

Conservative management of staghorn calculi: a single-centre experience

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Objective

To evaluate the outcomes of conservatively managed staghorn calculi, specifically looking at morbidity and mortality, incidence of infections and progressive changes in renal function.

Patients and Methods

A total of 22 patients with unilateral or bilateral staghorn calculi, who were treated conservatively, were included in the study. Patients were reviewed yearly with symptom assessment, urine culture and measurement of estimated glomerular filtration rate.

Results

The presentations to the urology department of staghorn calculi were incidental (41%), haematuria (36%), abdominal discomfort (5%) and recurrent urinary tract infections (UTIs; 18%). The reasons for conservative management in the cohort were comorbidities (59%), patient choice (36%) or poor access/anatomy (5%). In the whole cohort the rate of recurrent UTIs was 50%, the progressive renal failure rate was 14%, the disease-specific mortality rate was 9%, the dialysis

dependence rate was 9% and the rate of hospital attendances attributable to stone-related morbidity was 27%. Comparison of outcome measures between the unilateral and bilateral staghorn stones showed statistically significant differences in disease-specific mortality (0 vs 40%) and morbidity (12 vs 80%) in favour of the unilateral group. Although there was a lower incidence of UTIs (41 vs 80%), renal deterioration (6 vs 40%) and dialysis requirement (6 vs 20%) in the unilateral group, these findings were not statistically significant.

Conclusions

From the results, we conclude that conservative management of staghorn calculi is not as unsafe as previously thought. Careful patient selection to include unilateral asymptomatic stones with minimal infection, and thorough counselling with regard to the risks, could make conservative management a suitable option for specific patient groups.

Keywords

staghorn calculus, conservative management, renal lithiasis, calculi, urinary tract infection

Introduction

It has been 42 years since Blandy and Singh published their landmark paper, setting the standard for active management of staghorn calculi [1]. They retrospectively studied 54 patients with staghorn stones (nine bilateral and 45 unilateral) over the course of 17 years. Their results showed that patients developed symptoms or complications related to their stones and that the outcomes of conservatively managed patients were poor [1]. They also reported that over half of the patients in their cohort died from progressive renal failure. In addition to this, nearly half of the patients who were initially treated 'expectantly' progressed to requiring a nephrectomy. As a result of this, they concluded that management of staghorn calculi should consist of early and complete removal of the stone [1]. Their paper, along with well-founded evidence that staghorn stones cause significant morbidity and mortality, through UTIs and progressive

decline in renal function, has persuaded urologists to treat staghorn stones whenever possible [2–5]. These results may occasionally influence urologists in their decisions to surgically manage patients, who are unfit for a general anaesthetic, which may often lead to significant negative outcomes. Since the publication of the paper by Blandy and Singh, however, there has been little research carried out to help us consider if their results are truly relevant today. Two papers were identified in the literature from the 1980s which suggest that there may be a potential role for expectant management of patients who are inoperable. Both papers were published in German, but translations of the abstracts have been included in reviews [6,7]. One paper considered a cohort of 24 patients whose staghorn were deemed inoperable and who were therefore managed conservatively. The authors were unable to attribute any deterioration in renal function to the patients' lithiasis. All patients had a proven UTI. Six patients in the cohort died from causes attributable to the

stone [6]. The other paper followed 20 patients with inoperable stones who had already undergone previous surgical intervention. The authors of that paper too found that most patients had positive urinary cultures and reported that none of their patients experienced ‘serious complications’ [7]. Added to this, there is evidence that shows there is a significant rate of recurrence in patients with surgically treated stones [8]. Reports suggest up to one-third of patients experience a recurrence [9]. This would add weight to the argument that more data are needed to let patients who are relatively symptom-free, with poor physiological reserve, make an informed decision regarding conservative management.

For these reasons, we felt it necessary to further explore conservative management in a cohort of patients who were either deemed unfit for surgery or who declined surgical intervention.

Patients and Methods

A prospective cohort study was devised to consider the possibility of conservative (non-surgical) management in patients who were either truly asymptomatic or minimally symptomatic from their staghorn calculi and were unwilling or unfit to undergo surgical treatment. This was registered with the local hospital research and audit department. The primary outcome measures were incidence of UTIs, progressive changes in renal function and mortality rates in this group and the secondary outcome measure was the frequency of significant morbidity caused by the stones. This was quantified by analysing the rates of hospital admission for morbidity caused by the calculus and also the patients’ requirement for dialysis. A patient cohort was collated by identifying patients attending the urology outpatient clinic with complete or partial staghorn calculi. Patients with both unilateral and bilateral stones were included. The patients had to be either minimally symptomatic or asymptomatic at diagnosis and had either declined any surgical intervention or were deemed unfit for surgical management. The patients who were deemed to represent too high a surgical risk had been assessed by an anaesthetist before this decision was made. All patients were assigned an American Society of Anaesthesiologists (ASA) score. This was taken into consideration when assessing fitness for surgery. In general, patients with an ASA score of 4 were considered to be too high risk and clinical judgement was used when considering patients with an ASA score of 3.

Patients

The patients were assessed on a yearly basis in the outpatient urology clinic. The subjective symptom burden was noted, urine culture was performed and the patients’ renal function was monitored with estimated GFR (eGFR) calculated using

the Modification of Diet in Renal Disease study equation. The information collected was recorded in a patient database, and a chi-squared test was used in Microsoft Excel to aid analysis.

Results

Patient Demographics

A cohort of 22 patients was identified that included 27 affected kidneys (17 unilateral stones and five bilateral stones). The mean (range) patient age at diagnosis was 65.3 (32–86) years. The male:female ratio was roughly even (1:1.1). The median follow-up of the cohort was 6 years and the mean follow-up was 8.1 years. The patients predominantly presented to the urology department (Fig. 1) with either incidentally diagnosed stones (41%) or haematuria (36%). Other presentations were urinary tract sepsis (18%) and vague abdominal discomfort in one patient (5%). The reasons for conservative management included patients being deemed unfit for surgery (59%) and patients declining surgical intervention (41%). It is worth noting that none of the patients in the cohort were free from comorbidities (Fig. 2). Two patients (9%) had an ASA score of 2. Both of these patients declined surgical intervention despite having surgery offered. Nine patients were classified as having an ASA score of 3. Seven of these requested non-surgical treatment. The other two patients were deemed not to be candidates for surgery, one because of technical anatomical difficulties (comorbidities, including spina bifida and horseshoe kidney) and the other because of morbid obesity. The remaining 11 patients had an ASA score of 4 and were all deemed unfit for surgical treatment. There was a wide variety of comorbidities that resulted in patients not being considered candidates for surgery. The most commonly occurring conditions were ischaemic heart disease, diabetes mellitus, previous strokes and chronic obstructive pulmonary disease. Other conditions that occurred less frequently were spina bifida, Parkinson’s disease and active malignancy.

The raw data we collected are shown, alongside the outcome measures, in Table 1.

Fig. 1 Presentations to the urology department.

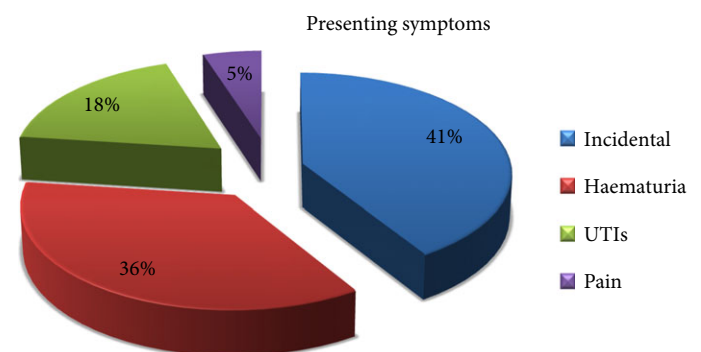
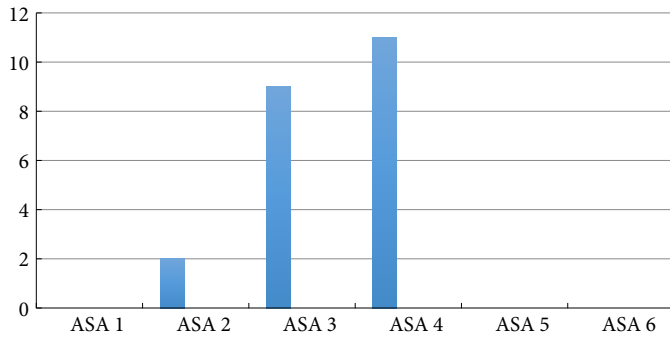


Fig. 2 American Society of Anesthesiologists (ASA) scores of the study cohort.



Primary Outcome Measures

Urinary tract infections

From these data we can see that half of the cohort had recurrent UTIs (50%, $n = 11$), and that a higher proportion of patients with bilateral stones (80%, $n = 4$) than unilateral stones (41%, $n = 7$) had recurrent infections. Patients who had more than one UTI were, in general, started on prophylactic antibiotics.

Progressive renal deterioration

Assessment of deterioration in renal function showed that 14% ($n = 3$) of patients had a progressive drop in eGFR of >30% during the follow-up period; again, with a higher proportion of those with bilateral stones in comparison to unilateral stones having this morbidity (40 vs 6%).

Mortality

Eight patients (36%) in the total cohort died during follow-up; however, of these patients, only two (9%) died from disease-specific causes. Both of these patients had bilateral complete staghorn calculi. The patients who survived follow-up (64%) had a mean to-date survival of 10.3 years. The patients who died from disease-specific causes had a mean survival of 4.4 years from the start of the study.

Table 1 Outcome measures.

Outcome measures	Unilateral (%)	Bilateral (%)	Whole cohort (%)
>1 UTI	7/17 (41)	4/5 (80)	11/22 (50)
Progressive renal deterioration	1/16 (6)	2/5 (40)	3/21 (14)
All-cause mortality	5/17 (29)	3/5 (60)	8/22 (36)
Disease-specific mortality	0	2/5 (40)	2/22 (9)
Dialysis	1/17 (6)	1/5 (20)	2/22 (9)
Hospital attendances	2/17 (12)	4/5 (80)	6/22 (27)

Secondary Outcome Measures

Dialysis dependence

Renal function deteriorated in two patients to a level that required dialysis. One patient who became dialysis-dependent had a unilateral stone and the other had bilateral stones.

Hospital admissions

To consider significant morbidity caused by the stone, we looked at the need for hospital admissions for stone-related problems. Six patients (27%) attended and were admitted to hospital during their period of follow-up; however, again there was considerable difference between bilateral and unilateral stones (80 vs 12%).

Statistical Analysis

A simple statistical analysis was undertaken of the data collected. A chi-squared test was performed to compare the difference between unilateral stones and bilateral stones. We then calculated the relative risk for these outcome measures using patients with unilateral stones as our control group. The results of these tests are shown in Table 2.

The relative risk of recurrent UTIs was 1.95 ($P = 0.127$). The value for renal deterioration was close to statistical significance ($P = 0.060$) and had a risk ratio of >6. Hospital admissions and disease-specific mortality were both statistically significant, with relative risks suggesting higher risk in patients with bilateral stones (6.8 for hospital admissions and 15.0 for disease-specific mortality).

Discussion

The results of the present study are discussed here on the study's own merits and in comparison with the previous study in 1973 by Blandy and Singh [1], with the aim of finding a treatment algorithm for the management of patients with staghorn calculi and minimal symptoms who either decline surgery or are unfit for intervention.

Table 2 Statistical analysis.

	Unilateral	Bilateral	P	Relative risk
Recurrent UTI	7/17	4/5	0.127	1.95
Renal deterioration	1/16	2/5	0.060	6.4
Hospital admission	2/17	4/5	0.003	6.8
Disease-specific mortality	0/17	2/5	0.006	15.0

Urinary Tract Infections

Urinary calculi and UTIs are inherently linked. This is attributable either to a stone being formed as a result of an infection (in ~15% of patients) or to an infection as a result of urinary tract calculi [2]. Studies on the composition of staghorn stones have shown infected stones rates of ~40–70% of all staghorn calculi [4]. A strong correlation between organisms isolated from the staghorn calculi and the urine of affected patients has been shown, with 70% of the patients having common organisms [4]. Studies have also shown that >50% of patients (some studies have reported up to 100% of patients) who have conservatively managed staghorn calculi have more than one positive urine culture during follow-up [4,6,7]. Because the patients in the present study were managed non-surgically it was not possible to determine confidently whether these stones harbour infective microorganisms or not; however, these data suggest that there may well be a proportion of infected stones that do not shed bacteria or colonize the urinary tract. Equally, there will be a proportion of sterile stones that do result in UTIs. It is therefore reasonable to conclude that, regardless of the cause of the stone, infection is a major factor causing morbidity in patients with conservatively managed staghorn calculi.

Antimicrobial prophylaxis is an area of interest in managing urinary tract calculi. There is evidence to suggest that prophylactic antibiotics in infected stones are beneficial [10], but most of the evidence on antibiotic prophylaxis relates to the surgically managed patient [10]. Given that there is strong concordance between the organisms in stones and in the urine, prophylactic antibiotics based on urine culture and sensitivity could provide significant symptomatic and survival benefits for conservatively managed patients.

Renal Deterioration and Dialysis Requirements

Deterioration in renal function is one of the major concerns when planning to manage someone with staghorn calculi conservatively. This concern is not unfounded, with studies showing that the proportion of patients who die from progressive renal failure is as high as 50% [1]. The results of the present study showed, more optimistically, that only three patients (14%) succumbed to progressive renal decline and that renal function deteriorated to a level that required dialysis in only two of these patients (9%). Unsurprisingly,

the rates of renal decline were higher in patients with bilateral calculi as compared with those with unilateral stones (40 vs 6%). The proportion of the patient cohort requiring dialysis was also higher in the bilateral stone group in comparison to those with unilateral stones (20 vs 6%). The absolute numbers for each of the dialysis groups was the same ($n = 1$); however, there was a trend towards higher dialysis requirements in patients with bilateral stones. Considering both renal decline and dialysis requirements, therefore, we can see that having an unaffected kidney provides a good reserve and helps protect against declining renal function.

This recognized deterioration in renal function has been attributed to several factors, including mechanical obstruction, renal parenchymal damage secondary to infection, chronic inflammation and fibrosis [11]. There are two pertinent points to note from this. Firstly, this highlights the importance of preventing and treating infections early in order to minimize parenchymal damage and help reduce stone growth. Secondly, preservation of residual renal function as well as protecting the unaffected kidney in patients with unilateral stones is of utmost importance.

There may be several reasons that the present study showed less of a decline in renal function than was observed in previous studies. First and foremost, significant advances have been made in the field of microbiology and in the availability of antibiotics and the understanding of their use. This has meant that better antimicrobial agents are available and we are able to target them more effectively. We are also considerably better at controlling risk factors for deteriorating renal function (such as high blood pressure and diabetes) [12–14]. In addition, growth of interventional radiology has helped us to treat patients who have sepsis with percutaneous drainage techniques, which not only has the benefits of reduced morbidity and mortality but also minimizes the nephron loss from these infections and obstructive events [15].

Mortality

The mortality associated with staghorn calculi has traditionally been considered to pose too high a risk to manage patients conservatively. Blandy and Singh reported that a high proportion (50%) of their cohort eventually experienced progressive renal failure and died as a result of this [1]. As detailed earlier, mortality, and more importantly, disease-specific mortality may not be as high as this. The patients who died from causes not attributable to their stones died from unrelated causes such as ischaemic heart disease and cancer. This is to be expected as, by definition, a large number of patients who are managed conservatively will have a significant set of severe comorbidities that have precluded surgery. When considering disease-specific mortality, it would

appear that there are several factors that would put patients at increased risk. In the present study patients who died from disease-specific causes, i.e. urinary sepsis and acute or chronic renal failure, had bilateral complete staghorn calculi. In these patients, an anaesthetic review was organized to further assess the surgical risks. At these reviews, the risks of general anaesthesia were deemed to outweigh the short- and long-term risks of sepsis and renal failure. Knowing that the biggest risks to these patients are sepsis and progressive decline in renal function, we can set out to try and prevent these, as described above.

Hospital Attendance

From the data on hospital attendances we can deduce that bilateral stones cause severe morbidity more frequently than do unilateral calculi. This adds further weight to the argument that bilateral stones should be taken more seriously, as they are associated with both higher morbidity and mortality.

Conservative Management

As it has been 42 years since Blandy and Singh published their landmark paper setting the standard for active management of staghorn calculi, it seems appropriate to compare the two studies.

There are two major differences between the results of the papers. Firstly, as previously mentioned, there was a significant difference in the rates of progressive decline in renal function and mortality. The results of the present study are consistent with more recent data on progressive renal decline [3]. The second major difference is that, in the study by Blandy and Singh, nearly 50% of the patients who were treated expectantly progressed to requiring a nephrectomy during follow-up. In the present study, none of the cohort needed any surgical intervention. These findings would support conservative management of staghorn calculi in appropriately selected patients.

There are several possible reasons for the aforementioned differences. Firstly, although the original paper looked at conservative management of patients with staghorn calculi, 20 of the patients included had a primary nephrectomy and 16 underwent a delayed nephrectomy as a result of intolerable symptoms or pyonephrosis [1]. This left only 18 patients who were truly conservatively managed, compared with the 22 patients in the present study. Another distinction between the studies is that the definitions used for 'silent' staghorn calculi differed. Blandy and Singh noted that their patients were far from asymptomatic, with some patients requiring a nephrectomy as a result of intolerable symptoms. This suggests that these stones may have been causing more problems than those in patients whose symptoms were more

tolerable. This led the authors to conclude that there is no such thing as an asymptomatic staghorn calculus [1]; however, since then, it has been reported that there are patients who are truly asymptomatic, although the numbers are small (~1%) [16]. It would also appear that there is a subset of patients who have trivial or minimal symptoms. It may also be the case that, because of the increased availability and diversity of radiological techniques, more incidental staghorn stones are detected that would have gone undiagnosed at the time when the paper by Blandy and Singh was published.

Factors that influence the decision to manage conservatively the aforementioned subset of patients are of utmost importance. Essentially, we noted two indications: patients who have minimal symptoms and decline surgical intervention and patients who are medically unfit for surgery. This could be another reason for the difference between the two papers; the criteria for conservative management were not explicitly outlined in the original paper.

Added to the above points, the recent advances in medicine discussed above could have influenced the differences in the results, particularly when considering declining renal function and mortality rates.

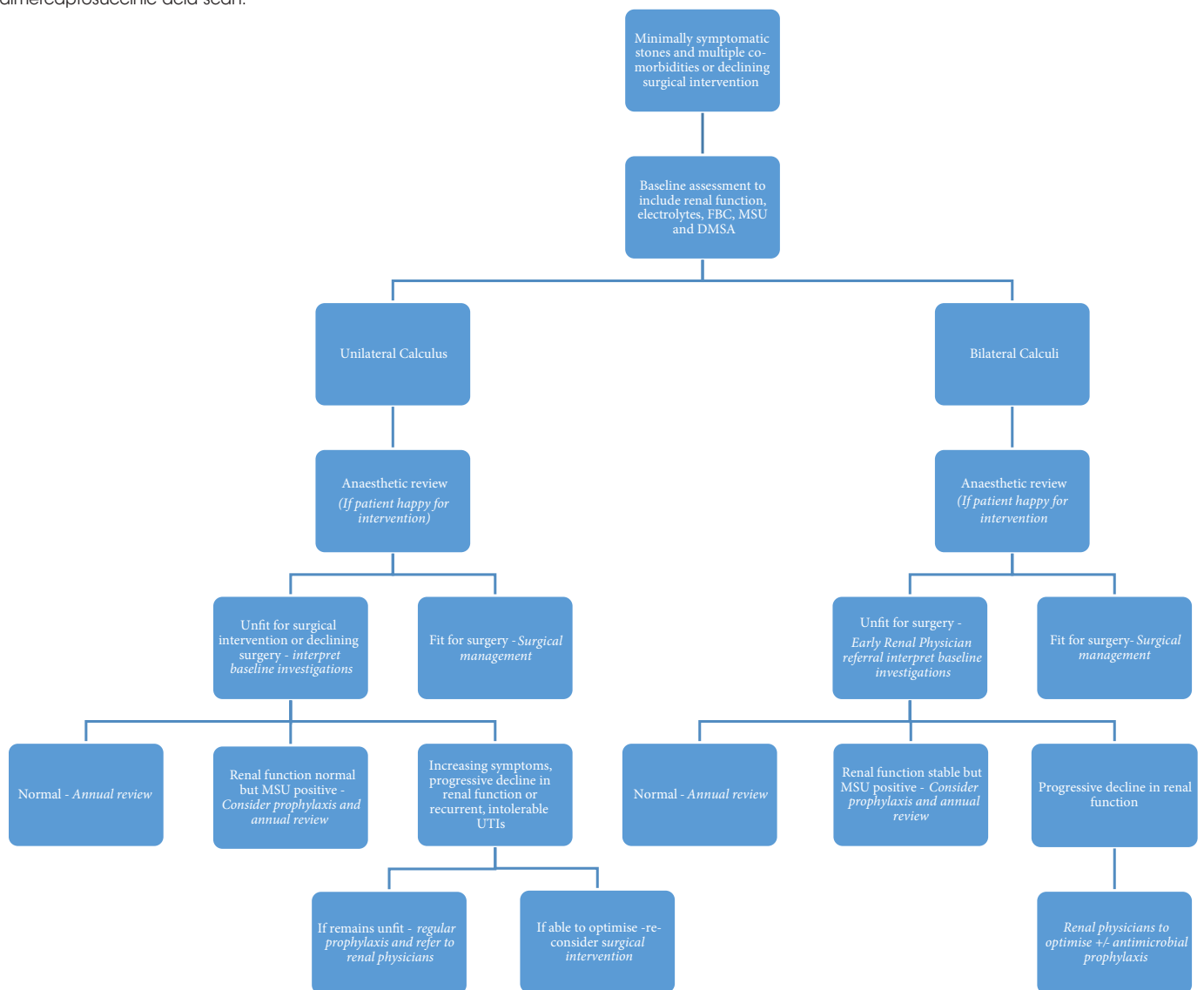
Limitations and Further Recommendations

The two main limitations of the present study are its small sample size and the relatively short follow-up. With regard to sample size, it is difficult to obtain a large sample of conservatively managed staghorn stones because, currently, active management of these stones is preferred. We believe that the present study includes a relatively large single-centre cohort for the UK, but that the next step would be to obtain national data on conservatively managed patients in order to expand on the results of this study. A national database would help to achieve this. To address the short follow-up period we are continuously monitoring these patients and collecting data on other patients in the Health Trust and are hoping to publish our longer-term results in the future. Another limitation is that we are unable to comment on the composition of the stones, especially with regard to rates of infected vs sterile stones. From the encouraging results of the present study, we can conclude that this is an area in which further research would be valuable.

Conclusions

The present study helps to counsel patients with regard to their chances of future problems when they are either unfit for surgery or decline intervention. As we have shown, patients with unilateral stones fare considerably better than those with bilateral stones. This is of course a logical conclusion to draw, but the specific negative outcomes and

Fig. 3 Management algorithm for patients unfit for surgery or who decline intervention. FBC, full blood count; MSU, mid-stream urine culture; DMSA, dimercaptosuccinic acid scan.



adding numerical value to these could be of value when counselling patients. We can state that patients with bilateral stones are nearly twice as likely to have recurrent UTIs and are more likely to have a progressive decline in renal function, by a factor of 6. Also, perhaps more importantly, bilateral stones are significantly more likely to lead to hospitalization for stone-related morbidity and also have significantly higher rates of disease-specific mortality. This information is useful for patients as it can inform discussions with patients who are unfit to undergo active stone management. In addition we hope that these data will help assist decision-making in stone multidisciplinary team meetings and outpatient clinics. Taking all of this into account, we have devised a recommended monitoring and treatment algorithm for these patients, which would allow us

to take an ‘active surveillance’ approach to ‘conservative management’ (Fig. 3). It is important to note that these recommendations relate to patients who have been deemed unfit for surgery in consultation with an anaesthetist or who decline surgical intervention.

In summary, we can state that conservative management of staghorn calculi, in the context of patients who are unfit for surgery or who decline intervention, is perhaps not as unsafe as previously thought. Careful patient selection, that is, patients with asymptomatic, unilateral stones where the patient is unfit for surgical intervention, and thorough patient counselling about the risks of conservative management could make it a suitable option for an appropriate subset of patients.

Conflict of Interest

None declared.

References

- 1 Singh M, Chapman R, Tresidder GC, Blandy J. The fate of the unoperated staghorn calculus. *BJU Int* 1973; 45: 581–5
- 2 Thomas B, Tolley D. Concurrent urinary tract infection and stone disease: pathogenesis, diagnosis and management. *Nat Clin Pract Urol* 2008; 5: 668–75
- 3 Teichman JM, Long RD, Hulbert JC. Long-term renal fate and prognosis after staghorn calculus management. *J Urol* 1995; 153: 1403–7
- 4 Shafi H, Shahandeh Z, Heidari B et al. Bacteriological study and structural composition of staghorn stones removed by the anatomic nephrolithotomic procedure. *Saudi J Kidney Dis Transpl* 2013; 24: 418–23
- 5 Rous SN, Turner WR. Retrospective study of 95 patients with staghorn calculus disease. *J Urol* 1977; 118: 902–4
- 6 Flamm J, Forstik F. Conservative treatment of staghorn calculi [abstract translated from German]. *Z Urol Nephrol* 1987; 80: 395–400
- 7 Burchardt P. Conservative treatment of staghorn and residual calculi [abstract translated from German]. *Urologe A* 1982; 21: 45–8
- 8 Streem SB, Yost A, Dolmatch B. Combination sandwich therapy for extensive renal calculi in 100 consecutive patients: immediate, long-term and stratified results from a 10-year experience. *J Urol* 1997; 158: 342–5
- 9 Akman T, Binbay M, Kezer C et al. Factors affecting kidney function and stone recurrence rate after percutaneous nephrolithotomy for staghorn calculi: outcomes of a long-term followup. *J Urol* 2012; 187: 1656–61
- 10 Zanetti G, Paparella S, Trinchieri A, Prezioso D, Rocco F, Naber KG. Infections and urolithiasis: current clinical evidence in prophylaxis and antibiotic therapy. *Arch Ital Urol Androl* 2008; 80: 5–12
- 11 Boonla C, Krieglstein K, Bovornpadungkitti S et al. Fibrosis and evidence for epithelial-mesenchymal transition in the kidneys of patients with staghorn calculi. *BJU Int* 2011; 108: 1336–45
- 12 Ptinopoulou AG, Pikilidou MI, Lasaridis AN. The effect of antihypertensive drugs on chronic kidney disease: a comprehensive review. *Hypertens Res* 2013; 36: 91–101
- 13 Gunst J, Schetz M. Clinical benefits of tight glycaemic control: effect on the kidney. *Best Pract Res Clin Anaesthesiol* 2009; 23: 431–9
- 14 Viazzi F, Leoncini G, Pontremoli R. Antihypertensive treatment and renal protection: the role of drugs inhibiting the renin-angiotensin-aldosterone system. *High Blood Press Cardiovasc Prev* 2013; 20: 273–82
- 15 Goldsmith ZG, Oredein-McCoy O, Gerber L et al. Emergent ureteric stent vs percutaneous nephrostomy for obstructive urolithiasis with sepsis: patterns of use and outcomes from a 15-year experience. *BJU Int* 2013; 112: E122–8
- 16 Vargas AD, Bragin SD, Mendez R. Staghorn calculus: its clinical presentation, complications and management. *J Urol* 1982; 127: 860–2

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Abbreviations: ASA, American Society of Anaesthesiologists; eGFR, estimated GFR.