# **Original Article**



# Do men with bladder stones benefit from treatment of benign prostatic obstruction?

Gianluca Maresca<sup>1,2</sup> (i), Samuel Mc Clinton<sup>1,2</sup>, Satchi Swami<sup>1,2</sup>, Ismail El-Mokadem<sup>1,2</sup> and James F. Donaldson<sup>1,2</sup>

<sup>1</sup>Department of Urology, Aberdeen Royal Infirmary – NHS Grampian, and <sup>2</sup>Academic Urology Unit (AUU), University of Aberdeen, Aberdeen, UK

# **Objective**

To identify whether men aged  $\geq$ 40 years with bladder stones (BS) benefit from treatment of benign prostatic obstruction (BPO).

#### Patients and methods

A regional, retrospective study of patients undergoing BS surgery between January 2011 and December 2018 was performed using a prospectively collected database. The primary outcome was BS recurrence after successful removal. Kruskal–Wallis and chi-squared statistical tests were used.

## **Results**

A total of 174 patients underwent BS removal and 71 (40.8%) were excluded due to BS formation secondary to causes other than BPO. Hence, 103 men aged  $\geq$ 40 years had BS successfully removed, of which 40% had a history of upper tract urolithiasis. These men were divided into three groups: those undergoing contemporaneous medical, surgical, or no BPO treatment. Age, diabetes, previous urolithiasis and previous BPO surgery were well matched between the BPO treatment groups. In all, 18 of these men (17%) had BS recurrence after 46 months follow-up.Recurrences were significantly lower following BPO surgery; one of 34 (3%) men versus five of 28 (18%) with no BPO treatment (P = 0.048) and 12 of 41 (29%) with medical BPO treatment (P = 0.003). Recurrences after medical and no BPO treatment were similar (P = 0.280). In all, 34 men (33%) had BPO complications that were similar between groups (P = 0.378).

#### Conclusion

This is the largest reported cohort of men, with the longest follow-up after BS removal. Most men aged ≥40 years with BS benefit from BPO surgery. However, the study findings also support a multifactorial aetiology for BS, which questions the dogma that BS are an 'absolute indication' for BPO surgery, as is stated in the Non-neurogenic Male Lower Urinary Tract Symptoms European Association of Urology Guideline. Assessment and management of all causative factors is likely to enable selection of which men will benefit from BPO surgery and to reduce BS recurrence rates.

# **Keywords**

benign prostatic obstruction, benign prostatic hyperplasia, bladder stones, EAU Guidelines, lower urinary tract dysfunction, lower urinary tract symptoms, metabolic stone formation

# Introduction

Bladder stones (BS) account for 4%–5% of all urinary tract stones in developed nations [1,2]; however, BS account for a disproportionately high proportion of deaths from urolithiasis (8%) [3].

Bladder stones can be classified as primary, secondary or migratory [4]. Primary BS are endemic in children in many developing nations, and are associated with dehydration, recurrent diarrhoea, and a diet deficient in animal protein [5]. Secondary BS occur in patients with associated lower urinary tract abnormalities including: BOO, neurogenic bladder dysfunction, bladder augmentation, foreign bodies, and chronic bacteriuria. Migratory BS form in the upper urinary tract before moving into the bladder [6,7].

When compared with upper-tract stones, BS affect men (85% vs 57%) and older patients (68 vs 45 years) more commonly in developed nations [1]. Benign prostatic obstruction (BPO)

is common in men aged ≥40 years [8], and thus BPO is presumed to be the commonest cause of BS. A reported 48%-80% of BS have been attributed to BPO [7,9], despite no urodynamic evidence to support this assumption [10]. This led to the dogma that BS are an 'absolute (BPO) operation indication' in men aged ≥40 years, which is stated in the European Association of Urology (EAU) Guideline on 'Non-Neurogenic Male Lower Urinary Tract Symptoms (LUTS)' [11].

The EAU Guideline on 'Bladder Stones' also recommends performing 'procedures for the stone and underlying BOO simultaneously in adults with BS secondary to BOO, where possible' [4]. However, the 2021 the AUA Guideline on BPH/ LUTS recommends BPO surgery for men with 'recurrent BS' [12]. The UK National Institute for Health and Care Excellence (NICE) Guidelines on LUTS in men (CG97), and Renal and Ureteric stones (NG118), do not provide guidance on treatment of men with BS [13,14].

There is a paucity of evidence to support the 'absolute' need for BPO surgery in all men ≥40 years with BS, particularly in the current era of medical and minimally invasive procedures for BPO [15,16]. The objective of this study was to determine whether men aged ≥40 years with BS benefit from medical or surgical BPO treatment.

# Patients and Methods

A prospective database of all patients undergoing BS surgery in our region was maintained. Electronic patient records were assessed. BPO management options were at the surgeon's and patient's discretion. Urodynamic assessments were not mandatory prior to BS removal and reporting of flow studies, post-void residual urine volumes (PVRs), stone size and numbers were poorly documented in this dataset. Patients were allocated into three BPO management groups: Group 1 received BS surgery only, without any BPO treatment; Group 2 received BPO medication, which was commenced at the time of BS management; and Group 3 received BPO surgery.

#### Inclusion Criteria

All men aged ≥40 years undergoing BS surgery in our region in an 8-year period (2011-2018 inclusive) were included. Patients residing in NHS Grampian, NHS Shetland or NHS Orkney catchment areas were included to reflect the population of the entire North East Scotland region. BS of any size, number, and composition, first-time or recurrent stone formers, and men who had received previous BPO surgery or medication were included.

# **Exclusion Criteria**

Patients with risk factors for secondary BS formation other than BPO were excluded: pre-existing bladder augmentation

or urinary diversion, neuropathic bladder dysfunction (including spinal cord injury, multiple sclerosis, Parkinson's disease and stroke), foreign bodies (including indwelling catheters), and urethral stricture or bladder neck stenosis. Men who had undergone previous radical prostatectomy were excluded. Men who were not rendered stone-free at their first operation and did not undergo a subsequent BS clearance procedure (e.g., due to development of comorbidities precluding surgery) were also excluded.

#### Bladder Stones Removal

All BS procedures were eligible for inclusion: transurethral cystolithotripsy (TUCL) or percutaneous cystolithotripsy, and open or laparoscopic cystolithotomy. All lithotripsy modalities were included: mechanical, laser, pneumatic or ultrasonic lithotripsy.

#### Benign Prostatic Obstruction Treatment Options

The BPO treatments were: no treatment (observation), medical treatment ( $\alpha$ -blocker and/or  $5\alpha$ -reductase inhibitor), or surgery. Surgery was mono-polar or bipolar TURP: either concurrently with BS removal or as a pre-planned, staged procedure.

#### **Outcomes**

The primary outcome was BS recurrence after complete removal. Secondary outcomes included stone-free rate (SFR). Recurrence and SFR were defined as any BS detected ≥3 months postoperatively. Modality of stone-free status assessment was at the surgeon's discretion: direct visualisation, CT, ultrasonography, or X-Ray. Clinical and imaging follow-up was at the surgeon's discretion.

Other secondary outcomes were: major postoperative complications, defined as Clavien-Dindo classification Grade III–V and occurring at  $\leq 30$  days [17]. BPO complications occurred >30 days postoperatively and included: acute urinary retention (AUR), recurrent UTIs, new bladder diverticulum formation and visible haematuria, overflow incontinence, upper-tract dilatation, or renal insufficiency due to BPO [11]. Unplanned BPO treatments included surgery, medication, or long-term catheterisation (indwelling or intermittent).

#### Data Analysis

Analysis used the median and interquartile range (IQR). Statistical analyses were performed using the Social Science Statistics Calculator using the Kruskal–Wallis and chi-squared tests [18].

# **Results**

# Causes of BS Formation

A total of 174 patients underwent BS procedures during the study period and 71 (40.8%) were excluded. The majority of

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exclusions (69 patients [97%]) were because BPO was deemed unlikely to have caused their BS: 27 were female, 25 men had neurogenic bladder dysfunction, 11 were men aged <40 years, and six men had other causes of BOO (urethral stricture or bladder neck stenosis). Other reasons for exclusion are listed in Fig. 1.

In all, 103 men aged ≥40 years met the inclusion criteria; these constituted 59.2% of all patients undergoing BS removal.

## Benian Prostatic Obstruction Treatment Groups

In all, 28 men (27%) were allocated to Group 1 (no BPO treatment), 41 (40%) to Group 2 (BPO medication), and 34 (33%) to Group 3 (BPO surgery). In Group 3, 25 men (74%) underwent concomitant BS and BPO surgery; nine (26%) underwent staged procedures.

#### **Baseline Characteristics**

Baseline and outcome data are summarised in Table 1. The BPO treatment groups were well matched for age (P = 0.872), previous urolithiasis (P = 0.139), previous BPO surgery (P = 0.762), and diabetes (P = 0.096). The median duration between previous BPO surgery and BS surgery was 7 years overall and was not significantly different between groups (P = 0.309): 7 years in Group 1, 12 years in Group 2 and 7 years in Group 3. Most men underwent TUCL (102 [99.3%]), one patient (0.97%) underwent percutaneous cystolithotripsy.

### Follow-Up

The overall median duration of follow-up was 3.8 years. This was not significantly different between groups (P = 0.352); however, it was numerically longer in Group 1 (median 58 months) than Group 2 (46 months) or Group 3 (39 months).

#### Bladder Stone Recurrence Rates

In all, 18 patients (17%) were found to have recurrent BS, with a median time to recurrence of 28 months. There were significantly more recurrences in Group 2 patients (12/41 [29%]) than in Group 1 (five/28 [18%]) and Group 3 (one/34 [3%]) (P = 0.011). When pairwise comparisons were performed, Group 3 was significantly different from both Group 1 (P = 0.048) and Group 2 (P = 0.003), whilst Group 1 vs Group 2 was not significantly different (P = 0.280).

#### Perioperative Outcomes

The SFR after one procedure was 92% and was similar between groups (P = 0.616). The SFR after two or fewer procedures was 100%. The SFR was 91% (20/22 patients) when BS and BPO procedures were carried out concomitantly, which is equal (P = 0.941) to the SFR for patients undergoing staged BS and BPO procedures separately: 92% (11/12 patients).

Two men (1.9%) had an intraoperative extraperitoneal bladder perforation treated with prolonged catheterisation (ClassIntra Grade 2) [19]. Six men (5.7%), two from each group (P = 0.925) experienced haematuria intraoperatively that responded to irrigation alone (ClassIntra Grade 1). There were no major postoperative complications. No patients required a blood transfusion or return to theatre.

# Benign Prostatic Obstruction Complications

A BPO complication was recorded in 34 men (33%) and was not significantly different between groups (P = 0.378). In all, 18 men (17.5%) had AUR, the most common BPO complication, which was similar between groups (P = 0.860). No patient developed overflow incontinence, upper tract dilatation, or renal insufficiency due to BPO. A total of 36 men (35%) later required an unplanned BPO treatment (medication, catheter, or surgery): this was similar between groups (P = 0.780).

#### **Discussion**

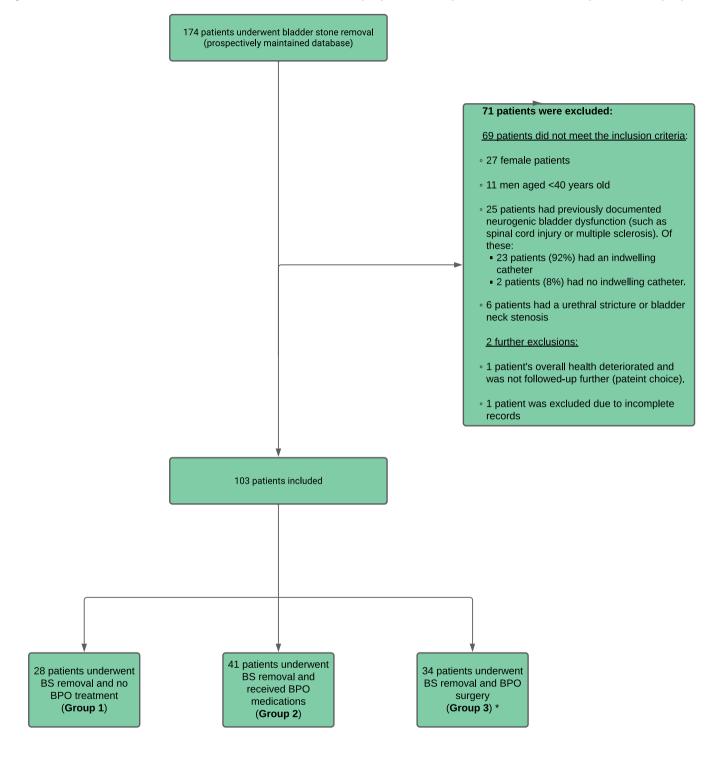
This study presents long-term BS recurrence rates and BPO outcomes in men aged ≥40 years after successful BS removal. This is the largest reported cohort of men undergoing BS removal and represents the longest follow-up. There were significant rates of BS recurrence, BPO complications and need for subsequent BPO treatment. This highlights the significant morbidity associated with BS.

This study also reports a large, contemporaneous cohort of adults undergoing BS removal in a developed nation: 40.8% of patients' with BS were not caused by BPO (Fig. 1). Another notable finding is that 40% of included men aged ≥40 years had previous upper-tract urolithiasis. These findings also support a multifactorial aetiology for BS.

Benian Prostatic Obstruction Treatment Options for Men Aged ≥40 years with BS

Age, diabetes, previous urolithiasis and previous BPO surgery were well matched between BPO treatment groups. Men undergoing BPO surgery were less likely to experience BS recurrence than men undergoing medical treatment or no BPO treatment (P = 0.003 and P = 0.048, respectively). This suggests a benefit for BPO surgery. However, interestingly, the rate of BS recurrence was not significantly different between no BPO treatment and BPO medications. However, the efficacy of BPO interventions was not proportional to the

Fig. 1 Study profile. \*22 patients underwent a TURP at the same time as TUCL (65%). The remaining 12 patients underwent a staged procedure (35%).



#### Abbreviations:

- BS: Bladder Stones
- BPO: Benign Prostatic Obstruction
- \* 22 patients underwent a TURP at the same time as Transurethral cystolithotripsy (65%). The remaining 12 patients underwent a staged procedure (35%).
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**Table 1** Outcomes in men aged ≥40 years undergoing BS removal by BPO treatment group.

| Outcomes                        |  | Overall    | Group 1<br>No BPO<br>treatment | Group 2<br>Medical<br>BPO treatment | Group 3<br>BPO surgery<br>(TURP) | P     |
|---------------------------------|--|------------|--------------------------------|-------------------------------------|----------------------------------|-------|
| Number of patients, $n$ (%)     |  | 103 (100)  | 28 (27)                        | 41 (40)                             | 34 (33)                          | N/A   |
| Baseline                        | Age, years, median (IQR)   | 72 (67–79) | 73 (63–78)                     | 72 (67–80)                          | 74 (67–78)                       | 0.872 |
| characteristics                 | Previous BS, n (%)   | 14 (13)    | 6 (21)                         | 4 (10)                              | 4 (12)                           | 0.342 |
|                                 | Previous upper-tract stone, n (%)  | 41 (40)    | 15 (54)                        | 15 (37)                             | 11 (32)                          | 0.204 |
|                                 | Previous urinary stones (any), n (%)   | 48 (47)    | 17 (61)                        | 15 (37)                             | 15 (44)                          | 0.139 |
|                                 | Previous BPO surgery, n (%)  | 11 (14)    | 4 (14)                         | 4 (10)                              | 3 (9)                            | 0.762 |
|                                 | Diabetes mellitus, n (%)   | 20 (19)    | 6 (21)                         | 4 (10)                              | 10 (29)                          | 0.096 |
| Follow-up, months, median (IQR) |  | 46 (22–87) | 58 (29–97)                     | 46 (24–82)                          | 39 (19–77)                       | 0.352 |
| Perioperative                   | SFR, first procedure, n (%)  | 95 (92)    | 27 (96)                        | 37 (90)                             | 31 (91)                          | 0.616 |
|                                 | SFR for 1-2 procedures, n (%)  | 103 (100)  | 28 (100)                       | 41 (100)                            | 34 (100)                         | N/A   |
|                                 | Major postoperative complication, n (%)  | 0 (0)      | 0 (0)                          | 0 (0)                               | 0 (0)                            | N/A   |
| Stone recurrence                | BS recurrence, n (%)   | 18 (17)    | 5 (18)                         | 12 (29)                             | 1 (3)                            | 0.011 |
|                                 | Time to BS recurrence, months, median (IQR)  | 28 (9–36)  | 35 (13–39)                     | 31 (17–41)                          | 23 (N/A)                         | N/A   |
| ВРО                             | BPO complications (total), n (%)   | 34 (33)    | 8 (29)                         | 15 (37)                             | 11 (32)                          | 0.781 |
|                                 | AUR, n (%)   | 18 (17.5)  | 5 (18)                         | 8 (20)                              | 5 (15)                           | 0.860 |
|                                 | Recurrent UTIs, n (%)  | 4 (4)      | 1 (4)                          | 1 (2)                               | 2 (6)                            | 0.704 |
|                                 | Bladder diverticulum, n (%)  | 3 (3)      | 1 (4)                          | 2 (5)                               | 0 (0)                            | N/A   |
|                                 | Treatment-resistant macroscopic haematuria due to BPH, n (%)                           | 9 (9)      | 1 (4)                          | 4 (10)                              | 4 (12)                           | 0.517 |
|                                 | Overflow incontinence, upper tract dilatation or renal insufficiency due to BPH, n (%) | 0 (0)      | 0 (0)                          | 0 (0)                               | 0 (0)                            | N/A   |
|                                 | Need for subsequent BPO treatment, n (%)   | 36 (35)    | 9 (32)                         | 16 (39)                             | 11 (32)                          | 0.780 |
|                                 | Need for BPO surgery, n (%)  | 5 (5)      | 0 (0)                          | 4 (10)                              | 1 (3)                            | N/A   |
|                                 | Need for catheterisation, n (%)  | 20 (19)    | 6 (21)                         | 9 (22)                              | 5 (15)                           | 0.697 |
|                                 | Need for new BPO Medication(s), n (%)  | 18 (17)    | 6 (21)                         | 4 (10)                              | 8 (24)                           | 0.239 |

likelihood of BS recurrence: BS recurrence rates were numerically lower in patients with no BPO treatment than medical BPO treatment (29% vs 18%, P = 0.280). This suggests that factors other than BPO treatment, which were not robustly assessed, affected the probability of BS recurrence, implying a multifactorial aetiology of BS.

Benign prostatic obstruction complications and need for unplanned subsequent BPO treatments (medication, catheter, or surgery) were, surprisingly, equal between groups. However, the commonest postoperative BPO complication was AUR, which could also be caused by detrusor failure rather than BPO. No patient underwent preoperative invasive urodynamics and documentation of uroflowmetry and PVRs was not consistent. In Group 3 (BS treatment and surgical BPO management) 15% of men required catheterisation for AUR during the follow-up period, which is similar to the reported rate following TURP in men without BS (12.5%)

Only one other non-randomised study, in just 64 men with BS, compared medical treatment (tamsulosin and finasteride) vs TURP [15]. Only one patient, in the TURP group, had a BS recurrence (3.4% vs 0%), after a median 39 months follow-up. In all, 34% of men on BPO medication subsequently required a TURP, compared with 10% in the present study. A high PVR prior to BS removal predicted the need for subsequent TURP (odds ratio 1.033, P = 0.014). There are no other comparatives

studies for BPO treatments in men undergoing BS removal.

# The Aetiology of BS in Men Aged >40 years

The finding of a lower rate of recurrence in men undergoing BPO surgery in this study supports the theory that BPO is the commonest cause of BS in men aged  $\geq$ 40 years [7,9]. An autopsy study found that men with histological evidence of BPH had an eight-fold higher incidence of BS than men without BPH (3.4% vs 0.4%), despite an equal incidence of upper-tract stones [21].

Studies using clinical data have consistently concluded that BPO is the commonest cause of BS in men aged ≥40 years [4,22]: 48%–80% of BS are attributed to BPO [7,9]. However, none of these studies included invasive urodynamics, the 'gold standard' diagnostic test for BPO [11]. The diagnosis of BPO was based on the presence of: a) LUTS, which are common with BS; and, b) benign prostatic enlargement, which is common in men aged ≥40 years but does not reliably confer the presence of BPO [8,11].

Lower urinary tract dysfunction (LUTD) is hypothesised to cause urinary stasis and thus BS form due to delayed washout of crystalline aggregates, which promotes nucleation, crystal growth, aggregation and thus stone formation [7,9,16]. BPO is the commonest cause of LUTS in men aged  $\geq$ 40 years [11]. However, we now recognise that there are many causes of

LUTS other than BPO, including: detrusor failure, neurogenic bladder dysfunction (which may be occult, e.g., diabetic autonomic neuropathy), urethral stricture, and bladder neck stenosis [4]; all of which are associated with BS formation [4].

Only one study reported invasive urodynamics in men with BS. Urodynamics were performed before and after shockwave lithotripsy for BS in 46 men aged 60-69 years. Just 51% had urodynamic evidence of BOO [10]. Surprisingly, the mean PVR was just 94 mL. Overall, 10% had detrusor under-activity, 68% had detrusor over-activity, and 18% had normal urodynamics. This suggests that in half of men, the prostate could be merely an innocent bystander, not implicated in BS formation. However, 74% of these men had a history of previous urolithiasis [10], significantly higher than the present (47%) and other studies (37%) [6]. This urodynamic study could therefore possibly slightly over-represent metabolic BS formers and underrepresent BS formed due to BPO.

In this study, 40% of men had had previous upper-tract stones and 40.8% of all patients undergoing BS removal in our study were excluded as other factors were more likely causes of BS (Fig. 1). These findings strongly support a metabolic pre-disposition to BS. Only 3%-4.7% of men who require surgery for BPO have formed BS [23,24]. Most men with BS have PVRs of <100 mL [10] and the majority of patients with BPO with high PVRs, do not form BS [6,25,26]. This suggests that urinary stasis or LUTD alone is insufficient for BS formation without another pre-disposing factor.

A study from the Mayo Clinic performed metabolic urine assessments in 57 men undergoing BPO surgery: men with BS were compared with a control group of men without BS who had either previous AUR or a high PVR. BS formers had lower urine pH (5.9 vs 6.4, P = 0.02), lower 24-h urine magnesium (106 vs 167 mmol, P = 0.01), and higher 24-h urine uric acid super-saturation rates (2.2 vs 0.6, P < 0.01) [6]. BS formers also had higher rates of previous upper-tract urolithiasis (36.7% vs 4%, P = 0.01) [6].

A metabolic pre-disposition is further supported by the chemical composition of BS (Fig. 2). The spectrum and prevalence of chemical compositions are comparable to those seen in upper-tract urolithiasis, which also vary between populations. Calcium stones predominate; uric acid stones constitute 9.6%-59% and infection (struvite) stones constitute 7.7%-46.9% of BS [27,28].

Renal stones occur in 16%-30% of adults with PUJ obstruction (PUJO) [29]. In the absence of recurrent infections, 76%-87% of PUJO stone-formers have metabolic abnormalities in addition to urinary stasis [29]. This suggests that another factor (metabolic abnormality or chronic bacteriuria) is typically required in addition to urinary stasis for lithogenesis to occur in both patients with BS and PUJO.

This evidence overwhelmingly suggests that the cause of lithogenesis must therefore be multifactorial in most or all patients with BS. Causative factors include: metabolic predisposition, LUTD, chronic bacteriuria, and abnormal material (including catheters, foreign bodies, and bowel mucosa/mucous) [4,22,28].

# Preoperative Investigations

Identifying and addressing all potential contributing factors to BS formation is therefore very likely to reduce recurrence rates after successful BS removal. Thorough assessment for the presence of LUTD, metabolic predisposition, presence of abnormal material and infection is therefore likely to be beneficial when planning BS treatment [4]. Assessment of the presence of BPO in men with BS can be challenging as BS typically cause LUTS [4]. However, there was no significant difference in both invasive and non-invasive urodynamic findings in men before and after BS removal in the only published urodynamics [10].

# Concomitant vs Staged BS and BPO Surgery

There are no previously reported studies that directly compare outcomes for staged vs concomitant BPO and BS surgery [4]. This study found no major intra- or postoperative complications in men undergoing concomitant or staged BPO and BS procedures and SFRs were equal (P = 0.941).

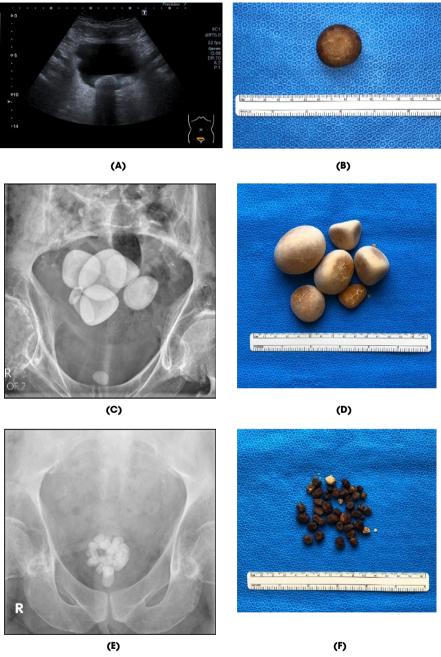
Three contemporary, retrospective studies report outcomes in men undergoing BPO surgery vs TUCL and BPO surgery concomitantly: they all report no difference in intraoperative or major postoperative complications and 100% SFRs [25,30,31].

One study in 1078 men undergoing TURP, of which 297 had a concomitant TUCL, found a higher rate of postoperative UTIs following concomitant TUCL (2.0% vs 0.6%, P = 0.044) [30]. There was no difference in rates of urinary incontinence (0.3% vs 0.3%, not statistically significant).

Two studies compared men undergoing holmium laser enucleation of prostate with or without concomitant TUCL: 54 of 963 men and 41 of 320 men underwent concomitant TUCL [25,31]. The larger study found higher UTI (7.4%) and sepsis (1.9%) rates in patients who underwent concomitant TUCL (3.1% and 0.1%) [31]. The smaller study found a higher rate of transient postoperative urinary incontinence (26.8% vs 12.5%, P = 0.03). Long-term continence rates were equal [25].

These small increases in the rates of minor (Clavien-Dindo Grade I–II), short-term postoperative complications in TUCL patients are expected as stones commonly harbour bacteria [32] and BS are associated with detrusor over-activity [6].

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These findings suggest concomitant BPO and BS surgery can be performed safely and effectively in carefully selected men. However, it is likely that men who are frail, have a history of recurrent UTIs, or who have a very large BS or prostate may be more safely and/or effectively treated with staged procedures.

Limitations and Strengths of this Study

Whilst data collection in this study was retrospective, a prospectively maintained log of consecutive patients undergoing BS removal was used. Urodynamics (including uroflowmetry and PVR) were not reliably recorded. Imaging was not routinely used to confirm stone-free status, which was typically assessed endoscopically; however, this is accepted practice, employed in some randomised controlled trials (RCTs) [33].

Surveillance imaging was not routinely performed; hence, BS recurrences were typically symptomatic. However, electronic records included all imaging, primary care referrals, prescription records, and hospital episode data. The median duration of follow-up varied amongst groups. While this was not statistically significant (P = 0.352), the clinical significance is unclear.

Men who underwent previous BPO surgery and later developed BS were included in the study. The median duration between previous BPO surgery and BS diagnosis was 7 years. It is therefore likely that significant prostatic regrowth had occurred since the previous BPO surgery. This study represents real-life outcomes in a contemporary UK population.

#### **Future Research**

Further studies are required: firstly, from an epidemiological perspective, to evaluate lower urinary tract function using urodynamics, including a cystometrogram, in men aged ≥40 years before and after BS removal. This would inform patient management: firstly, by robustly describing the probability of BPO in a man with BS, and secondly by verifying whether the presence or absence of BPO can be accurately assessed with BS still in situ. This will therefore inform whether men should undergo BS removal followed by assessment for BPO, or whether we can robustly assess for BPO prior to BS removal, thereby justifying concomitant BS and BPO surgery.

For men with BS and urodynamically confirmed BPO, prospective, well-designed RCTs are needed to compare medical, surgical, and newer minimally invasive BPO procedures in terms of BS recurrence rates and BPO outcomes [11]. Finally, prospective RCTs evaluating the safety and efficacy of concomitant vs staged BS and BPO procedures are also required.

# Conclusion

This study provides the best quality evidence available on BPO treatment in men with BS: the largest cohort and longest duration of follow-up. After successful BS removal in men aged ≥40 years, there are significant BS recurrence and BPO complication rates. BPO surgery is associated with a lower BS recurrence rate than medical or no BPO treatment. These findings support the recommendations in both the 'Bladder Stones' and 'Non-neurogenic male LUTS' EAU Guidelines that men aged ≥40 years with BS benefit from BPO surgery [4,11]. This study also provides evidence in

support of the recommendation to perform concomitant BS and BPO procedures, in selected men [4].

However, this study's findings that 40.8% of BS patients' stones formed due to pathology other than BPO, and 40% of men aged ≥40 years with BS had had previous upper-tract urolithiasis supports the emerging evidence that most BS are multifactorial in aetiology. Factors that may contribute to BS formation include: metabolic, infective, abnormal material (including catheters and bowel), and LUTD. This questions the dogma that BS are an 'absolute indication' for BPO surgery, as stated in the 'Non-neurogenic male LUTS' EAU Guideline [11].

It is likely that the majority of, but not all, men with BS will benefit from BPO surgery. Careful assessment and management of all factors that contribute to BS formation is likely to select which men will most likely benefit from BPO surgery, as well as reducing BS recurrence rates and their associated morbidity in all patients. Further studies on men with BS, which include urodynamics and randomisation to medical or surgical BPO interventions, are required.

# **Conflict of Interest**

None of the authors have any conflicts of interest to declare.

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Correspondence: Gianluca Maresca, Department of Urology, Aberdeen Royal Infirmary, Foresterhill Health Campus, Aberdeen AB25 2ZN, UK.

e-mail: g.maresca@outlook.com

Abbreviations: AUR, acute urinary retention; BPO, benign prostatic obstruction; BS, bladder stones; EAU, European Association of Urology; IQR, interquartile range; LUTD, lower urinary tract dysfunction; PUJO, PUJ obstruction; PVR, post-void residual urine volume; SFR, stone-free rate; TUCL, transurethral cystolithotripsy.