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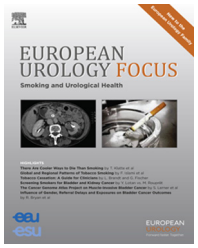

Clinical Trial Update – Stone Disease

The Swiss Kidney Stone Cohort: An Observational Study to Unravel the Cause of Renal Stone Formation

Beat Roth [a,*], *Olivier Bonny* [b],
on behalf of the Swiss Kidney Stone Cohort Investigators [†]

[a] *Department of Urology, University of Bern, Bern, Switzerland;* [b] *Nephrology Service, University of Lausanne, Lausanne, Switzerland*

Nephrolithiasis is a worldwide health care problem with a current lifetime risk of 18.8% in men and 9.4% in women in Western countries [1]. The incidence and prevalence of renal stone disease are increasing globally, irrespective of age, sex, and race [1,2]. Without a specific treatment, 5-yr and 20-yr recurrence rates are 40% and 75%, respectively [3,4]. In the USA, hospitalizations, surgery, and lost work time associated with kidney stones cost more than 5 billion USD annually [5]. Many factors predispose to the development of urinary stones, among which genetic variants and environmental conditions—especially dietary factors—are the most relevant leading to changes in urine (eg, excretion of citrate, oxalate, urate, sodium, phosphate, and calcium). In addition, supersaturation in urine plays a crucial role in the development of urinary stones [6–10].

To date, comprehensive epidemiological and genetic data on stone formers is sparse or even lacking. Medical evaluation of stone formers is widely underused [11]. A program aimed at better understanding of the development of urinary stones and prevention of recurrent stone formation is therefore appealing to establish a cause and effect association.

The Swiss Kidney Stone Cohort (SKSC), sponsored by the National Center for Competence in Research of the Swiss National Science Foundation (www.nccr-kidney.ch) was launched in 2014. It is a prospective observational cohort that aims to cover the whole of Switzerland. The SKSC is based in the five Swiss university hospitals (Basel, Bern, Geneva, Lausanne, and Zurich). The cohort includes recurrent stone formers or first-time stone formers with additional risk factors (Table 1). Patients undergo a baseline and several follow-up evaluations (after 3 mo and yearly thereafter). Patient evaluation consists of socioeconomic data, stone composition analysis, standard chemical and hormonal urine and blood analysis (2 × 24-h urine collections), analysis of crystalluria (quantitative and qualitative), food intake assessment (Food Frequency Questionnaire and EPIC-Globodiet structured recall interview by a trained dietician), physical activity assessment, and pulse-wave velocity in some centers. Samples of serum, plasma, and urine are stored in a biobank at each visit. Investigators record the data using a web-based application. All metabolic samples are analyzed by a unique central laboratory.

The study plan foresees a target number of 1000 patients with a follow-up of at least 3 yr. After an initially slow starting phase, recruitment of patients has increased steadily. So far, more than 420 patients have been enrolled and some of them have already been followed up for up to 2 yr (Fig. 1). The cohort should reach 1000 patients by 2020, with consequent last visit by the last enrolled patient in 2023. At the end of 2016, it was decided to add a urolithiasis-naïve control group of 250 subjects.

With more than 400 patients enrolled so far, SKSC has reached a critical number that allows further scientific studies and can start to answer unsolved questions in the field. Therefore, the collected data and biological samples are now available for studies or collaborations. Two calls for scientific projects have already been launched, and others will follow. The calls are open to access the SKSC data and samples, but no additional funding is provided and

* Corresponding author. Department of Urology, University Hospital Bern, CH-3010 Bern, Switzerland. Tel. +41 31 6323621; Fax number: +41 31 6322180.
E-mail addresses: urology.berne@insel.ch, beat.roth@insel.ch (B. Roth).
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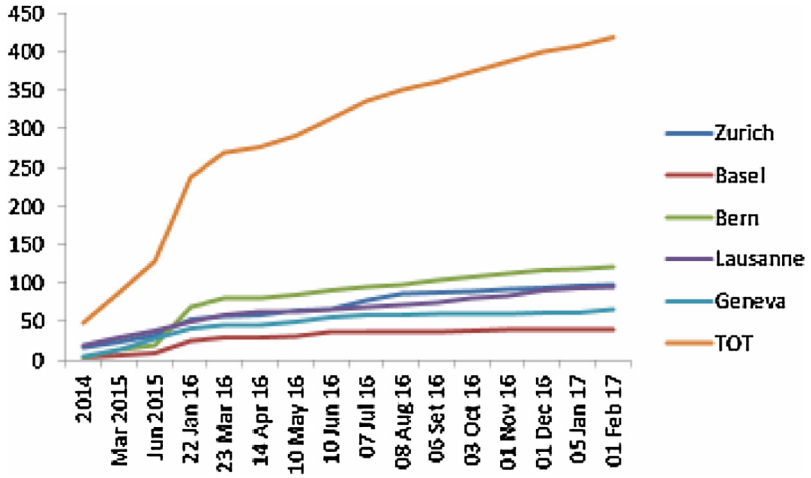

Fig. 1 – Number of patients included in the Swiss Kidney Stone Cohort for each of the five university hospitals and the total (TOT) over time.

Table 1 – Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criterion
• Signed informed consent	• No signed informed consent
• Male or female	
• Age >18 yr	
• Recurrent kidney stone events (more than 1)	
• Single kidney stone event with at least one of the following risk factors:	
– First event at age <25 yr	
– Positive family history	
– Non–calcium oxalate stones	
– Gastrointestinal disorders (eg, gastric bypass surgery, inflammatory bowel disease)	
– Osteoporosis	
– Nephrocalcinosis	
– Single kidney	
– Event during pregnancy	
– Gout	
– Metabolic syndrome	
– Residual intrarenal stones (>3 mo after stone treatment)	
– Bilateral or multiple stones	
– Chronic urinary tract infection	
– Chronic renal failure (estimated glomerular filtration rate <60 ml/min)	
– Kidney transplant	

investigators must secure their own budget. Two projects based on data already available have been accepted so far; one of these is evaluating the effect of shockwave lithotripsy on urinary pH, and the other is comparing food intake between the SKSC and a general population using food frequency questionnaires.

Partial data from the SKSC have already been presented at the 2016 and 2017 annual meetings of the European Association of Urology. Addition of a stone-naïve control group has considerably widened the field for relevant clinical and translational studies and will facilitate basic research in genetics, the molecular and cell biology of kidney stone formation and related diseases, and epidemiological and even interventional studies in the field of kidney stone disease.

Another major advantage of a nationwide running cohort is an established infrastructure and a standardized patient work-up in all centers, which sets the scene for multicenter interventional studies. The NOSTONE trial is the first study that is using the SKSC platform. NOSTONE (starting enrollment in March 2017) is a 3-yr prospective, multicenter, randomized, placebo-controlled, double-blind, parallel-group (4 arms: 50 mg or 25 mg or 12.5 mg of hydrochlorothiazide or placebo) trial that will include 416 adult patients with recurrent calcium-containing kidney stones. The primary outcome will be the incidence of stone recurrence (a composite of symptomatic or radiologic recurrence, with the latter assessed via low-dose computed tomography).

In conclusion, the SKSC presents unique opportunities for important research on the etiology, biology, and prevention of urolithiasis. Its nationwide character, standardized and extensive patient work-up, long-term follow-up, and significant number of patients recruited make the SKSC a valuable tool for better understanding of the pathophysiology of kidney stone formation. Research projects within the SKSC are encouraged, and collaboration can be proposed at http://sksc.nccr-kidney.ch/index.php?nav=108&scx=0&scy=0.

Conflicts of interest: The authors have nothing to disclose.

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