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Analysis of spontaneously passed urinary tract stones

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Abstract Most studies on epidemiology, composition, and recurrence of renal calculi include both spontaneously passed calculi and those retrieved after surgical manipulation or shock wave lithotripsy. The present study exclusively focused on epidemiology, composition, and recurrence of spontaneously expelled stones in patients from North and East Mallorca (Spain) which represents a geographically specific non-urban region of a developed country. The study involved 136 patients who spontaneously passed 205 renal calculi. All calculi were classified and sub-classified according to composition after macroscopic and microscopic examination. We also analyzed prevalence, gender, age, and stone recurrence rate over a period of 3 years. The peak incidence of spontaneously stone passage is within the fourth to sixth decade. Overall male to female ratio was 3/1. Calcium oxalate was the most prevalent composition (64.8%) followed by uric acid (25.3%), mixed stones (5.3%) and calcium phosphate calculi (4.3%). Uric acid stones were the most recurrent (50%) followed by calcium oxalate monohydrate papillary calculi (26.4%), calcium oxalate monohydrate un-attached calculi (19.2%), calcium oxalate dihydrate calculi (18.3%), calcium phosphate calculi (14%), and mixed calculi (12.5%). In conclusion, spontaneously passed stones in Mallorcan population have similar epidemiology, composition, and recurrence rate from that found in other developed countries. Calcium oxalate stones are largely the most spontaneously passed type of calculi and uric acid stones are the most frequently recurred. These findings are also found to be similar to those reported in previous studies examining both spontaneously and non-spontaneously passed stones.

Keywords Renal calculi · Spontaneously expelled stones · Recurrence · Epidemiology · Renal stone composition

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Introduction

Most publications looking at epidemiology, composition, and recurrence of renal stones include both spontaneous passed stones and fragmented calculi retrieved by ureterorenoscopy, percutaneous nephrolithotomy, or shock wave lithotripsy [1–4]. There are no many studies specifically looking at spontaneously passed renal calculi [5, 6]. As expected, these studies show that stone passage rate is inversely related to increasing stone size. In one study looking at spontaneously passed stones 96.6% were sized $\leq$10 mm and most of them (55%) were $\leq$5 mm [6]. Another study showed that calculi exclusively composed by calcium oxalate (CaOx) were more likely to be spontaneously expelled than calculi with any other composition [5]. They were followed by mixed CaOx and calcium phosphate calculi. Many of the passed stones in this study weighted less than 0.10 g [5].

Our objective was to analyze epidemiology, composition, and recurrence rates of spontaneously passed calculi in a population from North and East Mallorca (Spain). We specifically focused on spontaneously expelled calculi and the study of a geographically specific non-urban population in a developed country.

Materials and methods

We analyzed prevalence, gender, age, composition of spontaneously passed calculi and stone recurrence rate in 136 patients from North and East regions of Mallorca over a period of 3 years. Patients with previous history of recent surgical manipulation or lithotripsy were excluded from the study. A total of 205 renal spontaneously passed calculi were collected, dried, stored in sterile containers and were examined. All stones were immediately analyzed after passage. The procedure used to analyze and study renal calculi involved an appropriate combination of observation by means of macroscopic and microscopic conventional techniques (stereoscopic microscope Optomic) together with physical techniques such as infrared (IR) spectrometry (Brucker IFS 66 infrared spectroscope) and scanning electron microscopy (SEM) (Hitachi S-530) coupled with X-ray microanalysis (Oxford Link Isis) [7].

The study of the calculus begins with external aspect direct observation using a stereoscopic microscope. The calculus is then sectioned into two parts along a plane as close as possible to its geometric centre, in order to establish the internal structure.

An in-depth study of the fine inner structure of the calculus and the detection and identification of microcomponents (not identifiable using conventional IR spectrometry) requires the use of SEM coupled with X-ray microanalysis. In order to determine the importance of a given microcomponent, accurate knowledge of the fine structure of the calculus is mandatory, so that the initial zone of calculus development can be established. This zone is crucial in establishing the origin of the calculus.

The discrimination between unattached and papillary calculi was only applied to COM stones because only stones composed mainly by COM showed signs of papillary attachment [8]. As a particular characteristic, papillary stones are always linked to some alteration of papillary tissue, ranging from Randall's plaque to other less severe papillary injuries. Obviously, renal stone development is a multifactorial disease and other factors can coincide with unattached COM stones (deficit of crystallization inhibitors, hyperoxaluria,…). Consequently, apart from some common factors, papillary and unattached stones have different origin and consequently different etiology [8].

This methodology allows the classification of renal calculi into 11 main types (Table 1) and distinguishes papillary calcium oxalate monohydrate renal calculi (COM-P) from non-papillary (unattached) calcium oxalate monohydrate renal stones (COM-U) based on the presence or absence of a renal papillae fixation point.

To consider a stone as a mixed one, the second component has to represent at least the 20% (or more) of the whole calculus, in accordance with the classification used in the following papers [8, 9].

Table 1 Classification of renal calculi according to Grases et al. [8]

Classification of renal calculi	
1.	Calcium oxalate monohydrate papillary renal calculi (COM-P)
2.	Calcium oxalate monohydrate unattached renal calculi (COM-U)
3.	Calcium oxalate dihydrate renal calculi (COD)
4.	Calcium oxalate dihydrate/hidroxyapatite mixed renal calculi (COD/HAP)
5.	Hydroxyapatite renal calculi (HAP)
6.	Magnesium ammonium phosphate (struvite) renal calculi (STR)
7.	Calcium hydrogen phosphate dihydrate (brushite) renal calculi (BRU)
8.	Uric acid renal calculi (UA)
9.	Calcium oxalate/uric acid mixed renal calculi (CO/UA)
10.	Cystine renal calculi (CYS)
11.	Infrequent renal calculi

HAP and BRU stones probably differ in etiology [10]. However, due to the low number of such stones in the present study, they are grouped together as calcium phosphate stones, since such low number would not permit to establish significant conclusions.

The recurrence was determined considering the number of stone formers that develop at least a new calculus during the 3 years follow-up of the present study. For this reason, the study was divided in to two parts. The first one was the recruitment period of the patients whose calculi were able to be analyzed. This period comprised from October 2002 to October 2003. Finalized the recruitment period the patients were periodically controlled at the office. When they completed the established 36 months of follow up their study card was closed. The observation interval to establish the recurrence rate finished in October 2006 when all recruited patients completed 36 months of follow up.

Results

Distribution by gender and age

Distribution by age and gender is shown in Table 2. Papillary COM, COD, and HAP were most prevalent in younger ages (third and fourth decade) whereas un-attached-COM and uric acid stones were found to have higher prevalence in older people (fourth and sixth decade). Overall male to female ratio was 3/1. Except for calcium phosphate calculi (male to female ratio 0.7/1) all other calculi composition

Table 2 Distribution by age and sex

Type	*N* (patients)	Age (average age) (years)	Male (%)	Female (%)	Male/female ratio
COM-P	34	17–70 (41)	76	24	3/1
COM-U	26	28–98 (54)	77	33	3/1
COD	49	21–79 (45)	67	33	2/1
Uric Acid	20	30–83 (56)	85	15	6/1
Mixed Calculi	8	34–73 (49)	75	25	3/1
Calcium phosphate	7	31–52 (45)	43	57	0.7/1

COM-P papillary COM, *COM-U* un-attached COM

Table 3 Prevalence rates for types of spontaneously expelled upper urinary calculi

Stone type	*N* = 205	Prevalence (%)
Calcium oxalate	113/205	64.8
Uric acid	52/205	25.3
Mixed stones	11/205	5.3
Calcium phosphate	9/205	4.3

Table 4 Calcium oxalate stone subtypes

Calcium oxalate stones	*N* = 133	Percentage
Calcium oxalate monohydrate (COM)	77/133	57.8
Calcium oxalate dihydrate (COD)	56/113	42.1

was more frequently spontaneously passed by males. This was specifically significant for uric acid stones which showed a male to female ratio of 6/1.

Prevalence

The prevalence of the different types of spontaneously passed calculi in our population is shown in Table 3. Calcium oxalate (CaOx) stones were the most prevalent type of overall spontaneously passed stones (64.8%). They were followed by uric acid stones (25.3%), mixed stones (5.3%) and calcium phosphate stones (4.3%). Distribution of calcium oxalate calculi subtypes is represented in Table 4. The most prevalent CaOx calculi sub-type was COM (whewellite), which represented 37.5% of the total number of expelled calculi. Sub-classification of COM stones is shown in Table 5. COM stones were followed by COD calculi (weddelite), which represented 27.3% of the total number of expelled stones.

Uric acid stones were the second-most prevalent expelled stones after CaOx calculi. They represented 25.3% of the total stone number. Sub-classification of uric acid stones is shown in Table 6.

Mixed stones were the third-most prevalent group of calculi and represented 5.3% of all stones. The most frequent type of mixed stone was the combination of COM and uric acid, followed by the combination of COD and hydroxyapatite and COM and hydroxyapatite (Table 7).

Table 5 Calcium Oxalate Monohydrate sub-classification

Calcium oxalate monohydrate (COM)	*N* = 77	Percentage
Papillary calcium oxalate monohydrate (COM(P))	45/77	58.4
Un-attached calcium oxalate monohydrate [COM (U)]	32/77	41.5

Table 6 Uric acid stones subtypes

Uric acid type	*N* = 52	Percentage
Anhydrous	31/52	59.6
Dihydrous	21/52	40.3

Table 7 Mixed stone types

Mixed stones	*N* = 11	Percentage
COM + uric acid	8/11	72.7
COD + hydroxyapatite	2/11	18.1
COM + hydroxyapatite	1/11	9.0

Table 8 Calcium phosphate subtypes

Calcium phosphate type	*N* = 9	Percentage
Hydroxyapatite	6/9	67
Brushite	3/9	33

Calcium phosphate stones were the fourth-most prevalent group and accounted for 4.3% of all stones. Sub-classification showed that 67% were hydroxyapatite calculi and 33% were brushite calculi (Table 8). No cystine or struvite (magnesium ammonium phosphate) calculi was identified in the population studied.

Recurrence

Table 9 shows recurrence rate for each type of stone during a 3 years follow-up period. Uric acid stones represented the

Table 9 Recurrence rate at 3 years

Stone type	3 years recurrence rate (%)
Uric acid	50.0
COM papillary	26.4
Calcium phosphate	25.0
COM non-papillary	19.2
COD	16.6
Mixed stones	12.5

highest rate of recurrence. Fifty percent of the uric acid stone expellers subsequently developed at least one other calculi. Furthermore, 90% recurrently expelled uric acid stones. COM papillary calculi showed a recurrence rate of 26% and followed acid uric stones. Most recurrent calculi in this group were COM papillary (55%). Recurrence rates for other calculi were 19.2% for COM un-attached calculi, 18.3% for COD calculi, 14% for calcium phosphate calculi, and 12.5% for mixed calculi.

Discussion

Not many studies have investigated composition and recurrence rate of spontaneously passed urinary tract stones [5, 6] but they have shown that such stones are most likely to be CaOx calculi [3, 5]. In addition, CaOx stones, either pure or mixed, and calcium phosphate stones are the most likely calculi to be spontaneously passed as they are usually smaller than other calculi [6]. Such findings are similar to those reported in many broader urinary lithiasis studies showing that CaOx stones are the most prevalent type of urinary calculi formed in the upper urinary tract and bladder.

Another feature of the present study is the focus on a specific regional population. The findings from this population are consistent with those from larger international series showing that CaOx stones are the most prevalent type of renal lithiasis [1, 2] and that the most common subtype is COM [1, 4, 8]. The fact that in our study no cystine nor struvite (magnesium ammonium phosphate) calculi were identified, reflects that magnesium ammonium phosphate or staghorn stones can rarely be expelled spontaneously due to their large size, and that cystine calculi only develop in relatively rarely occurring homozygote individuals.

CaOx calculi are the most prevalent type of urinary lithiasis worldwide. They are followed by uric acid stones or ammonium containing calculi, respectively, depending on the patient belonging to developed or developing countries, respectively [2, 11–13]. The higher prevalence of uric acid calculi in developed countries reflect high-purine diets, while ammonium containing calculi in developing countries reflects the consequence of urinary infections. In our study, CaOx calculi were the most prevalent type and they were followed by uric acid stones, which is consistent with the studies involving developed countries [11, 12].

Our results also showed that all types of spontaneously expelled calculi were clearly more predominant in males, excluding calcium phosphate calculi which showed a slightly higher prevalence in women (0.7/1). Male prevalence was especially significant for uric acid stones which showed a male/female ratio of 6/1. The male/female ratio for the COM group in our study was 3/1 as described by other authors in the literature [2].

It is important to understand that it is difficult to determinate when the real lithogenic history of a patient begins because most calculi can be asymptomatic during a large period of time since their formation in the urinary tract. That is why we considered patients age as the age patients reported when they were recruited for the study. In our study, expelled calculi were most prevalent between the fourth and sixth decade, except for papillary COM and for COD calculi which showed a tendency to predominate between the third and fourth decade.

In order to analyze real recurrence rate for all type of stones, no preventive treatment was given to any patient. However, in order to determinate the recurrence rate of the lithiasis, it is important to take into account that a given patient can develop and expel more than one type of stones. We considered the most frequently expelled calculus composition as the reference when patients passed more than one type of stones. If they passed two different stones, the first expelled calculus was considered as the reference. Therefore, one of the patients initially expelled a hydroxyapatite calculus and this was followed by passage of two COD calculi; in this case, the patient was considered and managed as a COD stone former. When a patient first expelled a COM stone and after that a COD calculus, the patient was considered as a COM stone former. Our results show that most recurrent stones are uric acid stones followed by COM papillary and calcium phosphate calculi.

Conclusion

Our results show that spontaneously passed stones in the Mallorcan population have similar epidemiology, composition, and recurrence rate from that found in other developed countries. The peak incidence of spontaneously stone passage is within the fourth to sixth decade. All types of stones are most frequent in males than in females, except calcium phosphate calculi which are slightly predominant in females. Calcium oxalate stones are largely the most spontaneously passed type of calculi, predominantly COM.

They are followed by uric acid, mixed and calcium phosphate calculi. The most recurrent stone type is uric acid and it is followed by papillary COM, calcium phosphate, COM un-attached, COD, and mixed calculi. These findings are also found to be similar to those reported in previous studies examining both spontaneously and non-spontaneously passed stones.

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