertension, dyslipidemia, and diabetes).

Results: A total of 4,440 patients included in the final analyses were classified into four groups: calcium oxalate (CaOx) (n = 3213), CaOx + calcium phosphate (CaP) (n = 881), CaP (n = 115), uric acid (UA) (n = 191). The proportions of patients with recurrent and/or multiple stones significantly increased with the number of MetS traits only in patients with CaOx stone (P < 0.01, Table 1). However, similar associations were not observed in patients with other stone compositions. In patients with CaOx stone, there was a significant and stepwise increase in the odds of recurrent and/or multiple stones after adjustment for age and sex. In patients with 3 or 4 MetS traits, the odds was 1.8-fold greater compared with patients with 0 traits (OR, 1.78; 95 % CI, 1.29–2.42). In addition, the presence of MetS traits was associated with significantly increased odds of having hypercalciuria in patients with CaOx stone after adjustment for age and sex.

Conclusions: In patients with CaOx stone, MetS trait clustering is associated with greater severity of the disease and increased urinary calcium excretion. These results suggest that CaOx stone disease should be regarded as a systemic disorder linked to MetS.

COI: No.

Table1. Proportions of patients with recurrent and/or multiple stones by number of metabolic syndrome traits.

Stone composition	Total	No. of metabolic syndrome traits				P
		0	1	2	3-4	
CaOx	3,213	62.1%	66.6%	69.7%	76.5%	<0.01
CaOx+CaP	881	70.0%	71.9%	78.7%	73.3%	0.30
CaP	115	74.6%	65.6%	75.0%	90.0%	0.48
UA	191	69.4%	75.8%	72.7%	77.3%	0.85

MP-09

Hypocitraturia is much more important than hypercalciuria

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Introduction and objectives: For ages hypercalciuria has been known the dominant risk factor for stone recurrence in calcium containing stones. Aim of the present study was to evaluate the frequency of hypercalciuria and hypocitraturia in high-risk stone patients with special regard on recurrence rate and specific metaphylaxis.

Material and methods: From 2008 to 2013 104 high-risk stone patients were treated in our clinic. 72 of them underwent metabolic assessment. 70 patients fulfilled the criteria for our retrospective assessment (aged over 16 years, calcium containing stones). Metabolic assessment included blood chemistry, blood gas analysis and a 24-h urine collection. Urine analysis included calcium, citrate, oxalate, phosphate, magnesium and uric acid. In most patients specific metaphylaxis was recommended. Recurrence rate was observed during a follow-up period of at least 8 months.

Results: 22 of the patients had pure calciumoxalate stones, 6 had pure calciumphosphate stones and 42 presented with mixed calciumoxalate/calciumphosphate stones. In pure calciumoxalate stones 7 presented with hypercalciuria (>7 mmol/24 h) and 13 with hypocitraturia (<2.5 mmol/24 h). In pure calciumphosphate stones 71 presented with hypercalciuria and 4 with hypocitraturia. In mixed calcium containing stones 18 presented with hypercalciuria and 26 with hypocitraturia. In all calcium containing stones hypocitraturia was observed in 43 patients, hypercalciuria in 26 patients respectively. Hypocitraturia and was statistically significant ($p = 0.0161$) more common than hypercalciuria.

(Specific treatment was recommended with alkaline citrate and thiazide. In 12 patients receiving specific metaphylaxis stone recurrence was observed.)

Conclusions: 97 % of our patients had calcium containing stones. Hypocitraturia was significantly more common in these patients than hypercalciuria. Treatment of hypocitraturia seems to be the important factor in prevention of stone recurrence.

COI: No.

MP-10

Oxidative stress, inflammation and sialic acid content in renal tubular cells exposed to urine from nephrolithiasis patients and healthy individuals

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We previously demonstrated oxidative damage and inflammation in stone-forming kidneys of nephrolithiasis (NL) patients. Sialic acid has been proposed to be a crystal binding receptor, and cell-crystal interaction is a prerequisite event in the kidney stone formation. In this study, we tested the hypothesis that NL urine had a higher capability than healthy (H) urine to induce oxidative stress, inflammation and sialic acid expression in human renal proximal tubular (HK-2) cells. Twenty-four hour urine was collected from 5 pre-operative NL patients and 5 H individuals. HK-2 cells were exposed to 20 % (v/v) urine from each subject. H₂O₂ (50 μM) and TNF-α (10 ng/mL) were used as positive controls for inductions of oxidative stress and inflammation, respectively. Levels of protein carbonyl, intracellular reactive oxygen species (ROS), catalase activity, total

antioxidant status (TAS), NF-κB/p65, phosphorylated NF-κB/p65 and sialic acid in the treated cells were determined. Viability of HK-2 cells exposed to urine, H₂O₂ and TNF-α was not significantly altered. Protein carbonyl content and intracellular ROS generation were significantly increased, while TAS was significantly decreased, in H₂O₂-treated cells compared with the untreated controls. Compared with the H urine, NL urine significantly caused increases in protein carbonyl and intracellular ROS, and decrease in TAS. Levels of nuclear NF-κB/p65 and phosphorylated NF-κB/p65 in the TNF-α-treated cells were significantly increased compared to the untreated cells. Neither treatment with NL nor H urine caused significant activation of NF-κB in HK-2 cells. Sialic acid levels both in the H₂O₂-treated cells and the NL urine-treated cells were significantly increased compared with the untreated control. In conclusion, urine from kidney stone patients, but not from healthy individuals, was capable of inducing oxidative stress and sialic acid content in renal tubular cells. These changes might promote the formation of renal calculi. However, exposure of cells to sub-lethal dose (20 %) of NL urine was not able to cause significant activation of inflammatory transcription factor NF-κB.

COI: No.

MP-11

Neutrophil gelatinase-associated lipocalin (NGAL) as a biomarker of renal injury in patients with ureteric stones

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Introduction: An accurate assessment of the risk of renal injury in patients presenting with renal colic is challenging. Creatinine and urine output measurement have significant pitfalls in patients with normal contralateral kidneys.

A biomarker of renal injury may offer the opportunity for early detection and aid clinical management.

NGAL has shown good performance in the prediction of renal injury in several clinical scenarios.

Our objective was to analyze the kinetics of NGAL in patients presenting with acute ureteric obstruction secondary to stone.

Materials and methods: Serum (sNGAL) and urine (uNGAL, normalized to urinary creatinine) levels were measured pre-, intra- and postoperatively in 37 subjects with acute ureteric colic, and compared with two control groups (13 patients with non-obstructive renal stones undergoing elective surgery and 10 healthy controls).

Samples were analyzed with the NGAL Test™ (Bioporto Diagnostics, Denmark) a commercially available particle-enhanced turbidometric immunoassay.

Uni- and multivariate analyses were conducted to evaluate correlation of NGAL levels with commonly adopted clinical parameters.

Results: Levels of sNGAL decreased significantly after relief of ureteric obstruction (77 ng/mL vs 82 ng/mL, $p = 0.01$), whereas uNGAL increased. uNGAL levels in the urine from the obstructed kidney were significantly higher than in the bladder ($p = 0.003$).

In patients who passed their stone, at a median 4 weeks' follow-up NGAL levels were significantly lower ($p = 0.03$).

NGAL levels at presentation were significantly lower in healthy controls ($p = 0.003$).

In controls undergoing elective surgery, pre- and post-operative levels of pNGAL and uNGAL were not significantly different ($p = 0.61$ and $p = 0.09$).

On multivariate analysis female gender and a higher white cell count were the only factors correlated with higher NGAL levels.

Conclusions: To our knowledge this is the first study evaluating the kinetics of NGAL at different time points in patients with obstruction due to ureteric stones.

Relief of obstruction led to a significant decrease in sNGAL levels, though with a brief increase in urinary levels due to release of NGAL-rich urine from the obstructed side. Surgical intervention did not act as a confounder.

These observations suggest that this biomarker could help estimating renal injury due to obstructive stones and help as a marker of de-obstruction during follow-up.

COI: No.

MP-12

Comparison of stone culture using two different sampling methods (wet and dry)

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Introduction: Stone culture has been shown to be more accurate than urine culture in predicting the bacterial flora responsible for infection after treatment for urolithiasis.

In order to identify whether the bacterial yield differed depending on sample preparation, we compared microbiological results with two techniques.

Materials and methods: Paired stone samples were sent as ‘wet’ (in normal saline) or ‘dry’ immediately after PCNL or ureterorenoscopy. All samples were processed following standard laboratory protocol. Positive culture rates and specific bacterial growth were compared between the two groups and in relation to the type of intervention.

Results: 118 paired samples were obtained from 59 patients undergoing PCNL (31) or ureterorenoscopy (28). Overall 39 % of cultures were positive. 97 % of positive cultures grew a single organism. Female patients and PCNLs were more likely to have a positive culture.

Positive rates for dry (37.3 %) and wet (40.7 %) samples were similar ($p = 0.72$).

Results of dry and wet samples were discordant in 13.6 % of cases, without predominance of one technique.

There was no significant difference in the microbiological profile between sampling techniques ($p = 0.9$). The type of intervention did instead affect the type of bacteria, with a higher prevalence of *Proteus* in the PCNL group ($p = 0.009$).

Conclusions: Wet and dry sampling for stone culture seems to perform comparably. Based on the limited additional information, performing both cannot be recommended.

This study confirms however the importance of obtaining a stone culture at the time of intervention, to help subsequent clinical management.

COI: No.

MP-13

Impact of ureteral stones into the ureteral wall: is it possible to predict

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Aim: To determine the possible predictive value of certain acute phase reactants CRP and ESR as well as radiologic parameters on the degree of impaction in ureteral stones.

Patient and methods: A total of 80 adult patients with a single opaque proximal ureteral stone were evaluated. A non-contrast CT was performed in all cases and all possible radiologic predictive parameters calculated. Additionally, to outline the degree of impaction at the stone site, two serum acute phase reactants namely CRP and ESR levels were also assessed.

Results: Patients were divided into two groups as follows; Group 1 ($n:42$) patients with normal CRP levels and Group 2 ($n:38$) patients with elevated levels of CRP. The data obtained in the sub groups were first comparatively evaluated with radiological parameters and the possible correlation between CRP values and these parameters was well evaluated. While the serum CRP levels were normal in 42 cases, they were elevated in 38 cases. Evaluation of the data from CRP subgroups and radiologic parameters showed that elevated levels of serum CRP were closely related with mean values of ureteral wall thickness (UWT) as well as mean level of hydronephrosis with a statistically significant difference. Additionally, a correlation analysis between serum CRP levels and all other parameters mentioned above demonstrated a statistically significant correlation between UWT, degree of hydronephrosis and serum ESR values.

Conclusions: Evaluation of serum CRP and ESR values could let us to predict the UWT, a parameter which is closely related with the degree of stone impaction.

COI: No.

MP-14

Medical expulsive therapy following SWL in ureteral calculi: an effective approach for the improvement of health-related quality of life

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Aim: To evaluate the possible effects of medical expulsive therapy (MET) on the health-related quality of life (HRQOL) of the patients undergoing SWL.

Animals and methods: A total of 80 adult patients treated with SWL for 5–10 mm single radio-opaque upper ureteral stones were included. Patients were randomly divided into two main groups: (Group 1, $n: 40$) no specific medication apart from pain management; (Group 2; $n: 40$) MET (Tamsulosin) in addition to medical therapy for pain. Patients requiring DJ stent placement and/or auxiliary measures after SWL procedure were excluded from the study program due to the possible effects of these procedures on the HRQOL of the cases. The remaining 54 patients were further evaluated [Group1: SWL ($n = 26$); Group 2: SWL + MET ($n = 28$)] on these aspects. Patients were followed during 4-weeks period with respect to the analgesic requirement, number of renal colic attacks and emergency department visits along with the HRQOL scores by using EQ-5D index and mean EQ-5D VAS values.

Results: Mean values of patient age and stone burden were 39.41 ± 1.76 years and 48.20 ± 1.96 mm² respectively. Of all the 26 cases treated with SWL only; while 17 cases (65.4 %) became completely stone-free, on the other hand however, of the 28 cases undergoing SWL + MET; while 20 cases were completely stone free (71.4 %) after 4 weeks.

Evaluation of the cases during this follow-up period demonstrated that cases undergoing SWL only required significantly higher amount of analgesics when compared with SWL + MET group ($p = 0.0045$). In addition to the lower mean number of renal colic attacks and emergency department visits in SWL + MET group. Evaluation of the mean HRQOL in terms of EQ-5D index and EQ-5DVAS values in both groups again demonstrated higher mean values in patients undergoing SWL + MET ($p < 0.05$).

Conclusions: Our current data clearly show that in addition to the increased spontaneous stone passage rates; MET in patient treated with SWL for ureteral calculi could increase the HRQOL scores in these cases by lowering the number of both renal colic attacks and ED visits along with decreased analgesic need after the procedure.

COI: No.

MP-15

Precise identification of crystal deposits in the kidney tissue

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Background: Biopsies of native or transplanted kidneys in patients suffering chronic or acute renal failure are commonly stained for tissue examination and search for possible crystal deposits which are then identified by polarizing microscopy and staining by von Kossa's method revealing mainly calcium deposits.

Aim of the study: Revisiting the nature of crystal deposits in kidney tissue sections by infrared microscopy.

Method: 205 renal biopsies presumably containing crystal deposits were analyzed with the Spotlight 400 FTIR imaging System in the mid infrared spectral range to obtain infrared maps of tissue slides at high spatial resolution, down to 10 microns.

Results: Based on infrared analysis, we identified crystals in all biopsies including 78.8 % calcium-containing crystals, 15.3 % purine crystals of which 90.5 % of 2,8-dihydroxyadenine and 5.9 % drugs crystals.

Among birefringent crystals observed under polarized light, we identified 60.2 % of calcium oxalate monohydrate, 2.6 % of lipids, 13.1 % of 2,8-dihydroxyadenine, 7.8 % of uric acids and urates, 5.9 % of drug crystals (triamterene, *N*-acétysulfadiazine, ciprofloxacin, indinavir, atazanavir); and among non refringent crystals: 27 % of carbapatite, 14.6 % of amorphous carbonated calcium phosphate, 3.9 % of drug crystals (fosfarnet, vancomycine) and 1.5 % of other phosphates. Overall, we identified 26 different types of crystals. Surprisingly, we found mixtures of crystalline phases in a high proportion (23.8 %) of biopsy samples.

Discussion: Crystals may be related to various pathological conditions. Identification of dihydroxyadenine prompt to treat the patient with allopurinol. In transplanted patients, we found a negative correlation between the amount of calcium phosphate deposits and the graft survival. The high occurrence of mixed crystals may be a marker for successive episodes of kidney dysfunction related to different mechanisms. We therefore suggest that FTIR microspectroscopy is a major diagnostic tool for crystal identification and should be proposed to any patient with a past history of stone disease and presenting with an unexplained renal failure of the native or grafted kidney.

Conclusion: A precise identification of crystal deposits in the kidney tissue may be a major tool for the diagnosis of an unexplained renal failure. Common histological procedures clearly fail to identify accurately crystals deposits and should be completed by infrared analysis.

COI: No.

MP-16

FTIR microspectroscopy is a major diagnostic tool for 2,8-dihydroxyadenine nephropathy

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Adenine phosphoribosyltransferase (APRT) deficiency is a rare autosomal recessive disorder characterized by 2,8-dihydroxyadenine (2,8-DHA) crystalluria that can cause nephrolithiasis and chronic kidney disease.

The prevalence of this disease is unknown because many cases are undiagnosed or mistaken with other urolithiasis (mainly uric acid). However, the prevalence of heterozygous mutation is around 1 % in general population.

Method: 594 kidney biopsies presumably containing crystal deposits were analysed with the Spotlight 400 FTIR imaging System in the mid infrared spectral range to obtain infrared maps of tissue slides at high spatial resolution, down to 10 μm . When required, an optional ATR imaging accessory was used, improving the spatial resolution by a factor four, down to 3 μm at 1000 cm^{-1} .

Results: Among the 594 biopsies, 20 (3.36 %) contained 2,8-DHA crystals not identified by histological examination: 6 on native kidney in patients presenting with renal failure (3 acute, 2 chronic and 1 terminal renal failure); in 4 cases, crystals were first identified as calcium oxalate by histological examination and drug crystals were suspected in another case. Twelve patients were diagnosed on their renal transplant (12 on the first transplant, 2 on the second kidney transplant). In 8 cases, calcium oxalate crystals were suspected by histological examination. Allopurinol therapy allowed to recover 50 % to 2/3 of the kidney function in most patients. Only two transplants were lost.

Discussion: 2,8-DHA crystals in biopsies were originally misdiagnosed as calcium oxalate crystals because identification is done visually without infrared analysis. In our study, we have 3.36 % of renal biopsies that contain 2,8-DHA, an unexpected high frequency. We therefore suggest that FTIR microspectroscopy is a major diagnostic tool for 2,8-DHA identification and should be proposed to any patient with a past history of stone disease and presenting with an unexplained renal failure of native or grafted kidney.

Conclusion: APRT deficiency remains a misdiagnosed genetic disease. An early diagnosis should be performed based upon crystalluria study or infrared (or X-ray diffraction) analysis of stones in order to treat early patients and avoid the risk for renal dysfunction as a result of a diagnostic failure.

COI: No.

MP-17

Hyperoxaluria induced tubular ischemia: the effects of verapamil on the antioxidant capacity of the affected kidneys

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Aim: To evaluate the potential protective effects of a calcium channel blocker (Verapamil) on the oxidative stress related changes with an emphasis on the antioxidant capacity of the kidneys an experimental study in rats was performed.

Animals and methods: A total of 44 rats have been included. Hyperoxaluria was induced in Group 1 by continuous administration of ethylene glycol (EG). Animals in Group 2 received Verapamil in addition to EG. Animals in Group 3 constituted the control group. In addition to the evaluation of tissue and serum levels of three scavenging enzymes, NO, MDA and T-AOC; the presence and degree of crystal formation in renal parenchyma were evaluated in all animals after 7 and 28 days.

Results: Our data demonstrated that in addition to the lower level of all three scavenging enzymes (SOD, CAT and GSH) particularly during late phase evaluation (4 weeks); the total antioxidant capacity (T-AOC) of these kidneys were also higher when compared with the animals receiving EG only. Tissue and serum levels of both NO and MDA indicated the preventive effect of Verapamil on the oxidative stress induced changes. Very limited or no crystallization in the kidneys treated with verapamil during early and late phase examination was observed when compared with considerable crystal formation in Group 2 animals.

Conclusions: Verapamil treatment may preserve the oxidant capacity of the kidneys and subsequently limit the crystal deposition induced by hyperoxaluria. Verapamil could therefore be considered in the management of kidney stone formation particularly in cases with recurrent kidney stone disease.

COI: No.

MP-18

Probability of renal stone formation (PSF) in obese patients before and after gastric bypass surgery; effect of a preventive strategy

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Background: Prevalence of obesity has increased worldwide, and so did the number of gastric bypass procedures (100 procedures/year in our center). Gastric bypass leads to metabolic disorders that raise lithogenesis risk. We wanted to estimate the stone risk of a cohort of obese patients naïve of nephrolithiasis scheduled for gastric bypass surgery.

Methods: Standard metabolic work-up was performed in obese patients scheduled for gastric bypass surgery in the following month. To estimate stone risk we calculated the probability of stone formation (PSF) according to Robertson. PSF can be calculated for uric acid (UA), calcium oxalate (CaOx), calcium phosphate (CaP) or mixed crystals, and correlates with the incidence of nephrolithiasis.

Results: of the first 6 patients prospectively enrolled (mean \pm SD): all females, aged 35.3 ± 9.0 years, weighing $120.8 \text{ kg} \pm 19.4$, BMI $46.6 \text{ kg/m}^2 \pm 5.9$. Results of the 24 h urine analyses are depicted in table 1. Based on the PSF values, four patients (1,3,4,6) had a severe risk (PSF > 0.9) of CaOx lithogenesis, and one of them (patient 4), simultaneously had a moderate risk (PSF 0.7–0.9) of UA lithogenesis.

Conclusions: Obese patients without history of nephrolithiasis scheduled for gastric bypass are already at high risk of CaOx lithogenesis prior to surgery, a fact largely underestimated by most surgical teams. We are currently carrying out a prospective

randomized study assessing the benefit of a dedicated preventive strategy (which will be presented) aiming at reducing the stone risk after bypass surgery.

COI: No.

Table 1 24 h urine collection analyses

Patient	#1	#2	#3	#4	#5	#6
Volume (ml/24 h)	1180	2550	1430	880	1500	800
pH	6	6.5	6.5	5.5	5.5	5.5
creatinine (mmol/24 h)	16.0	11.5	13.7	10.3	15.6	16.9
Na (mmol/24 h)	136	153	342	141	164	168
K (mmol/24 h)	72	84	54	41	40	79
Ca (mmol/24 h)	6.08	1.76	9.55	6.44	4.58	3.13
phosphate (mmol/24 h)	25.1	26.0	45.5	29.5	27.2	34.2
urea (mmol/24 h)	367	160	535	384	390	362
uric acid (mmol/24 h)	4.33	4.21	5.71	3.67	4.67	2.02
Mg (mmol/24 h)	5.25	5	4.98	3.89	2.64	4.87
citrate (mmol/24 h)	4347	4287	5764	2895	2768	6976
oxalate (mmol/24 h)	523	507	635	383	278	734

MP-19

Silodosin, the selective alpha 1A adrenoceptor antagonist, facilitates expulsion of size 5–10 mm distal ureteral stones

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Introduction and objectives: We reported that alpha 1A adrenoceptor (AR) is the main participant in phenylephrine-induced human ureteral contraction. We therefore decided to carry out a prospective randomized study to evaluate the effects of silodosin, a selective alpha 1A AR antagonist, as a medical expulsive therapy (MET) for distal ureteral stones.

Methods: A total of 112 male patients, who were referred to our department for the management of symptomatic unilateral distal ureteral calculi of less than 10 mm, were randomly divided into two groups: group A (56 patients) who were instructed to drink 2 L of water daily and group B (56 patients) who received the same instruction and were also given silodosin (8 mg/daily) for a maximum of 4 weeks. Expulsion rate, expulsion time and need for analgesics were examined.

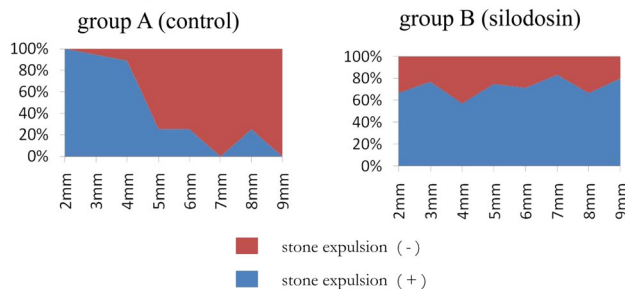
Results: The expulsion rate was 55.3 % (56 patients) for group A and 72.7 % (55 patients) for group B ($P = 0.106$). The expulsion rate for <5 mm was 92.9 % (28 patients) for group A and 69.2 % (26 patients) for group B ($P = 0.053$). The expulsion rate for ≥ 5 mm was 17.9 % (28 patients) for group A and 75.9 % (29 patients) for group B ($P = 0.001$). The expulsion time was 13.40 ± 5.90 and 9.29 ± 5.91 days, respectively ($P = 0.012$). Analgesics were required 1.5 ± 3.1 and 0.3 ± 0.9 times, respectively ($P = 0.382$). Stone size in expulsion cases was 3.64 ± 1.25 and 5.23 ± 2.32 mm,

respectively ($P = 0.003$). In all stone sizes, group B showed high expulsion rate (Fig.).

Conclusions: Due to the high likelihood of spontaneous passage of stones up to 5 mm, MET is less likely to increase the stone-free rate. Here, we have shown that MET for distal ureteral stones by silodosin was effective for stones ≥ 5 mm. We believe that silodosin might have potential as a MET for distal ureteral stones.

COI: No.

Expulsion rates related to stone size



MP-20

The impact of prostatic stones for the procedures of Holmium-Laser enucleation of prostate

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Introduction and objectives: Prostatic stones are usually not related to severe clinical symptoms. At the initial step of Holmium-Laser enucleation of prostate (HoLEP), prostatic stones sometimes influence the procedure to go into the layer between peripheral zone (PZ) and adenoma around verumontanum. We analyze the patterns of prostatic stones and show how to manage these patterns.

Methods: From June 2012 to January 2016, 104 cases performed by one surgeon (MS) were analyzed. HoLEP were performed mainly by two or three lobe technique based on anteroposterior technique. Around the apical lesion, first, urethral mucosa is incised beside the verumontanum bilaterally. Next, the transvers mucosal incision at distal verumontanum is made. When prostatic stones exist, stones were seen after this maneuver. Conditions of prostatic stones were checked by videoclip.

Results: The mean patient age, enucleated volume and enucleated time was 69 years (range 52–83), 33.4 (1–152) grams and 38.9 (14.1–126) minutes, respectively. Two patterns that influenced the procedure were identified: (1) with many small prostatic stones by curing up in small cavity and (2) with relatively large prostatic stones (over 4 mm) berried in PZ. For the pattern 1), just to provide the energy intermittently or decrease the frequency is the way to find the correct plane. For the pattern 2), we need more attentions; the proper layer is seemed shallower than we expected because the mucosa embedded PZ could lead deeper plane than correct plane.

Conclusion: Prostatic stones are said to be a landmark between the PZ and adenoma during TURP. However, during HoLEP, we need to find the right plane between PZ and adenoma in the early and important step. We identified the patterns that could cause the difficulty to keep appropriate plane by large and/or many prostatic stones. Surgeons should pay more attentions in finding prostatic stones during HoLEP.

COI: No.

MP-21

Endoscopic therapy for pediatric stone disease, our experience in more than hundred cases

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Introduction and objectives: Treatment approaches for urinary stones changed during the last years. Extracorporeal shock wave (ESWL) is more and more replaced by endoscopic procedures like ureterorenoscopy (URS) and percutaneous nephrolithotomy (PCNL). ESWL is still the first treatment for children with ureteral stones, but it is not a promising option for stones >10 mm in diameter, or for impacted, calcium oxalate monohydrate or cystine stones. In this special cases ureteroscopy or PCNL with smaller-caliber instruments should be used as the first choice of treatment.

Material and methods: Between 2009 and 2015 we treated 126 children aged between 0 and 18 years (median 9.2 years) successfully in our Department. The children were referred because of complex stone situations such as staghorn calculi, cystine stones, bilateral stones or obstructive ureteral stones. All stones were removed endoscopically (URS 4.5 F; PCNL 7-15F). The obtained stone material was analysed—if necessary—children underwent metabolic evaluation and received subsequently preventive medication.

Results: Endoscopic stone treatment (URS n = 79, PCNL n = 47) in children with stone disease is a secure and effective option for complex stones. The overall mean hospital stay for PCNL was 7.5 days (min. 2, max. 19) and for URS 3.7 days (min. 1, max. 8). Overall primary stone-free rate was 76.2 % after a second look 94.5 %. Second look procedures or retreatment was required in 28.1 %. The median stone size was 13.1 mm for PCNL (min. 6 mm, max. 35 mm) and 6.2 mm for URS (min. 1 mm, max. 15 mm). Overall-complication-rate was 11 % and comparable to those in adults. Three children reacted with fever (temperature >38.5 °C). One child developed hyponatremic hypervolemia post-operatively, which needed intensive care treatment for 3 days. We did not find any severe bleeding after URS or PCNL, no transfusion was needed.

Conclusions: Endoscopic therapy for pediatric stone disease should be the first option in complex situations when ESWL is not a promising option. Children should be referred to specialized stone centers, where smaller-caliber instruments are available. The combination of careful and complete endoscopic stone clearance and subsequent metabolic therapy according to the stone type stone prevention is essential in complex cases.

COI: No.

MP-22

New anatomical classification of the pelvicalyceal system for endoscopic intrarenal surgery

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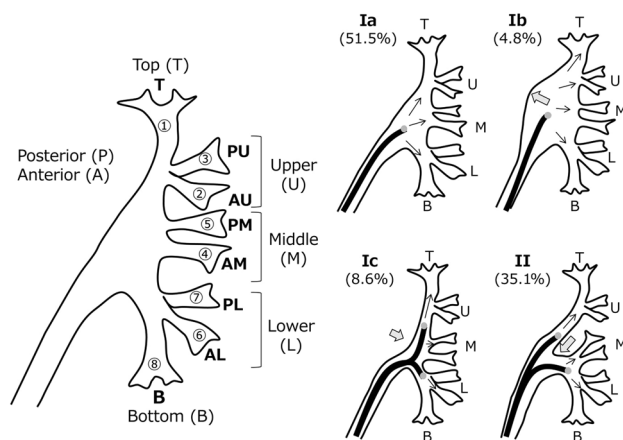
Background and purpose: We currently have many opportunities to perform endoscopic intrarenal surgery. However, anatomical differences in the renal pelvicalyceal system make it difficult to describe detailed ureteroscopic findings and share common information about the stone position or appropriate puncture site for the percutaneous approach. The aim of this study was to propose a new nomenclature for renal calyces and anatomical classification of the pelvicalyceal system.

Materials and methods: We prospectively collected data on a total of 181 consecutive patients (353 kidneys) who underwent CT urography at our institution. We constructed three-dimensional (3D) images of the pelvicalyceal systems and performed virtual ureteroscopy if necessary. Seventeen kidneys with deformation due to severe hydronephrosis or large renal masses were excluded from this study.

Results: We systematically categorized each minor calyx into five levels: top (T), upper (U), middle (M), lower (L), and bottom (B). The upper, middle and lower calyces were typically found in pairs: anterior (A) and posterior (P). The top and bottom calyces generally formed compound papillae. The most common total number of minor calyces was eight (50.3 %), followed by seven (29.5 %). We also classified the form of the pelvicalyceal systems into type I (64.9 %, 218/336) and type II (35.1 %, 118/336) according to the branch patterns of the renal pelvis. In type I, the renal pelvis bifurcated into the upper branch (to T and U) and lower branch (to M, L, and B). Type I was subclassified into three types: type Ia (51.5 %, 173/336), the standard type; type Ib (4.8 %, 16/336), with a wide convex pelvis; and type Ic (8.6 %, 29/336), with a narrow concave pelvis.

Conclusions: This new anatomical classification can divide the renal pelvicalyceal system into two types (subdivided into four types) and name each minor calyx. This new methodology can thus make it possible to share common intrarenal information, leading to the development of concrete treatment strategies.

COI: No.



MP-23

Efficacy of ESWL training using human body-typed stone-targeting phantoms

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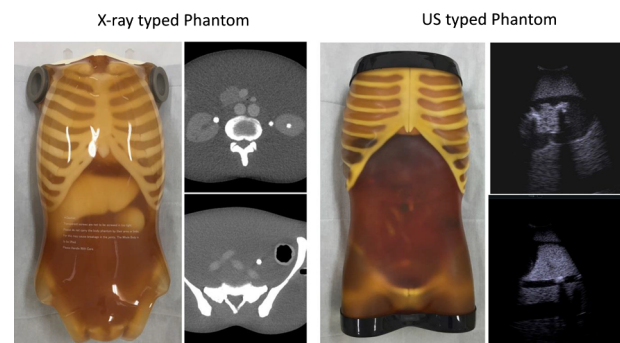
Introduction and objectives: We previously reported that training for extracorporeal shock wave lithotripsy (ESWL) could largely improve its success rates. We produced two phantom types for stone-targeting training to introduce a new ESWL instrument. The aim of the study is to demonstrate the efficacy of the training and ability of the model to improve success rates.

Materials and methods: Two human body phantom models for X-ray and ultrasound targeting were created. The whole body and the organs (liver, kidneys, spleen, pancreas, and bowels) of both phantoms were made of urethane elastomer, while the model stones placed inside were composed of epoxy resin. Using these two phantom types, technical training was performed for the targeting methods of X-rays alone and dual imaging (X-ray + ultrasound) on the introduction of Dornier Gemini[®] as a new ESWL instrument.

Results: This training was performed for six doctors in charge of ESWL treatment and they acquired all manuals. The indication for ESWL was determined according to Japanese urolithiasis guideline, and 38 operations were performed between April 1 and October 9, 2015. The stone locations were as follows: renal pelvis, 20; pelvic-ureteric junction, 3; proximal ureter, 8; middle ureter, two; and distal ureter, 5. Except for the four cases of distal ureter with X-ray targeting, dual imaging was used. An OptiCouple was used for all operations and generated bubbles were removed by passage of the operators' hand through between patients' skin and therapy head appropriately. The ESWL success rate confirmed by computed tomography was 100 % and no additional treatments were needed. In terms of complications, one patient developed a febrile urinary tract infection.

Conclusion: Operation training using phantoms on a new ESWL introduction demonstrated extremely higher success rates than the reported ones.

COI: No.



MP-24

Stone density: probably most important predictive factor on the stone free rate of endoscopic treatment (RIRS)?

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Treatment of renal stones has seen significant changes over the last few decades with a shift from open surgery to minimally invasive interventions.

Kidney stones over 1 cm in diameter are the common urologic problem. European and American Associations of Urology has published guidelines on Urolithiasis and presented the most effective tools to treat large stones.

On the other hand many experienced endourologic centers choose other modalities from their armamentarium. With advances in the designs of ureterorenoscopes (URSs), especially the introduction of Holmium:YAG (yttrium aluminum garnet) laser into the market and worldwide accepted use of this laser during URS, most of kidney stones can nowadays be managed by flexible ureterorenoscopy (RIRS).

No current available method is validated for predicting stone free rate after retrograde intrarenal surgery (RIRS). In most cases the stone size is the dominant factor for treatment modality choice.

Our aim was to evaluate the efficacy of RIRS for the treatment of mid-size renal stones (1–3 cm) and to analyze the stone density (Hounsfield units) as predictive factor of stone free in order to identify which patients may have benefit from this technique.

Method: A retrospective analysis on 84 patients who underwent retrograde endoscopic procedures for reno-ureteral stones—*intra renal retrograde surgery (RIRS)* between October 2014 and November 2015 was performed.

A patients were divided in three groups by stone density with comparable stone size—Group A (<800 HU), Group B (800–1000 HU), Group C (>1000 HU).

Results: Analyzing the RIRS the stone-free rate after single treatment was (defined as no residual stone or fragments up to 3 mm) 87 % in patients Group A, 84 % in Group B and 28 % in Group C.

Conclusion: A significant reduction of success rate was found in patient with high density stones (>1000 HU). For this group of patients other treatment modalities must be used, especially for stones greater than 15 mm.

COI: No.

MP-25

Stone size was the only independent predictor of residual stone and multiple procedures of ECIRS

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Introduction and objectives: It would be very helpful for surgeons and patients to predict postoperative outcomes before operations and multiple attempts have been made to develop reliable predictive tools grading the complexity of standard percutaneous nephrolithotomy (PNL). Stone size and the number of involved calyces have been reported to be major predictors of successful PNL. However, few have been reported about clinical predictors or classification systems for endoscopic combined intrarenal surgery (ECIRS). The aim of this study was to identify the predictors of treatment results after ECIRS. **Methods:** We retrospectively reviewed the charts of 75 patients with renal stones who underwent ECIRS between February 2008 and April 2015. We investigated the stone-free rate (SFR), the number of primary procedures and the perioperative complications, and analyzed the factors contributing to these three outcomes by using logistic regression analysis. Stone free was defined as residual fragments less than 4 mm and primary procedures as ECIRS and conventional transurethral lithotripsy. Perioperative complications included extravasation, excessive bleeding and postoperative fever >38 °C.

Results: The median age was 56 years (21–83 years) and 43 patients (57.3 %) were male. The median stone size was 417 mm² (102–2365 mm²). The SFR was 69.3 % (52/75 cases) with average number of primary procedures of 1.48. On multivariate analysis, an increasing stone size was the only independent predictor of residual stones and multiple primary procedures ($p < 0.01$ and $p = 0.04$, respectively, Table). Overall, 24 patients (32.0 %) experienced perioperative complications. Female ($p = 0.01$), increasing Hounsfield units of the stone ($p < 0.01$) and no or mild hydronephrosis ($p = 0.04$) were significantly associated with perioperative complications.

Conclusions: Increasing stone size was the only independent predictor of residual stone and multiple procedures of ECIRS. In contrast, increasing number of involved calyces was not predictive,

which might be responsible for the combined antegrade and retrograde access.

COI: No.

Table. Multivariate analyses of associations between various parameters and residual stones/ multiple primary procedures

Variable	residual stones			multiple primary procedures		
	Odds ratio	95% CI	P value	Odds ratio	95% CI	P value
Age	0.99	0.93–1.04	0.63	1.03	0.97–1.08	0.33
Male	4.31	0.63–29.08	0.13	0.88	0.21–3.55	0.86
Stone size	1.01	1.00–1.00	<0.01	1.00	1.00–1.00	0.04
Number of involved calyces	0.98	0.38–2.59	0.96	2.11	0.88–5.02	0.09
Hounsfield units	1.00	0.99–1.00	0.30	1.00	0.99–1.00	0.14
Skin to stone distance	1.02	0.97–1.06	0.25	1.02	0.98–1.06	0.27
Degree of hydronephrosis	1.23	0.27–5.51	0.78	1.38	0.36–5.05	0.65
Unfavorable nephrostomy tract	4.95	0.70–34.66	0.10	3.93	0.74–20.86	0.10

MP-26

Peri-operative outcomes of percutaneous stone surgery in patients with urinary diversions

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University College London Hospital, UK

Introduction: Percutaneous nephrolithotomy is challenging in patients with urinary diversions.

Besides the difficulties in retrograde access, these patients present complex stones and medical comorbidities. Internationally adopted stone complexity scores place them in the highest-risk categories.

Our aim was to review the success rate and peri-operative outcomes of PCNLs for these patients in a highly specialized tertiary centre.

Materials and methods: We reviewed all PCNLs performed between 2008 and 2014 in patients with any form of urinary diversion.

Stone parameters (size, density and complexity according to Guy's score) and peri-operative outcomes (operative time, bleeding, changes in renal function, complications, length of stay and stone-free status) were compared between cases and 50 controls with normal lower urinary tract.

Subgroup analyses were performed to compare different types of diversion (ileal vs colonic and continent vs non-continent).

SPSS software was used for statistical analysis.

Results: 42 patients were included (5.2 % of all PCNLs performed). Types of diversion included conduits, neobladders and continent diversions created for a range of benign and malignant indications. Stone complexity was higher in the diversion group (Guy's score 3 or 4 in 83.3 vs 48 %, $p = 0.001$), with a higher prevalence of struvite composition and positive stone culture compared to controls ($p < 0.001$).

Ultrasound-guided access was successful in 100 % of cases. Operative times were shorter (95 vs 80 min, $p < 0.01$) owing to the absence of retrograde catheter insertion.

Complication rates were similar between groups ($p = 0.6$), but length of hospital stay was marginally longer in diversion patients (6 vs 4 days, $p = 0.03$).

Stone free rate was comparable (52.4 vs 65.3 %, $p = 0.3$).

Patients with ileal conduit had a longer hospital stay compared to other types of diversion ($p = 0.001$), while colonic continent diversions had a higher percentage of infected struvite stones (80 vs 47.1 %, $p < 0.001$).

Conclusions: Within a specialized tertiary centre, peri-operative outcomes of PCNLs in patients with urinary diversions appear to be non-inferior.

Proficiency in ultrasound-guided access has the benefit of a reduced operative time, which contributes to a better post-operative course.

The knowledge of biochemical and microbiological profiles associated with specific types of diversion could contribute to a more insightful pre- and perioperative management.

COI: No.

MP-27**Can we identify predictors for the risk of embolization following percutaneous nephrolithotomy?**

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Introduction: Bleeding requiring angiographic embolization is an uncommon but serious complication of percutaneous renal surgery, reported in approximately 2 % of cases. We reviewed our PCNL series to identify predictors for risk of embolization.

Materials and methods: All patients who underwent embolization between 2008 and 2014 were identified from our PCNL and Interventional Radiology databases. Patient demographics, stone characteristics and peri-operative outcomes were compared with 50 consecutive non-embolized control PCNL patients.

Results: 12/850 patients underwent embolization (1.4 %) at median 8.5 days (1–21) following PCNL. 50 % of patients were embolized at day 10 or beyond. Haemodynamic instability was common in the early group, whereas haematuria was the main feature of patients presenting later. No significant differences in age, gender and stone characteristics were identified, nor for calyx of access, operative time or stone-free rate. Post-operative CRP was higher in embolized patients (median 29 vs 8, $p = 0.02$), who also had a significantly higher proportion of infected struvite stones, consistent with a trend towards more complex stones (Guys score III/IV). Interestingly the decrease in haemoglobin on post-operative day 1 was similar to controls, with levels dropping to a median 69 mg/dL pre-embolization.

Conclusions: Embolization following PCNL is uncommon and predicting patients at risk is challenging. In particular, the haemoglobin on the first postoperative day does not help identify a significant bleeding risk and does not change clinical management in otherwise well patients. If haemoglobin change is to be used as a marker for the national PCNL registry, a later measurement might act as a more useful guide to the complexity of the procedure. Patients who have persistent haematuria should be managed cautiously, especially if they have struvite stones and raised post op CRP.

COI: No.

MP-28**Evaluation of predictive factors for post-operative pyrexia of transurethral lithotripsy (TUL)**

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St. Luke's International Hospital, Japan

Purpose: To revise the predictive factors for post-operative pyrexia of transurethral lithotripsy (TUL) in the treatment of ureteral calculi.

Materials and methods: We performed a retrospective analysis of 65 patients who underwent TUL between October 2014 and December 2015 at our hospital. At our hospital, the clinical pathway of TUL is hospitalization for 2 days and one night. 64 (98.5 %) patients were discharged on schedule. Antibiotics were administered before TUL for all patients with febrile urinary tract infection, symptomatic pyuria and pre-stenting, while it was not always used for patients with asymptomatic pyuria.

Results: There were 40 males and 25 females with a mean age of 60.5 (22–85). Stones were classified into 28 renal calculi cases and 37 ureteral calculi cases. Ureteral stones were located in the upper, middle, and lower third of the ureter, 24, 5, and 8 cases, respectively. The mean diameter of the largest stone was 11.8 (6–25) mm, and the cumulative stone diameter was 13.6 (6–32) mm. A preoperative stent was inserted in 27 (41.5 %) patients. Flexible ureteroscopy and a ureteral access sheath was used in 49 (75.4 %) procedures. The mean operative time was 86 min. Stone free rate (<2 mm) was 86 % (56/65). Second TUL was performed in 5 (7.7 %) patients and they were finally stone free. Other 4 patients whose residual stones were within 4 mm did not need additional treatment. Post-operative high fever (>38 degrees Celsius) was seen in 3 patients (4.6 %). However, they could be discharged because their blood test results only showed slight inflammatory reaction. We examined predicting factors for post-operative pyrexia, which were age, gender, stone size, operation time, pre-operative pyuria, and whether the patient had pyelonephritis as an initial symptom or not. Patients with post-operative pyrexia were likely to have had pyelonephritis ($P = 0.059$). The number of patients whose initial symptom was pyelonephritis is 10. All cases were managed with double-J ureteral stent, and they were operated on at least one month later.

Conclusion: Patients with history of pyelonephritis are likely to develop post-operative pyrexia. Pyelonephritis cases are carefully operated, and evaluating the period of antibiotics and timing for TUL is important.

COI: No.

	Post-operative fever(-)	Post-operative fever(+)	P value
Total number of patients	62	3	
Age, year, range	60.5 (22-85)	76 (31-80)	0.625
Sex, no (%)			0.554
Male	39 (63)	1 (33)	
Female	23 (37)	2 (67)	
Stone diameter (mm), range (mm)	12 (6-32)	12 (10-21)	0.798
Operaton time(min)	81 (22-159)	120 (46-132)	0.668
Preoperative pyelonephritis, no (%)	8 (13)	2 (67)	0.059
Pyuria, no (%)	25 (40)	2 (67)	0.565

MP-29**The reasons of inaccuracies admitted in the evaluation of postoperative complications by Clavien-Dindo grading system in the endoscopic treatment of urolithiasis**

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Introduction: Clavien-Dindo classification used for postoperative surgical complications assessment was approved by the EAU as an instrument for comparing different centers treatment results in the endoscopic treatment of urolithiasis. However, the absence of an internationally accepted standard for postoperative course of endoscopic treatment of urolithiasis defining a clear boundary between normal and complicated postoperative courses, leads to inaccurate estimation of light postoperative complications in various centers. Moreover, the complexity of urinary stones for the endoscopic treatment should be determined based on the capabilities of the method.

M&M: We conducted the analysis of the results of endoscopic interventions of 1027 patients with stones located in the upper urinary tract (597 men—58.1 % and 430 women—41.9 %), aged 4–84 years (38.9 ± 15.6). The average size of stones was 30.3 ± 0.6 (3–150) mm. Stones were removed either by percutaneous (948 cases) or transurethral (79 cases) access. Each patient had a pneumatic litho-

tripsy. This made an objective evaluation of the effectiveness of the treatment in different groups possible.

Results: To determine the exact boundary where a postoperative complication begins, we accepted the standard (Tabl. 1).

The completeness of the stones removal for “simple” stones made up 15 (3.4 %), for “complex” ones—122(21.0 %), that is 63 (16.4 %) in II g. and 59(29.9 %) in III g., $P < 0.01$ between all groups.

According to the systematization of Clavien–Dindo there were 250 complications in 195 patients, distributed as follows: I 64(6.2 %), II 111(10.8 %), IIIa 33(3.2 %), IIIb 39(3.8 %), IVa 3(0.3 %), IVb 0, V 0.

Conclusions: For the correct evaluation of light postoperative complications in the Clavien–Dindo system, it is advisable to use a common accepted standard of postoperative course of endoscopic treatment of urolithiasis in all centers.

Patients with upper urinary tract stones should be divided into groups with “simple” and “complex” stones from the position of endoscopic surgery taking into account its capabilities. Then, in the urological community, the question of which residual stones should and should not be regarded as a complication after endoscopic treatment of urolithiasis and included to the system will become clear.

COI: No.

Criteria of standard - uncomplicated postoperative period of endoscopic surgery of nephrolithiasis.

Insignificant (moderate) staining of urine with blood along nephrostomy or ureteral or urethral catheter, that does not lead to the formation of blood clots, and impairment of drainage that does not require additional fluid (more than 1 liter), diuretic therapy and haemostatics;
Increasing the patient's body temperature up to 37.9 C without chills, within not more than 48 hours, which does not require antipyretic, infusion therapy (more than 1 liter);
Locating of intraoperatively placed ureteral, urethral catheters from 12 hours to 7 days (under surgeon's direction) without the development of infectious and inflammatory process and additional interventions;
A single session of routine antegrade pyelography before removing the drainage;
Clinically insignificant residual stones;
Clinically significant residual stones at any localization after surgery for complex stones.

MP-30

Active stone removal can prevent stone-related deaths in bedridden patients with upper urinary tract calculi

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Introduction and objectives: Controversies exist as to whether to perform active stone removal in bedridden patients with upper urinary tract stones because of their perioperative risks. However, there have been few reports on the optimal treatment of urinary tract calculi in bedridden patients. The purpose of the present study was to clarify whether stone removal in bedridden patients improves their prognosis.

Methods: We retrospectively reviewed the charts of 64 bedridden patients (Eastern Cooperative Oncology Group performance status 3–4), 20 men and 44 women, treated for upper urinary tract stones from January 2009 to April 2015. Stone event-free survival rate and the overall survival rate were calculated by Kaplan–Meier method.

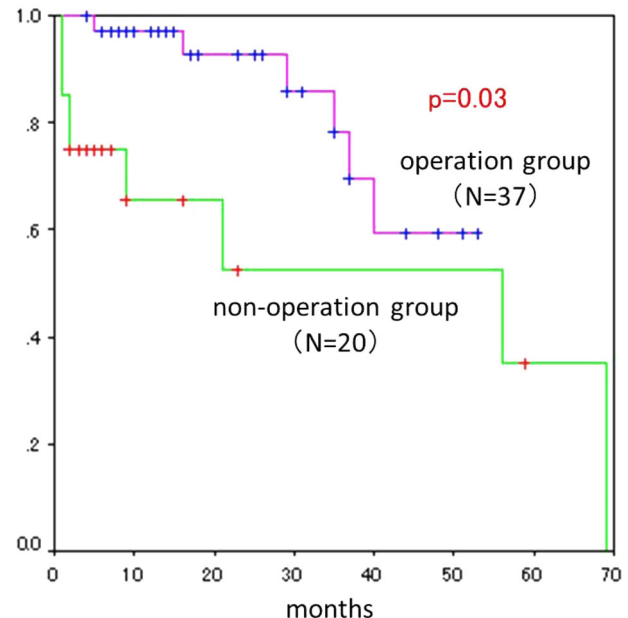
Results: The median age was 81 years and median stone size was 11 mm. Fifty-three patients (82.8 %) presented with acute pyelonephritis. Of 64 patients, 7 patients (10.9 %) experienced spontaneous stone expulsion and 37 patients (57.8 %) underwent active stone removal (operation group), while 20 patients (31.3 %) were treated without operation (non-operation group). Of 37 patients in operation group, 6 patients (9.4 %) underwent ESWL, 25 patients (39.1 %) did ureteroscopy, 5 patients (7.8 %) did percutaneous nephrolithotomy and 1 patient (1.6 %) did nephrectomy. Overall stone free-rate was 77.8 % and perioperative complication was

observed in 8 patients (12.5 %). Two-year stone event-free survival rate in operation group was 86.1 %. Two-year overall survival rates in operation and non-operation groups were 92.7 and 52.5 %, respectively ($p = 0.03$, Figure). No stone-related death was observed in operation group, while 7 out of 9 patients (77.8 %) died of stone-related events in non-operation group.

Conclusions: Active stone removal in bedridden patients can prevent stone-related death and improve their prognosis.

COI: No.

Fig. Overall survival rate



MP-31

Risk factors for loss to follow-up in patients with upper urinary tract stones after surgical treatment

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Introduction and objective: After surgical treatment for urolithiasis, regular follow-up is critical in preventing and monitoring stone growth or new stone formation. The aim of the present study was to investigate risk factors for loss to follow-up in patients with upper urinary tract stones after surgical treatment.

Methods: We retrospectively identified 287 consecutive patients treated with extracorporeal shock wave lithotripsy (SWL), ureteroscopy (URS) or percutaneous nephrolithotomy (PNL) between January 2010 and December 2013. Kaplan–Meier estimates were calculated for probability of loss to follow-up. In cases where physician did not make a follow-up appointment or patient did not come on the appointment day, the date taken for the event was the date of the last visit. Data were censored on the day of last visit for patients who were referred to another urology clinics. Cox proportional hazard models were utilized to identify risk factors for loss to follow-up. Characteristics considered included age, gender, number of stone episodes (first time or recurrent), number of stones (single or multiple), stone location (kidney or ureter), stone size, type of

surgery, number of surgical procedure, residual stones, type of outpatient clinic (general or specialized stone clinic).

Results: Overall, 91 patients were lost to follow-up with a median follow up of 632 days (range 2–1968 days). Of these, 53 events (58.2 %) were due to patient behavior, while 38 events (41.8 %) were attributed to physician. 1-, 2- and 3-year probability of loss to follow-up were 23.6, 29.1 and 35.4 %, respectively. Independent and significant risk factors for loss to follow-up identified in Cox proportional hazard models were 60 years old or younger, ureteral stone, SWL, single surgical procedure and general clinic (Table).

Conclusions: Our findings will help physicians recognize patients who require additional support by stone specialist for retention in follow-up program, including younger patients, those with ureteral stones and those who underwent less invasive or single surgical procedure.

COI: No.

Table. Multivariate Cox proportional hazard analysis of risk factors for loss to follow-up in 287 patients with upper urinary tract stones after surgical treatment.

Variables	HR	95% CI	P
≤ 60 years / >60	1.73	1.11 - 2.71	0.02
Male / female	0.91	0.57 - 1.44	0.68
First time episode / recurrent	1.22	0.78 - 1.90	0.38
Single stone / multiple	1.30	0.85 - 2.00	0.23
Ureteral stone / kidney	1.83	1.15 - 2.91	0.01
Stone size	0.93	0.59 - 1.48	0.77
Surgery			
SWL / PNL	3.58	1.03 - 12.5	0.04
URS / PNL	2.20	0.62 - 7.84	0.22
Single surgical procedure / multiple	1.91	1.11 - 3.27	0.02
Residual stones	0.93	0.42 - 2.02	0.85
General clinic / specialized	2.64	1.65 - 4.21	<0.01

FREE POSTER

FP-01

Age-related differences in impacts of ambient hot season on clinical presentation of acute renal colic in stone formers

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Purpose: Although the rise in ambient temperature is a risk factor for renal colic due to urolithiasis, it remains unclear whether stone patients would have different sensitivity to the change in the temperature by aging. We aimed to examine impacts of hot season and age of patients on clinical presentation of renal colic.

Patients and methods: We retrospectively reviewed medical archives of consecutive 106146 patients who visited the emergency department (ED) of Nihonkai General Hospital between Apr, 2007 and Mar, 2015. Total 358 patients symptomatic for urolithiasis were included in this study after exclusion of patients who met the following criteria: no pain, abnormal vital signs, moderate to severe

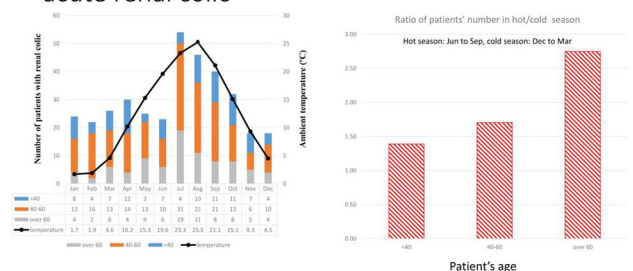
infection of urinary tract or active malignancy. The present study was approved by the institutional ethical committee. The patients were classified into three age-groups under 40 years, 40–60 years and over 60 years (n = 88, 184 and 86, respectively). Relationships among age, mean ambient temperature, month and season at ED visit were analyzed. Ratio of patient's number in hot (Jun to Sep) to cold (Dec to Mar) seasons was obtained by calculation of the number of stone patients who presented at the hot season divided by those at the cold. Information on regional climate was obtained from an open access database which are publicly provided by Japan Meteorological Agency in Ministry of Land, Infrastructure, Transport and Tourism. Statistical analysis was done with R package.

Results: The number of stone patients presenting with renal colic climbed up by 2-fold in hot season, compared with that in other seasons (Fig., left). The actual increase in patients' number was most remarkable for the age-group of 40–60 years. In contrast, ratio of patient's number at hot/cold season became higher in parallel to aging (Fig., right). However, the trend was not statistically significant but marginal (p = 0.087, Cochran-Armitage test), probably because of the small number of patients in this study.

Conclusion: The increase in ambient temperature at hot season would tend to affect clinical presentation of colic attack due to nephrolithiasis in the middle-aged patients quantitatively and the elders over 60 years qualitatively.

COI: No.

Impacts of ambient hot season and age of patients with nephrolithiasis on clinical presentation of acute renal colic



FP-02

The correlation between abdominal obesity and stone analysis in Korean patients

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Objective: Recent epidemiologic and clinical data suggest that metabolic syndrome is involved in the pathogenesis and progression of stone disease. The purpose of our study was to assess to relation between subcutaneous adipose tissue, visceral adipose tissue, and stone analysis in Korean patients.

Materials and methods: Between 2011 and 2014, 774 patients underwent stone surgery (ureteroscopic stone extraction, laparoscopic ureterolithotomy, Percutaneous nephrolithotomy) at a tertiary center. Stone surgery was performed by three surgeons. 689 patients were enrolled and the data were collected retrospectively in medical records. Each subject underwent cross-sectional CT scan of the abdomen at the level of L4. Assessment of total, visceral and subcutaneous abdominal fat compartments was performed by single slice CT. Analyses were performed using Alice software (version 4.3.9; Parexel, Waltham, MA).

Results: The median age was 56 years. 262 (38 %) patients had male and 427 (62 %) patients had female. In stone analysis, 351 (51 %) patients had calcium stone, 83 (12 %) patients had carbonate stone, 214 (31 %) patients had uric acid stone and 41 (6 %) patients had struvite stone. There were performed to assess the association of the visceral adipose tissue, subcutaneous adipose tissue, Total adipose tissue, area ratio (V/V + S, %), outer circumference (cm). In male group and female group, the visceral adipose tissue (123.6 ± 49.2 , 120.4 ± 48.2), area ratio (46.0 ± 9.3 , 38.6 ± 8.7) and outer circumference (86.5 ± 8.0 , 85.9 ± 8.8) were not significantly different but subcutaneous adipose tissue (146.2 ± 61.4 , 189.0 ± 58.7), total adipose tissue (269.8 ± 95.3 , 309.4 ± 91.8), were significantly different. In calcium stone, and uric acid stone, subcutaneous adipose tissue (163.6 ± 65.9 , 163.8 ± 64.4), total adipose tissue (279.5 ± 99.6 , 299.0 ± 94.0), area ratio (41.7 ± 9.1 , 45.6 ± 10.4) and outer circumference (85.2 ± 8.2 , 86.8 ± 6.5) were not significantly different, but the visceral adipose tissue (115.9 ± 45.9 , 135.2 ± 52.4) was significantly different.

Conclusion: In man and female, subcutaneous adipose tissue and total adipose tissue in woman increases the proportion of findings showing an increase in stone incidence.

In Uric acid stone visceral adipose tissue increases the proportion of findings showing an increase in stone incidence. So, we check the central obesity and then diet, exercise, change lifestyle will help prevent the uric acid stone through reducing abdominal fat.

COI: No.

FP-03

Pregnancy decrease the incidence of stone recurrence in female patients with urolithiasis

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Background: The recurrent rate of female patients with urolithiasis after pregnancy has not been well studied. This cohort-study investigated the recurrent rate of in female stone patients after pregnancy by means of nation-wide database in Taiwan.

Materials and methods: Retrospective cohort study was applied from National Health Insurance Research Database, Taiwan. All female patients age larger than 20 years diagnosed with urinary stone before pregnancy (ICD-9-CM: 592 and 594) from 2000 to December 2012 were enrolled. The two selected samples (pregnancy cohort and non-pregnancy cohort) were from the beneficiaries of the NHI in Taiwan, and the end of follow-up is Dec. 31, 2011. The match ratio was 1:1. We recorded the stone recurrent rate after pregnancy with the initial diagnosis of stones. Control group was female stone patients without event of pregnancy during follow-up period.

Results: There were 1009 female stone patients had pregnancy after the initial diagnosis of stone disease. The average age in pregnancy cohort was 28.23 ± 5.47 and was not differed from non-pregnancy cohort (28.06 ± 5.15). The mean of follow-up was 7.89 years and 7.62 years for cohort group and compared cohort group. The recurrent rate of stone was 14.3 % (144/1009) and 22.8 % (230/1009) in the study group and cohort group, respectively. Compared with non-pregnant, pregnant were significant associate with decreasing risk of secondary calculus of kidney (adjusted HR = 0.55, 95 % CI 0.44–0.67).

Conclusion: The recurrent rate in female stone patients after pregnancy was significantly lower than female stone patients who without event of pregnancy. The cause should be further studied.

COI: No.

FP-04

The role of metabolic abnormalities in stone patients at different age groups

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Introduction: Urinary stone disease is usually seen maximum in the age group of 30–50 years. However the reason why the middle age is mostly involved in forming urinary stone is not clearly understood. This study was performed to find out the variations in the metabolic parameters in the different age groups.

Materials and methods: 1469 patients who attended the urinary stone clinic were selected for the study. They were classified into different age groups—less than 30 years, 31–59 years and more than 60 years. 24 h. urine samples of all the patients were collected in thymol and assessed for 24 h. calcium, phosphorus, uric acid, magnesium, creatinine, oxalate, citrate, sodium and potassium. Blood was collected for estimation of serum calcium, phosphorus, uric acid, magnesium and creatinine. All the differences in means of biochemical values of the three different age groups were compared using ANOVA test using the SPSS software program.

Observations: It was observed that the maximum number of patients were seen in the 30–59 years (78.7 %), followed by 22.7 % in the young age and 8.5 % in the elderly. On comparing the various metabolic factors studied, the promoters of stone formation particularly 24 h urine calcium—33 mg/day ($p < 0.001$), urine phosphorus—668 mg/day ($p < 0.01$), uric acid—389 mgs/day ($p > 0.01$), urine sodium (252 mg per day), serum calcium (11.1 mg per day) serum uric acid (5 mg/day) and urine sodium—252 mg/day ($p < 0.05$) were significantly higher in the middle age group and the variation among the groups was statistically significant. The urine oxalate—76 mg/day (NS) was also high in the group, but this was not statistically significant. Urine citrate—761 mg/day ($p < 0.01$) was least in the young age and urine creatinine—6.5 g/day ($p < 0.05$) was elevated in the elderly patients.

Conclusions: From the findings of the study, it is concluded that the metabolic parameters are different in different age groups and the changes in the metabolic parameters are likely to be responsible for increased possibility for stone formation in the 4th and 5th decades of life.

COI: No.

FP-05

Influence of sex in the metabolic parameters of stone formation

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Introduction: It is generally known that stone formation is more common in males. However the metabolic studies do not provide clear cut ideas on why the males are affected more with urinary stone disease. This paper is based on the study on 1469 patients in the stone clinic.

Materials and methods: The metabolic cause for stone formation in 1469 patients was studied during the last 5 years. They were analyzed metabolically for 24 h. urine calcium, phosphorus, uric acid, magnesium, creatinine, oxalate, citrate, sodium and potassium. Blood was

collected for the estimation of serum calcium, phosphorus, uric acid, magnesium and creatinine. The mean value was identified for the males and females and student test in SPSS software program was conducted for statistically identifying the significance of the difference.

Observations: 75 % of the patients were male. The known promoters of stone formation namely urine calcium—232 mg/day ($p < 0.001$); urine phosphorus 667 mg/day ($p < 0.001$), urine uric acid—394 mg/day ($p < 0.001$), urine oxalate—76 mg/day ($p < 0.05$), urinary sodium—254 mg/day ($p < 0.05$), serum uric acid—5 mg% ($p < 0.05$) were statistically significantly higher in the male patients. Serum calcium was slightly higher at 1.7 mg% in males but was not statistically significant. The urine creatinine, urine citrate, serum phosphorus and serum magnesium were not significantly different. The value of the urinary inhibitors namely magnesium—6.4 mg/day ($p < 0.001$) and urinary potassium 49 mg/day ($p < 0.001$) were higher in the males, both of which were statistically significant.

Conclusions: The male patients had significantly higher urinary risk factors compared to the female. Most of the values were statistically highly significant. Urinary citrate did not show any significant change. Urinary magnesium was also higher in the males. There is a definite metabolic preponderance for the male towards formation of stones.

COI: No.

FP-06

Recovery from nephrotoxicity in rats administered both melamine and cyanuric acid

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Background: Melamine was recently identified as a risk factor for renal calculi following the milk powder contamination in China. However, the long-term natural history of melamine exposure and its renal effects remain unknown. We evaluated renal function and other adverse health effects using a rat model administered melamine and cyanuric acid, considering age and sex.

Methods: Twelve male F334/N rats each of ages 6, 10, and 26 weeks ($N = 36$) were equally assigned to Group M + C or controls. Group M + C rats were administered 12 mg kg⁻¹ day⁻¹ of melamine and cyanuric acid for 28 days. Serum and urine samples and kidney sections were evaluated on day 28. Six-week-old male and female F344/N rats were administered 12 mg of melamine and cyanuric acid for 28 days. Body weights were measured weekly; on days 0, 28, 90, and 180 after the 28-day period of melamine and cyanuric acid administration, serum samples and kidney sections were obtained.

Results: Although the control group had no crystals, 6-week-old Group M + C rats had more crystals compared to the 10- and 26-week old Group M + C rats. Male rats also had significantly more crystals than females of the same age. Male rats were affected to a greater extent than females.

Conclusion: Younger rats experienced more severe renal failure and greater renal crystal deposition following melamine and cyanuric acid administration. However, after melamine and cyanuric acid administration cessation, crystal deposition and renal failure immediately improved and did not cause growth arrest. Therefore, early diagnosis of melamine-associated calculi is critical.

COI: No.

FP-07

Toward a new insight of calcium oxalate crystals in fly by nano-computerized tomography

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Background: Here, we introduce a new tool for the study of anatomical structure for fly. As consequence of technical development, the invention of micro-CT has been introduced to the small animal such as rat and mice. A new insight of internal microstructure of objects with 150–200 nm so called nano-CT allows us to check more detail structures. In another word, the structure could be seen in a nano-level.

Materials and methods: We used previously developed animal model of calcium oxalate (CaOx) crystal deposition on the Malpighian tubules of drosophila melanogaster as study animal. The lithogenic flies were breed for 3 weeks. Samples were simply prepared for further scanned by micro-CT/nano-CT, Bruker Skyscan 1272 (Kontich, Belgium) to scan samples at 0.8 μm (800 nm) resolution. CT scanning was performed at 40 kVp of voltage, 250 μA of current, 1750 ms of exposure time and without filter. Reconstruction of sections was carried out with GPU-based scanner software (NRecon). Further analysis on specific region of interests by using DataViewer software (Skyscan). Area with high HU level (>7000) was defined as CaOx deposition for further 3D analysis.

Results: Image of whole lithogenic fly was compared with control. High HU level was detected in the region of Malpighian tubules which can be identified as CaOx crystals. There was no crystal image in the control group. The image was same as human non-contrast CT for the diagnosis of stone disease.

Conclusion: Nano-CT clearly demonstrated the calcium oxalate crystals in the Malpighian tubules of fruit fly. The image system provide a new vision on study animal will facilitate further study of stone disease. With the development of new technology on nano-CT, more delicate and advanced image will be presented in the future.

COI: No.

FP-08

Pattern of crystalluria relating to severity of stone disease

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Introduction: Urinary stone formation is closely related to crystalluria pattern. Crystals are seen in some normal individuals, but presence of large number, large size, aggregation or clumping of calcium oxalate monohydrate (COM), calcium oxalate dihydrate (COD) or uric acid (UA) crystals is pathological. This paper correlates the pattern of crystalluria with severity of stone disease and clinical progress of the disease of 1200 stone patients studied in 6 years.

Materials and methods: All patients attending the stone clinic were graded as Grade A, B, C, D or E based on stone episode rate and severity. The crystalluria pattern of the patients was classified as nil (0), minimal (+1), moderate (+2) or bad crystalluria (+3, +4, plenty) of any variety. The patients were metabolically analysed for 24 h urine volume, calcium, phosphorus, uric acid, magnesium, creatinine, oxalate, citrate sodium and potassium and serum calcium, phosphorus, uric acid, magnesium and creatinine. The values were compared

between the groups. The clinical progression of the stone disease was recorded.

Observations: The extent of crystalluria did not show any statistically significant variation between the different grades of severity of stone disease. Many patients with significant crystalluria did not form repeated stones. But many patients with severe grades of stone disease had significant crystalluria. Presence of uric acid crystals was seen more to be related to uric acid stone episodes. The presence of uric acid crystals in many calcium oxalate repeat stone formers indicated relationship between uric acid crystalluria and calcium oxalate stone formation. Many patients with significant COD crystalluria, COM crystalluria or a combination of these developed recurrent stone formation and with passage of stones even when metabolic picture showed normal values.

Conclusions: It is concluded that the presence of crystals in urine is a valuable parameter to study the stone patient more than the urine and blood metabolic profile. There is no generalised correlation between the extent of crystalluria and the extent of stone disease. Further studies are required at individual crystal level to understand the relationship between the specific crystals and metabolic pattern of the stone patients.

COI: No.

FP-09

Does stone episode depend on metabolic status?

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Introduction: Several papers have been presented to explain the relationship between the metabolic parameters of the individuals and the extent of stone formation. However, it has been recognized that in several situations, the metabolic pathologies are not present, but stone formation continues unabatedly. Conversely, the metabolic abnormalities may be present in an individual, but the extent of stone formation may be very much restricted. This study was undertaken to find out whether the metabolic changes occur during periods of activities.

Materials and methods: Of the 1200 patients studied during a period of 4 years, the patients who had repeated metabolic assessments done on four different occasions or more were analysed. All patients were metabolically assessed by performing the 24 h urine volume, calcium, phosphorus, uric acid, magnesium, creatinine, oxalate, citrate, sodium and potassium and serum calcium, phosphorus, uric acid, magnesium and creatinine at times of symptomatic stone activity and at times of dormancy. The values of same patient were analysed for statistically significant variation in the values at the different times of assessment using ANOVAR in SPSS software.

Observations: There was no statistically significant difference between the biochemical parameters of patients at time of active stone disease and times of stone inactivity. Minimal though statistically insignificant higher values were observed in the urine uric acid level (674 mg/24 h against 612 mg/24 h) in the active stone group, compared to the inactive group. In the rest of the patients, there was no difference during the different periods of assessment irrespective of the presence or absence of clinical or radiological active stone formation and growth.

Conclusions: The biochemical milieu of the urine and blood did not directly involve the stone forming process. However, the metabolic profile may in some patients with idiopathic calcium oxalate stone formation have a role in the summation effect which has been

described earlier. It is concluded that the metabolic studies may be performed in the stone patients attending the stone clinic for the first time, but it is not necessary to repeat the metabolic evaluation at every attendance for individual stone episodes.

COI: No.

FP-10

Are metabolic changes different in recurrent stone formers and one time stone formers?

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Introduction: Several papers have been presented in the recent past about the role of metabolic changes in active stone formation. Stone formation is well known to be a culmination of intermittent metabolic activity of the formation of crystals—nucleation—aggregation and growth. Some patients form stones only once in a life time, whereas others have multiple stone episodes during the whole life time needing repeated stone retrievals. For understanding the metabolic profile of these patients who had high grade stone disease, this study was performed to identify the correlation between the recurrent stone formers and single episode stone formers.

Materials and methods: 1000 stone formers attending the stone clinic were classified into single episode stone formers and multiple episode stone formers. The biochemical study was performed for the 24 h urine volume, calcium, phosphorus, uric acid, magnesium, creatinine, oxalate, citrate, sodium and potassium and serum calcium, phosphorus, uric acid, magnesium and creatinine. The biochemical changes were compared between the recurrent stone formers and the one time stone formers. Student t test was performed on all the values using statistical software package SPSS.

Observations: There were 33 % recurrent stone formers and 67 % single episode stone formers in the study. On metabolic assessment, it was observed that there was no statistically significant difference in the biochemical values between the recurrent stone formers and the single stone formers in any of the urine or blood parameters studied. This indicates that biochemical abnormalities alone do not decide the actual process of stone formation in majority of the patients with idiopathic calcium oxalate stone disease.

Conclusions: Stone nucleation and growth are not directly proportional to the metabolic status of the patient. Other factors play a role in the precipitation of crystal formation and growth into macroscopic stones. The possibility of summation effect of various lithogenic factors need to be considered as causative factor in the nucleation and growth of the urinary stone.

COI: No.

FP-11

Epithelial to mesenchymal transition (EMT) in vivo and in vitro induced by calcium oxalate (CaOx) and oxalate (Ox)

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The epithelial to mesenchymal transition (EMT) is a biological process that provides a polarized epithelial cell acquiring a mesenchymal cell phenotype that will allow it to increase the capacity migration and invasion, calling it myofibroblast. Hyperoxaluria is associated with kidney stones, interstitial fibrosis, and progressive renal failure. Interestingly, bone morphogenic protein-7 (BMP-7) has emerged as an antifibrotic cytokine.

This study analyzed if oxalate (OX) and calcium oxalate (CaOx) could induce EMT in vitro in proximal tubule cells (HK-2) and in vivo in mice subjected to hyperoxaluria by offering hydroxy-proline (HPL). Additionally, tested the possible beneficial action of the BMP-7 in this event. The EMT was evaluated in vitro by phenotypic characterization, invasion, cell migration, gene expression (PCR-Real Time) and protein expression (immunofluorescence or Western Blotting) of e-cadherin, cytokeratin and α -smooth muscle actin (α -SMA) and TGF- β , its mediator (Table 1). We measured in vivo renal function, oxalate urinary concentration and the number of urinary crystals. The deposition of collagen fibers type I and III, TGF- β expression and TEM markers (e-cadherin and α -SMA), were respectively analyzed by Masson Trichrome staining, immunohistochemistry and immunofluorescence.

The results showed that HK-2 cells stimulated with Ox and CaOx decreased expression of E-cadherin, cytokeratin and increased expression of α -SMA and TGF- β . The cells acquired migration ability and cell invasion with consequent phenotypic change. BMP-7 was efficient in prevent this event. Hyperoxaluric mice exhibited impairment of renal function, urinary stone formation and increased oxalate excretion. We have also observed decreased expression of E-cadherin and increased expression of α -SMA, with deposition of collagen type I and III fibers, events that were prevented by BMP-7.

The Ox and CaOx were able to induce epithelial to mesenchymal transition in vitro and in vivo, and the TGF- β was its main mediator. BMP-7 was effective in reversing EMT phenomenon. Supported by FAPESP, CNPq, CAPES and FOR.

COI: No.

	HK-2	Ox	CaOx	TGF-b	Ox + BMP-7	CaOx + BMP-7
e-cadherin	1.02±0.15	0.11±0.04	0.35±0.03	0.09±0.07	5.64±0.52	5.04±0.52
Cytokeratin	1.07±0.29	0.04±0.02	0.05±0.02	0.10±0.01	2.75±0.22	3.86±0.60
a-sma	0.94±0.07	7.17±1.91	5.99±1.34	13.59±0.47	0.03±0.02	0.18±0.01

FP-12

Calcium oxalate monohydrate crystals in urinary stone metabolism

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Introduction: The calcium oxalate precipitates in the urinary tract initially as unstable calcium oxalate trihydrate which is seen only in renal tubules of experimental work which gets dehydrated to calcium oxalate dihydrate, that may be present in normal individuals and seen in pathological number and sizes in the urinary stone patients and calcium oxalate monohydrate (COM) which forms a definite pathology in urinary stone patients. This study was undertaken to find out the relationship between the presence of COM crystalluria and the various biochemical parameters in the urinary stone patients.

Materials and methods: 1469 patients attending the stone clinic in the last 5 years were analyzed for urinary deposits to look for the presence or absence of urinary calcium oxalate monohydrate crystals. Based on the report, the patients were classified into those with calcium oxalate monohydrate (COM) crystals and those without. 24 h.

urine of all the patients was collected in thymol and assessed for 24 h. calcium, phosphorus, uric acid, magnesium, creatinine, oxalate, citrate, sodium and potassium. Blood was collected for estimation of serum calcium, phosphorus, uric acid, magnesium and creatinine. All the biochemical values were compared between the two groups using student 't' test using the SPSS software program.

Observations: 9.8 % of the patients had COM crystalluria. It was seen that urinary magnesium and urinary oxalate were lower in the patients with calcium oxalate monohydrate crystals 5.7 mg% vs 6.3 mg% ($p < 0.05$) and 63 mg% vs 76 mg% ($p < 0.05$) respectively. It is very clearly recognizable that the patients with COM crystals were having a lower urinary oxalate. This is explained by the precipitation of the oxalate as crystals reducing the urinary levels. The urinary magnesium level also probably plays an important role in the formation of calcium oxalate monohydrate crystals. No other parameter was statistically significantly different. Urinary citrates were slightly lesser in the COM crystallurics, but not statistically significant. Renal function was not affected in COM crystalluric patients.

Conclusions: The presence of COM crystals has to be taken seriously in deciding the treatment and prophylaxis of urinary stone diseases. Metabolic abnormalities may not have a significant role in the formation COM crystals.

COI: No.

FP-13

The presence of calcium oxalate dihydrate crystals and stone metabolism

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Introduction: Calcium oxalate dihydrate (COD) crystals are normally present in 12 % of population and pathologically present in good number of urinary stone patients. The correlation between presence of COD crystalluria and metabolic abnormality in the stone forming individual has not been studied extensively. This paper intended to study the role of COD crystals in the variation in metabolic aspects of urinary stone forming patients.

Materials and methods: 1469 patients attending the urinary stone clinic were analysed for the presence of extent of calcium oxalate dihydrate crystals. Based on the observations, patients were classified into two, those with COD crystals and those without. 24 h. urine of all the patients was collected in thymol and assessed for 24 h. calcium, phosphorus, uric acid, magnesium, creatinine, oxalate, citrate, sodium and potassium. Blood was collected for estimation of serum calcium, phosphorus, uric acid, magnesium and creatinine. All the means of biochemical values were compared between the two groups using student *t* test using the SPSS software program.

Observations: It was seen that COD crystals were present in 17.7 % of the patients. On analyzing the biochemical data, it was observed that the patients who had COD crystals had significantly higher urinary calcium—238 mg/day ($p < 0.05$) urinary phosphorus—696 mg/day ($p < 0.05$), compared to the patients with no COD crystalluria. Inhibitors like urinary citrate—788 mg/day ($p < 0.05$), urinary magnesium—5.7 mg/day ($p < 0.05$) and urinary potassium—43.8 mg/day ($p < 0.050$) were significantly lesser in patients with COD crystalluria. The urine oxalate was lesser in the patients with COD crystalluria. This could be explained by the possibility that the oxalate was taken away for the formation of oxalate crystals. Interestingly, the uric acid levels in the blood and urine were not related to the COD crystalluria.

Conclusions: The presence of COD crystals in the urine is definitely related to biochemical milieu of the urinary stone patient. The presence of COD crystals may be part of the metabolic process which is responsible for the stone formation and that may be the reason for the findings of the present study.

COI: No.

FP-14

Presence of RBC in urine related to biochemical profile of stone formers

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Introduction: The presence of RBCs in urine definitely indicates either the presence of crystals or the movement of stones producing urothelial injury and then the RBCs as deposits. The present study was undertaken to assess the biochemical changes that are recurring in patients with RBCs in the urinary deposits and those without RBCs in the urinary deposits.

Materials and methods: 1469 patients were assessed for urine deposits in early morning urine samples and random samples, collected on two consecutive days and classified into two groups—those with presence of RBCs in the deposits and those without RBCs. The RBCs seen in urine as part of urinary tract infection proved by urine culture studies were excluded. 24 h urine samples of all the patients were collected in thymol and assessed for 24 h calcium, phosphorus, uric acid, magnesium, creatinine, oxalate, citrate, sodium and potassium. Blood was collected for estimation of serum calcium, phosphorus, uric acid, magnesium and creatinine. All the means of biochemical values were compared between the two groups using student 't' test using the SPSS software program.

Observations: Statistical analysis showed that there was a statistically significant difference between the biochemical values of the group having RBCs in urine and those without. The inhibitors urinary magnesium—6.5 mg % ($p < 0.05$) and urinary potassium—63 mg % ($p < 0.05$) were significantly lower in the group with RBC. The urine citrate was also lower, but the difference was not statistically significant. Serum calcium—11.6 mg% was significantly higher in the RBC group, but was not statistically significant. However, urine calcium—218 mg/day ($p < 0.05$) and urine sodium—232 mg/day ($p < 0.05$) were significantly lower in the RBC group.

Conclusions: The study indicates that the presence of RBCs in the urine may be due to the stone forming metabolic tendency of the patient. Presence of RBC in the urine of patients without definite radiological or moving stone may indicate active crystal formation in the urinary tubules of the kidney. However, RBC produced mechanically by injury to the urothelium the by the moving stone may be not the cause, but the effect of stone disease.

COI: No.

FP-15

The relevance of pus cells in urine in the metabolism of urinary stone formers

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Introduction: Presence of pus cells (PC) in the urine usually denotes urinary tract infection. However it has been observed that in several patients with urinary tract stone disease, the urinary deposit showed significant number of pus cells in the urine in the absence of proved infection by urine culture and sensitivity. It has been observed in the earlier studies that the presence and number of pus cells in the urine have been high in several patients with urinary stone disease. This study was undertaken to find out the role of urinary PC in the metabolic process of stone formation.

Materials and method: 1469 patients were studied in the last 5 years for the presence of PC in the urine and the patients were classified into two as those with PC (PC group) and those without PC (no PC group). The PCs seen in urine as part of urinary tract infection proved by urine culture studies were excluded. 24 h urine samples of all the patients were collected in thymol and assessed for 24 h. calcium, phosphorus, uric acid, magnesium, creatinine, oxalate, citrate, sodium and potassium. Blood was collected for estimation of serum calcium, phosphorus, uric acid, magnesium and creatinine. All the differences in means of biochemical values of PC group and the No PC group were compared using student 't' test using the SPSS program.

Observations: 83 % of the patients studied had PC in urine. The biochemical values of the 24 h urine and serum parameters in the two groups showed no significant difference between the PC group and the No PC group. Though not statistically significant, the promoters, urine oxalate, urine sodium, serum calcium and serum uric acid were higher in the PC group and the inhibitors urine citrate and urine potassium were lower in the PC group, though not statistically significant.

Conclusions: The findings of the study point to the fact that the presence of pus cells may be an effect of the stone and not a cause of stone disease. However more detailed studies may recognise metabolic role for PC in urine.

COI: No.

FP-16

Presence of genetic diversity in Asian and European cystinuria mutations

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Purpose: Cystinuria is autosomal recessive disease caused by a defect in the cystine transporter rBAT (SLC3A1)/BAT1 (SLC7A9). We have previously identified Japanese unique mutation; P482L, that is responsible for over 70 % of patients. Here we present the mutational analysis result of Korean and Japanese cystinuria patients and discuss about the difference between Asian and European cystinuria patients.

Material and methods: 92 cystinuria Japanese patient's blood samples were obtained, from Chiba university hospital and a collaborative hospital in Japan. Genomic Analysis data of 8 Korean patients were provided from Seoul national university under collaboration study. Mutations in rBAT/BAT1 were studied by direct sequencing. Cystine concentrations in urine were assessed by 24-h acidic urine collection.

Results: Among Korean cystinuria patients, 75 % of patients possess mutation in rBAT and 25 % of patients possess mutation in BAT1. Concerning rBAT mutation, 1820del was most frequent Korean mutation (37.5 %) but only found 1.1 % in Japanese patients, and not reported in European countries. T216 M was second common Korean mutation (25 %) but only 1.1 % in Japanese but found 71.4 % in Yugoslavian and 66.7 % in Turkish patients. 1500 + 1G>A in intron 8 was found in 12.5 % of Korean patients but not found in Japanese but found in 11.1 % of French Canadian and 2.6 % in North American patients. 1820delT and C673R mutations were only found in Japanese and Korean patients. Concerning BAT1 mutation, heterozygote exon 12 deletions were most frequent Korean mutation (37.5 %). This mutation was not found in Japanese, while found in Spanish (1.4 %), Italian (5.4 %) and German (4.4 %). Although 70 % of Japanese cystinuria patients possess P482L mutation, this mutation was only found in one (12.5 %) Korean patients. Genotype distribution of Korean patients were rather similar to European patients than Japanese patients.

Conclusions: Those data indicated the presence of genetic diversity of Asian and European cystinuria mutations

COI: No.

FP-17

Inhibitory effect of Rooibos tea on urinary stone formation in a rat model

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Objective: We have previously reported that oxidative stress plays an important role in the formation of stones in the urinary tract. Rooibos tea grows naturally only in South Africa, is a beverage rich in antioxidants. Therefore, we examined the inhibitory effect of rooibos tea on urinary stone formation in rats.

Methods: Seven-week-old Sprague–Dawley rats were divided into the tap-water group (control group, n = 6) and rooibos-tea group (treatment group, n = 6). Ethylene glycol (EG) and vitamin D₃ were administered for 2 weeks by using a stomach tube. Ten milliliters of the urine collected over 24 h was centrifuged at 1500 rpm for 5 min. Sediment was observed in using 400-fold magnification. The average number of crystals observed in 3 fields of view was measured. We compared the 2 groups in terms of the urinary excretion of calcium oxalate crystals.

Result: The amount of calcium oxalate crystals excreted in the urine of the mice administered rooibos tea was lower than that excreted in the urine of the mice administered tap water.

Conclusion: Rooibos tea possibly inhibits urinary stone formation.

COI: No.

FP-18

The effect of green tea for the early period of renal crystal formation

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Introduction: We previously suggested the involvement of renal tubular epithelial cell (RTC) injury in the pathogenesis of renal stones, and reported the importance of RTC injury for renal crystal formation. And it is reported that the green tea (GT) has a cell injury-inhibiting effect. In this study, we investigated early period of renal crystal formation and the effect of green tea.

Materials and methods: Mice treated with normal water or GT received daily intra-abdominal injection of glyoxylate (GOX) for 6 days. Animals were sacrificed and their kidneys examined before and 6, 12, and 24 h and 3 and 6 days after GOX administration. Crystal formation was detected using Pizzolato staining and polarized light optical microscopy. Immunohistochemical staining and western blotting for superoxide dismutase (SOD), 4-hydroxynonenal (4-HNE) and malondialdehyde (MDA) were performed to detect oxidative stress, lipid peroxidation, and RTC injury, respectively. Immunohistochemical staining and western blotting for osteopontin (OPN) were also performed. RTC microstructural damage and crystal nucleation were observed using TEM.

Results: In normal water-treated mice, we detected renal crystals in progressively higher numbers after 3 and 6 days but could not detect crystals after 6, 12, or 24 h. After 6, 12, and 24 h, we detected decreased levels of SOD and increased levels of MDA and 4-HNE. GOX administration increased OPN expression. TEM revealed collapse of the mitochondria and microvilli of the RTC, aggregation in the renal tubular lumen, and crystal nucleation after GOX administration. In GT-treated mice, we detected renal crystals 6 days but not after 3 days. During early period of renal crystal formation, the cell injury-inhibiting effect of GT reduced the collapse of RTC mitochondria, decreased the amount of cell debris, and delayed crystal formation. OPN expression was lower in GT-treated than in normal water-treated mice.

Conclusions: We suggest that GOX produces crystal formation by injuring mitochondria, which release free radicals that cause inflammation via OPN and injure the RTC. As a result, cell debris appears in the lumen of the renal tubule and crystals form. GT appears to inhibit this process.

COI: No.

FP-19

Febuxostat reduces calcium oxalate monohydrate crystal-induced upregulation of MCP-1 in MDCK cells

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Background: Renal cellular exposure to oxalate (Ox) and/or Calcium Oxalate (CaOx) crystals leads to the production of reactive oxygen species (ROS), development of oxidative stress followed by injury and inflammation. Renal injury and inflammation appear to play a significant role in stone formation.

Nearly one-third of patients with calcium stones have hyperuricemia. It is well known that uric acid (UA) contributes to not only UA stone formation but also CaOx stone formation.

Febuxostat is a potent nonpurine selective inhibitor of xanthine oxidase (XO), which is a critical source of ROS approved for the treatment of hyperuricemia to reduce serum urate concentration, and also has an effect to reduce oxidative stress.

Methods: Monolayers of 90 % confluent Madin-Darby canine kidney (MDCK) cells were exposed to 25, 50, 100 mM febuxostat for 12 h, and 4–67 $\mu\text{g}/\text{cm}^2$ calcium oxalate monohydrate (COM) crystals for 6 h. mRNA expression of monocyte chemoattractant protein 1 (MCP-1) was determined by real-time reverse transcription polymerase chain reaction (real-time RT-PCR) analysis.

mRNA microarray was applied to evaluate the expression of MDCK cells exposed to COM crystals and febuxostat.

RNA was isolated using a miRNeasy MiniKit (Qiagen). ssDNA was hybridized to an Affymetrix CanGene1.0 st array. Gene arrays were processed with a GeneChip fluidics station 450 and double staining was captured using a GeneChip Scanner 3000 7G.

Results: Exposure to COM crystals leads to time and concentration dependent activation of MCP-1 expression. Febuxostat suppressed time and concentration dependent decrease of the mRNA expression of MCP-1 in COM crystals treated MDCK cells.

Genes encoding for inflammatory genes were significantly up-regulated in the group, which was exposed COM crystals only, however these genes were down-regulated in the group, which was exposed both COM crystals and febuxostat in MDCK cells.

Conclusions: Febuxostat down-regulated COM crystals-induced mRNA expression of MCP-1.

Association analysis demonstrated several genes involved in the stone formation process.

Febuxostat might have a preventive effect for inflammation on renal epithelium, which plays an important role in urinary stone formation, and provide a potential therapeutic treatment for urinary stone disease.

COI: No.

FP-20

Evaluation of flavonoids of *Ziziphus Lotus L* for antiurolithiatic activities

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The species of *Ziziphus Lotus L*. is a very common shrub in arid and semi-arid region in Algeria. Fruits and leaves of this species are traditionally used for treatment of many diseases. The use of Herbal medicines and their efficacies in renal stone allowed us to study the inhibitor effect of the extract of *Ziziphus Lotus* on the inhibition of COD crystal. The objective of this study is to evaluate in vitro the activity antilithiatic of the extracts of the leaves of this shrub, by the model of turbidimetry, by means of a spectrophotometer.

The extracts are prepared with solvents of increasing polarity (Diethyl ether, Ethyl acetate, and water distilled). The comparison of turbidimetric slopes with and without inhibitor, we concluded that flavonoids have an inhibitory effect very strong, and the most polar flavonoids are most effective because of their high hydroxyl groups.

COI: No.

FP-21

Role of mitochondrial permeability transition in kidney stone formation

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Introduction and objective: We recently reported that renal tubular cell injury induced by oxidative stress and subsequent mitochondrial collapse is the initial step in the process of kidney stone formation. Recently, it was shown that the mitochondrial permeability transition (MPT) is involved in mitochondrial collapse. Cyclophilin D (CypD) is a mitochondrial matrix protein involved in MPT. Thus, we hypothesized that CypD-dependent MPT causes mitochondrial collapse and is a trigger of kidney stone formation. In this study, we investigated whether mitochondrial collapse depends on CypD and determined its relationship to kidney stone formation using CypD-deficient mice.

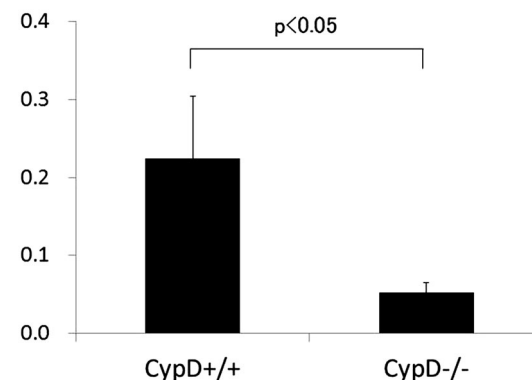
Methods: We administered 80 mg/kg glyoxylic acid, a precursor of oxalic acid, intraperitoneally for 6 consecutive days to 8-week-old male CypD-deficient mice (CypD^{-/-}, n = 6) and wild-type mice (CypD^{+/+}, n = 6). We removed the kidneys of the mice in each group 6 days after glyoxylic acid administration. Stone formation and morphology were evaluated using a polarization microscope and Pizzolato staining, and the stone formation rate was estimated using image analysis software. The form of mitochondria was observed using a transmission electron microscope (TEM). Superoxide dismutase (SOD) and malondialdehyde (MDA), markers of oxidative stress, osteopontin (OPN), a stone matrix protein, and caspase 3, a marker of apoptosis, were evaluated by immunohistochemical staining and western blotting.

Results: The stone formation rate of CypD^{-/-} mice (0.05 %) was significantly lower than that of CypD^{+/+} mice (0.22 %). Expression of MDA, OPN, and caspase 3 was lower in CypD^{-/-} mice than in CypD^{+/+} mice. Expression of SOD was higher in CypD^{-/-} than in CypD^{+/+} mice. Based on TEM observations, CypD^{+/+} mice had a disorganized internal structure and rupture of the double membrane of the mitochondria suggesting mitochondrial collapse, but such morphological changes were rare in CypD^{-/-} mice.

Conclusions: According to the results of this study, during kidney stone formation, CypD influences MPT by generating mitochondrial collapse via oxidative stress, leading to renal tubular cell injury and kidney stone formation. Thus, the mechanism of CypD-dependent MPT underlies kidney stone formation.

COI: No.

(%) The stone formation rate



FP-22

Cancelled.

FP-23

Cancelled.

FP-24**A single blind, parallel trial of L-Hydroxyproline in healthy adult subjects**

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As calcium oxalate is the most common constituent of urinary stones animal model of the urolithiasis has been established by feeding L-hydroxyproline, an endogenous precursor of oxalate. However, the influence of oral L-hydroxyproline on human urinary oxalate excretion has not been clearly demonstrated. We herein report a clinical study examining the influence of daily ingestion of L-hydroxyproline on urinary oxalate levels with a focus on measuring oxalic acid excreted in the urine.

We performed a single-blind, parallel designed study. Forty healthy subjects (20 males and 20 females, 33.4 ± 9.4 years of age, who has no history of kidney disease) were divided into 4 groups with 10 subjects in each group with same sex ratio. L-hydroxyproline doses of 0, 500, 1000 and 2000 mg were taken daily after breakfast for 12 weeks. Medical interviews, physical examinations, vital sign measurements, anthropometric measurements, blood examinations and 24-h urine sample collections were conducted every 4 weeks at the hospital. A male and two female subjects were withdrawn from this study because of pregnancy or urinary tract infection so the final number of subjects was 37. The baseline characteristics of subjects of each group were not different statistically. On the 24-h urine test, almost no markers changed, but there was a significant change in total L-hydroxyproline excretions in the 2000 mg L-hydroxyproline group compared to control group at the point of 8 weeks after first intake. Moreover, oxalic acid levels also increased significantly in the 2000 mg group at the point of 8 and 12 weeks after first intake. However, all values returned to basal values after 4 weeks from the last L-hydroxyproline intake. These results suggest that 2000 mg L-hydroxyproline daily intake might affect oxalate metabolism of healthy subjects. The metabolic significance of L-hydroxyproline is still unclear and further investigation is warranted.

COI: Yes.

COI Relation: This study was funded by KYOWA HAKKO BIO CO., LTD. Saori Akizuki, Koji Morishita and Ayako Kamimura are employees of KYOWA HAKKO BIO CO., LTD. Haruo Ito was a consultant of KYOWA HAKKO BIO CO., LTD.

FP-25**Different presentations of stone disease and metabolic status**

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Introduction: A patient is considered as a stone patient if he has a definite stone identified radiologically or a stone has been passed or retrieved. However several patients with stone disease suffer from

severe colic without evidence of large stones and significant symptomatic crystalluria. This study was undertaken to classify the different groups of stone patients and to study whether the metabolic profile of the patients was different in the different groups.

Materials and methods: 1600 patients presenting to the stone clinic were classified as five groups, A—patients who had one episode of colic or crystaluria at the time of presentation, B—patients who had recurrent episodes of colic or crystaluria without any definite stones, C—single episode of definite stone as identified by stone passage or radiological stone or stone retrieval history, D—recurrent stone formation, whereby there is one episode or more of definite stone formation along with repeated colic or crystaluria episodes and E—severe disease, meaning recurrent stone formers with stone episodes along with colic or crystalluria episodes of more than five, considered as very bad history of stone formation. The metabolic parameters of 24 h urine and blood were assessed on all the patients and in different groups, an analysis of variance performed using SPSS software to find out variations in the pattern of biochemical profile of 24 h urine and blood in the different categories of stone patients.

Observations: There was no statistically significant variability in any of the urinary or blood parameters studied in the different ranges of the risk groups as classified in the study. This indicates that the stone formation in general is not influenced by the metabolic parameters as such. They probably have a supporting role in the actual process of nucleation and growth.

Conclusion: It is concluded from the study that the risk of significant stone formation is not directly related to the metabolic aspects of urine and blood of these individuals. Possibility of summation effect of various precipitating factors should be considered as relevant to stone nucleation and growth.

COI: No.

FP-26**Urinary oxalate in relation to metabolic parameters in stone disease**

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Introduction: It is well recognised that the majority of idiopathic stones in the human urinary tract are formed of calcium oxalates. The urinary oxalate is not usually assessed, but in situations where the assessment is done, the oxalate level is recognised to be very high. This study was conducted in the urinary stone clinic in order to assess the relevance of urinary oxalate level in the metabolic status of the stone forming individual.

Materials and methods: 1469 patients were assessed for metabolic status and based on the 24 h urinary oxalate level, they were classified into three groups normo-oxaluria group (<40 mg/day) moderate hyperoxaluria group (40–80 mg/day) and severe hyperoxaluria (>80 mg/day) group. 24 h urine samples of all the patients were collected in thymol and assessed for 24 h calcium, phosphorus, uric acid, magnesium, creatinine, oxalate, citrate, sodium and potassium. Blood was collected for estimation of serum calcium, phosphorus, uric acid, magnesium and creatinine. All the variations in means of biochemical values in the three groups were compared using ANOVA in the SPSS software program.

Observations: Significant variations were observed in the study. Majority of pathological values of the promoters was observed in the severe hyperoxaluric group. The 24 h urine calcium—279 mg/day ($p < 0.001$), urine phosphorus—699 mg/day ($p < 0.05$), urine uric acid—438 mg/day ($p < 0.05$) and urinary sodium—292 mg/day ($p < 0.05$) were significantly high in the severe hyperoxaluria group. Urine creatinine—4.9 g/day ($p < 0.01$) and serum creatinine—1.7 mg% were highest in this group explaining possible maximal renal damage in this group. However, inhibitors namely urine citrate 984 mgs/day ($p < 0.01$), urine magnesium—8.4 mg/day ($p < 0.05$) and urine potassium—59 mg/day ($p < 0.05$) were highest in this group. The promoter serum parameters like serum calcium—11.4 mg% ($p < 0.05$) and serum uric acid—5.0 mg% (NS) were highest in the moderate hyperoxaluria group.

Conclusions: The level of urinary oxalate probably has a significant role to play in the nucleation and growth of urinary stones. This indicates that control of urinary oxalate is of prime importance in prevention of stone disease. Reduction of urinary oxalate can be easily achieved by administration of appropriate doses of pyridoxine.
COI: No.

FP-27

Role of serum calcium in the metabolism of stone formation

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Introduction: The calcium metabolism has been closely believed to be related to the process of stone formation. However, the recent trend in prophylaxis does not give value for the calcium metabolism. This study was undertaken to assess the relative role of serum calcium in the metabolic parameters relevant to the process of stone formation in the human urinary tract.

Materials and methods: 1469 patients who attended the urinary stone clinic were metabolically analysed. Based on the value of serum calcium the patients were classified into two groups as hypercalcaemics (more than 11 mg%) and normocalcaemics (less than 11 mg%). The 24 h urine samples of all the patients were collected in thymol and assessed for 24 h calcium, phosphorus, uric acid, magnesium, creatinine, oxalate, citrate, sodium and potassium. Blood was collected for estimation of serum calcium, phosphorus, uric acid, magnesium and creatinine. All the differences in means of biochemical values of the two groups were statistically analysed using student 't' test using the SPSS program.

Observations: 13.5 % of the total patients had hypercalcaemia. The hypercalcaemic group had significantly higher levels of urine calcium—277 mg/day ($p < 0.001$) and urine potassium 56 mg/day ($p < 0.001$). The identification of high potassium in the hypercalcaemic group is not explainable. Even though the other parameters were not statistically significantly different in the 2 groups, the promoters like urine phosphorus—680 mg/day and urine uric acid—401 mg/day were higher in the hypercalcaemic group.

Conclusions: Even though serum calcium is not proved to be primarily responsible for the initiation and growth of stone in the urinary tract, it has been surmised from the findings of the present study that the calcium levels may be responsible for the precipitation and growth of urinary stones in a small number of recurrent stone formers.
COI: No.

FP-28

Urine uric acid and metabolic profile in urinary stone formation

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Introduction: Uric acid metabolism is well known to be involved in the formation of uric acid stones. But the role of urine uric acid in the nucleation and growth of calcium oxalate stones in the urinary tract is not recognised. This study was undertaken to assess the relationship of urine uric acid level to the other metabolic factors in the formation of calcium oxalate urinary stones.

Materials and methods: 1469 patients attending the urinary stone clinic were studied and based on the urine uric acid values, classified as normouricosuric—below 600 mg/day and above—600 mg/day (hyperuricosuric) groups. 24 h urine samples of all the patients were collected in thymol and assessed for 24 h calcium, phosphorus, uric acid, magnesium, creatinine, oxalate, citrate, sodium and potassium. Blood was collected for estimation of serum calcium, phosphorus, uric acid, magnesium and creatinine. All the differences in means of biochemical values of hyperuricosuric group and normouricosuric group were compared using student 't' test using the SPSS program.

Observations: Of the patients studied, 7.5 % had urine uric acid above 600 mg/day. On comparing the mean values of the hyperuricosuric group with the normouricosuric group, it was observed that there was a statistically significant increase in the values of promoter biochemical parameters namely urine calcium—307 mg/day ($p < 0.001$), urine phosphorus—802 mg/day ($p < 0.001$), urine oxalate 103 mg/day ($p < 0.001$), urine sodium 347 mg/day ($p < 0.001$) and serum uric acid 5.6 mg % ($p < 0.05$) in the hyperuricosuric group. However the inhibitors urine magnesium—3.5 mg% ($p < 0.001$) and urine potassium—69 mg/day ($p < 0.001$) were also significantly higher in the hyperuricosuric group. The serum creatinine—2.8 mg% was also significantly higher in the group. This indicates a possible deterioration in renal function in the group of patients with hyperuricosuria.

Conclusion: Several biochemical parameters are significantly different in the normouricosuric and hyperuricosuric patients. However the inhibitor urine magnesium was higher in the hyperuricosuric group. It is concluded that uric acid metabolism is involved in the nucleation and growth of urinary stone. Hence control of uric acid is essential for the successful prophylaxis of calcium oxalate stone formers.

COI: No.

FP-29

Black stones and white stones the metabolic difference

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Introduction: Several stones are passed in the urine and several are retrieved by open surgery, interventional procedures or extracorporeal shock lithotripsy. Most of the stones are not collected and analyzed. Different methods of analysis have been utilized all over the world and the value of many is doubtful. This study was performed to see whether the external colour and appearance of stone mattered in the metabolic status of the individual forming the stone.

It was seen that the black stones were oxalate, calcium oxalate monohydrate or calcium oxalate dihydrate. The white stones could also be either of these oxalates.

Materials and methods: 235 stones of calcium oxalate predominant variety were identified and selected for the study. They were classified into white stones and black stones. They were further classified into spiculated stones and bosselated stones. The metabolic profile of the patients was studied on the 24 h urine and blood and compared in four groups—calcium oxalate monohydrate black, calcium oxalate monohydrate white, calcium oxalate dihydrate black and calcium oxalate dihydrate white. Yellow uric acid stones were excluded.

Observations: The black stones were more in calcium oxalate monohydrate rather than calcium oxalate dihydrate. When ANOVA was performed using SPSS software, there was no statistically significant variation in the pattern of biochemistry either in 24 h urine or blood between white stones and black stones and between the calcium oxalate monohydrate stones and calcium oxalate dihydrate stones.

Conclusions: It is concluded that colour of the stone may not just be due to injury produced by the spiculations of the stone as many of the black stones had bosselated surface and not spiculated surface. The colour of stones may be due to other factors rather than the injury produced by the irregular surface of the stones. Many of the black stones had white interior and white stones had black interior. As the size of the stones was very small in majority of the cases, intricate analysis of different layers was not possible. Further studies are needed in this direction to identify the clinical significance of the colour of the stones.

COI: No.

FP-30

Microplate method for measurement of urinary supersaturation to indicate stone recurrence of calcium oxalate

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Introduction: Urinary stones have an estimated lifetime morbidity of 15.1 % in males and 6.8 % in females; in other words, one out of seven males and one out of fifteen females are affected with this disease at least once in their life in Japan. The stone forming urinary environment may be conducive to spontaneous nucleation of calcium oxalate. We reported a simple and easy method using microplates to measure the metastable limit (ML), which indicate the upper limit of supersaturation dissolution. We evaluate the efficacy of the microplate method in this study.

Materials and methods: We studied 100 healthy males between 20 and 65 years of age, who have no history of urinary stone, and 40 patients of males with single stone formers (SF) and 40 patients of males with recurrence calcium oxalate stone formers (RSF). The ML by the microplate method, 200 μ l aliquots of each urine sample were treated with sodium oxalate to give final concentrations of 0–1.5 mmol. The urine samples were then incubated at 37 °C for 20 min and the minimum amount of oxalate necessary to induce nucleation detectable by inverted microscopy was taken to be the measured ML of each urine. In addition, we considered whether there was a difference in a result to a spot urine and 24 h urine.

Results: We confirmed that ML is correlated with the urinary calcium concentration in healthy subjects, SF and RSF. There was no significant difference between healthy subjects and RSF in urinary magnesium concentration, and ML was found to be correlated with urinary the concentration of oxalate and citrate acid in healthy subjects only. The microplate method was shown to valuable and useful in spot urine as well as in 24 h urine.

Conclusions: These results suggest that ML is a simple and easy way to measure the urinary calcium level and that ML could be a useful test item in outpatient settings as a convenient indicator for preventing recurrence of urinary stones in the future.

COI: No.

FP-31

Can we predict a urinary stone composition by dual energy analysis of computerized tomography?

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Objective: Recently, a qualitative diagnosis of urinary stone composition using computerized tomography (CT) scanner with dual energy (DE) sources has become possible. In the case of uric acid stones, there are few differences between Hounsfield unit (HU) values at higher voltages (135 kV) and lower voltages (80 kV). On the other hand, calcium containing stones have higher HU values at lower voltages than at higher voltages. We investigated whether DE-CT analysis was useful clinically to know urinary stone compositions.

Method: Aquilion™ PRIME (Toshiba Medical Systems) was used for DE-CT scanning. We reviewed 2,838 stones collected from 2,233 patients who underwent DE helical scanning in the process of diagnostic imaging for upper urinary tract stones. The urinary stone compositions predicted by DE-CT analysis were compared with the result of Fourier transform infrared spectroscopy (FTIR) of the delivered stones after various interventions. The stone fragments were also subjected to ex vivo DE-CT scanning if their volume was sufficient. The results of the ex vivo study were compared with those obtained from in vivo DE scanning.

Results: 448 stones were analyzed by both DE-CT and FTIR. The main stone compositions were 279 calcium oxalate monohydrate (COM), 120 calcium oxalate dihydrate (COD), 27 uric acid, 11 carbonate apatite, 4 brushite, 4 cystine, and 3 struvite. The positive predictive value for the stone estimated definitely by DE-CT analysis was 89 % for calcium oxalate stones and 85 % for uric acid stones. The correlation of HU at 135 and 80 kV of each stone was calculated. Calcium oxalate monohydrate was “HU(135 kV) = 0.663 × ”-HU(80 kV)” ($R^2 = 0.970$) and uric acid was “HU(135 kV) = 1.012 × ”HU(80 kV)” ($R^2 = 0.992$).

Conclusion: Based on the results, it is possible to know the stone compositions, such as uric acid and calcium containing stones, by DE-CT analysis before the interventions for stone removal. If we could make a definitive diagnosis of uric acid stones, the patients would receive stone dissolution therapy by urine alkalization. DE-CT analysis for the urinary stones will be useful for not only estimation of stone fragility and stone skin distance but also predicting the stone composition.

COI: No.

FP-32

Efficacy of dual energy CT on urolithiasis diagnosis and treatment

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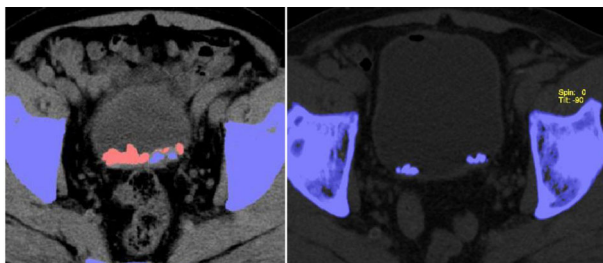
Introduction and objectives: To find out the information about the chemical composition of urinary stones is very important for treatment and prevention of stone recurrence. Recently DECT can demonstrate chemical composition and its location of mixed stones easily. From this point, we reviewed our DECT data and evaluated the efficacy of DECT on stone treatment, especially focused on uric acid stone.

Materials and methods: We retrospectively reviewed DECT data which was obtained between November 2011 and December 2015. DECT data from 101 patients with known or suspected urolithiasis were analyzed in this study. Our preliminary data showed the results of infrared spectroscopic analysis and DECT-based diagnosis were identical regarding calcium and uric acid composition. For the patients with uric acid stone or uric acid-calcium mixed stones, oral chemical dissolution therapy (potassium citrate/sodium citrate) started and the change of stone composition was monitored using DECT.

Result: Male 73 and female 28 patients were examined. Average ages of patients was 62.4 ± 14.4 year (19–91) and average BMI was 24.3 ± 4.2 kg/m² (13.7–37.3). Stone sites were bladder 18, ureter 40 and kidney 43. Average stone size was 12.3 ± 8.9 mm (2–45) and stones were located in bladder (n = 18), ureter (n = 40) and kidney (n = 43). Fifty-three out of 101 patients had biochemical stone analysis and we compared DECT stone compositional results to the results of infrared analysis. The compositional stone differentiation was correct in 52 out of 53 (98.1 %). Accuracy rate was as follows; calcium stone 97.8 % (46/47) and uric acid stone 100 % (6/6). Oral chemo-dissolution therapy generally increased urine pH from 5.0 to 7.0. Duration to achieve a stone-free status was 3–7 months. DECT for mixture stones clearly showed distribution of calcium and uric acid compositions, and distribution change with oral chemo-dissolution therapy (Figure). In this way, the situation of uric acid and calcium compositions was easily visualized by DECT.

Conclusions: DECT is able to accurately diagnose the stone from the image component and precisely demonstrate the composition distribution of urinary stones. DECT may be very useful for the treatment and prevention of stone recurrence.

COI: No.



Figures: DECT clearly demonstrated composition of the residual fragments left after transurethral cytolitholapaxy (left). After 7 months of follow-up with potassium/sodium citrates treatment, residual fragments of uric acid completely disappeared and a few calcium fragments remained (right). Red:uric acid, Blue:calcium.

FP-33

The efficacy of KUB and ultrasonography for the detection of renal stone

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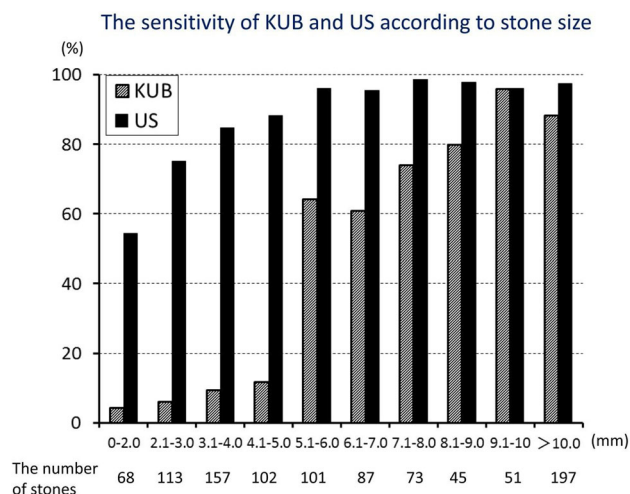
Objective: To assess the efficacy of kidney ureter bladder radiograph (KUB) and ultrasonography (US) for detecting renal stone using non-contrast enhanced CT (NCCT) as a standard reference.

Methods: From January 2012 to September 2014, 822 patients underwent KUB, US and non-contrast enhanced CT on the same day. The sensitivity and specificity of KUB and US to detect renal stone were evaluated. Whether the stones detected by KUB overlapped with those by US was analyzed. We compared the sizes of stones determined in the longest axis of KUB, US and NCCT, and performed group classification based on size to examine whether stone sizes measured by KUB, US and NCCT were similar.

Results: Of 1644 kidneys, NCCT detected at least one stone in 994 kidneys. Of those, KUB detected at least one stone in 488 kidneys, yielding a sensitivity of 49.1 % and a specificity of 99.1 %. In contrast, US detected at least one stone in 882 kidneys, yielding a sensitivity of 88.7 % and a specificity of 68.3 %. Interestingly, stones were detected in 476 kidneys by both KUB and US. Expectedly, the detection rate increased with stone size, but the detection rate for stones less than 5 mm was low in KUB. Furthermore, stone sizes obtained by KUB and US were positively correlated with those obtained by CT, and stone size measurement by KUB and NCCT were concordant in 320 (66 %) out of 488 cases, and that by US and NCCT were concordant in 620 (70 %) out of 882 cases.

Conclusion: KUB is of limited value for detecting renal stones, particularly those less than 5 mm.

COI: No.



FP-34

Changes in renal papillary density after hydration therapy in calcium stone formers

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Background: Calcium stone formers have higher values of renal papillary density compared with unaffected subjects. This phenomenon might be due to lithogenic processes leading to the deposition of calcium and formation of Randall plaques. To date, the effect of hydration therapy on renal papillary density of calcium stone formers is not known.

Methods: We enrolled 19 calcium stone formers (>50 % of the stone made of calcium salts) who were prescribed >2 L/day of a hypotonic, oligomineral water low in sodium and minerals (fixed residue at

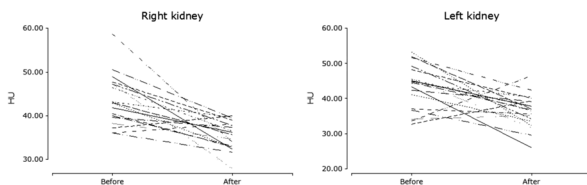
180 °C <200 mg/L) after endoscopic removal of their stones. Renal papillary density was evaluated on CT scans performed before the urological procedure and 6 months after the hydration course and expressed in Hounsfield Units (HU) as an average of 6 papillae per kidney. Differences were analyzed with the paired *t* test.

Results: Average age of the 19 enrolled patients was 56.8 ± 18.2 years, 17 (89.5 %) of whom were males. Average values of papillary density before urological interventions were 43.6 ± 5.9 HU for the right kidney and 43.4 ± 6.2 HU for the left kidney. After 6 months of hydration, average values decreased to 35.5 ± 3.3 HU for the right kidney and 36.4 ± 4.7 HU for the left kidney; the difference was statistically significant for the right kidney (average difference -8.2 HU, 95 % confidence interval [CI] $-11.6, -4.7$; $p < 0.01$) as well as for the left kidney (-7.1 HU, 95 % CI $-11.0, -3.1$; $p < 0.01$) (Figure 1).

Conclusions: In calcium stone formers, hydration therapy is associated with a significant reduction in renal papillary density. Our data suggest a potential role of hydration therapy in reducing the medullary deposition of calcium and formation of Randall plaques.

COI: No.

Figure 1. Renal papillary density before and after hydration therapy in calcium stone formers



FP-35

The clinical role of procalcitonin for urinary tract infection caused by urinary stone

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Procalcitonin is a 13 kDa 116-amino acid prohormone of calcitonin. In 1993, Assicot et al. reported increased procalcitonin concentrations in patients with sepsis and infection. Further clinical studies indicated that bacterial inflammation and sepsis, but not viral infections or autoimmune disorders, could induce high concentrations of serum procalcitonin.

Urinary tract infection in some cases can progress to urosepsis, for which the treatment options include urinary intervention. No biomarkers to determine whether a urinary intervention is indicated are currently available.

This study was carried out to determine the usefulness of serum procalcitonin concentrations as an early marker to decide upon intervention for urinary tract infection caused by urinary stone.

The subjects were 25 patients (median age: 71, male/female: 11/14) with urinary tract infection caused by urinary stone in whom we measured serum procalcitonin concentration at the start of treatment. We evaluated relation between urine culture, blood culture and serum procalcitonin concentration, and also whether serum procalcitonin concentration can be a utility index of urinary intervention (Percutaneous nephrostomy etc.). Further, we estimated whether serum

procalcitonin concentration can be a prediction factor of DIC, urosepsis.

We considered about clinical role of serum procalcitonin concentration on the treatment strategy of urinary tract infection caused by urinary stone.

COI: No.

FP-36

Effect of vitamin D supplementation on urinary calcium excretion in women with hypercalciuria

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Introduction: Adequate 25 OHD serum levels are fundamental for normal bone and mineral homeostasis. Despite this, there is resistance to correct vitamin D deficit in patients with idiopathic hypercalciuria (IH), with or without renal lithiasis (RL) because of the fear to aggravate hypercalciuria.

Objective: To evaluate urinary calcium in IH patients with and without RL after the correction of vitamin D deficit.

Materials and methods: We selected 48 women with IH (defined as an excretion of >220 mg/UCa/24 h or >4 mg/Kg); mean age 55 ± 10 years, BMI 24.3 ± 4 , with normal renal function. They were not taking medications that could affect calcium/phosphorus metabolism. All of them were receiving a diet with 0.8 to 1 gr of calcium/day. 20.8 % had renal lithiasis and 91.6 % had osteopenia/osteoporosis. 25OH Vitamin D serum levels <30 ng/dl were considered as insufficiency and levels <20 ng/dl were considered deficiency.

Results: 25 OHD levels increased from 19.8 ± 5.9 to 33.1 ± 14.3 ng/dl ($p < 0.0001$) after supplementation, while there was no change in urinary calcium. The mean dose of ergocalciferol administered was 17.451 ± 9.560 IU/week. Median follow-up was 12.2 ± 10 months.

Conclusions: Ergocalciferol administration to patients with IH, with or without renal lithiasis, corrects vitamin D deficit without increasing urinary calcium.

COI: No.

FP-37

Calcium oxalate stone formation can be prevented

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Introduction: Prevention of stone disease has not been satisfactory in any part of the world. This paper presents the experience of the authors in preventing stone formation during the last three decades.

Materials and methods: Thousands of patients with stone disease were followed up for minimum of 10 years. Metabolic investigations were done at the time of presentation and repeated occasionally. They were started on low dose prophylaxis (allopurinol 100 mg and pyridoxine 40 mg) and asked to review 2 monthly to assess the clinical status of pain and extent of urinary deposits including RBC, PC and crystals. When symptoms completely subsided and the urine was clear, the dose of drugs was appropriately reduced. If the symptoms

worsened or urine showed persistent deposits, the dose was increased to up to 600 mg of allopurinol daily and 240 mg of pyridoxine daily. Side effects if any were recorded at the time of follow up.

Observations: 96.4 % of patients had good control of the stone forming process recognized by the clearance of symptoms and absence of crystals from the urine deposits. At the end of 10 years, the stone episode rate reduced from 2.78 to 0.037. 35 % of the patients stopped drugs when symptoms were relieved and stopped coming for follow up. Of these, 16.5 % returned to the clinic with urinary symptoms or vague low abdominal pain. In them, crystalluria was significant in 65 % and radiological and ultrasonically significant stones in 7 per cent. Such patients were started on chemotherapy/chemoprophylaxis depending upon their status. In patients who become asymptomatic after the administration of drugs, urine deposits mainly RBCs, pus cells and crystals were present in 18 per cent of patients. They got symptoms and urinary deposits cleared by appropriate doses of the prophylactic regime. 3 per cent of the patients required interventional procedures.

Conclusions: It is concluded that proper metabolic assessment and appropriate prophylactic regime with varying doses of allopurinol and pyridoxine will prevent further stone formation in 96 % of the patients.

COI: No.

FP-38

Are diuretics indicated in urinary stone prevention?

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Introduction: Various diuretics are administered to stone patients for increasing the urine outflow and thus supporting the passage of stones down the ureter. The concept of administering diuretics has not been understood properly by the clinician's in general. This paper is presented to recognize the role of diuretics in management of patients with urinary stone disease.

Materials and methods: Details of 330 patients with history of administration of diuretics were recorded and studied. The type of diuretic, doses and duration of treatment were recorded. The patients were followed up for a minimum of 3 years to assess the impact of the treatment on the process of stone formation and growth and clinical symptoms.

Observations: The majority of patients were given thiazide diuretics for a long period. The other diuretics included furosemide, dityde and others. The patients were taking the drug for the long period in the 78 % of the patient. 58 % of the total patients had associated hypertension and in good number of patients, the indication for giving diuretics was not clear to the patient, as to whether the diuretic was indicated for the hypertension or the stone disease. The patients getting diuretics did not benefit in the movement down of stones in 92 % of the patients and they had to be stopped.

Conclusion: Diuretics are blindly been given for the stone patients without recognizing the scientific reasons. The scientific reasons include the administration of thiazide diuretics—hydrochlorothiazide in the dose of 12.5 mg for reducing the hypercalciuria in patients with idiopathic hypercalciuria for long periods of time. The hypercalciuric effect is recognized maximum at the dose of 12.5 milligrams. At the dose of 25 milligrams or more, the hydrochlorothiazide acts more as a diuretic than a hypocalciuric agent. The misuse of diuretics in patients with calcium oxalate stone disease can be minimized by recognizing

the role of different diuretics in the urinary system and recognizing the action of hydrochlorothiazide in calcium metabolism in specified doses.

COI: No.

FP-39

Stone clinic effect the missing factor

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Introduction: It's mentioned that the stone clinic effect is responsible for improvement of the prophylactic pattern of the urinary stone patient. Lot of discussion has gone by trying to decipher the stone clinic effect. However the urine deposits are rarely studied. What was generally described as the stone clinic effect is that the patient drinks plenty of water on the day of the visit so as to satisfy the clinician. This study was undertaken to recognize the influence of stone clinic effect on patients with urinary stone disease. The role of analysing urine deposits in every patient presenting to the stone clinic for prophylaxis or treatment has been studied.

Materials and methods: 500 patients presenting to the stone clinic were assessed for previous visits to other stone clinics in the last 2 years. The types of investigations performed during these visits and the influence of these on the patient's prophylactic pattern were recorded. The changes in the pattern of chemotherapy/chemoprophylaxis advised for the patients were recorded. The decisions taken in the stone clinic based on the urinary deposits and clinical examination were recorded.

Observations: From these patients, it was recognized that in no situation of a stone clinic, the patients were advised to have urine deposit examine routinely before meeting the clinician. The patients are generally advised to have ultrasound scan of the abdomen before the patient is attending the stone clinic. It was observed that only 5 % of the patients attending other stone clinics were asked to perform the urine deposit studies before visiting the clinician. The dose of drugs and type of treatment were not modified based on the appearances of the urinary deposit at the time of the visit.

Conclusion: Prophylaxis of the stone patient should be adjusted by the appearance of the urinary deposits on the day of assessment and multiple assessments are necessary in order to recognize stone activity in the form of blood cells and crystals in the urine deposits.

COI: No.

FP-40

Role of stone analysis in stone prevention

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Introduction: In most parts of the world, stones are passed spontaneously or retrieved. In most of the situations, the stone is lost, as the patient is not advised to collect the stones. Even if the stones are collected by the patients, most are discarded later. Even when the stone is analyzed, it is either qualitative or semi quantitative estimation to look for the presence of oxalate, phosphate and magnesium

or quantitation as calcium oxalate, calcium phosphate or uric acid. Sophisticated analysis including the scanning electron microscopy, transmission electron microscopy, Fourier Transform Infra Red spectroscopy are performed very minimally in research centres. This paper was undertaken to assess the role of recognition of stone composition in deciding prophylaxis.

Materials and methods: 640 patients who had stone analysis done were followed up for a period of 3 years for stone prophylaxis. Of these, 66 % were pure calcium oxalate monohydrate or calcium oxalate dihydrate stones. The patients were administered chemoprophylaxis using different doses of allopurinol and pyridoxine and followed up for stone incidents and metabolic profile.

Observations: It was observed that, the dose of prophylaxis was more for patients forming calcium oxalate monohydrate stones. This indicates that the metabolic background of the monohydrate stone was worse than the metabolic profile of the patients producing calcium oxalate dihydrate stones. In patients with recurrent stone formation, 23 % of the patients had variations in the composition of the stones during repeated episodes indicating that the mechanism of stone formation is variable in the same patient during the different episodes of stone disease. The stone analysis pattern was different in the different periods of time.

Conclusions: A simple stone analysis shows whether the stones are primarily calcium oxalate monohydrate, calcium oxalate dihydrate, uric acid or mixed stones. This is very important and simple for the clinician and the prevention strategy should be decided by the type of stone. Patients forming calcium oxalate monohydrate stones should be more seriously considered for prophylaxis.

COI: No.

FP-41

Problems with citrate therapy

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Introduction: The concept of stone prophylaxis had been centered on reducing the promoters and increasing the inhibitors. However, various treatment modalities have failed to prevent stone recurrence in the recent past. Citrates have been given as inhibitors for patients in most parts of the world. Citrates are blindly given to patients with proved or suspected stone problem without assessing the urinary citrate level. This study has been undertaken to assess the role of citrate in the management of patients with active stone disease.

Materials and methods: 800 urinary stone patients with active stone disease and idiopathic calcium oxalate stone formation were metabolically assessed and treated with different modes of prophylaxis, namely oral citrates alone, citrates + magnesium, citrates + magnesium + B6 (pyridoxine) and citrates along with allopurinol and pyridoxine. The patients were assessed at the end of 2 monthly intervals to a minimum of 1 year. The effect of prophylaxis was assessed by reduction in the clinical symptoms and impact on urinary deposits namely RBC, PC and crystals. The side effects of the drugs were studied.

Observations: When followed up for 1 year, 63 % of the patients discontinued the drug due to symptoms of intolerance, primarily gastrointestinal upsets and abdominal discomfort. In the patients who presented at 2 monthly intervals, there was no significant reduction in the extent of symptoms, extent of crystalluria or extent of blood components namely RBC & PC in the urine. Study of clinical and

investigative status of the patients on the different groups of treatment mentioned showed that the reduction in symptoms was present in different groups and the extent of crystalluria differed in different extents in the different groups. Alkalinisation of urine was observed in 83 % of the patients studied.

Conclusions: It is concluded from the study that citrate administration produced alkalinisation of urine but no significant reduction in the extent of RBC and PC or extent of crystalluria. Citrate administration could be beneficial in patients to increase urinary citrate. Citrates should be administered only to patients with hypocitruria. Long term treatment is not advisable as patients develop intolerance to the drug.

COI: No.

FP-42

Summation effect on stone nucleation a new concept for prophylaxis

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Introduction: Various aetiological factors are proposed as cause for initiation and growth of urinary stones, including basic biochemical parameters in blood and urine and various experimental possibilities like macromolecules, glycosamino glycans, Tamm Horsefall mucoprotein, and anti oxidants. The protocols for prophylaxis have to be centered on causative factors in individual patients. This paper has attempted to identify a simple, feasible, patient friendly and successful prophylactic modality for preventing stone formation.

Materials and methods: 1200 patients attending the urinary stone clinic in the last 5 years were investigated for identifying metabolic risk factors. Their demographic pattern, family history, geographic location and dietetic predilections were also assessed. The patients were administered prophylactic drugs and followed up for a minimum period of 5 years. The stone episode rate was compared with the pre treatment status. The metabolic factors of the patients were statistically tested using multiple regression analysis to identify the independent variables, which had influence on the stone forming factors responsible for the initiation and growth of stones.

Observation: Statistical studies of various metabolic and demographic factors correlated with the seriousness of the disease process in terms of permanent and temporary risk. It was recognised that the factors responsible for stone nucleation and growth are different in different individuals. The most important and common factors responsible for stone formation included the male sex, middle age, domicile in Gulf countries, presence of calcium oxalate dihydrate and monohydrate crystals and elevation in the urinary oxalate and uric acid levels.

Conclusion: It is concluded from the study that urinary stone disease is multi factorial in etiology. Prophylaxis should be based on individual situations, taking into consideration the relevance of each metabolic or demographic parameter identified in the individual. The findings also conclude that summation effect is the prime factor responsible for stone nucleation and growth. Stone formation can be prevented by reducing essential parameters like urinary uric acid and oxalate, which catalyze the process of stone nucleation and growth. They are primarily allopurinol and pyridoxine in combination in appropriate doses. Other drugs, though beneficial cannot be administered for long due to intolerance and side effects.

COI: No.

FP-43**Expectant management and active stone removal for asymptomatic renal stones**

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Introduction: Controversy exists as to whether asymptomatic renal stones should be treated or managed expectantly. Japanese Guidelines on Urolithiasis recommend active stone removal for the stones with growing tendency, calyceal dilation or >10 mm in diameter. The aim of the present study was to evaluate the clinical outcomes of expectant management and active stone removal for patients with asymptomatic renal stones.

Patients and methods: We retrospectively reviewed the charts of 105 patients with asymptomatic renal stones who presented between January 2010 and December 2014. Of these, 79 patients (88 stones; median stone size, 5 mm) were managed expectantly (group 1) and 26 patients (median stone size, 15 mm) underwent active stone removal (group 2). We investigated Kaplan–Meier estimates of the cumulative incidence rates of stone related event and intervention in both groups, and stone-free rate and perioperative complications in Group 2. Stone related event was defined as spontaneous passage, stone growth ($\geq 50\%$ in diameter) or the need for intervention with SWL, URS or PNL.

Results: In group 1, 11 stones (12.5 %) passed spontaneously, 6 stones (6.8 %) grew larger and 8 stones (9.1 %) were treated with SWL (7 stones) or URS (1 stone) with a median follow-up of 15.2 months. Three-year cumulative incidence rates of stone related event and intervention were 41.7 % and 16.2 %, respectively. In group 2, 24 patients (92.3 %) met the criteria for active stone removal recommended in Japanese Guidelines on Urolithiasis. Overall stone-free rate was 88.9 % following SWL (10 patients), URS (10 patients) and PNL (6 patients). Mild extravasation and postoperative fever >38 °C was observed in 1 (3.8 %) and 3 patients (11.5 %), respectively. Only 1 patient experienced spontaneous passage of residual stone with a median postoperative follow-up of 22.6 months.

Conclusions: Natural history of asymptomatic renal stones in the present study was similar to previous reports. While, minimally invasive surgery provided acceptable outcome in patients who met the criteria for active stone removal recommended in Japanese Guidelines on Urolithiasis. Our data can help patients and physicians make informed decisions regarding the management of asymptomatic renal stones.

COI: No.

FP-44**Planning of percutaneous nephrolithotomy using three dimensional computed tomography**

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Objective: To optimize the surgical procedure with the PCNL, we developed the preoperative three-dimensional (3-D) planning method for the access route in PCNL using the 3-D combined computed tomographic urography (3-D cCTU). The aim of this study was to

evaluate the feasibility and efficacy of this novel planning technique for PCNL.

Materials and methods: We conducted a retrospective study from April 2013 to Dec 2015. A total of 14 patients with complex renal stones (staghorn stone or multiple caliceal stones) planned for PCNL were included in this study. The access route for PCNL was planned by the imaging application before the operation using the patient specific 3-D cCTU. The image of skin, bone, kidney ureter, liver, spleen, and the virtual 3-D puncture line was drawn in 3D virtual field to avoid the organ injury and to access the proper renal calyx for aimed stone from the body surface. At the operation, the puncture of the PCNL was performed under combination of ultrasound and fluoroscopic guidance with image assistance of planned puncture line. The feasibility and efficacy of the 3-D planning was evaluated with the operational outcome.

Results: Median stone size was 3.5 cm (2.3–7.0), 7 of the 14 patients (50 %) had staghorn calculi. In 13 patients out of 14 patients (92.8 %), the puncture of access tract for PCNL could be achieved successfully as that was planned preoperatively. Median total operation time was 158 min and median time for planning was 58 min. There were no intraoperative or postoperative complications and patients did not require blood transfusion. Two patient (14 %) required secondary PCNL for residual stone. Based on CT examination, the complete stone clearance rate at 3 months was 71.4 %. All patients had stable renal function and unobstructed drainage at 3 months after the operation.

Conclusion: Preoperative planning of complex stone situations with 3D-CT had a significant impact on operative procedure, resulting in a low number of access punctures.

COI: No.

FP-45**Recurrence rate of the upper urinary tract stones**

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Purpose: The aim of this study is to evaluate the recurrence rate of the upper urinary tract stones.

Patients and methods: A retrospective review of the patients was performed. From April 2010 to March 2011, total of the 414 patients with upper urinary tract stones were identified and the patients were followed up to March 2015. Stone recurrence was defined as a new stone was detected after treatments or spontaneous passages.

Results: 327 were male and 87 were female. The mean age was 55 years old. There were 107 renal stones and 307 ureteral stones. Spontaneous passages were confirmed in 107 patients. 70 patients were treated by ESWL, 31 patients were treated by PCNL and 206 patients were treated by TUL. A median follow up time was 19.8 months (0–70.8). There were 97 recurrences (23.4 %) during follow up. Median interval to recurrence was 20.1 months (0.6–65). Recurrence rate was 4.5 % in spontaneous passage, 4.4 % in ESWL, 1.9 % in PCNL, 12.6 % in TUL.

Conclusions: Recurrence rate was different among the treatments. The patient treated with TUL had the highest rate of stone recurrence. This might be due to tiny fragments that could not be removed during treatment and not be detected in early period of follow up. To reduce recurrences we should try to remove all fragments.

COI: No.

FP-46**Our initial experience of endoscopic combined intrarenal surgery (ECIRS) in the Galdakao-modified supine Valdivia position**

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Purpose: To review our initial experience of ECIRS in the Galdakao-modified supine Valdivia position for upper urinary tract stone disease.

Materials and methods: We retrospectively reviewed our records of 19 patients who underwent ECIRS in the Galdakao-modified supine Valdivia position for upper urinary tract stone disease. The Guy's stone score was employed to grade the complexity of ECIRS. Patient characteristics, operative parameters and outcomes were assessed. Treatment success was defined as stone-free status or asymptomatic insignificant residual fragments <4 mm.

Results: The distribution of cases according to the Guy's stone score was 5.3 % classified as grade I, 36.8 % as grade II, 36.8 % as grade III, and 21.1 % as grade IV. All patients had single percutaneous access tracts under combined ultrasonographic and fluoroscopic guidance. 11 patients (57.9 %) required secondary procedures. Mean operative time for the primary procedure was 137.1 min with mean estimated blood loss of 379 ml. Mean hospital stay was 17.9 days. Fever (>38.5 °C) was the most common perioperative complication and 5 patients developed fever postoperatively (26.3 %). No patient required transfusion. Stone-free rate and success rate after the primary procedure were 26.3 and 36.8 % respectively. Final stone-free rate and success rate were 52.6 and 68.4 %, respectively. According to grades defined by the Guy's stone score, stone success rates were 62.5 % for grade I/II and 18.2 % for grade III/IV, respectively.

Conclusions: More than half of our cases were relatively complex, which led to lower stone-free rate and success rate than reported by others. However, our initial experience still confirmed safety of the Galdakao-modified supine Valdivia position. Further experience and improvement of the procedure are required for better outcome at our institution.

COI: No.

FP-47**Treatment of upper urinary tract stones over 2 cm in size with TUL assisted PNL (TAP)**

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Background: The aim was to retrospectively assess the results of treatment of upper urinary tract stones over 2 cm in size with TUL assisted PNL (TAP).

Methods: The subjects were 12 Japanese patients who underwent TUL assisted PNL (TAP) as an initial treatment of upper urinary tract stones over 2 cm in size and could be followed up for at least 3 months, between 2014 and 2015. Treatment effect was evaluated by ct scan at 3 months after treatment. A stone-free status or status of stone fragmentation to 2 mm or smaller was considered to indicate effective treatment.

Results: Median stone size was 29.0 mm (16–56). Access sheath was applied from upper calyces in 2 case, middle calyces in 7 cases, lower calyces in 9 cases.

Mean operative time was 278 min. At 3 months after treatment, the stone-free rate was 66.6 % (8 of 12 cases). Complications of this therapy included renal subcapsular hematoma and pyelonephritis in 1 case each.

Conclusions: Initial experience of TUL assisted PNL (TAP) seems to be an effective and safe as a treatment in patients who have renal stones over 2 cm in size.

COI: No.

FP-48**A clinical outcome of endoscopic management for 20 mm or more of large renal calculi**

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Introduction: The JUA (Japanese Urological Association) guideline recommends that percutaneous nephrolithotripsy (PNL) is most appropriate for management of 20 mm or more of the large renal stones including staghorn calculi. This is similar to the AUA and EAU guidelines. We evaluated the clinical outcome of surgical management by PNL, uretero-renal surgery (URS) for large renal calculi and the endoscopic combined intrarenal surgery (ECIRS).

Materials and methods: We evaluated a total of 73 patients who underwent PNL or URS for 20 mm or more of the large renal stones, including staghorn calculi between August 2013 and September 2015, retrospectively. We diagnosed the stone size and hydronephrosis by using Computed Tomography (CT) and X-ray. The initial treatment was performed by PNL or URS in all cases. We retrospectively examined the operation time and the complications of intraoperative and postoperative. The stone free was defined as less than 4 mm fragments after the treatments.

Results: The median stone length was 39.0 mm in the PNL group (n = 33) and 24.2 mm in the URS group (n = 40) (p < 0.0001). The median operation time in each groups was 148.5 min and 152 min (p = 0.839). Thirty-eight cases (52.1 %) were necessary for the concomitant secondary management, including 18 cases were performed by PNL and 7 cases by the ECIRS. The URS and the shock wave lithotripsy (SWL) were 15 cases and 5 cases. Intraoperative complications were 4 cases (12.1 %) in the PNL group and 2 cases (5.0 %) in the URS group (p = 0.399). Postoperative fever was 23.3 % of all cases, was no significance in both groups. All of them were cured immediately by receiving antibiotics. Stone free rate (SFR) of all cases was 81.0 % and all ECIRS for secondary management was 100 %.

Conclusion: This study showed that there was no significant difference between the PNL and URS for the operation time and the complications of intraoperative and postoperative for large renal calculi. We should select the initial management method for the large renal calculi according to the individual case. Furthermore, the ECIRS was the most appropriate for secondary management, because of improvement of the SFR for the large renal calculi.

COI: No.

FP-49

Comparison of percutaneous nephrolithotripsy and retrograde intrarenal surgery for renal stone with a diameter of 20 to 40 mm

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Objective: For renal stone larger than 20 mm, percutaneous nephrolithotripsy (PCNL) is considered to be a first-line treatment. According to stone and patient characteristics, retrograde intrarenal surgery (RIRS) with flexible ureteroscope or shockwave lithotripsy (SWL) become an alternative treatment options. We retrospectively evaluated the efficacy and safety of PCNL and RIRS in management of renal stones 20–40 mm in diameter.

Patients and methods: Between January 2008 and February 2015, Of patients with renal stone 20–40 mm, 35 were treated with PCNL, 48 with RIRS. The average age of the patient was 57.4 years (31–88). There were 58 male and 25 female patients. Stone-free rate (SFR) was defined as no residual stone or stones ≤ 4 mm on CT or KUB.

Results: Mean stone size of the PCNL group was significantly larger than that of the RIRS group (39.6 mm vs. 31.7 mm, $p < 0.05$). SFR after single procedure was achieved in 37.1 % of patients for the PCNL group and 39.6 % of patients for the RIRS group, respectively. Because of residual stones, one patient of the PCNL group needed the same operation, and 2 patients in the RIRS group. SWL was performed for 21 patients in the PCNL group, for 26 patients in the RIRS group. Final SFR was 94.3 % in the PCNL group and 91.6 % in the RIRS group. SFR for preoperative stone size of 20–30 mm and 31–40 mm was 93.8 and 94.7 % in the PCNL group, 97.1 and 76.9 % in the RIRS group, respectively. In terms of postoperative complications, blood transfusions were needed in one patient in the PCNL group. Ureteral injury in one patient of the RIRS group was conservatively treated by ureteral stent. Fever (≥ 38.0 °C and consecutive 3 days) occurred in 8 patients of the PCNL group and 3 patients of the RIRS group.

Conclusion: Our study suggests that RIRS for renal stone 20–40 mm has a low complication and SFR comparable to PCNL. Especially for selected patients with renal stone 20–30 mm, RIRS can be an effective alternative to PCNL.

COI: No.

FP-50

Wideband doppler ultrasound-guided mini-endoscopic combined intrarenal surgery as an effective and safe procedure for management of large renal stones: a preliminary report

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Objectives: To evaluate the efficacy and safety of wideband doppler ultrasound-guided mini-endoscopic combined intrarenal surgery (mini-ECIRS) for large renal stones.

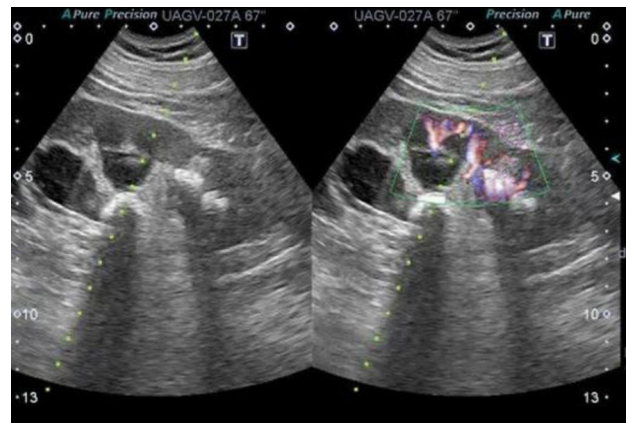
Methods: From January 2013 to September 2015, this study included forty-one patients with large renal stones (>30 mm) who were

performed mini-ECIRS using retrograde flexible ureteroscopy and miniature nephroscope by wideband doppler ultrasound guidance in modified valdivia position. Surgical parameters, including stone free rate (SFR), operative times, modified Clavien grade complications, especially related with hemorrhagic complications, and hemoglobin drop were recorded and analyzed. A comparison was made using univariate analysis to determine risk factors that affected hemoglobin drop ≥ 1 g/dl.

Results: Mean stone size including 41.4 % staghorn calculus was 45.5 ± 14.7 mm. Percutaneous accesses into calices using wideband Doppler ultrasound were successful in all cases. Mean total operative time was 148.4 ± 51.3 min. Mean mini-ECIRS time (from first percutaneous puncture to end of procedure) was 106.2 ± 36.0 min. Initial stone free rate was 73.2 % ($n = 30$). Final stone free rate after auxiliary treatment was 97.5 % ($n = 40$). Hemoglobin drop was 0.54 ± 0.65 g/dl. 3 post-operative minor complications (7.3 %) occurred. On univariate analysis, there were no significant risk factors on hemoglobin drop ≥ 1 g/dl.

Conclusions: Wideband Doppler ultrasound guided mini-ECIRS is beneficial, versatile, and safe treatment option for large renal stones >30 mm in size. Especially, visualizing vascular flow and running of blood vessels in real time according to Wideband Doppler ultrasound may decrease bleeding and hemorrhagic complications.

COI: No.



FP-51

Successful removal of a staghorn calculus by mini-endoscopic combined intrarenal surgery in a child

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Introduction: The incidence of pediatric urolithiasis has been increasing by 6–10 % annually over the past two decades, and the associated morbidity and recurrence rate are considerably high. Urogenital abnormalities and metabolic disorders are some of the causative factors of pediatric urolithiasis, and medical management of pediatric urolithiasis has been widely developed. Less-invasive therapy for pediatric urolithiasis is available because of the miniaturization of equipment and improved optical techniques; however, surgical treatment strategies, especially for large calculi, remain controversial, not only because of the variable success rates but also because of postoperative complications, such as the need for

transfusion and decreased renal function. Here, we describe the case of a 2-year-old boy with a left renal staghorn calculus who was treated with a single session of mini-endoscopic combined intrarenal surgery (ECIRS) in the prone split-leg position with pre-ureteral stenting and the directional enhanced flow imaging ultrasonography.

Case: A 2-year-old boy presented with a left renal partial staghorn calculus measuring 27 × 15 mm. The patient did not show any metabolic risk factors, such as hypercalciuria, hyperoxaluria, hypocalciuria, or cystinuria, as per the results of a 24-h urine examination. We used directional enhanced flow imaging ultrasonography (D-eFLOW), which enabled successful renal puncture of the lower calyx. We performed mini-ECIRS using a 7.5/8.4 Fr flexible ureteroscope (URS) and 18 Fr mini-percutaneous nephrolithotomy (PCNL) tract (Karl Storz). For fragmentation, a 200- μ m holmium:YAG laser fiber and lithoclast lithotripsy with a 12-Fr mini-nephroscope were used for retrograde intrarenal surgery (RIRS) and mini-PCNL, respectively. Retrograde irrigation washed small fragments through the sheath. In addition, all stones were completely removed during this single session without any major intra- and postoperative complications.

Conclusion: To our knowledge, ours is the first case of successful mini-ECIRS in a child. Novel techniques for secure renal puncture and effective fragmentation using D-eFLOW and URS not only increased the success rate of the surgery but also avoided postoperative complications. We believe this technique provides an important therapeutic option for a large renal calculus in pediatric patients.

COI: No.

FP-52

Impact of preoperative stenting to flexible ureterorenoscope on outcomes and patient quality of life

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Introduction: Technical improvements and introduction of disposables have led to an increased use of flexible-ureterorenoscope (f-URS) for both, renal and ureteral stones. We evaluated the effect on the outcomes and patient quality of life (QOL) by placement of a preoperative stent.

Materials and methods: The patients were divided into two groups depending on whether they had a stent placed before f-URS. 15 patients, pS (–) who had not a stent placed f-URS, and 13, patients pS (+) who received preoperative stent placement. pS (+) group placed a Boston Scientific, MA 6Fr Percuflex Plus Stent®. F-URS with the ureteral access sheath Navigator® 13/15Fr (Boston Scientific, MA). Stones were fragmented with holmium: YAG laser using ureteroscope type5 (Olympus, Tokyo). The follow-up examination included a noncontrast enhanced computed tomography scan 4 weeks later. The stone-free rate was defined as the complete clearance of stones or fragments <4 mm. The Ureteral Stent Symptom Questionnaire (USSQ) was administered to pS (+) group before and after 1–2 weeks the ureteral stent placement.

Results: The mean stone size was 10.3 and 11.8 mm in the pS (–) and pS(+) groups, respectively. The mean operative time was no difference between pS (–) and pS (+) (121.5 vs 117.8 min). The overall stone-free rate 4 weeks after procedure was 93.3 % in the pS (–) group and 92.3 % in the pS (+) group. Acute pyelonephritis, which is one of the complication after f-URS was developed 13.3 and 7.7 % in the pS (–) and pS (+) groups. pS (+) was associated with residual sensation and hematuria in USSQ.

Conclusions: Preoperative ureteral stents can complete URS for reduce the operator of stress with a good viewing. However, some

patients acknowledge the decline of QOL and urinary tract infection by ureteral stent placement. Routine stent placement is not necessary before all f-URS procedure, but we have demonstrated that it is associated with passive ureteral dilation, however preoperative ureteral stents have also been associated with hematuria and urinary tract infection.

COI: No.

FP-53

Effectiveness of preoperative stenting with flexible ureterorenoscopic lithotripsy for renal stones

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Introduction and objectives: Flexible ureterorenoscopy (fURS) with Ho:YAG laser can be performed safely and effectively for renal stones. However, ureteral stenosis sometimes make it difficult to approach renal stones at first attempt. Placement of a preoperative stent may enhance stone clearance by dilating the ureter to facilitate both access and stone removal. The aim of this study is to evaluate effectiveness of fURS and preoperative stenting for renal stones.

Method: From January 2010 to March 2015, we retrospectively reviewed the records of patients treated with fURS for renal stones at our institution, and analyzed about the age of patient, stone characteristics (size, number, operating time, presence of ureteral stent before and after fURS, and stone-free rate. Stone-free is defined as no stones or less than 2 mm fragment after fURS.

Result: There were 77 patients (46 men, 31 women), and 146 renal stones were treated with fURS. The median age of patients was 60 years old. The median stone size was 8 mm (2–30 mm). The mean operating time was 108 min (18–214). The rate of presence of ureteral stent before fURS was 71.4 % (55/77). The totally success rate of fURS was 92.2 % (71/77). Preoperating stenting group tend to reduce operating time, despite total amount of stones is larger than preoperative no stenting group. We could approach for renal stones with fURS first attempt in all patients in preoperative stenting group. However, 5 patients, who were in preoperative no stenting group, we could not approach renal stones at first attempt due to ureteral stenosis and finished with ureteral stenting.

Conclusion: Flexible ureteroscopic lithotripsy for renal stones can be performed with a high success rate. Preoperative stenting is an effective and safe method in managing renal stones with fURS.

COI: No.

FP-54

The evaluation of urination-related QOL after ureteroscopic lithotripsy with indwelling the ureteral stent: loop tail stent vs pig tail stent

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Background and purpose: We evaluated the urination-related QOL at early postURSL for upper urinary calculi with indwelling the ureteral stent. Therefore we aimed to evaluate the effect of the type of stent used on urination-related QOL.

Patients and methods: Of 135 patients who underwent URSL between May 2014 and March 2015 in our hospital, 70 patients in whom the stent tail was left inside the bladder without crossing the midline and answered to a questionnaire (Core Lower urinary tract Symptoms Score, CLSS) on pre- and postoperative urination-related QOL were retrospectively analyzed.

Results: The number of men was 42 and women was 28, the median age was 63 years. A significant symptom aggravation was observed for five CLSS items: nocturia ($P = 0.006$), urgency ($P = 0.01$), urgency incontinence ($P = 0.03$), bladder pain ($P = 0.0001$), and urethral pain ($P < 0.0001$) between pre- and postURSL. Comparing Loop tail stent and Pig tail stent, patients stenting loop tail stent improved significantly bladder pain ($P = 0.03$) more than Pig tail stent at post URSL.

Conclusions: Stenting a Loop tail stent improved the urination-related QOL rather than a Pig tail stent at early postURSL.

COI: No.

FP-55

Relationship between infectious fever and clinical parameters following percutaneous nephrolithotomy (PNL)

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Objective: Percutaneous nephrolithotomy (PNL) is widely used procedure especially in larger renal stone.

In many cases infectious stone was found in PNL patients, therefore infectious complication should be considered after operation. The aim of this study was to analyze which patient should be enrolled to prior administration of antimicrobial agents for patients who received PNL.

Materials and methods: We retrospectively reviewed the records of 25 patients with renal or ureteral stones who underwent PNL in the modified Valdivia position in our hospital between November 2012 and January 2015. Three days (in total 7 administrations) of antimicrobial prophylaxis (AMP) was postoperatively performed using cephalosporin in second generation, and no administration prior to PNL was performed. Fever is defined as more than 38 degree centigrade. Relationship between fever and several clinical parameters regarding PNL was statistically analyzed.

Results: The mean age, stone size, stone burden and operating time was 55.6 ± 11.2 years, 25.1 ± 10.8 mm, 457.7 ± 460.7 mm² and 161.2 ± 27.5 min, respectively. Fever was observed in five patients (20 %). In four of five patients urine culture showed more than 10^4 /ml.

More patients with urine culture more than 10^4 /ml ($p < 0.01$) or diabetes mellitus ($p < 0.01$) were significantly subject to infectious fever.

Conclusion: Our study suggested that it may not be necessary for patients with urine culture less than 10^4 /ml or without diabetes mellitus to be administered AMP prior to PNL.

COI: No.

FP-56

Prevention of postoperative high fever of transurethral lithotripsy after treatment of obstructive pyelonephritis due to ureteral stone

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It is important to prevent complications such as high fever after transurethral lithotripsy (TUL). Especially, in case of TUL after treatment of obstructive pyelonephritis due to ureteral stone, the incidence of postoperative high fever and sepsis is higher. In our hospital, for prevention of postoperative high fever, we have taken strategy as follow from 2013 (1. operating time <120 min, 2. selection of appropriate antimicrobial agents against preoperative urine culture, 3. without using pumping system as possible to prevent an increase in renal pelvic pressure). We investigated for changes in the incidence of postoperative high fever.

Between January 2011 and December 2015, TUL was performed in 55 patients who were treated for obstructive pyelonephritis due to ureteral stone. We divided into two groups that TUL was performed from 2011 to 2012 (Group A; 26 patients) and from 2013 to 2015 (Group B; 29 patients). There was no significant difference in age, sex, stone location and stone diameter between group A and group B. Median operating time was 86 min and 66 min, and stone free rate was 80.8 % and 75.9 % in group A and B. However, the incidence of postoperative high fever was 53.8 % and 24.1 % in group A and group B.

In conclusion, stone free rate was slightly reduced, but we could dramatically reduce the incidence of postoperative high fever. These strategies are important to prevent postoperative high fever of transurethral lithotripsy after treatment of obstructive pyelonephritis due to ureteral stone.

COI: No.

FP-57

Two cases of reduced port laparoscopic pyeloplasty concomitant with pyelolithotomy

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Abstract: Recently, a number of cases of reduced port surgery has been performed in the field of urology. This report describes our experience of two cases of ureteropelvic junction obstruction (UPJO) complicated with renal stones for which reduced port laparoscopic pyeloplasty concomitant with pyelolithotomy were performed.

Case1: A 12-year-old boy who presented with gross hematuria after playing soccer. Ultrasonography and CT scan, showed left hydronephrosis and renal stones. Diuretic renogram was also performed, and UPJO was detected.

Case2: a 24-year-old male in whom left hydronephrosis and kidney stones were detected during a detailed examination for hematochezia. The case also showed an obstructive pattern by diuretic renogram. We

decided to perform pyeloplasty because the both cases had symptomatic hydronephrosis and obstructive pattern by diuretic renogram.

Operation: The procedure was started with an umbilical incision, placement of an EZ-Access, and insertion of two 5-mm ports. For Case 1, operation was performed with the intraoperative addition of one 3-mm port and two 2-mm ports. For Case 2, operation was performed with the intraoperative addition of two 3-mm ports. A flexible cystoscope was inserted via the EZ-Access into the renal pelvis. The kidney stones were crushed using a Ho-YAG laser. Then the stone fragments were removed using a basket forceps. Subsequently, pyeloplasty was performed using the Anderson-Hynes method. No intra-operative or post-operative complication was observed in both cases. Furthermore diuretic renogram after pyeloplasty showed improved UPJO in the both cases. The both cases have progressed favourably after the operation because of no recurrence of hydronephrosis or renal stones.

Conclusion: Reduced port surgery produces excellent esthetical outcomes and also can perform safety pyeloplasty concomitant with pyelolithotomy. The technique can be regarded as beneficial especially for young patients.

COI: No.

FP-58

Surgical outcomes in laparoscopic lithotomy for upper urinary tract stones

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Introduction and objectives: Percutaneous nephrolithotomy (PCNL) is currently considered the first-line treatment in the management of large renal stones. Although the better surgical results, there is also greater risk for significant morbidities such as bleeding than other less invasive modalities. Recent several studies reported laparoscopic pyelolithotomy is comparable to PCNL in terms of surgical outcomes for removing renal stones. We evaluated the surgical outcomes in laparoscopic lithotomy (LL) for upper urinary tract stones.

Methods: Between November 2011 and April 2015, 19 patients underwent LL for upper urinary tract stones. Patients were placed in the flank position under general anesthesia. Procedures were performed by both transperitoneal approach and retroperitoneal approach. The renal pelvis and ureter were exposed and incised using scissors, and the stone was removed using the grasping forceps. The collecting system was observed through the trocar using a 5.3-Fr flexible ureteroscopy or 8.1-Fr flexible cystoscopy. After double-J stent insertion, the ureterotomy incision was closed with 4/0 monofilament sutures. Patients with ureteropelvic-junction-obstructions (UPJO) were performed Anderson-Hynes dismembered LP.

Results: In 19 cases, pure LL was performed in two cases and LL and LP were performed in 17 cases. Mean operative times were 248 (194–325) min. Mean estimated blood loss was small amount and there was no intraoperative complication. The median number of the stones were 2 (1–20). Median maximal stone's diameters were 7 (3–25) mm. Stone-free rate were 73.7 %. Unsuccessful cases were all renal stones. 2 cases were not able to grasp the stone by forceps due to the small size and 1 case was not able to slip through the infundibulum.

Conclusions: LL is an effective and safe modality for managing upper urinary tract stones. UPJO accompanied renal stones are good indications of LL and LP simultaneously.

COI: No.

FP-59

Clinical usefulness of presepsin in obstructive acute pyelonephritis due to upper urinary calculi

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Introduction and objectives: Presepsin may be useful in identifying patients with sepsis and its diagnostic superiority has been confirmed by several preliminary studies. Obstructive acute pyelonephritis (OAPN) is not uncommon, and often causes serious conditions including systemic inflammatory reaction syndrome (SIRS) and disseminated intravascular coagulation (DIC). We assessed the clinical usefulness of presepsin in patients with OAPN associated with upper urinary tract calculi.

Methods: We prospectively studied 14 patients with OAPN due to upper urinary tract calculi who were admitted to our hospital. Emergency drainage for decompression of the renal collecting system was performed in all cases. The materials at baseline were collected before the drainage. A diagnosis of DIC was made based on the diagnostic criteria of the Japanese Association for Acute Medicine. We assessed the occurrence of SIRS and DIC during treatment period of OAPN.

Results: Overall, 8 patients (57 %) showed SIRS, and 2 (14 %) patients showed DIC. There were no significant difference in various patient characteristics and blood biochemical parameters at baseline, including presepsin, between SIRS and non-SIRS groups. Presepsin and serum creatinine at baseline in DIC group showed significantly higher than that in non-DIC group ($p = 0.03$ and $p = 0.04$, respectively). However, there were no significant difference in conventional inflammatory biomarkers at baseline, including CRP and procalcitonin, between DIC and non-DIC groups.

Conclusions: This results suggest that presepsin might be useful for prediction of DIC in patients with OAPN due to upper urinary calculi, however further studies will be needed to confirm this issue.

COI: No.

FP-60

Clinical implication of intraoperative stone culture in transurethral ureterolithotripsy

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Objectives: To evaluate the correlation between preoperative urine culture (UC) and intraoperative stone culture (SC) and the impact of SC findings on clinical decisions.

Methods: Preoperative UC and intraoperative fragmented SC were prospectively obtained in all patients undergoing transurethral ureterolithotripsy between January 2015 and November 2015.

Results: The study group consisted of 62 patients. Of these 62 patients, 39 (62 %) had sterile UC and SC results. Both urine and renal stones were colonized in 12 patients (19 %); in 2 of them, the UC and SC showed different pathogens. A colonized SC associated with a sterile UC was found in only 2 patients. Five patients (8 %) had postoperative pyelonephritis, and the UC and SC showed same pathogens in all 5 cases. Positive SC was significantly more prevalent in cases with preoperative treatment for urinary tract infection (UTI)

than cases not required for UTI treatment ($p < 0.001$). The positive SC cases showed significantly high value of CRP than the negative SC cases ($P < 0.01$). The postoperative pyelonephritis cases had significantly high grade hydronephrosis than the cases with no postoperative pyelonephritis ($P = 0.04$).

Conclusions: Case histories of preoperative UTI treatment and high value of CRP suggest positive SC. High grade hydronephrosis is a risk factor of postoperative pyelonephritis in SC positive cases.

COI: No.

FP-61

Effect of *Oxalobacter formigenes* colonization on urinary oxalate excretion

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Kidney stones are a disease of worldwide prevalence with significant public health implications. About 60–80 % of stones are composed of calcium oxalate (CaOx). Hyperoxaluria is a major risk factor. *Oxalobacter formigenes* (*OF*), a member of the human colonic microbiota, plays a major role in net colonic oxalate absorption and secretion. We now report *OF* colonization rates in a young healthy population, the stability of colonization, the effects of antibiotic treatment, and *OF* colonization on urinary oxalate (Uox) excretion.

We followed 64 healthy subjects tested for *Helicobacter pylori* (HP), who were treated with antibiotics (amoxicillin and clarithromycin for 2 weeks) for HP eradication. Using species-specific PCR, we tested for *OF* colonization at baseline and at follow-up. Urine samples 3 h after a low oxalate standard meal were analyzed for Uox, factored for urine creatinine (Cr).

Of the 65 subjects (M/F: 23/42; mean age 25.2 ± 5.7 years) tested for *OF*, 28 (43 %) were positive at baseline. Of 7 *OF* + subjects at baseline, subject to HP elimination, 6 became *OF*-negative at 12 wks, only 2 reverted to positive at week 24, and 4 patients remained negative at follow up (Mean 22.5 ± 4.2 weeks). Of 18 untreated positive people with follow assessments, 16 (89 %) remained positive at follow up (Mean 23.0 ± 4.2 week), but of 24 untreated negative subjects, only 3 (12 %) were positive at follow up (mean 20.2 ± 6.8 weeks), significantly fewer than the untreated positives ($p = 0.001$ by Fisher exact test).

We tested Uox/Cr in 137 samples from 46 subjects with no antibiotic exposure at different time points. We found that the presence of *OF* was associated with 14 % lower Uox/cr as compared with its absence (17.0 ± 0.0 vs 19.4 ± 0.1 mg/g, $p = 0.04$).

We conclude that *OF* colonization status remains stable over a follow-up period of several months, with antibiotics suppressing colonization in the majority of people in the short term. The differences in urinary oxalate levels with respect to *OF* status is consistent with its protective effects for the prevention of calcium oxalate kidney stones.

COI: No.