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Management of high recurrent urolithiasis patients: the long term interdisciplinary approach is the key

Abstract

Background: Urolithiasis is a pathology that can be highly recurrent, leading to frequent urological interventions, even with specific management. Objective: We want to verify, whether an interdisciplinary long-term approach during a single day-care program decreases the recurrences rate requiring urological intervention.

Design, Setting, and participants: Patients with recurrent stone events were included in a prospective study of 18 months of interdisciplinary management. During the first day (T0), a team of health professionals diagnoses the lithogenic process and analyzes the causes of recurrences to determine preventive measures. Then, patients were re-evaluated at 6 and 18 months later to check the recurrences of stone events and the efficacy of preventive measures. Primary endpoints were urological intervention and urinary tract infection rates at baseline and 6 and 18–months. Secondary endpoints were blood and urine parameters changes and quality of life assessed by an open-ended survey.

Outcome measurements and statistical analysis: the rate of recurrence and urological intervention was checked before the interdisciplinary day (T0) and at 18 months (T18). Blood and urine samples were analyzed to evaluate the lithogenic process, such as the 24h urine, morning urine, and eGFR. Statistical analyses were performed with Statistica 10.

Results and limitations: Out of 157 patients included in the study between 2007 and 2010, 82 (52%) came back 18 months later. After 18 months, 83% did not show any recurrences. The frequency of surgical intervention was 0.65(0.21-1.42) intervention per year before the management and reach 0(0-0) after 18 months ($p<0.0001$). The 24h diuresis volume was improved from 2.00 (1.50-2.50) to 2.33(1.80-3.05) L/d ($p<0.01$). Initial extreme values of pH have shown a significant improvement for both initial acid (<5.5, $p<0.001$), and alkaline (>6.5, $p<0.01$) pH. Modification of Diet in Renal Disease (MDRD) was stable (81+-23 VS 80+-22 ml/min/1.73m^2 ($p>0.05$)). However, all parameters of 24h urine, as calciuria and oxaluria, did not show significant change.

Conclusion: The long-term interdisciplinary management of the recurrent stone former was useful to reduce recurrences and decrease uro-logical intervention.

Keywords: high recurrence, urolithiasis, interdisciplinary management

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Introduction

Urolithiasis is a widespread pathology with an increasing prevalence of around 10%[1,2] in developed countries, leading some authors to speak from the "stone boom millennium".[3]

Without specific management, the recurrence rate is above 50% and can reach 70%,[1] but even with prevention measurements, this rate can still reach 10 to 15% for some patients,[4] such as in genetic disorders.[5] The management and the consecutive urological intervention of stone kidney costs every year 2,1 billion dollars.[3,6]

The causes of failure to prevent recurrences are not easily determined and can be numerous and varied: lack of information to settle down the diagnosis (eg. no stone analysis), wrong diagnosis, absence of specific recommendations, or even no management of associated pathologies. Also, patients' misunderstanding of prevention treatment, or incapacity to follow it, are the other causes of recurrences, just as the absence of long-term follow-up.[7,8] Those patients with very high recurrent stone disease can be demotivated, despite having consultations with a nephrologist, and are often lost in follow up.

To accurately identify risk factors, and causes of recurrences and to treat them properly, we decided to create an original and adapted management based on a long-term interdisciplinary approach.

The aim of this article is to evaluate the effect on recurrences of this method by comparing parameters, such as a decrease in urological intervention rate, before management and 18 months later.

Material and methods

Study design

This is an interventional prospective study on higher recurrent (at least 3 urological interventions) stone former patients. In this study, the impact of interdisciplinary-based management will be investigated in poorly controlled recurrent stone formers adult people. The study flow is presented in (Figure 1).

Study settings

This 18-month prospective study will be conducted in a tertiary care Nephrology care hospital of Pitie-Salpetriere, located in Paris, France. The recruitment and data collection will be performed between January 2007 and December 2010.

Study population

Eligibility criteria for the study include poorly controlled higher recurrent stone formers (at least 3 urological interventions) adult patients (age ≥18years) regardless of gender; speaking and understanding French and/or English languages; having no significant

comorbidity; being not involved in any trial/study related to urolithiasis during last 3 months and able to attend regular visits. Participants will be excluded if they are unable to answer the questionnaire independently or have hearing, vision, or cognitive impairments.

Sample recruitment procedures

Patients are identified from the hospital chart and invited to participate in the study. If the patient is willing to participate in the study, an appointment will be scheduled and the purpose of the study will be explained to the patient. Each patient will be his or her own control for the comparison between baseline and 6 and 18 months.

Study aims

Primary aim: To investigate the effectiveness of an interdisciplinary management program on recurrences of urolithiasis by the frequency of urological interventions, and urinary tract infection rates before and after 18 months.

Secondary aim: To examine the impact of an interdisciplinary management program on self-care behaviours and patients' stone knowledge, blood and urines parameters changes and quality of life assessed by an open-ended survey

Study procedure: After the signature of the informed consent letter, patients with the active stone disease despite being followed by a nephrologist before this study were managed by an interdisciplinary team of health professionals. They undergo a first-day care program to diagnose the precise lithogenic process and analyze the causes of recurrences to determine adequate preventive measures. Then, to allow a long-term follow-up, patients came back 6 and 18 months later, where their status was re-checked. Details about patients' demographics and lab profiles will be obtained at the first visit, and at 6 and 18-month follow-ups.

Our long-term interdisciplinary approach is described in (Figure 1):

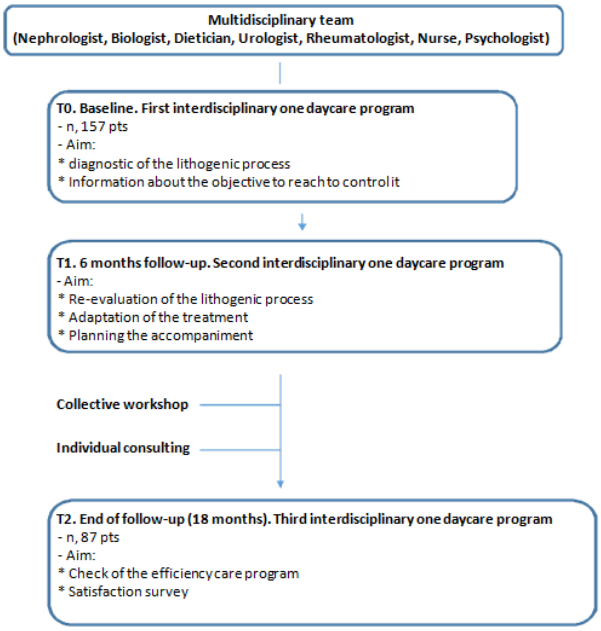

Figure 1 Flow chart of the study.

Baseline interdisciplinary daycare =T0

The goal of this day is to integrate historical and medical data to identify precisely the lithogenic process on clinical, radiological, biological, and dietetic aspects.

The patient's history is reviewed by specialists, including a radiologist, an urologist, a dietician, a nurse, a psychologist, a biologist, a rheumatologist, and a nephrologist during an interdisciplinary daycare program. During this day, the rate of recurrences requiring a surgical intervention between the first urological intervention in the life and this day T0 is calculated.

A nephrologist and an urologist together with a radiologist carefully review the entire medical story, which is already helpful for the diagnosis of stone formation.[9,10] The evolution of each stone is described from the first manifestation until the proven expulsion, and/or the surgical intervention. The stone-free state in between two different colics must be confirmed or not to be able to differentiate a recurrence (new stone construction after an authenticated free stone state) from a relapse (same stone). They are precisely noted based on imaging monitoring. This eliminates the wrong recurrence with for instance many surgical interventions on the same very hard stone as brushite.

Biological (blood and urine) analysis interpretation was performed with a dietician who can collect and analyze dietary habits and evaluate actual intakes during an entire week. The extended blood and urine tests included metabolic evaluation and sequentially samples including the morning first urine were performed during this first interdisciplinary daycare program. Crystalluria, which was performed by a trained biologist, and shown to the patient in our unit, can sometimes settle the diagnosis of the lithogenic process, as in the case of cystinuria, where pathognomonic hexagonal crystals are observable. Finally, the best way to analyze the stone if available is the spectrophotometric analysis with infra-red analysis, which was completed by Daudon's morphoconstitutional classification.[11]

A physical examination by a nurse was performed to measure body weight, waist-to-hip ratio, height, and blood pressure and to check the quality of life (integrating sleep and sexual disorders). Nurses also checked the urine volume and the ability of the patient to measure his own volume of urine during the day.

This interdisciplinary evaluation allows to identification of high-rate recurrent patients, gives them clues regarding the pathophysiological diagnosis, advises to reveal the lithogenic process, usually masked at that time of the management by dietetics disorders, and begins the educational program focused on changing daily dietetic habits. After the initial evaluation, and at the issue of the interdisciplinary consultation, the patient who has accepted to enter the long-term care program receives recommendations to correct dietetic errors and to reach the defined objectives to prevent recurrences. The accompaniment is mandatory with ETP individual consultation and collective workshops too especially for the ones suffering from genetic disorders instance cystinuria.

The second interdisciplinary day-care program: 6 months later

The aim of this one-day care program is to re-evaluate the medical management and control of the lithogenic process and its consequences. During this day, many of them reveal a lithogenic condition that needs a dynamical evaluation of calcium (Pak test) and/or phosphate metabolism (calcium-phosphate metabolism). According to the results of these explorations, genetic analyses are performed to prove our hypothetic disorder. At the issue of interdisciplinary evaluation, the measures of prevention are re-defined.

The urological interventions are organized when it is possible, in patients with identified lithogenic process and controlled risk, to minimize the number of surgical interventions. The type of urological intervention is discussed together with the nephrologist, depending

on the nature of the lithogenic process and depending on the quality of its control. The diagnosis of underlying pathologies leading to the lithogenic process is in part settled down at this time of the program. The repercussion of urolithiasis on the bone is evaluated too.[12,13]

Patients with calcium-dependent lithogenic process undergo bone density measurement: if the BMD is low with osteoporosis, the treatment is discussed together with the rheumatologist, given the fact that it is mandatory to correct and to prevent the progression of osteoporosis even in high urolithiasis recurrence rate patient. Evaluation of bone metabolism gives information concerning the lithogenic pathway that can be linked to it and guides the prevention treatment. The goals of global management are dual on one hand the prevention of stone recurrence and on the other hand the prevention of osteoporosis progression.[14]

After the second interdisciplinary day evaluation patients are aware that they need a lengthwise follow-up, which means perseverance and time, from both sides: from the team and from themselves! During this phase of the program, most of the patients have a specific treatment for their underlying disease that is required for the reduction of the recurrence rate. Recommendations are in most of cases applied at this time of the program. The dietetic advice is checked by urinary analyses until the objectives of recurrences rates are achieved. It takes time to change dietetic habits but most of them keep them in the long term. Everything is done to help the patient during the entire care program to achieve his objectives, including psychological support and pain control.[15,16]

If the specific lithogenic process is identified in most patients at this point of the interdisciplinary approach, recurrences are not controlled in all of them. For the latter, living in very complex clinical conditions, perseverance is required to progress further. The ones who have active stone formation despite stressed management for a long period and their active participation to the program will need more time (up to 12 months) to be successful in terms of controlled risk. Most of our very high-rate recurrence patients have a genetic disorder like cystinuria, Dent disease, renal phosphate loss, normocalcemic hyperparathyroidism… Time is essential to understand why the process is not controlled from both sides (team and patient). Careful re-evaluation of the progression factors leading to recurrence is made, through a multistep analysis allows improvement of prognosis. If a recurrence has occurred during this period, it must be analyzed together with all the caregivers to identify where the failure of the management process occur. All these steps of the program are explained again in detail to the patient.

Third interdisciplinary day care program: 18 months later

The last interdisciplinary evaluation occurs 18 months after the first step.

To evaluate the efficiency of the control of lithogenesis, we compared many parameters that reflect stone activity on the first day of the multidisciplinary consultation (T0) and 18 months later (T18). First, we directly checked the absence of recurrences during the 18 months of follow-up, which were determined as follows: any surgical intervention, except for the removal of stone that was present before T0, spontaneous stone elimination, nephritic colic, and new or bigger stone on imaging between T0 and T18. Then, the most important outcome for the clinical evaluation of patient recurrences is the decrease in urological intervention frequency. It has been calculated as the ratio of the number of all types of interventions per year since the first stone episode. Urological intervention includes ureteroscopy, shock-wave lithotripsy, placement, or removal of any catheter, percutaneous nephrolithotomy, and nephrostomy. About biological measurements, stone composition, determined by infrared spectrophotometry, gives important clues about risk factors of urolithiasis but was not always available.[15,17] Urine volume, oxalate, calcium, uric acid, phosphate, citrate, sodium, urea, and creatinine have been measured on 24h urine. Daily salt and protein intakes were calculated thanks to these results. On morning spot urine, specific gravity, pH, creatininuria, and urea were measured.[17–27] Crystalluria, which consists in the observation and description of crystals in the morning urine, was performed too.[28–30] Moreover, renal function has been evaluated with the MDRD formula and creatinine clearance. At the end, a qualitative questionnaire was distributed to patients to get their feedback about the experience, and to evaluate their good comprehension of preventive recommendations.

Qualitative survey scale

A qualitative survey was performed by asking open-ended questions to patients through phone conversation and discussing their experiences throughout the years of follow-up.

Questions	Responses			
	Very true	True	Quite true	Not true
I know my objectives to reach to prevent stone recurrences				
I find that my file is useful and will help me to reach my objectives in terms of concentration of urines				
I consider that interdisciplinary management is useful to prevent my recurrences leading to surgery				
I am clearly satisfied with the interdisciplinary care because it improved my quality of life				
I will recommend this interdisciplinary care for one of my family who suffers under recurrent stone events				

Statistical Analyses

Statistical analyses were performed using Statistica version 10 (for windows 8, released in 2010, StatSoft Inc. 1984-2015). The distribution of data was tested by the Shapiro-Wilk test. Normally distributed continuous data are reported as mean ±SD, and skewed continuous data are reported as the median and interquartile range (25–75 percentiles). Comparisons of results between T0 and T18 were realized with paired t-test for normally distributed continuous data, with Pearson's chi-squared test for binary data, and with Wilcoxon test for skewed continuous data. All comparisons are considered significant when $p<0.05$.

Results

Between 2007 and 2010, 157 patients were initially recruited. Among them, 82 came back 18 months later. There were 43 men and 39 women, and the average age was 48+/-13 years old. Body Mass Index was 24 (21-27) at T0 and did not show any significant change at T18: 25(21-26) ($p>0.05$). All results are shown in Table 1.

Urological intervention frequency was 0.65(0.21-1.42) intervention a year, before the first day, and decreased to 0(0-0) at T18 ($p<0.0001$) (Figure 2). The proportion of patients who did not show any recurrences at 18 months is 83% (68/82).

Table 1 High recurrent urolithiasis patients: characteristics and outcome

	T0	T18	p-value
Man	43 (52%)		
Age	48 (+/- 13)		
BMI	24 (21-27)	25 (22-26)	
Urological intervention (n/year)	0.65 (0.21-1.42)	0 (0-0)	<0.0001
Recurrence after T18		14 (17%)	
pH	6.0 (5.3-6.8)	6.0 (5.4-6.5)	
Initial pH <5,5	5.0 (5.0-5.5)	5.6 (5.2-6.3)	<0.001
Initial pH >6,5	6.8 (6.8-7.0)	6.3 (6.0-6.7)	<0.01
Specific gravity	1020(1010-1030)	1020(1015-1025)	
Presence of crystals	37(45%)	43(52%)	
Calcium(mmol/L)	2.4(1.6-4.8)	3.0 (2.1-5.3)	
eGFR (ml/min/1,73 m2)	81(+/- 23)	80 (+/- 22)	
Volume (L)	2.0 (1.4-2.5)	2.4 (1.9-3.0)	<0.01
Oxalate (mg/24h)	35.5 (22.5-52.0)	33.0 (20.1-44.4)	
Calcium (mmol/24h)	5.82 (+/- 3.0)	6.22 (+/- 3.4)	
Uric acid (mg/24h)	511 (413-600)	536 (399-657)	
Phosphate (mmol/24h)	24.9 (+/- 7,5)	27.1 (+/-10,4)	<0.05
Citrate (mg/24h)	496 (320-746)	400 (257-639)	<0.05
Sodium (mmol/24h)	137 (102-210)	142 (108-184)	
Salt intake (g/24h)	8 (6-12)	8 (6-11)	
Urea (mg/24h)	22.1 (17.1-27.2)	22.4 (17.8-26.7)	
Protein intake (g/kg/24h)	1.08 (+/- 0.33)	1.09 (+/- 0.29)	
Creatinine Clearance (ml/min)	105 (+/- 44)	103 (+/- 43)	

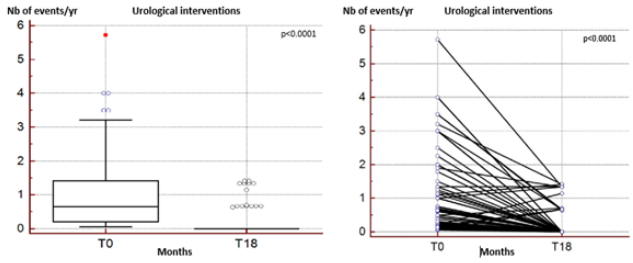

Figure 2 Primary end points. Statistically significant decrease in urological procedures.

Calculi analysis was performed in 67 cases (82%). Most the stones were containing calcium (51%), with 33% of stones including calcium oxalate dihydrate, as a major or minor component. Phosphates were well represented too (29%), and infection (defined by the presence of Struvite or Whitlockite, or carbonatation of carbapatite > 15%) was the cause of recurrence in 7% of patients. Cystine and uric acid stones stood for 16% and 11% of stones, respectively in our cohort.

Before interdisciplinary management, the median 24h urine volume, which reflects daily fluids intake, was 2.0 (1.4-2.5) L/d and reached 2.4 (1.9-3.0) L/d after 18 months (p<0.01) (Figure 3). Creatinine, in µmol/kg/d, allowed us to verify that urine was correctly collected by patients. There was no change in 24h urine calcium, oxalate, and uric acid: initial calciuria was 5.8 +/-3.0 mmol/24h and reached 6.2 +/-3.4mmol/24h (p: 0.59), oxaluria evolved from 35.5 (22.0-52.0) to 33.0 (20.1-44.4) mg/24h (p:0.59). Uric acid was 511 (413-600) at the beginning of the study, and 536 (399-657) mg/24h at the end (p: 0.09). However, we observed a significant decrease in citraturia, an inhibitor of stone formation, after the management: 496 (320-746) to 400 (257-639) mg/24h (p<0.05). There was also a significant change in phosphaturia, which passed from 24.9 +/-7.5 to 27.1 +/-10.4mmol/24h (p<0.05). Daily salt intake, calculated from 24h urine sodium, was initially 8 (6-12) g/d, and became 8 (6-11)g/d after 18 months (p<0.05). In the same way, daily protein intake shifted from 1.08 +/- 0.33 to 1.09 +/- 0.29g/kg/24h.

Renal function evaluation, calculated with MDRD and clearance of creatinine on 24h urine did not show deterioration after 18 months. Creatinine clearance, measured on 24h urine, was 105 +/- 44 ml/min at the beginning of the study, and 103 +/- 43 at T18 (p>0,05). eGFR, which was 81+/-23 at T0 did not statistically change at T18 (80+/-22ml/min/1.73m^2) (p>0.05). The understanding of information about crucial endpoints to prevent recurrences was good or very good in 97%. The personal file was useful to help them to reach the endpoints of 80%, and the satisfaction rate was 89%.

On morning urine, crystalluria was positive in 45% at T0, and 52% at T18 (p>0.05). There was no significant modification of urine specific gravity too: 1020 (1010-1030) before and 1020 (1015-1025) at the end of the study (p>0.05). There is a significant difference when measuring pH in two different groups of "extreme value": patients with initial urine pH lower than or equal to 5.5 (median: 5.0 (5.0-5.5)) get the higher value after the management (5.6 (5.3-6.3)) (p<0.0001). In opposition, for the ones with alkaline pH, higher than 6.5 at T0 (except for cystinuria patients for whom alkalinization is the first therapeutic recommendation[26]), the pH decreased from 6.8 (6.8-7.0) to 6.3 (6.0-6.7) (p<0.01) (Figure 2).

Qualitative survey: Most of the patients were relieved to have a clear diagnosis and a lower renal colic and urologic procedures incidence. They explained they could live well without forming new stones with relatively few modifications to their lifestyle. Most of them were very satisfied with the significant decrease in urological interventions and medications. They all expressed their gratitude for being able to live without stone recurrence by applying preventive measures that did not significantly change their lifestyle. The question "why do I have kidney stones" had disappeared: they could have more energy to focus on the objectives to reach instead of being depressed by painful recurrences. They explained that it was crucial to be accompanied by a multidisciplinary group to achieve their goals.

Discussion

The main results of this prospective study demonstrate that a multidisciplinary-based program is effective in significantly improving urinary symptoms (stone recurrence, urological intervention, urinary tract infection rates) and quality of life of higher recurrent stone former adult patients.

Our long-term interdisciplinary approach included 3 days of care spread over time. Baseline interdisciplinary daycare (T0) was mandatory to understand the lithogenic process. Carefully revisiting all clinical and radiological events in a sometimes lifelong stone story is not necessarily performed on a routine basis and affords a much better overview of the patient's disease. Thereafter, the step at 6 months (T6), is crucial because it allows the reliability of the information given by the patients. There is a critical educational phase in our program focused on helping patients restore normal calcium intake to have better conditions to analyze the next biological data. In very high-rate recurrence patients, dietetic disorders or bad habits are very frequent: some dietetic disorders may enhance the lithogenic risk (increased salt, too much protein, too much oxalate intakes, and lack of drinking intakes), while some dietetics habits may mask it, within most patients a very low calcium intake below 300mg/d. The 25OH

vitamin D3 level is often very low, and we give supplementation until it reaches 35ng/mL before interpreting the patient's calcic status. A psychosomatic evaluation of the stone's former personal history allows a link between personal events and recurrences and is helpful to "predict" the risk of recurrences. Patient education is a critical step in this program since patient involvement, in an attempt of decreasing stone formation, is essential. The different axis of patient evaluation from an educational perspective are the patient's willingness to unravel the diagnosis of the disease (sometimes critical in familial forms), the patient's readiness for changing daily dietetic habits, and the patient's ability to understand and manage lifestyle changes that are. Finally, the last interdisciplinary evaluation occurs 18 months after the first step. It is necessary to appreciate the efficiency of management and to verify that recurrence risk is completely controlled. The recurrence process, if it goes on, means that the prevention strategy management has failed. To understand where and why it failed at the end of the program, the precise diagnosis of recurrence risk factors is made, and the causes of failure can be identified and corrected. Although describing the scientific evidence for reducing recurrences with increasing water intake, a recent review showed that there is no strong evidence that dietary recommendations have benefits on recurrences.[21] It means that it is not enough in high recurrences patients. But a long-term modification of dietary habits needs a motivated patient and a motivated physician. The long-term interdisciplinary approach helps a lot to support both of them.

Our selected patients had a history of urological intervention frequency of 0.65 interventions a year (median) and reached 5.71 for some. This is a quite high rate, considering costs for public health,[28] and main risks for patients, who undergo the risk of complications, even if they are rare.[29,30] According to us, this is a more important clinical endpoint than the biological evaluation of stone disease, which sometimes seems random. It is also the main criterion cited by patients in the satisfaction survey. The number of urological interventions and urinary infections could be improved in a span of only 18 months (Figure 3), which is very quick, but it is worth verifying this result after more years. Even for patients with more than one intervention a year, there are only a few recurrences: only 5 on 32 of them had a new intervention. This may partially be explained by the 24h urine volume improvement. Indeed, the 24h diuresis volume is another very important parameter to consider, because it has been shown in many papers to be the most efficient tool to prevent stone recurrences. Before starting the interdisciplinary management, patients had already received, in specific consultation with a urologist and/or nephrologist, the crucial information for lithiasis prevention, which is to have a urine volume of 2-2.5L a day at least.[31–34] Despite this recommendation, half of the patients did not reach this goal before the study (median was 2.0 (1.4-2.5) L/d) (Figure 3). This level of diuresis is good, but still not enough for half of the studied population to prevent stone recurrence. However, at the end of the study, 24h diuresis median reached 2.4 (1.9-3.0) L/d vs T0 ($p<0.01$). It means that participation in the interdisciplinary daycare program brought solutions to almost all patients to overcome this little, but crucial, lack of daily hydration. Here are the tools used to reach this goal: presentations about lithogenesis, direct visualization of their own crystalluria by patients, group effect, and psychosocial counselling for some. Results about 24h diuresis encourage to motivate patients to continue increasing their water intake even when it's close to aim.

However, crystalluria and specific gravity on a morning spot of urine could not be improved. Observation of urine crystals has shown that their presence in more than 50% of spaced urine samples is significantly associated with recurrences. Some other parameters, such as crystal volume in cystinuria, are also a sign of recurrence.[25–27] On the opposite, the presence of some crystals, such as amorphous phosphates, is also observable in non-stone former, showing it cannot be correlated with significant metabolic disturbance. In our report, the simple presence of crystals has been checked, but not the other parameters of crystalluria, which is sometimes not enough to predict the risk of recurrence. Urine specific gravity on a morning spot should be lower than 1012 to avoid crystal growth in urine.[35] It means that water intake should be better distributed between day and night.

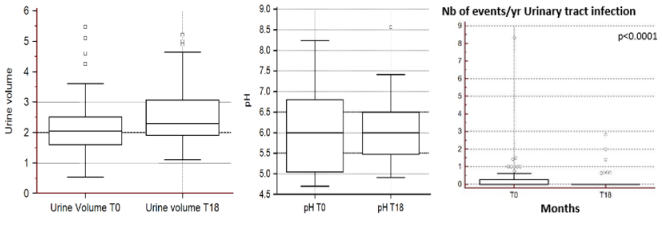

Figure 3 Secondary end points. Significant increase in diuresis at 18 months follow-up.

When pH is acid, there is an increased risk for some ion precipitation, such as uric acid and cystine, while phosphates crystallize easily when pH is more alkaline. The patients with an "extreme" (lower than 5.5 or higher than 6.5) initial pH value, have better control of pH after the management, which become closer to a central value (about 6), and so, a lower lithogenesis risk. The saturation level of components such as cystine and uric acid is exponentially increased by pH alkalinization.[5,34] When patients are sorted by stone composition, we can observe that thanks to the interdisciplinary approach, pH variations are specific and oriented in the function of stone nature (Figure 2).

Other biological parameters of 24h urine such as calcium, uric acid, sodium, and urea concentration were excessive and could not be improved. The absence of a decrease in calciuria can be related to many factors: first, vitamin D supplementation promotes calcium intestinal absorption, leading to increased calcium filtration. It goes on the same way for phosphate, therefore it could also explain the phosphaturia increase, which is significant ($p<0.05$), but does not exceed the threshold of hyperphosphaturia. Then, calciuria is directly enhanced by the raise of natriuria, which decreases calcium reabsorption. Indeed, salt consummation could not be improved to the recommended levels (below 6g a day) as well as protein intake (recommended value: 0.8-1g/kg/d), who are also likely to increase calciuria, but also oxaluria. The absence of good control in urine sodium and urea, which are directly linked to the consummation of salt and protein, shows how much it is difficult for patients to have a balanced diet, and could be the cause of poor results in 24h urine evaluation.[21,36]

The chronic stone disease can lead to renal failure due to consecutive infection, staghorn stone, long-period obstruction, and tubular deposit and is linked to comorbidities (such as diabetes mellitus), etc.[5,37–40] That is why it is an important endpoint to evaluate during the follow-up. In our study, MDRD could be preserved at the same level for 18 months, even for the 13 patients who presented a CKD - determined by a MDRD under 60 at T0 - at the beginning of the interdisciplinary care program, renal function is not worsened ($p>0.05$). Typically, 4 had congenital cystinuria, which produces frequent urolithiasis that grows quickly if unwell treated.

Bias and remarks

Only 52% of patients came back at 18 months, which shows that long-term follow-up is hard to establish. However, this number is

under-evaluated because of some patients didn't come exactly at 18 months, but some months later, so, they were not considered in the study. The reasons for giving up the care program are many and may include difficulty to come at the hospital centre. Indeed, many patients who came lived in far regions from Paris. Others patients who did not suffer anymore did not deem it necessary to come in a period without stone event. Many of them came more than 3 years after.

A criticism of this study could be that all biological parameters could not be improved: this could be due to a little number of patients and to different lithiasic pathology. This leads to heterogeneity and lack of statistical power in comparing results before and after the interdisciplinary approach, as well as between groups of patients (no significant difference could be found between different kinds of urolithiasis). Despite no significant change in some parameters, a decrease in recurrences and in urological intervention is encouraging because it is an important goal in urolithiasis treatment. Yet the improvement in the recurrence rate of surgical intervention despite the lack of calciuria emphasizes the importance of increased diuresis.

Conclusion

Our study shows that a long-term interdisciplinary management of highly recurrent stone formers allows a significant decrease in recurrence rate and urological intervention as well. In our tertiary stone clinic, all high-rate recurrences patients had multifactorial underlying processes, including metabolic disorders. The analysis of this process is mandatory to prevent recurrences.

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Author contributions

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Software: IT, VC, EC

Validation: IT, VC, PC

Formal analysis: IT, VC, EC

Investigation: IT, LP, MPD, RRP, RI, CB, HI

Resources: NA

Data curation: IT, PC

Writing—original draft preparation: IT, VC, HI

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