Original Article

Journal of Feline Medicine and Surgery
2021, Vol. 23(4) 331–336

DOI: 10.1177/1098612X20950312
journals.sagepub.com/home/jfm

This paper was handled and processed by the European Editorial Office (ISFM) for publication in *JFMS*

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Factors associated with positive urine cultures in cats with subcutaneous ureteral bypass system implantation

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Abstract

Objectives The aims of this study were to report the postoperative incidence of subcutaneous ureteral bypass (SUB)-associated bacteriuria and risk factors in a large population of UK cats, to identify the commonly implicated isolates in these cases and to report associations of positive postoperative urine cultures with device occlusion or a need for further surgery.

Methods Electronic clinical records were reviewed to identify cats with ureteral obstruction that underwent unilateral or bilateral SUB implantation between September 2011 and September 2019. In total, 118 client-owned cats were included in the study population. Information recorded included signalment, history, surgical and biochemical factors, urinalysis and culture results. Multivariable logistic regression was performed to identify variables associated with a positive postoperative culture.

Results In total, 10 cats (8.5%) had a positive postoperative culture within 1 month postsurgery and 28 cats (23.7%) within 1 year postsurgery. Cats with a positive preoperative culture were significantly more likely to have a positive culture within 6 months postoperatively (odds ratio [OR] 4.09, 95% confidence interval [CI] 1.18–14.18; $P = 0.026$). Of the 14 cats with a positive preoperative culture, six (42.9%) returned a positive culture within 1 year postoperatively, and in four cases (66.7%) the same isolate was identified. Cats with a higher end-anaesthetic rectal temperature were significantly less likely to return a positive culture within 3 months (OR 0.398, 95% CI 0.205–0.772; $P = 0.006$) postsurgery. Cats culturing positive for *Escherichia coli* at any time point (OR 4.542, 95% CI 1.485–13.89; $P = 0.008$) were significantly more likely to have their implant removed or replaced.

Conclusions and relevance Perioperative hypothermia and preoperative positive culture were independent predictors of a postoperative positive culture and this should be taken into consideration when managing these cases. Positive postoperative culture rates were higher than have previously been reported.

Keywords: Subcutaneous ureteral bypass; SUB; bacteriuria; ureterolithiasis

Accepted: 22 July 2020

Introduction

Intraluminal ureteral obstruction is an occurrence of increasing incidence in feline medicine, with ureterolithiasis implicated in the majority of cases.[1] Ureteral obstruction may also be diagnosed secondary to stricture, stenosis, iatrogenic injury, thrombi and neoplasia.[2]

Successful management of ureteral obstruction depends on prompt renal decompression to prevent permanent loss of glomerular filtration capacity.[3] Historically, where medical treatment failed, nephrectomy was indicated; however, in recent years, many institutions have adopted

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ureteral bypass using the subcutaneous ureteral bypass (SUB) system placement as the treatment of choice.[4]

The SUB system consists of two catheters, placed in the renal pelvis and bladder lumen, connected to a shunting port sited in the subcutaneous tissue,[4] allowing urine to bypass the affected ureter. SUB placement mortality rates compare favourably to more traditional surgical techniques, with 0–13% perioperative mortality reported[5,6] vs 18% perioperative mortality for both traditional interventions[1] and ureteral stent placement.[6] Intraoperative complications are reported to occur in 7% of cases[5] and perioperative complications necessitating surgical intervention reported in 7% and 9% of cases, respectively,[5,6] with device occlusion, device leakage and urethral obstruction most commonly observed.

Bacteriuria following SUB placement is reported in 8–21% of cats.[5,7] Therefore, identifying factors predictive of device colonisation and the clinical impact of this may help guide client decision-making.

Risk factors for positive urine cultures in cats with SUB system implantation have previously been described in a small population of 43 cats within an American institution;[8] this study population included cats that underwent SUB system or ureteral stent placement. The authors reported that of all variables assessed only use of postoperative antibiosis was associated with likelihood of positive urine culture. Berent et al[5] reported that both positive preoperative culture and postoperative use of an indwelling catheter were associated with positive postoperative culture; however, other factors were not assessed.

The microbial profile of SUB system-associated bacteriuria has been reported twice previously,[5,8] both studies from American cat populations. The clinical implications of SUB-associated bacteriuria, in terms of association with device obstruction and requirement for surgical intervention, have not been previously reported.

The objectives of this study were thus three-fold. First, to report the postoperative incidence of SUB-associated bacteriuria and risk factors in a large population of UK cats; second, to identify the commonly implicated isolates in these cases; and, third, to report associations of positive postoperative urine cultures with device occlusion or need for further surgery.

Materials and methods

The clinical records of all cats with implantation of a SUB system at the Queen Mother Hospital for Small Animals, London, between September 2011 and September 2019 were reviewed. Cases were excluded if they had not survived to discharge. Only cases with a minimum of one urine culture performed at least 2 weeks postsurgery were included. Information recorded included signalment, history, surgical and biochemical factors, in addition to urinalysis and culture results. Initial diagnosis of ureteral obstruction was made via abdominal ultrasound performed by board-certified radiologists or residents in training, with pyelography performed to confirm aetiology as required.

Surgery was performed by board-certified surgeons or residents in training, with general anaesthesia supervised by board-certified anaesthetists or residents. A SUB device (Norfolk Vet Products) was implanted as described by the manufacturer,[4] under fluoroscopic guidance.

In cats with an active urine sediment, intravenous antibiotic administration was initiated preoperatively; surgery was delayed up to 48 h during antibiotic treatment if the clinical condition allowed. Cats with an active sediment were continued on a therapeutic course of antibiotics for 4–6 weeks postoperatively based upon culture and sensitivity results of urine obtained preoperatively or from the renal pelvis at surgery.

Cats that survived to discharge were scheduled to revisit the hospital approximately 1 month postoperatively, at which point a urine sample was collected via aspiration of the subcutaneous port via a sterile technique. Follow-up appointments were then recommended every 3 months for the first 2 years and every 6 months thereafter, when the same technique was performed. From February 2019 standard hospital protocol was revised to include flushing of the systems with 2.5 ml of sterile tetrasodium ethylenediaminetetraacetic acid (TetraEDTA) per port post-sample collection.

Cats with positive urine cultures were generally administered a 3–8-week course of appropriate antibiosis based on culture and sensitivity results with culture performed during and at least 1 week post-treatment. Where empirical antibiosis was required pending culture, a 4–6-week course of oral potentiated amoxicillin was prescribed with a change of agent as required on return of culture results. Antibiosis was often stopped or not re-prescribed for cats with recurrent or persistent positive urine cultures without lower urinary tract signs.

All samples were submitted to the same laboratory. Samples were streaked with an inoculation loop onto MacConkey agar and Columbia agar supplemented with 5% sheep blood. Samples were incubated for up to 24 h in 5% carbon dioxide at 37°C.

Bacterial identification was based on Gram staining, colony type and morphology, in addition to routine biochemical testing. Isolate sensitivity was established with the Kirby–Bauer disc diffusion method performed in accordance with Clinical and Laboratory Standards Institute guidelines.[9]

Statistical analysis

Descriptive analysis was used for signalment, treatment and sample data. Data were analysed with SPSS version 24 (IBM) with significance set at $P < 0.05$. Variables were tested for normality using a Shapiro–Wilk test. Normally

distributed data are reported as mean ± SD and non-Gaussian data are reported as median (range).

A χ^2 test was used to compare the likelihood of device explantation in bacteriuric cats, between those with clinical signs and those without.

Univariable logistic regression analysis was initially used to assess predictive factors for the following six models: first positive culture results within 1 (0–30 days), 3 (0–90 days), 6 (0–180 days) and 12 (0–365 days) months; for device occlusion at any time point; and for device removal at any time point. Variables for which $P < 0.1$ were then further explored using a multivariable analysis, with backward elimination to identify variables for which $P < 0.05$.

Results

One hundred and twenty-four cats had a SUB implanted between 16 April 2012 and 6 September 2019, but six cats did not survive to discharge. Therefore, 118 cats met the inclusion criteria.

Age at the time of device placement was 7.17 ± 3.35 years. Of the 118 cats included, 70 (59.3%) were neutered females, 47 (39.8%) were neutered males and one (0.8%) was an entire male. Breeds representing >2% of the population are summarised in Table 1.

Median body weight at the time of surgery was 4 kg (range 2.1–9.7 kg); median body condition score was 4/9 (range 1–9).

In 93 cats (78.8%) a SUB system was placed due to ureterolithiasis, four cats (3.4%) presented owing to iatrogenic injury (three owing to inadvertent ureteral ligation during ovariohysterectomy and one owing to stricture formation post ureterotomy), one cat (0.8%) was diagnosed with a ureteral stricture in the absence of ureteroliths or known prior trauma, and in 20 cats (16.9%) the underlying pathology was not confirmed.

Forty-six (39.0%) cats had a bilateral system placed and 72 (61.0%) a unilateral system. Of the unilateral systems, 41 (56.9%) were left-sided and 31 (43.0%) right-sided. Median surgical and anaesthesia time were 105 mins (range 50–275 mins) and 200 mins (range 125–420 mins), respectively. Sixty-four cats (54.2%) received potentiated amoxicillin perioperatively, 39 cats (33.0%) received cefuroxime and in 15 cats (12.7%) perioperative antibiotic choice was not recorded.

Table 1 Breeds representing >2% of the population of 118 cats with subcutaneous ureteral bypass system placement

Breed	n	%
Domestic shorthair	71	60.2
Domestic longhair	8	6.8
Burmese	5	4.2
Birman	4	3.4
Ragdoll	4	3.4
British Blue	3	2.5
British Shorthair	3	2.5
Persian	3	2.5

Cats were hospitalised for a median of 6 days (range 2–23) postsurgery.

Pre- and postoperative (obtained between 1 and 3 months postsurgery) clinicopathological data are summarised in Table 2.

Altogether, 110 cats had a preoperative culture performed and of these 14 (12.7%) were positive. Thirteen cultures identified a single isolate and one culture identified two isolates. The most frequent isolates were *Escherichia coli* (42.9%) and *Enterococcus faecalis* (28.6%). Of the 14 cats with positive preoperative cultures six (42.9%) had a positive postoperative culture, all between day 20 and day 176 postsurgery. Of these six cultures, four (66.7%) identified the same isolate both pre- and postoperatively. Of these four cultures, two isolated *E coli*, one *E faecalis* and one *Staphylococcus pseudintermedius.*

At least 1 month follow-up was available for all 118 cats. Of these, 10 (8.5%) had a first positive postoperative culture within 1 month postsurgery. The most common organisms isolated were *E coli* (40%) and *Pseudomonas aeruginosa* (30%). Only one of these 10 cats had had a positive preoperative urine culture, and the bacteria cultured was different (*E coli* preoperatively and *S pseudintermedius* postoperatively).

A minimum of 3 months of follow-up were available for 112 cats, and of these 15 (13.4%) had a first positive culture within 3 months postsurgery. A minimum of 6 months of follow-up were available for 95 cats, and of these 25 (26.3%) had a first positive culture within 6 months postsurgery. A minimum of 1 year of follow-up

Table 2 Clinicopathological data for 118 cats that had subcutaneous ureteral bypass systems placed, collected preoperatively and postoperatively between 1 and 3 months after surgery

	Preoperative data	Postoperative data
Urine pH	6 (5–8.5)	5.5 (5–7.5)
Creatinine (µmol/l)	603 (121–2128)	206.5 (96–1014)
Blood urea nitrogen (mmol/l)	35.1 (5.7–118.5)	15 (7.4–67.3)
Urine specific gravity	1.015 (1.007–1.050)	1.021 (1.010–1.050)

Data are median (range)

was available for 68 cats. Of these, 28 (41.2%) had a first positive culture within 1 year postsurgery. Of the first positive cultures returned within the first year postsurgery, 23 (82.1%) were single isolates and five (17.9%) were mixed cultures of two isolates. The isolates identified in single organism cultures are summarised in Table 3.

Cats with a positive preoperative culture were significantly more likely to have a positive postoperative culture within 6 months postoperatively (odds ratio [OR] 4.09, 95% confidence interval [CI] 1.18–14.18; $P = 0.026$) than those with a negative preoperative culture in multivariable analyses. This was not statistically significant within 1 ($P = 0.787$), 3 ($P = 0.935$) or 12 ($P = 0.328$) months postsurgery.

In multivariable analyses cats with higher end-anaesthetic rectal temperatures were significantly less likely to return a positive culture by 1 month (OR 0.404, 95% CI 0.203–0.803; $P = 0.010$) and 3 months (OR 0.398, 95% CI 0.205–0.772; $P = 0.006$) postsurgery but not by 6 months ($P = 0.121$) or 12 months ($P = 0.555$) postsurgery.

Age, sex, breed, weight, body condition score, perioperative antibiotic choice, reason for device placement, outdoor access, preoperative urea, creatinine, urine pH and specific gravity, and length of hospitalisation, anaesthetic and surgery were not significantly correlated with the likelihood of returning a positive culture at any time point when investigated with univariable analysis (all $P > 0.1$) and were not included in the multivariable model.

Use of TetraEDTA as part of a maintenance protocol from 1 month postsurgery was not significantly correlated with the likelihood of returning a positive culture within 3 months postoperatively and was not included in this multivariable model.

Site of implant and sex were included in the multivariable regression analysis but were not statistically associated with the likelihood of returning a positive culture at any time point ($P > 0.05$).

Of the 28 cats returning positive urine cultures within 12 months postsurgery, 10 (35.7%) were asymptomatic, with no noted device complications, two (7.1%) were asymptomatic with device obstruction diagnosed on imaging, 11 (39.3%) had lower urinary tract signs and/or secondary pyelonephritis and five (17.9%) had transient lower urinary tract signs, which were at times absent in the presence of bacteriuria.

Eleven cats with a positive culture had their implants removed or replaced. Of these, seven (63.6%) had either transient or perpetual clinical signs and four (36.4%) were asymptomatic. Seventeen cats with a positive culture did not have their devices removed. Of these, nine (52.9%) had transient or perpetual clinical signs, and eight (47.0%) were asymptomatic. There was no significant association between the presence of clinical signs and the likelihood of device removal in cats with bacteriuria ($P = 0.539$).

In total, 26 devices became obstructed over the period studied in 22 cats (18.6%): 18 (15.3%) due to device mineralisation, seven (5.9%) due to a catheter kink and one (0.8%) due to a blood clot. Of the 18 devices (17 cats) with mineralised obstructions nine were revised or replaced, three cats were euthanased and the owners of five cats declined surgical intervention due to minimal or absent clinical signs.

Cats culturing positive for *E coli* at any time point (OR 4.542, 95% CI 1.485–13.89; $P = 0.008$) were significantly more likely to have their implant removed or replaced when investigated with multivariable analysis. This was not significant for cats culturing positive for *P aeruginosa* ($P = 0.09$) or *E faecalis* ($P = 0.059$) when investigated with multivariable analysis, or cats with positive cultures preoperatively or within any time point postoperatively when investigated with univariable analysis ($P > 0.1$).

Cats with a positive urine culture preoperatively or within any time point postoperatively were not significantly more likely to develop a device occlusion than cats without a positive culture at any time point when investigated with univariable analysis ($P < 0.1$). However, cats with *P aeruginosa* cultured at any time point postoperatively were significantly more likely to develop an implant obstruction (OR 5.0, 95 % CI 1.138–21.98; $P = 0.033$); this was not significant for *E coli* ($P = 0.583$) or *E faecalis* ($P = 0.532$) positive cultures when investigated with multivariable analysis.

Table 3 Novel, single-culture isolates within 1 year postsurgery (n = 28)

Organism	n	%
Escherichia coli	11	39.3
Enterococcus faecalis	4	14.3
Pseudomonas aeruginosa	4	14.3
Staphylococcus pseudintermedius	1	3.6
Klebsiella pneumonia	1	3.6
Coagulase-negative staphylococcus	1	3.6
Enterobacter cloacae	1	3.6
Unidentified diptheroid	1	3.6
Unidentified coliform	1	3.6

Discussion

This study presents the results from a large number of urine cultures collected from cats with SUB systems placed in a UK referral centre over an 8-year period. Positive cultures were obtained from 28 of the 118 cats (23.7%) at some time point within 12 months postoperatively, with 8.5% returning a positive culture within 1 month postoperatively.

A study by Kopecny et al[8] reported 25% of cats returned a positive postoperative urine culture; however, it is difficult to compare these results with those reported here as the population studied included cats

with ureteral stent placement, the time points assessed were different and only 6/48 samples were collected via sterile subcutaneous port aspiration. It is also interesting to note that this paper reported that only 2.1% of cats returned a positive preoperative culture vs 12.7% of the cases reviewed here, 0% of the cases reported by Wolff et al[7] and 25% of the cases reported by Berent et al.[5] The latter papers reported a postoperative positive culture rate of 21% within 10 days postoperatively[7] and 24% at any time point;[5] however, direct comparison is challenging owing to the differences in data handling and proportion of cases lost to follow-up. Discrepancies may also reflect a difference in sampling methods or previous management of the cats presented for surgery.

The most commonly cultured isolate in this study, both preoperatively and at any time point postsurgery, was *E coli.* Berent et al[5] also reported *E coli* as the predominant isolate cultured from preoperative urine collection; however, in both that paper and that of Kopecny et al,[8] *E faecalis* was reported as the most common isolate cultured from postoperative samples. *E coli* and *E faecalis* are both commensals of the feline gastrointestinal tract[10] and thus the most likely mechanism of urinary tract infection is ascending colonisation by pre-existing enteric microflora. In the present study, *P aeruginosa* was the second most commonly cultured organism at 1 month and joint second most commonly cultured organism (in addition to *E faecalis*) at 12 months postsurgery. *P aeruginosa* is a ubiquitous environmental organism, commonly implicated in opportunistic nosocomial infections.[11] In this study, culturing *P aeruginosa* at any time point was significantly associated with risk of device obstruction but not significantly associated with device removal. This discrepancy is likely due to clients declining removal owing to financial constraints, or because the native ureter(s) had regained patency and the infection was subclinical or resulting in only mild clinical signs.

The only factors identified as predictive of postoperative positive culture were positive preoperative culture and lower end-anaesthetic rectal temperature. In this cohort, 4/14 cats with a positive presurgical urine culture cultured positive for the same isolate within 176 days postsurgery. Berent et al[5] also demonstrated that preoperative bacteriuria was significantly associated with postoperative bacteriuria; however, in this study it is not clear what proportion of cats returned the same isolate at both cultures. Perioperative hypothermia has not previously been investigated as a risk factor for postoperative implant infection. Beal et al assessed the effect of hypothermia on surgical site infection rates in dogs and cats, and found no significant relationship;[12] however, this paper reported incision infections rather than implant-associated infections.

In human patients, perioperative hypothermia has been shown to be associated with surgical wound infections. It is thought that this occurs as a result of the induction of peripheral vasoconstriction, leading to reduced tissue oxygenation and subsequent impaired chemotaxis, phagocytosis and antibody production.[13] In one study of human patients undergoing colorectal surgery, core temperature at the end of surgery was highly correlated with wound infection up to 2 weeks postsurgery, with a 19% incidence rate in the hypothermic group vs 6% in the normothermic group.[14] In our study, hypothermia was associated with increased risk of bacteriuria up to 3 months postsurgery; it is possible that later positive cultures represent initial false-negative cultures or subclinical cases that missed the 1 month recheck.

In the present study, *E coli* was associated with the need for device removal/replacement. This finding highlights the clinical significance of bacterial colonisation in these cases. In the cases reviewed here, the most common reason for implant removal/replacement was bacterial infection. This is in contrast to previous work, which reported mineralisation to be the most frequent reason for device exchange, causing occlusion in 24.2% of devices.[5] In our study population, occlusion due to device mineralisation occurred in only 15.3% of cases and led to device removal or replacement in only 8.5% of cats. The discrepancy in these figures may be attributable to multiple factors, such as differences in diet and water mineralisation levels.

In this population, clinical signs were seen in 57.2% of cats with positive urine cultures, but only 39.3% of cats showed persistent lower urinary tract signs or pyelonephritis, suggesting that many cats with positive urine cultures after device placement are not clinically affected; that is, they have subclinical bacteriuria. This reflects previous work by Berent et al,[5] in which only 62.5% of persistently affected cats had clinical signs suggestive of a urinary tract infection. The optimal way to manage cats with SUB implants and positive urine cultures without lower urinary tract signs remains a topic of debate. In our study, the presence of any lower urinary tract signs was not associated with an increased likelihood of device removal, but for some of these cats the clinical signs were only transient and overall case numbers for cats with positive urine cultures were small. Further work to investigate the optimal management strategies for cats with SUB implants and positive urine cultures, both symptomatic and subclinical, are warranted.

Our postoperative maintenance protocol was changed in February 2019 to include the instillation of TetraEDTA into the devices following sample collection. In this population there was no significant difference in the likelihood of returning a positive culture at 3 months postoperatively for cats receiving routine TetraEDTA flushing vs those that did not. Correlation with positive culture at later time points postsurgery could not be investigated in this population as timing of data collection meant follow-up length was limited in cats receiving the updated

protocol; however, this is an area that warrants further investigation.

The main limitations of this study are attributable to its retrospective design, with available follow-up and preoperative details variable. Although revisits were advised at standardised intervals, many patients did not revisit when advised. Additionally, cultures reported here may represent either clinical urinary tract infections or subclinical bacteriuria. Although an attempt has been made to retrospectively classify the cats as asymptomatic or otherwise, this distinction was made by reviewing historical data, which may not have been complete. Equally, categories were not always clearly defined; for example, some cases showed transient clinical signs that waxed and waned independent of treatment whereas others had persistent signs.

Conclusions

Postoperative bacteriuria occurred at least once within 12 months postoperatively in 23.7% of cats and was a risk factor for device removal/replacement. Both perioperative hypothermia and postoperative positive culture were predictive of postoperative positive culture and this should be taken into consideration when managing these cases.

Acknowledgements The authors would like to thank Dr Yu-Mei Chang for her assistance with this project.

Conflict of interest The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding The authors received no financial support for the research, authorship, and/or publication of this article.

Ethical approval This work involved the use of non-experimental animals only (including owned or unowned animals and data from prospective or retrospective studies). Established internationally recognised high standards ('best practice') of individual veterinary clinical patient care were followed. Ethical approval from a committee was therefore not necessarily required.

Informed consent Informed consent (either verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (either experimental or non-experimental animals) for the procedure(s) undertaken (either prospective or retrospective studies). No animals or humans are identifiable within this publication, and therefore additional informed consent for publication was not required.

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