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Bacterial Urinary Tract Infections Associated with Transitional Cell Carcinoma in Dogs

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Background: Urinary tract infections (UTI) are believed to be common in dogs with transitional cell carcinoma (TCC), but incidence and contributing factors have not been reported.

Objectives: To determine the frequency and bacterial agents associated with UTI in dogs with TCC and define contributing factors.

Animals: Eighty-five dogs with a history of urogenital TCC undergoing treatment with chemotherapy that had at least 1 urine culture performed.

Methods: Medical records and culture results were retrospectively reviewed and ultrasound images were reviewed when available. Clinical factors were evaluated statistically for association with positive culture.

Results: Fifty-five percent (47/85) of dogs had at least 1 positive culture during the course of treatment. Female dogs (80%, 40/50) were more likely than male dogs (29%, 10/35) to have at least 1 positive culture. Ultrasound examination determined that female dogs were more likely to have urethral (74%, 31/42) or trigonal tumor involvement (71%, 30/42) compared to male dogs (32%, 9/28 and 43%, 12/28, respectively). The most commonly isolated organisms were *Staphylococcus* spp. (23.9%, 29/121) and *Escherichia coli* (19.8%, 24/121). Dogs with urethral involvement of TCC were significantly more likely to have at least 1 positive culture than dogs without urethral involvement (75%, 30/40 versus 30%, 9/30).

Conclusions: Urinary tract infection is common in dogs with TCC highlighting the importance of regular monitoring for bacterial cystitis in dogs with TCC. In addition, clinical factors such as tumor location and sex may be predictive of positive culture and can help clinicians assess the risk of UTI.

Key words: Canine; Neoplasia; Urethral.

Canine urinary tract cancer accounts for approximately 1.5–2% of all reported malignancies in dogs with transitional cell carcinoma (TCC) being most common.[1–5] TCC is believed to have a multifactorial etiology with risk factors including exposure to pesticides, obesity, female sex, neuter status, and breed.[1,2,5–7] Factors that affect response to treatment include stage at time of diagnosis and tumor location.[2] The majority of urinary TCC in dogs are intermediate to high grade papillary infiltrative tumors, commonly found in the trigone, that ultimately progress to partial or complete obstruction of the urinary tract.[1–3,5] Urinary tract infections (UTI) may occur when the healthy host defense of the bladder is altered. TCC may cause a failure of host barriers as a result of abnormal patterns of voiding, decreased mucosal defenses caused by changes in the uroepithelium, and by decreased antibacterial properties caused by alterations of urine pH or host defense peptides, thereby predisposing to UTI.[8–12] Previously, published studies have shown that underlying illness contributing to immunosuppression is a risk factor for development of persistent or recurrent infections, suggesting that patients with cancer, those receiving chemotherapy or both may be at higher risk of UTI.[10,13,14] Possible sequelae to untreated bacterial UTI include renal failure, pyelonephritis, lower urinary tract dysfunction, septicemia, prostatitis, discospondylitis, or anemia.[8–11,15,16]

Abbreviations:

CLSI	Clinical Laboratory Standards Institute
MIC	minimum inhibitory concentration
TCC	transitional cell carcinoma
UTI	urinary tract infections
VMTH	Veterinary Medical Teaching Hospital

Although TCC causes functional and anatomic abnormalities that may perpetuate or predispose to UTI, the actual incidence of infection in tumor-bearing dogs is unknown. The objectives of this study were to determine the distribution, characteristics, and bacterial isolates of UTI in a population of dogs undergoing treatment for TCC and to determine whether a correlation exists between UTI development and patient or tumor variables in this population.

Materials and Methods

Study Population

A search of the University of California, Davis William R. Pritchard Veterinary Medical Teaching Hospital (VMTH) medical record database was conducted for the years 2002–2011. Dogs were included if they had a confirmed histologic or cytologic diagnosis of TCC, were treated with chemotherapy and had at least 1 urine sample cultured. Urine samples obtained postmortem were excluded from the study. Information obtained from the medical

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records consisted of breed; age at diagnosis; sex; neuter status; tumor location; number of cultures; culture results including bacterial type(s), numbers, and antibiotic susceptibility data; timing of cultures related to chemotherapy; and, antibiotic history before presentation. Tumor location at the time of diagnosis was determined by review of archived ultrasound images (when available) and evaluated by a single board-certified veterinary radiologist (REP), who was unaware of the clinical features and culture results. Locations were categorized as apical, midbladder, trigone, prostatic gland, urethral, or some combination of these, and data from tumors involving >1 location at diagnosis were included in multiple categories.

Bacterial Isolation, Identification, and Susceptibility Testing

A 10 μL sample of urine was inoculated on 5% sheep blood and MacConkey agars[a] and agar was incubated at 35°C in the presence of 5% CO_2 and observed daily for bacterial growth. Samples were considered negative for bacterial growth after 5 days of incubation. Bacteria were identified using conventional microbiological techniques including colony morphology, hemolysis pattern, Gram stain, tubed media, spot tests, and bacterial identification strips.[b,17] Criteria for positive culture for each collection method were based on standard published information.[10,11] Cultures were considered positive if they yielded ≥1000 colony forming units/mL in a cystocentesis, surgically obtained, or prostatic aspirate sample; ≥10,000 colony forming units/mL in a catheterized sample; and, ≥100,000 colony forming units/mL for a voided sample or a sample with unknown collection method. Bacterial types and fastidious behavior were grouped by genus. *Staphylococcus* spp. was subdivided based on coagulase activity. *Escherichia coli* was classified based on hemolytic status.

Antimicrobial susceptibility testing was performed by the broth microdilution method using microtiter plates.[c] Interpretation of minimum inhibitory concentrations (MICs) was based on criteria from the Clinical Laboratory Standards Institute (CLSI).[18,19] During the study period, a change in laboratory antimicrobial susceptibility testing and interpretation of bacterial urinary isolates occurred. Initially, urinary bacterial isolates were tested and results were interpreted based on estimated urinary antimicrobial concentrations rather than plasma concentrations. However, because these were not criteria utilized by the CLSI and were not comparable to subsequent testing, these results have not been reported or analyzed in this study.

Statistical Analysis

Bacterial species and tumor location were quantified based on total frequency determined. A 2-sided Fisher's exact test was performed to evaluate correlations among patient sex, tumor location, and UTI history. Neuter status was not taken into account when categorizing patients by sex because of the low number of intact patients. Tumor location was assigned based on ultrasonographic appearance, and statistical analyses included only dogs with images available for review. Dogs were categorized as having had ≥1 UTI or no confirmed history of UTI. Values of $P < 0.05$ were considered significant and all statistical tests were performed using commercial software.[d]

Results

Signalment

Eighty-five dogs met inclusion criteria. There were 50 females (59%; 3 sexually intact and 47 spayed) and 35 males (41%; 2 sexually intact and 33 neutered). Median age at the time of diagnosis was 10 years (range, 4–15 years). The most common breeds were mixed breeds (20/85, 23%), followed by Labrador retriever (8/85, 9.4%), golden retriever (5/85, 5.8%), German shepherd (4/85, 4.7%), beagle (4/85, 4.7%), and miniature dachshund (4/85, 4.7%). A total of 30 other breeds were represented by ≤3 dogs.

Tumor

Pretreatment ultrasound images were available for review for 70 dogs. Sixty percent (42/70) of dogs had trigonal involvement, 57% (40/70) had urethral involvement, 71% (20/28) of all males had prostatic involvement, 23% (16/70) had midbladder involvement and 14% (10/70) had apical bladder involvement. Fifty-eight percent (41/70) of dogs had tumors involving ≥1 location at the time of diagnosis. Female dogs were significantly more likely to have urethral involvement when compared to male dogs (74% versus 32%, $P = 0.001$) with TCC (Fig 1A). Female dogs also were more likely to have trigonal involvement when compared to male dogs (71% versus 43%, $P = 0.03$; Fig 1B). There was no correlation between midbladder or apical location and sex in this population of dogs.

Bacterial Isolation

A total of 238 cultures were performed with a median of 2 cultures (range, 1–21) per dog. Sixty-nine percent (164/238) of cultures were obtained by cystocentesis, 14% (33/238) by voiding, 12% (28/238) by catheterization, 2% (4/238) were surgically obtained, 3% (8/238) had an unknown method of collection, and 0.4% (1/238) was obtained by aspiration of the prostate gland. Neither the surgically obtained samples nor the prostatic aspirate were positive for bacterial growth. Only 1 sample without known collection method was positive for bacterial growth. Thirty-five percent (83/238) of all cultures were positive and 55% (47/85) of dogs had at least 1 positive culture result. Thirty-three percent (54/164) of cultures obtained by cystocentesis, 55% (18/33) of cultures obtained by voiding, and 32% (9/28) of cultures obtained by catheterization had positive culture results. Voided sample cultures were more likely to be positive when compared to cystocentesis ($P = 0.03$) samples. Positive culture rates were similar between cystocentesis and catheterized collection methods ($P = 1.0$). Eighty percent (40/50) of female dogs and 29% (10/35) of male dogs had at least 1 positive culture. Females were significantly more likely to have at least 1 positive culture ($P = 0.0001$; Fig 1C). Sixty-seven percent of dogs (57/85) had a urine culture obtained before starting chemotherapy and 25% (14/57) of those cultures were positive. Sixty-seven percent (56/83) of all positive samples were recultured. Of these, 30% (17/56) grew the same organism that initially was found on the positive culture whereas 28% (16/56) of the repeated cultures grew a different organism. Fifty-five percent (31/56) of the cultures were determined to have no

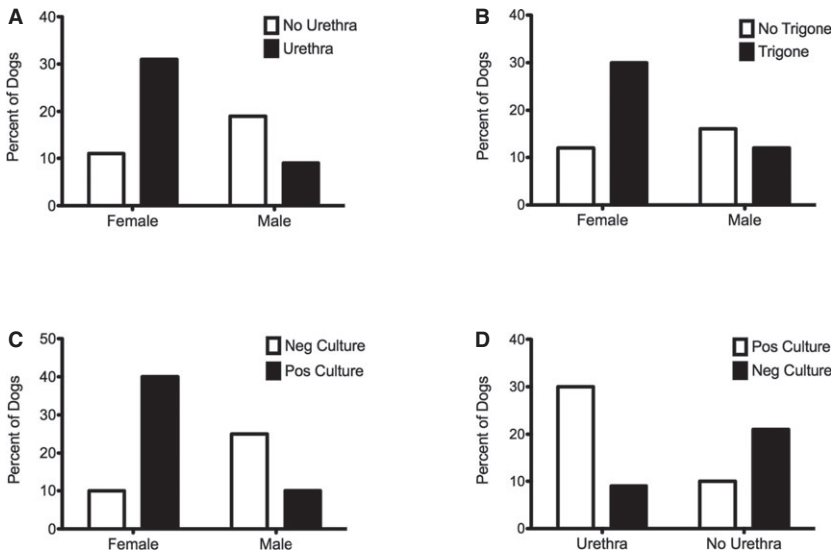

Fig 1. Significant findings of tumor location and lower urinary tract infection in dogs with transitional cell carcinoma. (**A**) Female dogs were significantly more likely to have urethral tumor involvement than males with urethral tumor involvement ($P = 0.001$). (**B**) Female dogs were significantly more likely to have trigonal tumor involvement than males with trigonal tumor involvement ($P = 0.03$). (**C**) Female dogs were significantly more likely to have at least one positive culture than male dogs with a positive culture ($P < 0.0001$). (**D**) Dogs with urethral involvement were significantly more likely to have at least one positive culture than dogs without urethral involvement ($P = 0.0002$).

growth on repeated culture. Thirty-two percent (27/83) of positive cultures were not retested at the VMTH. Forty-two of the positive cultures were evaluated for antibiotic susceptibility using urine MIC cut-offs. Thirty-two positive cultures were evaluated using serum MIC cut-offs, and MIC data were not available for 8 positive cultures.

From 83 positive cultures, 123 bacterial isolates were identified. One culture was mixed and another culture containing 1 organism was defined as an aerobic gram-positive, nonspore-forming, rod. These 2 cultures were excluded from classification of organismal types. The most common bacterial isolates included *Staphylococcus* spp. at 23.9% of isolates; 13.2% (16/121) were coagulase-positive *Staphylococcus* spp. whereas 10.7% (13/121) were coagulase-negative *Staphylococcus* spp. (Table 1). The next most common genus was *E. coli* at 19.8% of isolates; 14% (17/121) were nonhemolytic *E. coli* and 5.8% (7/121) were hemolytic *E. coli*. These results were followed by *Streptococcus* spp. at 18.2% (22/121), *Enterococcus* spp. at 7.4% (9/121), *Pseudomonas* spp. at 7.4% (9/121), *Pasteurella* spp. at 5.8% (7/121), *Mycoplasma* spp. at 3.3% (4/121), *Proteus* spp. at 2.5% (3/121), *Bacillus* spp., *Enteric* spp., *Actinomyces* spp. and *Aerococcus* spp. each represented 1.7% (2/121) with 5% of other bacteria (1 each of *Haemophilus* sp., *Enterobactor* sp., *Stenotrophomonas* sp., *Acinetobacter* sp., *Serratia* sp., and *Corynebium* sp.). The total number of positive cultures with >1 organism was 44.6% (37/83). One bacterial isolate was found in 55.6% (46/83) of positive cultures, 33.7% (28/83) of cultures had 2 isolates, 8.4% (7/83) of cultures had 3 isolates, and 1.2% (1/83) of cultures had 4 isolates. One culture obtained by cystocentesis was labeled mixed with 3 colonies of growth. Of the cultures for which MIC data were not available, 4 contained *Streptococcus* spp. and 1 each contained *Enteric* spp., *Pseudomonas* spp., *Mycoplasma* spp., *Staphylococcus* spp., and *Pasteurella* spp. Thirty-two percent (11/47) of all dogs with at least 1 positive culture grew an *E. coli* bacterial isolate (Table 1). This result was followed by *Streptococcus* spp. at 27.6% (13/47), *Staphylococcus* spp. at 23.4% (11/47), *Enterococcus* spp. at 19.1% (9/47), *Pseudomonas* spp. at 14.9% (7/47), *Pasteurella* spp. at 12.8% (6/47), *Mycoplasma* spp. at 8.5% (4/47), *Proteus* spp. at 6.3% (3/47), *Bacillus* spp., *Enteric* spp., *Actinomyces* spp., and *Aerococcus* spp. at 4.3% (2/47). One dog each grew *Haemophilus* sp., *Enterobactor* sp., *Stenotrophomonas* sp., *Acinetobacter* sp., *Serratia* sp., and *Corynebacter* sp.

Table 1. Frequency of bacterial isolates from all positive cultures and frequency of dogs with positive culture having cultured specific bacterial organisms.

Bacterial Type	% of Isolates	% of Dogs With At Least One Positive Culture
Staphylococcus spp.	23.9	23.4
Escherichia coli	19.8	32.0
Streptococcus spp.	18.2	27.6
Enterococcus spp.	7.4	19.1
Pseudomonas spp.	7.4	14.9
Pasteurella spp.	5.8	12.8
Mycoplasma spp.	3.3	8.5
Proteus spp.	2.5	6.3
Bacillus spp.	1.7	4.3
Enteric spp.	1.7	4.3
Actinomyces spp.	1.7	4.3
Aerococcus spp.	1.7	4.3
Other	5.0	12.8

Seventy-five percent (30/40) of dogs with urethral involvement, 62% (26/42) of dogs with trigonal tumor involvement, 56% (9/16) of dogs with midbladder location, 40% (4/10) of dogs with apical bladder involvement, and 25% of male dogs with prostatic involvement (5/20) had at least 1 positive culture. Dogs with urethral involvement of TCC were significantly more likely to have at least 1 positive culture than dogs with no urethral involvement (75% versus 30%, $P = 0.0002$; Fig 1D). When considering only females, dogs with urethral involvement still were more likely to have at least 1 positive culture than dogs without urethral involvement ($P = 0.01$). No other correlation was found between location and positive culture.

Twenty-two dogs had 87 urine cultures obtained after the laboratory policy change for antimicrobial susceptibility testing and interpretive criteria of urinary isolates. Twelve of these dogs had at least 1 positive culture (range, 1–16) and 32 positive cultures from these dogs had MIC data available for review. Six dogs (50%, 1 male, 5 female) had at least 1 culture with ≥1 organisms with acquired antibiotic resistance to ≥1 antimicrobial drugs. One dog had a resistant coagulase-negative *Staphylococcus* sp., a resistant coagulase-positive *Staphylococcus* sp. and *Aerococcus* sp. This dog had recurrent resistant infections and had 16 positive cultures over time containing 5 different genera of bacteria, 3 of which were resistant to ≥1 antimicrobial drugs. One dog had *Aerococcus* sp. One dog had resistant nonhemolytic *E. coli* and hemolytic *E. coli*. Two dogs had hemolytic *E. coli*. Lastly, 1 dog had a resistant nonhemolytic *E. coli*.

Antimicrobial History

A total of 69% (59/85) of dogs had a known history of systemic antimicrobial administration before diagnosis and first culture collection. Drug type was not known for 9 of these dogs. Both amoxicillin/clavulanic acid and enrofloxacin each were prescribed to 38% (19/50) of dogs, cephalexin to 24% (12/50) of dogs, amoxicillin to 22% (11/50) of dogs, and metronidazole to 6% (3/50) of dogs. Cefpodoxime, chloramphenicol, trimethoprim-sulfa, and ciprofloxacin each were prescribed to 2 dogs and 1 dog each received marbofloxacin, orbofloxacin, florfenicol, ampicillin, doxycycline, nitrofurantoin, and cefovecin. Forty percent (20/50) of patients had a history of >1 prescribed antibiotic. All 5 of 5 dogs with enrofloxacin-resistant bacteria had a known history of enrofloxacin administration and 2 of 3 dogs with amoxicillin/clavulanic acid-resistant bacteria had a known history of amoxicillin/clavulanic acid administration. Dogs without a known history of antimicrobial administration were not more likely to have a positive first culture compared to dogs prescribed a systemic antimicrobial drug ($P = 1.0$).

Discussion

In our study, positive urine cultures were found to be common in dogs with TCC. Fifty-five percent of dogs had at least 1 positive culture result during the course of treatment. In addition, 25% of dogs that had a urine culture obtained before starting chemotherapy had positive results. These findings suggest that all dogs diagnosed with TCC undergoing chemotherapy should have a culture performed before starting treatment and cultures should be repeated regularly throughout treatment. Undiagnosed and untreated UTI can lead to renal failure, pyelonephritis, lower urinary tract dysfunction, septiciemia, prostatitis, discospondylitis, or anemia and can, themselves, be life-limiting.[9–11,15]

Results of our study are consistent with previous studies with regard to signalment and tumor location in dogs with TCC. Similar to previous studies, female dogs were more likely to have TCC of the lower urinary tract than male dogs (59% versus 41%).[20] Causes for this difference are speculative. Because male dogs have an increased frequency of urination for territorial marking as compared with female dogs, this behavior could provide decreased exposure time of carcinogens to the uroepithelium for male dogs.[2] Female dogs also may have more direct contact with environmental carcinogens based on squatting behavior and higher body fat accounting for a possible increased risk of sequestration of lipophilic environmental carcinogens.[2] The results of this study showed the most common locations of tumor involvement were trigonal (60%) and urethral (57%). However, 58% of dogs had large tumors that were not isolated to 1 location at the time of diagnosis, making initial tumor origin difficult to determine.

We also found female dogs to be significantly more likely to have urethral and trigonal tumor involvement than male dogs. Although the reason for this difference between the sexes is unclear, a previous study found a similar anatomical difference between the sexes with 26/57 (46%) female dogs and only 4/35 (11%) male dogs having urethral tumors.[20] Unlike our study, there were similar frequencies of trigonal involvement between sexes in that study with 23/57 (40%) female dogs and 13/35 (37%) male dogs having trigonal involvement.[20] The previous study used cystoscopy and cystotomy to interpret tumor location, whereas ultrasonography was used in our study, suggesting that possible diagnostic shortcomings alone cannot explain the anatomical difference in tumor location between sexes. Therefore, it is unclear if female propensity for urethral and trigonal tumor location is because of an unknown mechanism causing a sex-related predilection.

Bacteria were isolated from 35% of all cultures, and culture results with >1 organism were common at 43.3% of positive cultures. The most common organisms cultured in our study were *Staphylococcus* spp., 23.7% followed by *E. coli* at 19.7% and *Streptococcus* spp., 18.2%. In comparison, the most prevalent organismal isolate in the canine urinary tract in previously published studies was *E. coli*, ranging from 37 to 55%.[15,21] The most likely organisms to invade the urinary tract are thought to be those of the colonic microbiotia. When evaluating the total number of dogs rather than the total number of bacterial isolates, *E. coli* was the most common isolate in dogs with at least 1 positive

culture at 32%, followed by *Streptococcus* spp. at 27.6% and *Staphylococcus* spp. at 23.4%. One dog in our study had 21 cultures performed (18 cystocentesis, 2 voided, and 1 unknown collection method), with a large proportion of the organisms consisting of *Staphylococcus* spp. and this case likely skewed results. It is unknown if the distribution of organisms in this study is the result of compromised local or systemic host defenses or a result of previously empirically prescribed antibiotics. The change in laboratory policy relating to MIC testing and interpretation made it difficult to fully explore antibiotic resistance in this population, but 27% of dogs with cultures collected after the procedural change and 50% of dogs with positive cultures had at least 1 organism with acquired antimicrobial resistance. Although data were collected regarding antibiotic history before presentation to the VMTH, the dosage, frequency, duration of antimicrobial treatment, antimicrobial type, or some combination of these often was not available. More than half of all dogs that presented to the VMTH previously were prescribed antibiotic treatment with 40% having received >1 antibiotic type. Results also showed no difference in likelihood of having a positive first culture based on previous antibiotic history. Characteristics and actual incidence of antibiotic-resistant organisms is difficult to ascertain because of the small population of dogs with urinary isolate antimicrobial susceptibility information. Both the bacterial isolates and their susceptibility patterns in this study might be specific to the western United States and therefore differences may be found in other regions of the country. Further study into antibiotic-resistant infections in dogs with TCC is needed.

The results of this study indicate that patient and tumor factors such as sex and location of tumor may indicate likelihood of infection. Seventy-five percent of dogs with urethral involvement and 62% of dogs with trigonal tumor involvement were diagnosed with at least 1 UTI during the course of treatment. In addition, more than half of dogs with a midbladder tumor location had a history of UTI. Dogs with urethral tumors statistically were more likely to have UTI than dogs with tumor location in another region. This study may indicate that dogs with tumors closer to the urethra are more likely to have UTI. Interestingly, only 25% of males with prostatic involvement were found to have UTI. Dogs with prostatic tumors might be less likely to develop UTI, but UTI in dogs with prostatic tumors also might be more difficult to detect by urine culture alone. Only 1 dog in this study had a prostatic aspirate cultured and further study into the utility of this culture method is necessary.

This study also found that female dogs were significantly more likely to have a positive culture (74% compared to male dogs with TCC at 28%). This information is in agreement with previous studies that showed female dogs are more likely than males to have uncomplicated UTI.[9,12,22] Although the actual cause is uncertain, bacteria may be able to gain entrance to the urinary tract by ascension through the shorter urethra of female dogs.

The results of this study must be interpreted cautiously, taking into account inherent limitations. One limitation of this study results from the inclusion of only dogs undergoing chemotherapy for TCC. This population was chosen because dogs receiving regular treatment at the VMTH were more likely to have repeated urine culture data available for review. Chemotherapy may cause some immunosuppression that could predispose to UTI, and these inclusion criteria may have selected for dogs more likely to develop UTI. Therefore, these results may not be applicable to dogs with TCC not receiving chemotherapy. Furthermore, the impetus for a clinician to submit a urine culture often was not documented in the medical record. Whether cultures were performed as a consequence of clinical signs or for routine screening were unknown. This study also included only dogs that had at least 1 culture performed during the course of treatment, potentially resulting in selection bias if clinicians submitted urine samples for culture because of suspicion of infection. The clinical signs of UTI and progressive TCC however are similar, and both may prompt urine culture thereby decreasing bias. Furthermore, bias may have been further minimized because it is standard practice at the VMTH to culture urine before starting chemotherapy and to culture regularly thereafter in dogs with TCC. Nonetheless, a future prospective study assessing the actual incidence of UTI in dogs with TCC is needed to confirm these findings without the inherent biases of a retrospective study.

In this study, 69% of cultures were obtained by cystocentesis. Fine-needle aspirates of patients suspected to have urinary tract TCC historically have been discouraged because of concern about implantation of cells along the needle tract. Needle tract implantation overall is considered rare.[23] It has been reported that abdominal wall TCC occurred in 6/367 patients having had ultrasound-guided fine-needle aspiration of the prostate gland or urinary bladder.[24] This number excluded dogs that had a previous cystotomy performed. It is common practice at our institution to collect urine from dogs with TCC by ultrasound-guided cystocentesis at a location as distant from the tumor as possible. The risk and complications of undiagnosed UTI are thought to be higher than the risk of tumor seeding. Although the purpose of this study was not to determine the incidence of needle tract seeding in this population, only 1 dog in the study was known to develop abdominal wall metastasis secondary to seeding. Furthermore, this dog was confirmed to have a previous history of a cystotomy for surgical resection of bladder TCC. No dogs in this study were confirmed to have needle tract seeding secondary to a cystocentesis alone, but, necropsies were not performed on all dogs after death or euthanasia to confirm the rate of actual tumor seeding. Although the majority of cultures in this study were obtained by cystocentesis (69%), voided cultures (14%) were statistically more likely to be positive. This finding may indicate the possibility of more false positives, despite the published organismal cut-offs, or alternatively, may result from detection of true infections in dogs with

tumors present in the prostate gland or urethra. Further study into these findings is necessary.

In conclusion, these results confirm the clinical suspicion that UTI is are common in dogs with TCC with 25% of dogs having a positive culture at diagnosis and over 50% of dogs having at least 1 positive culture during the course of treatment. These results also highlight the importance of regular monitoring for UTI, including relapse and reinfection after treatment of dogs with TCC. Tumor location and sex were predictive of positive culture in this study, and may guide a clinician's decision as to how aggressively a patient should be monitored for UTI. Further prospective investigation into UTI incidence and the relationship between UTI risk, sex, and tumor location is warranted.

Footnotes

[a] Hardy Diagnostics, Santa Maria, CA.
[b] API, bioMerieux, Durham, NC.
[c] Sensititre, ThermoFisher Scientific, Oakwood Village, OH.
[d] GraphPad Prism for Windows version 5.0c, GraphPad Software, San Diego, CA.

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Conflict of Interest Declaration: Authors disclose no conflict of interest.

Off-label Antimicrobial Declaration: Authors declare no off-label use of antimicrobials.

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