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ARTICLE

Percutaneous nephrolithotomy and modern aspects of complications and antibiotic treatment

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ABSTRACT

Objective: The incidence of urinary stones is increasing across the globe. Surgical treatment includes extracorporal shock-wave lithotripsy (ESWL), ureterolithotripsy (URS), percutaneous nephrolitotomy (PCNL) and rarely open surgery. This single center study describes complications to PCNL focusing on infections, bacterial growth/resistance and antibiotic prophylaxis/treatment.

Materials and methods: All patients treated for kidney stones with PCNL at Ängelholm Hospital in north-western Scania, Sweden from January 2009 to December 2015 were included. A dipstick test and a bacterial culture was made on all patients. Kidney stones were analysed for composition and cultured for bacteria.

Results: In total, 186 patients underwent PCNL, all receiving perioperative antibiotics. Thirty percent (56/186) had a positive urinary culture taken before surgery and 33.3% (62/186) had positive stone culture. The concordance between urinary and stone culture was 57.1%. Both positive stone and urinary culture increased the risk of complications after surgery ($p = 0.002$ and $p = 0.017$, respectively). Complications occurred in 16% (30/186). Eight patients (4.3%) developed sepsis. The most common bacteria in urine were *Enterococcus faecalis* and *Escherichia coli*, both 20%. The most common stone-bacteria reported was *Enterococcus faecalis* (26%).

Conclusion: This study has a total complication rate of 16%, approximately 10% of those are severe. The most common complication to PCNL was infection (60%), followed by bleeding (5.4%), reoperation (1.6%) and pain (0.5%). The high prevalence of *E. faecalis* might need to be considered, however the results should be validated in a larger cohort, possibly with a higher rate of antibiotic resistance, before a change of guidelines regarding prophylactic antibiotics could be proposed.

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Ureteroscopy; infection; complications; ureteric stone

Introduction

Kidney stones are common globally. The prevalence and incidence rates are 1.7–14.8% and 114–720/100,000 individuals, respectively. Epidemiologic data from seven Western countries show that incidence and prevalence are increasing [1]. In Sweden, the prevalence of nephrolithiasis was 10% for males and 3% for females in the 1970s [2], now gender differences are starting to equalize [3].

Kidney stones are composed of minerals, often containing organic components. Supersaturation of a mineral in the urine leads to stone formation. Calcium oxalate/calcium phosphate stones are the most common (80%), other components are struvite, uric acid and cysteine [4]. Struvite stones or 'infection stones' form in the presence of urease producing bacteria, sometimes growing quickly to large stones, 'staghorn calculi' [5].

Nephrolithiasis is multifactorial and can be caused by several different underlying diseases and numerous genetic (hypercalciuria, gout and cystinuria) [6] and environmental factors [7]. Weight, body mass index [8] and diabetes mellitus [9] also increase the incidence of kidney stones, sometimes as parts in the metabolic syndrome. Dietary risk factors are sodium and animal protein intake. The single most important factor to reduce stone formation is hydration.

Stones are formed in the kidneys and can move to the ureter, leading to obstruction and causing renal colic. Ureteric stones up to 7 mm most often pass spontaneously. The majority of stones greater than 7 mm require urological intervention [10]. Open renal stone surgery is now rarely performed, since the development of extracorporeal shock wave lithotripsy (ESWL), flexible ureteroscopy and percutaneous nephrolithotomy (PCNL) [11].

PCNL, first described by Fernström and Johansson in 1976 [12], is today the modality of choice for patients with kidney stones greater than 1.5–2 cm, lower pole stones greater than 1–1.5 cm, staghorn stones and shock-wave resistant stones [10].

Known complications to PCNL are fever (2.8–32.1%), bleeding requiring transfusion (0–45%), organ injury (0–1.7%) and sepsis (0.3–5%) [13]. The EAU Guidelines recommend

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urinary culture and treatment of all urinary infections preoperatively [10]. Positive stone culture and pelvic urine culture seem to be better predictors of urosepsis than midstream bladder urine [14].

This study evaluates the treatment and complication outcomes of PCNL performed during 2009–2015 at a single centre in Sweden. The aim was to identify risk factors causing complications focusing on postoperative infectious complications.

Materials and methods

This is a single-centre observational study. We included all patients operated on with PCNL at the Urology Clinic in north-western Scania County (Ängelholm Hospital) between the years 2009–2015 ($n = 186$). The main part of the data were prospectively gathered according to protocol, Clavian and the more complex situation of all antibiotic treatment was retrospectively gathered from medical charts. All operations were on Mondays or Tuesdays and the culture was taken for 1 week (this differs, however, sometimes due to the patients). The aim was that the patient should receive adequate antibiotic and start at least 3 days before surgery.

The primary outcome of the study was the incidence of sepsis and febrile urinary tract infections. Secondary outcomes were other complications (e.g. bleeding, complications requiring re-surgery/intervention, bacterial growth, stone composition, antibiotic prophylaxis/treatment and residual stones). Data collected was: Age at intervention, sex, body mass index, preoperative urine culture including resistance pattern, stone culture, pre-, per- and postoperative antibiotics, stone composition, stone cultures, stone free rate (SFR), sepsis and bleeding complication, days of hospitalization following surgery, comorbidity, catheter use and mortality rate (Figure 1). Exposure variables: positive urinary and/or stone culture, antibiotic prophylaxis. We considered patients with residual stones < 4 mm as stone free and used this as a cut-off when calculating SFR. The diagnosis of sepsis was determined by the treating physician and re-evaluated with qSOFA according to the SEPSIS-3 consensus definitions [15]. Complications were registered and categorized according to CROES modified Clavien-Dindo [16,17] (Appendix 1). Complications requiring medical care were divided into subgroups; acute (< 30 days) and late onset (> 30 days). Treatment indications were kidney stones > 1.5 cm, infectious stones, continual discomfort such as pain or bleeding/infection due to the stone, ESWL-resistant stones and anatomic anomalies preventing stone passage through the urinary tract. All patients had a dipstick and a urinary culture taken preoperatively. A new culture was taken if the patients developed infections symptoms. Targeted antibiotic therapy according to culture results and resistance pattern was administered prior to surgery. In cases of negative dipstick or culture, patients received standard antibiotic perioperative (Cefotaxime 1 g $\times$ 2 intravenously). Intravenous antibiotic therapy was started on the morning of the day of surgery and continued until the removal of the nephrostomy tube, normally on day 2 after surgery. Regarding additional antibiotic treatment this was decided by the treating surgeon and related to infectious symptoms considering the cultures taken. All patients underwent a CT scan preoperatively to assess the anatomy and location of the stone. The surgical procedure was initiated by cystoscopy and placement of a ureteral catheter (open-end, 7 Ch.) on the treating side (normally guided by a Terumo® stiff guide wire with floppy end, 0.035"). A regular catheter (14 Ch.) was placed and the patient turned to prone position. With guidance of contrast and fluoroscopy, a dorsal normally caudal renal calyceal papilla was punctured, 9–30 Ch. dilatations were done before placing an Amplatz™ sheath. The stones were fragmented by ultrasound (EMS Swiss Lithoclast®) and a nephrostomy 18 Ch. with open end was left in place, to be removed usually 2 days after surgery.

Long-term mortality was evaluated through the Swedish population registry, on 7 May 2018. The follow-up time varied between 2 and 9 years. No mortality was registered within 3 months following PCNL. Chi-square and Fisher's exact test were used for statistical calculations where appropriate. Regarding cultures the laboratory diagnosis is based on colony counts following culture, which reflect the concentration of bacteria in urine and, hence, the likelihood that the bacteria grown arise from a UTI rather than contamination. UTI is normally caused by a single bacteria present in a high concentration, usually $\geq 10^*8$ CFU/L.

All urine samples were transported in refrigerated boxes to a central microbiology laboratory, Lund University Hospital, Lund, Sweden, and cultured on selective media (10 µL on CNA agar, 10 µL on Uricult chromogenic agar) (Figure 2).

Growth was identified to species level and susceptibility tested according to the standard methods used at the laboratory at the time of culture. Bacterial growth was semi-quantified as scarce ($< 10^*7$ CFU/L), intermediate ($10^*7 - 10^*8$ CFU/L) or rich ($> 10^*8$ CFU/L). Workup was performed if there was growth of 1–2 primary or secondary pathogens. Growth of three or more species was just reported as 'mixed flora'.

Urinary stones were placed in standard urine collection tubes and transported in refrigerated boxes to the same laboratory. Upon arrival at the laboratory they were transferred to Trypticase Soy Broth, crushed and/or sonicated for 2 min, vortexed and 3 droplets each were cultured on blood-, hematin- and Uricult chromogenic agars. All growth was identified to species level and susceptibility tested without quantification.

Stone analysis were performed at Sahlgrenska University Hospital using ATR FT-IR.

This study was approved by the regional ethics review committee in Lund (Dnr 2017/15).

Results

All 186 patients undergoing PCNL during 2009–2015 at Ängelholm Hospital are presented in Tables 1 and 2. Of the patients, 1.6% (3/186) had a urethral catheter, 14.5% (27/186) had a double JJ-catheter and 11.8% (22/186) had a

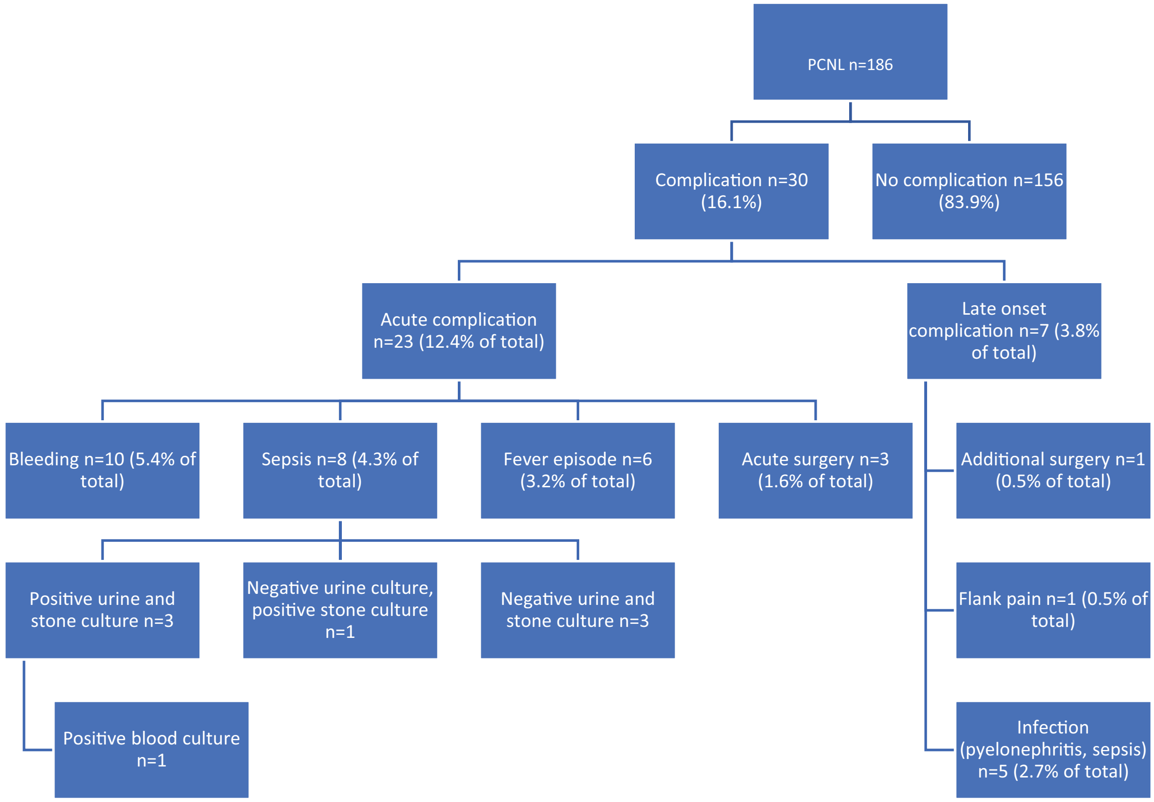

Figure 1. Flow chart of patients and complications. Acute complication = complication prior to discharge. Late onset complication = complications after discharge, but within 30 days. Additional surgery does not include surgery with the sole purpose of removing residual stones.

nephrostomy catheter preoperatively. Of all, 30.1% (56/186) had a positive urine culture preoperatively (Tables 3 and 4). The most common bacteria were *Enterococcus faecalis* (*E. faecalis*) and *Escherichia coli* (*E. coli*), with 19.6% (11/56) in both cases, followed by *Streptococcus agalactiae*, 12.5% (7/56). Mixed flora was common, 23.2% (13/56) (Figure 3(a)). One culture was positive for *E. coli* with carbapenemase production (carbapenem-hydrolyzing oxacillinase-48 (OXA-48)).

Stone culture were positive (> 10^3 colony forming units/ml) in 33.3% (62/186) (Table 3). The most common bacteria reported were *E. faecalis*, 25.8% (16/62) followed by coagulase-negative staphylococci, 24.2% (15/62) and *E. coli*, 16.1% (10/62) (Figure 3(a)). Both positive urine and stone culture were found in 18.8% (35/186). The concordance rate between urine and stone cultures was 57.1% (20/35), and 60% of these (12/20) also displayed the same resistance pattern. A positive urine culture increased the risk of complications. Microbial pathogens growing in cultures from stone or urine are shown in Table 5.

Of the 186 stones, only 176 were available for analysis. In complex stones the combination of calcium, oxalate and phosphate was the most common, occurring in 58.5% (103/176). Calcium were detected in 92.0% (162/176), oxalate in 79.5% (140/176) and phosphate in 69.9% (123/176) of the stones. Other components analyzed were ammonium, urate, magnesium, uric acid, struvite, carbon dioxide and trioxide and cysteine (Figure 4).

All patients received antibiotic prophylaxis (Table 3). The most common intravenous antibiotic was Cefotaxime, 78% (145/186), followed by aminoglycosides, 24.2% (45/186). Most patients received intravenous antibiotics preoperatively alone (83.3% (155/186)). Patients with a positive culture received oral antibiotics followed by intravenous antibiotics (13.4% (25/186)). Additional postoperative antibiotics, after removal of the nephrostomy tube, were given to 48.9% (91/186) of the patients. Of these, Ciprofloxacin (500 mg × 2 for 7 days), 47.3% (43/91) and Pivmecillinam (200 mg × 3 for 7 days) ,25.3% (23/91) were the most commonly used antimicrobial agents (Table 3).

Out of the patients with a positive urine culture, 44.6% (25/56) received oral antibiotics tailored to culture results and resistance pattern prior to admission and the rest of the positive cultures were considered bacterial contamination. The patients receiving antibiotics prior to admission had a higher risk of developing any complications ($p = 0.008$), but not sepsis ($p = 0.315$) compared to those who did not receive per oral antibiotics.

A total complication rate of 16.1% (30/186), 23 during hospital stay and seven occurring within 30 days, was found in this study. Positive urinary culture or stone culture was associated to the development of any complication, $p = 0.017$ and $p = 0.002$, respectively (Table 5).

Stone free rate was 65.6% (122/186). Treatment of residual stones were: watchful waiting, $n = 40$, ESWL, $n = 15$, ureteroscopy, $n = 8$, and endoluminal antegrade approach, $n = 1$.

No other possible risk-factors show any significant correlation with complications (age, sex, body mass index, stone composition, stone free rate (SFR), comorbidity, catheter use and mortality rate).

No significant association was found between serious postoperative infectious complications defined as sepsis and

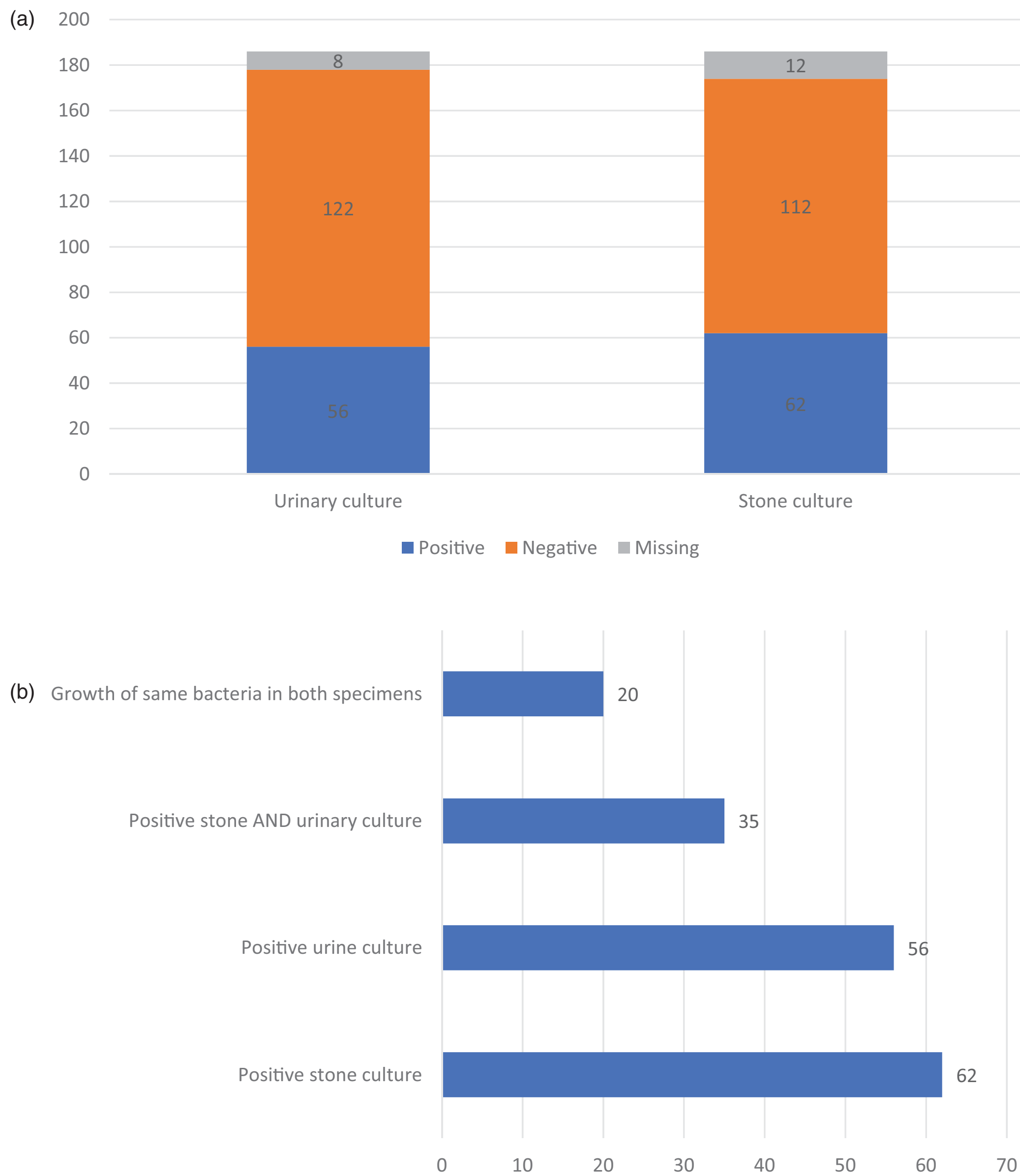

Figure 2. (a) Overview of urinary and stone culture ($n = 186$). (b) Overview of culture and concordance in the 186 patients.

Table 1. Patient demographics and complications.

		All patients ($n = 186$)	No complication ($n = 156$)	Complications ($n = 30$)
Age, mean (95% CI)		59.6 (57.3–61.9)	59.2 (56.7–61.6)	61.8 (55.5–68.1)
Sex male, % (*n*)		55.9% (104)	57.1% (89)	50.0% (15)
Body Mass Index, Median (95% CI)		27.1 (26.8–28.3)	27.4 (26.5–28.2)	27.5 (26.3–30.7)
Comorbidity, % (*n*)		76.9% (143)	76.3% (119)	80.0% (24)
Clavien-Dindo Classification Score, % (*n*)	0	83.9% (156)	100% (156)	–
	1	7.5% (14)	–	46.7% (14)
	2	7.5% (14)	–	46.7% (14)
	3	1.1% (2)	–	6.7% (2)
	4	–	–	–
	5	–	–	–
Any Catheter		26.7% (50)	43 (27.6%)	7 (23.3%)
Ureteral Catheter		1.6% (3)	2 (1.3%)	1 (3.3%)
JJ-Stent		14.4% (27)	22 (14.1%)	5 (16.7%)
Nephrostomy tube		11.8% (22)	20 (12.8%)	2 (6.7%)
Mortality rate, % (*n*)		11.3% (21)	10.9% (17)	13.3% (4)

positive urinary or stone culture. Of the sepsis patients, 37.5% (3/8) had negative cultures from both urine and kidney stone. Only one patient had a positive blood culture (1/8), *E. coli* with ESBL Carba in both urine and stone.

Nearly all of the patients (5/6) who developing fever postoperatively received an extra dose of intravenous aminoglycoside ($n = 4$) or carbapenem ($n = 1$) and per oral antibiotics following discharge. Looking at all complications, 12.4% (23/

186) suffered from one or more complications before being discharged from the hospital. Bleeding, defined as patients given a transfusion, occurred in 5.4% (10/186), sepsis was diagnosed in 4.3% (8/186), fever episode in 3.2% (6/186) and reoperation in 1.6% (3/186).

Of all 3.8% (7/186) of patients who sought medical care or required additional intervention within 30 days from being discharged, five of these had infectious complications, including one patient with abscess, two with pyelonephritis and two with urosepsis. One patient had hematuria and flank pain and one patient needed additional surgery (ureterolithotomy) due to residual stone.

Long-time mortality, median follow-up (range 2–9 years) postoperatively, was 11.3% (21/186) (Tables 1 and 2). Of these, 61.9% (13/21) were older than 70 years at the time of surgery and the majority, 90.5% (19/21), was diagnosed with at least one comorbidity; 52.4% (11/21) had a BMI of 25 or higher. No deaths were registered within 3 months of surgery. Median of hospital stay postoperatively was 3 days (ranging from 2 to 23 days).

Discussion

In this cohort 4.3% had sepsis and 3.2% had febrile UTI, which is in line with previous showing an incidence between 0.3 and 5% [13]. Ramaraju et al. [18] reported a SIRS incidence of 24.1% in patients given a third generation cephalosporin and aminoglycoside. Erdil et al. [19] reported a SIRS incidence of 16.7% when given antibiotics according to urinary culture preoperatively or single dose third generation cephalosporin preoperatively in the case of sterile urine. These high numbers is possibly explained by the increase of the intrarenal increased pressure during surgery, recognized by many as a source of postoperative fever. Urosepsis was seen in 1.5% patients given culture specific antibiotics or second generation cephalosporin according to Sharma et al. [13,19]. The criteria for the sepsis diagnosis has been re-evaluated recently and discrepancies in diagnosing has complicated the comparison of studies on the subject [15]. In this study, the treating doctor's encoding of sepsis in the patient chart was the deciding factor and additional data of the patient's condition was extracted to evaluate the judgment.

Our proportion of the patients having a positive urinary culture (30.1%) and stone culture (33.3%) are similar to other studies (3.2–51% and 9.4–48%, respectively) [14,20–23]. A not insignificant part of the patients had both positive urinary and stone culture. The concordance rate was 57.1%, compared to 22.6–83.3% in several studies [20–23].

Mariappan et al. [14] demonstrated a greater risk of developing urosepsis by bacteria from infected stones or pelvic urine compared with bladder urine. No such increase in risk was seen in our study, which could be explained by the fact that the current prophylactic regime works or be a consequence of the study being under powered. Having a positive urinary or stone culture, however, was an independent general risk factor for developing complications in this study. Out of the eight sepsis patients, one had a positive blood culture with the same type of bacterium in urine, stone and blood. Three patients with sepsis had negative urinary and stone cultures, this being an aseptic inflammatory response could be true but we still lack the explanation of this fever reaction and false negative cultures could still be a part of the problem. Regarding catheters one would assume that this would increase the risk of complications. This study fails to show any significant connection. Bacterial stone growth was associated with a hose connecting the external environment with the internal parts of the body namely nephrostomy or ureteral catheters. Double JJ-catheter seems to not have this effect.

In the patients with infectious complications, positive stone culture was more prevalent than a positive urine culture. This might indicate a successful eradication of bacteria in the bladder by preoperative antibiotics (not effective on the stones). Exposure to antibiotics prior to surgery could also promote development of resistant bacteria and increase the risk of sepsis [24]. Receiving antibiotics according to urinary culture increased the risk of complication, but not sepsis specifically, in this study. This is probably a result of confounding by indication, meaning that the positive urinary culture accounted for the risk and not the antibiotics *per se*. Among the patients with positive urinary culture, no advantage of giving per oral antibiotics could be seen in this study. However, these results should be interpreted with caution due to the small size of the study. Further studies should investigate the benefit of per oral antibiotics prior to

Table 2. List of comorbidities and coding.

	All patients ($n = 186$)	ICD-10 codes
Malignancy	22.0% (41)	C00–97
Diabetes mellitus	13.4% (25)	E10–14
Psychiatric disease	2.7% (5)	F04–99
Dementia	2.2% (4)	F00–03
Hypertension	27.4% (51)	I10, I15
Arrhythmia	6.5% (12)	I44–45, I47–49
Airway disease and COPD	10.2% (19)	J40–47
Bowel disease	26.3% (49)	K00–73, K75–87
Liver cirrhosis	0% (0)	K74
Urogenital disease (stone excluded)	72.6% (135)	N30–39, N40–42
Renal disease	7.5% (14)	N00–19

Table 3. Antibiotic treatment.

	All patients ($n = 186$)
Antibiotic prophylaxis	100% ($n = 186$)
(Standard Operation Procedure was Cefotaxime 1g × 2 intravenously or according to culture resistance >1 h before surgery)	
Preoperative per oral antibiotics according to urinary culture	13.4% ($n = 25$)
Perioperative iv antibiotics	
(used until nephrostomy tube was removed normally <3 days after surgery)	
Cefotaxime	78.0% (145/186)
Aminoglycoside	24.2% (45/186)
Other	2.2% (4/186)
Postoperative per oral antibiotics	48.9% ($n = 91$)
(used after nephrostomy tube was removed)	
Ciprofloxacin	47.3% (43/91)
Pivmecillinam	25.3% (23/91)
Other	31.9% (29/91)

Table 4. Antibiotic treatment specified.

	All patients ($n = 186$)	Complications ($n = 30$)	Positive urinary culture ($n = 56$)
Antibiotic prophylaxis	100% ($n = 186$)	100% ($n = 30$)	100% ($n = 56$)
Preoperative antibiotics according to urinary culture	13.4% ($n = 25$)	26.7% ($n = 8$)	44.6% ($n = 25$)
Preoperative antibiotics	17.7% ($n = 33$)	26.7% ($n = 8$)	44.6% ($n = 25$)
Amoxicillin	27.3% (9/33)	0	5
Ciprofloxacin	18.2% (6/33)	1	3
Pivmecillinam	18.2% (6/33)	0	2
Trimetoprim	15.2% (5/33)	1	3
Nitrofurantoin	12.1% (4/33)	0	2
Trim-Sulpha	12.1% (4/33)	0	2
Flucloxacillin	6.0% (2/33)	0	1
Cefadroxil	3.0% (1/33)	0	0
Clindamycin	3.0% (1/33)	0	0
Perioperative antibiotics	100% ($n = 186$)	100% ($n = 30$)	100% ($n = 56$)
Cefotaxime	82.8% (154/186)	23	32
Aminoglycoside	23.6% (44/186)	6	22
Cefuroxime	1.6% (3/186)	1	1
Ceftazidime	0.5% (1/186)	0	1
Meropenem	0.5% (1/186)	0	0
Piperacillin/Tazobact	0.5% (1/186)	0	0
Postoperative antibiotics	48.9% ($n = 91$)	76.7% ($n = 23$)	85.7% ($n = 48$)
Ciprofloxacin	47.3% (43/91)	2	1
Pivmecillinam	25.3% (23/91)	2	2
Nitrofurantoin	9.9% (9/91)	0	1
Amoxicillin	6.6% (6/91)	1	3
Aminoglycoside	6.6% (6/91)	7	20
Trimetoprim	5.5% (5/91)	0	5
Cefadroxil	4.4% (4/91)	0	4
Carbapenem	4.4% (4/91)	0	4
Trim-Sulfa	3.3% (3/91)	0	3
Piperacillin/Tazobact	3.3% (3/91)	0	3
Flucloxacillin	1.1% (1/91)	0	1
Other	1.1% (1/91)	0	1

surgery in order to avoid unnecessary administration of antibiotics.

The most common bacteria found in stone culture were *Enterococcus faecalis* and coagulase-negative staphylococci. Nevo et al. [25] showed bacterial resistance of 67% for second generation cephalosporins and 9% against Meropenem in *E. faecalis*. The high prevalence of *E. faecalis* must be taken into consideration. A potential strategy to minimize antibiotic use and to optimize prophylaxis would be to use a broader spectrum antibiotic, such as Piperacillin-Tazobactame as a standard, regardless of the pre-operative urinary culture. A reasonable duration would be until potential 'extra risks' catheters, namely urethral catheter and the nephrostomy, were removed, approximately 7–8 doses in all.

Richards et al. [26] reported *Enterococcus* as a frequent opportunistic pathogen in nosocomial infections and are clinically challenging to treat due to widespread resistance to antibiotics [27]. Coagulase-negative staphylococci infections are considered opportunistic and are associated with implant surgeries and immunocompromised patients [28]. Is the incidence of stone culture coagulase-negative staphylococci in this study due to sampling contamination or the presence of a nephrostomy/ureteral catheter and lacks clinical relevance? This is of course debatable, but some of the medical knowledge may indicate this. However, incidence of coagulase-negative staphylococci in renal calculi are reported by two other studies [14,29]. Of patients having bacteria in their urine preoperatively, only half received antibiotics according to culture. This can partly be explained by the proportion of mixed flora lacking bacterial resistance patterns and thereby considered to be contamination. The EAU Guidelines recommends urinary culture and treatment of all urinary infections preoperatively [10] and prophylaxis with aminoglycosides and second-generation cephalosporins. The broader spectrum antibiotics such as third-generation cephalosporins and carbapenems should be used for treatment indication only [30]. The standard perioperative drug of choice in our study was Cefotaxime, a third-generation cephalosporin. Aminoglycosides were the drug mostly used as additional iv therapy. Again, a general reflection is that none of these drugs are effective on *E. faecalis*.

The total complication rate in this cohort was 16.1%. Other complications apart from infection were bleeding, 5.4%, the need for additional surgery, 2.1%, and pain, 0.5%. Regarding the modified Dino-Clavien classification of surgical complications is not fully representative for complications in urological surgery. Therefore, there is a risk of underestimation of complications.

The population undergoing PCNL was to a large extent affected by comorbidities. This can be a result of the population's higher age compared to the normal population or a reflection of underlying diseases causing kidney stones. BMI being > 25 for the included patients may indicate that an excess of food intake could be one of the factors causing urinary stones. Taylor et al. [8] reported an association between higher BMI and increased risk of kidney stone formation.

Stone analysis shows that 92% (162/176) of stones contained calcium and the most common combination of calcium, oxalate and phosphate was found in 58.5% (103/176)

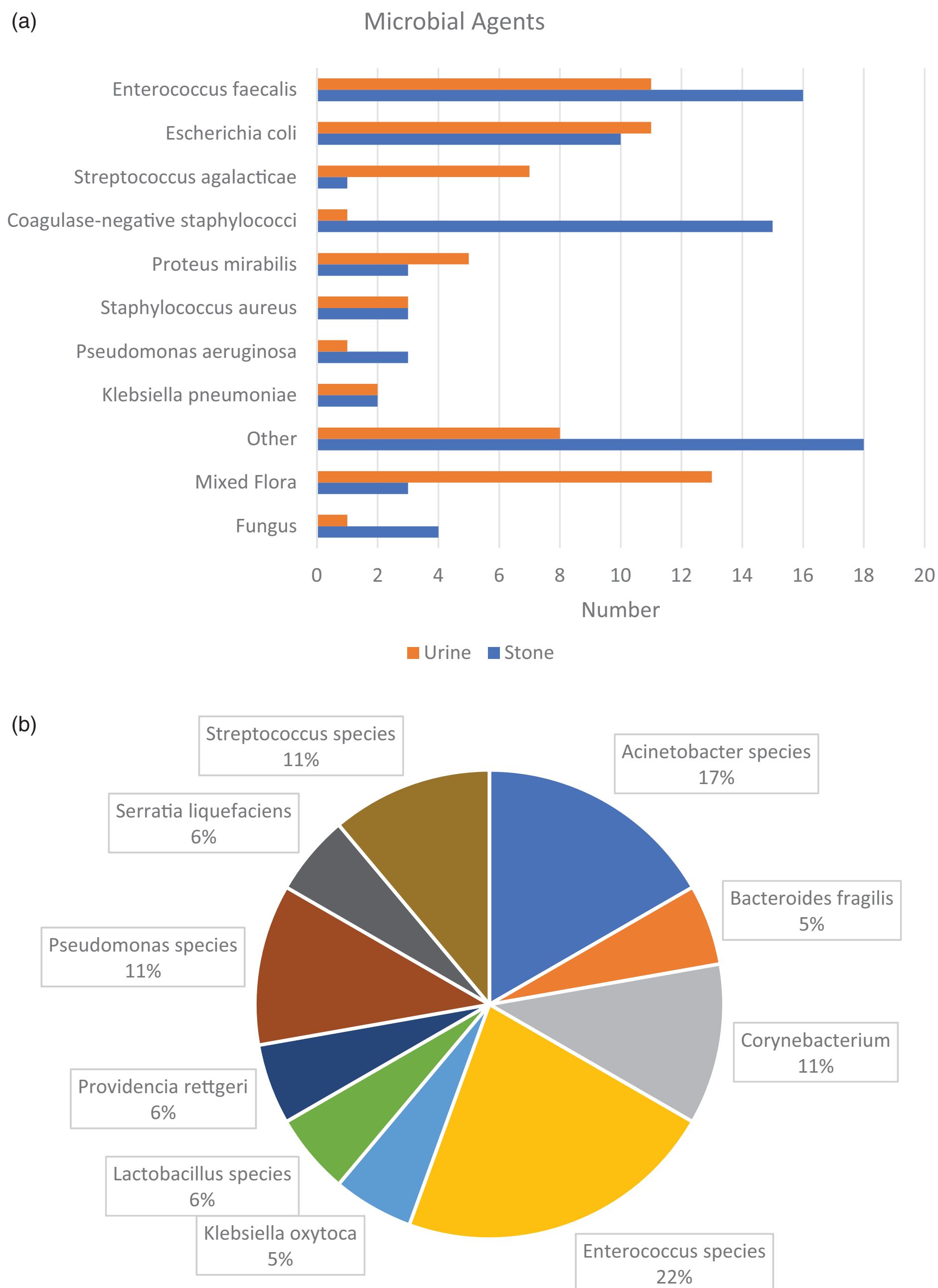

Figure 3. (a) Microbial agents in cultures of urine and stone. (b) Specification of 'other' stone microbial agents.

Table 5. Chi-square and Fisher's Exact test showing statistical significance (p-value < 0.05).

	p-value	OR	95% CI
Positive preoperative urinary culture			
To sepsis	0.678	1.716	0.371–7.942
To any complication	0.017	2.659	1.167–6.056
Positive stone culture			
To sepsis	0.135	3.187	0.735–13.817
To any complication	0.002	3.469	1.504–8.001
Preoperative antibiotic culture targeted treatment to sepsis	0.315	2.116	0.402–11.124
Preoperative antibiotics according to urinary culture to any complication			
All patients	0.008	3.713	1.447–9.527
Positive stone culture			
JJ Catheter	0.563	0.330	−0.098–0.194
To Ureteral Catheter	0.019	6.252	0.096–0.271
To Nephrostomy	<0.005	21.720	0.209–0.486
Comorbidity to any complication	0.658	1.244	0.473–3.273

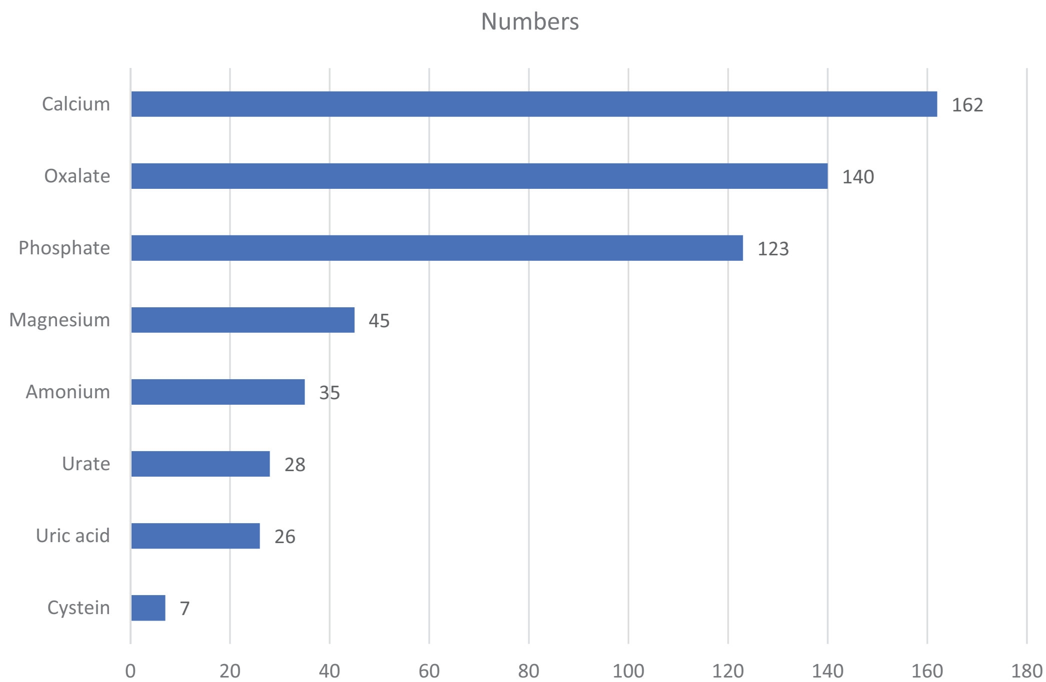

Figure 4. Stone content ($n = 186$). (Most stones containing a mix of agents and the most common mixture being Calcium/oxalate and Calcium/phosphate).

of the stones. This is substantially lower than the 80% previously reported [4]. Explanations could be a higher intake of meat and food in general, leading to a shift in stone configuration, concentrating, for example, more ammonium and uric acid in the urine.

The mortality rate in this study was 11.3%, compared to 0.9% for the total Swedish population in 2016 [31,32]. The reasonable explanations for our mortality rate are the older population and its high rate of comorbidities in the study population. No deaths were in proximity to surgery (first death 5 months after surgery).

This study has a high proportion of cultures and stone analysis taken, presenting an overview of complications and rates and provides modern information on patients undergoing PCNL. The limitation of this study is the number of patients ($n = 186$), which fails to reach statistical correlations between cultures and risk for sepsis complication.

In conclusion, positive urinary and stone cultures do not conform in all cases. Still they are seen frequently among patients undergoing PCNL and are associated with an increased risk of complications. This study has a total complication rate of 16%, of those ~10% are severe. Infectious complications stand for more than 60%. This study should be validated in a larger cohort, possibly with a higher rate of antibiotic resistance before a change of guidelines regarding prophylactic antibiotics should be proposed but if so the high prevalence of *E. faecalis* might need to be considered.

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Authors' contributions

MW, MR, and AL; Sample and data collection: MW, MR. Analysis and interpretation: MW, JB, MP, AL; Drafting the manuscript for important intellectual content: MW, JB, MP, JS, and AL.

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Appendix 1

Grade I	Deviation from the normal postoperative course without the need for intervention
Grade II	Minor complications requiring pharmacological intervention, including blood transfusion and total parenteral nutrition
Grade IIIa and b	IIIa: Complications requiring surgical, endoscopic or radiological intervention, but self-limited, without general anesthesia
	IIIb: Complications requiring surgical, endoscopic radiological intervention, but self-limited, with general anesthesia
Grade IVa and b	IVa: Life threatening complications requiring intensive care unit management; single organ dysfunction, including dialysis
	IVb: Life threatening complications requiring intensive care unit management; multiorgan dysfunction
Grade V	Death of a patient

The CROES modified Clavien-Dindo Classification [17,18], for classifying surgical complications.