Acute pyelonephritis in cats is frequently caused by *Escherichia coli* resistant to potentiated penicillins but has a better prognosis than other causes of acute kidney injury

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Received September 5, 2023
Accepted October 16, 2023
doi.org/10.2460/javma.23.08.0488

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OBJECTIVE
To describe the clinical findings, microbiological data, treatment, and outcome of a population of cats with suspected acute pyelonephritis (APN).

ANIMALS
32 client-owned cats.

CLINICAL PRESENTATION AND PROCEDURES
Retrospective case series from 2 veterinary teaching hospitals between January 1, 2014, and December 31, 2020. Cats were included if they had a positive bacterial urine culture and a clinical diagnosis of acute kidney injury.

RESULTS
Older female cats with underlying chronic kidney disease have a higher probability to develop bacterial culture-positive acute kidney injury or APN. *Escherichia coli* was the most commonly cultured bacterial species, and *E coli* isolates with susceptibility testing were resistant to amoxicillin-clavulanate but susceptible to fluoroquinolones or third-generation cephalosporins. Of the 20 cats with available follow-up information in the medical record, 14 were alive at 3 months after hospital discharge. Markers of renal function including creatinine (\(P = .008\)), BUN (\(P = .005\)), and phosphorus (\(P < .001\)) at the time of presentation were all higher in nonsurvivors compared with survivors.

CLINICAL RELEVANCE
The survival rate with feline APN is higher than previous reports of acute kidney injury when all etiologies are considered. Nonsurvivors had more pronounced azotemia upon initial presentation. Amoxicillin-clavulanate was a poor empirical antimicrobial in this cohort based on the microbiological data.

Keywords: acute kidney injury, feline, bacteriuria, urine culture, pyelonephritis

Sudden renal parenchymal damage due to a variety of etiologies (e.g., ureteral obstruction, pyelonephritis, renal ischemia, toxicosis) is an important clinical condition in cats resulting in acute kidney injury (AKI). Considering all etiologies together, feline AKI carries a guarded prognosis.\(^1,2\) Bacterial pyelonephritis as a cause of AKI in cats can often be difficult to diagnose.\(^3,4\) A presumptive diagnosis of acute pyelonephritis (APN) is often made in a patient with AKI and a positive aerobic bacterial urine culture.\(^5\) Quantitative culture and susceptibility testing of urine remain the standard of care to both aid in the diagnosis of APN and guide appropriate antibiotic therapy,\(^3,4\) but results are typically not available for several days after submission. Consequently, empirical treatment with antibiotics is typically recommended while urine culture results are pending.\(^1,5\)

Choosing the most appropriate antibiotic for empirical treatment of APN in cats is difficult due to a lack of documented microbiological information on these patients. In addition, scarce data are available in cats with APN to support antibiotic treatment durations and clinical outcomes.

In dogs with APN, gram-negative organisms from the *Enterobacteriaceae* family are cultured more commonly than gram-positive organisms, and *Escherichia coli* is the most commonly cultured bacterial species.\(^6\) This is similar to people with APN, where *E coli* is
consistently the most commonly cultured organism.7 The reported prevalence and susceptibility patterns of causative bacterial agents in feline APN patients are very limited. The most common species cultured from cats with lower urinary tract disease are E coli, Streptococcus spp, Staphylococcus spp, Enterococcus spp, and, at a lesser frequency, Proteus mirabilis.10,11 In cats asymptomatic for urinary tract disease, Enterococcus spp are the most common bacterial isolate, followed by E coli.12 Both E coli and Enterococcus spp are the most common organisms cultured postoperatively from cats with a subcutaneous ureteral bypass device or ureteral stent placement, and these cats may have clinical pyelonephritis and/or cystitis or have subclinical bacteruria.13-15

In dogs, empirical treatment for APN with antimicrobials with known efficacy against Enterobacteriaceae (eg, fluoroquinolones, third-generation cephalosporins) is often recommended.9 Fluoroquinolones are favored over β-lactam antibiotics for the treatment of APN in women.16 Enrofloxacin has been specifically advocated for empirical treatment of APN in veterinary medicine.4,5 In cats with lower urinary tract infections, antimicrobial susceptibility data show that there may be a higher prevalence of feline uropathogen isolates susceptible to enrofloxacin compared to amoxicillin-clavulanate.9,17 The most commonly encountered uropathogens in cats with suspected APN has not been reported until recently, but susceptibility data and outcome were not included.

The primary objectives of this retrospective study were to describe a clinical population of cats diagnosed with suspected APN including clinical signs, clinicopathological data, imaging findings, targeted bacterial urinary pathogens cultured and microbial susceptibility results, antimicrobial therapy prescribed, and outcomes. Three-month survival after hospital discharge was a secondary outcome of the study. Potential clinical markers of disease severity (clinical signs, Hct, WBC count, BUN, creatinine, phosphorus, electrolytes, albumin, urine specific gravity, International Renal Interest Society [IRIS] stage, and urinary tract ultrasound findings) were compared between cats that survived versus nonsurvivors.

Methods

Case selection

The medical records from 2 veterinary teaching hospitals (Kansas State University Veterinary Health Center [KSUVHC] and University of Wisconsin-Madison Veterinary Care [UWVC]) of client-owned cats with a urine culture performed between January 1, 2014, and December 31, 2020, were retrospectively reviewed. Cats with a clinical diagnosis of suspected APN were included in the study cohort if they met all 4 of the following criteria: (1) confirmed bacteriuria by a positive aerobic bacterial urine culture collected via cystocentesis; (2) presence of at least 1 consistent clinical sign of AKI such as lethargy, hyporexia, anorexia, vomiting, polyuria/polydipsia, peruria, hematuria, fever, and renal or abdominal pain; (3) acute clinical signs that developed within 1 week of presentation; and (4) new or worsening azotemia (increase in creatinine of ≥ 0.5 mg/dL since the last documented value) as defined by the IRIS as an AKI grade II or higher. Cats were excluded from the study if there were insufficient data in the medical records to determine clinical signs and renal status. Cats were also excluded if the primary cause of the azotemia was determined to be postrenal in origin but included if pyonephrosis was suspected. Additionally, patients euthanized within 24 hours after presentation were censored from outcome analysis.

Data collection

Data collected from the medical record included signalement, clinical signs, known comorbidities, presenting clinicopathological data (CBC, biochemistry panel, urinalysis), urinary tract ultrasonographic abnormalities, microbiological data from a quantitative urine culture, antimicrobial therapy including empirical treatment as well as treatment following urine culture and susceptibility results, and outcome. Records were reviewed for the 2 months prior to presentation to document any historical antimicrobial therapy. Subsequent antimicrobial therapy following the initial treatment for APN was not recorded. A fever was defined as a rectal temperature of > 102.1°F.19 Anemia was defined as an Hct below the laboratory’s reference interval. Neutrophilia was defined as a neutrophil count above the laboratory’s reference interval. Microscopic bacteriuria was defined as bacteria identified on a urine sediment examination, and pyuria was defined as ≥ 5 WBCs/high-powered field on urine sediment examination. Specific urinary tract ultrasonographic changes assessed were the presence or absence of renomegaly, hydropneic renal cortices, renal pelvic dilation, ureteral dilation, retroperitoneal disease such as effusion or hydropneic tissue, and presence or absence of degenerative changes to the kidneys.20,21 It was documented as to whether cats were still alive at discharge as well as 1 month and 3 months following discharge since the majority of cats were lost to follow-up after this timeframe.

Noted differences were observed between the reporting of quantitative urine cultures and antimicrobial susceptibility testing results by the microbiology laboratories of the 2 institutions. There was disparity in reporting the maximum number of CFUs per milliliter of the cultured bacterial isolates, the use of selective and cascading reporting of antibiotic susceptibility testing, and the use of plasma versus urinary breakpoints in reporting antibiotic in vitro susceptibility results for the penicillins and potentiated penicillins (eg, ampicillin, amoxicillin-clavulanate) of urinary isolates. Due to these noted differences, the microbiology results in this study are reported as a maximum of > 10,000 CFUs/mL for bacterial isolates cultured.

Statistical analysis

Statistical analysis was performed with Prism, version 9.5.1 (GraphPad Software Inc). Data were
assessed for normality via the Shapiro-Wilk test, but none of the variables met the normality assumption except for Hct. Continuous variables were therefore reported as median and range, and differences between groups were compared via an unpaired t test or Mann-Whitney U test when appropriate. Categorical variables were reported as numbers and percentages, and differences between groups were compared via the Fisher exact test. Logistic regression was used to evaluate the association of IRIS AKI grade with survival. Antimicrobial susceptibility data for the E coli isolates were presented as minimum inhibitory concentration (MIC) frequencies and percentage of susceptible isolates. Feline plasma MIC breakpoints were used when available.22 Statistical significance was set at \( P < .05 \).

**Results**

A combined total of 2,603 urine samples from feline patients were submitted for aerobic culture to the Kansas State Veterinary Diagnostic Laboratory (n = 1,017) and UWVC microbiology laboratory (n = 1,586) between January 1, 2014, and December 31, 2020. Of the urine samples with positive bacterial growth (n = 532), 32 cats were diagnosed and treated for suspected APN (KSUVHC, 25; UWVC, 7). The remaining cases with positive bacterial growth were cats with an incomplete diagnostic evaluation or incomplete medical record to determine the cause of bacteriuria (n = 338), did not have azotemia (n = 72), had azotemia but did not meet the criteria for APN (44), were diagnosed with a urethral obstruction (30), were diagnosed with a ureteral obstruction (5), had a culture performed from urine collected from a subcutaneous ureteral bypass device (5), had a culture performed from a voided urine sample (4), or was a recheck following treatment of APN (2).

**Study cohort**

The median age of cats with suspected APN was 15 years (range, 4 to 20). Twenty-nine cats were spayed females, 1 cat was an intact female, and 2 cats were neutered males. There were 24 domestic shorthairs, 4 domestic medium hairs, 1 domestic longhair, 2 Maine Coons, and 1 Siamese. Two cats received amoxicillin-clavulanate for 24 hours or less prior to presentation, and the remaining cats did not receive antimicrobials within the 2 months prior to presentation.

Most of the cats in this cohort had at least 1 co-morbidity identified (Table 1). Approximately half of the population (17/32 [52%]) had underlying chronic kidney disease (CKD), and 6 of 32 (19%) cats had no concurrent or underlying medical condition identified. For the cats with a diagnosis of CKD, previous creatinine concentrations were available for comparison in 13 of 17 and had increased by 1.4 mg/dL (range, 0.6 to 6.2) over 32 days (range, 15 to 112). At least 1 clinical sign of lower urinary tract disease (periuria, pollakiuria, or stranguria) was present in 13 of 32 (41%) cats (Table 2). All these cats had at least 1 additional clinical sign including lethargy, anorexia or hyporexia, vomiting, or an increased rectal temperature. Three cats had hematuria, but only 2 of them had other clinical signs of lower urinary tract disease. Only 7 of 32 (22%) were considered to have a fever, of which 2 had rectal temperatures of 102.2°F.

**Clinicopathological data**

Twenty-eight cats had a CBC performed, and all cats had a chemistry panel performed upon initial presentation (Table 3). Two additional cats had a PCV performed at presentation. Seventeen (57%) cats had an anemia. A leukocytosis was present in 10 of 28 (36%) cats, but a neutrophilia was present in 19 of 28 (68%) cats. Band neutrophils were present in 14 of 28 (50%) cats, and the median band neutrophil count of these 14 cats was 600/μL (range, 200 to 2,900). Based on initial serum creatinine concentrations, 9 (28%) of the cats were IRIS AKI grade II, 13 (41%) cats were IRIS AKI grade III, 6 (19%) cats were IRIS AKI grade IV, and 4 (12%) cats were IRIS AKI grade V. Twenty-five cats had a urinalysis performed concurrently with the urine culture, and 2 additional cats had just a urine specific gravity checked at the time of the urine culture. Of the cats with a urine sediment evaluation, microscopic bacteriuria was identified in 21 of 25 (84%), and pyuria was present in 14 of 25 (56%).
An abdominal ultrasound performed by a board-certified radiologist or resident under the supervision of a board-certified radiologist was completed in 20 cases. Renomegaly was only appreciated in 3 of 20 (15%) cats, and hyperechoic kidneys were appreciated in 8 of 20 (40%). Of the 8 cats with hyperechoic kidneys, 7 of them had evidence of underlying CKD such as small, irregular kidneys and loss of corticomedullary distinction. There were 3 other cats with CKD that had abdominal ultrasound performed, and these kidneys were not reported to be hyperechoic.

Pyelectasia was present in 12 of 20 (60%) cats, and pyelectasia was unilateral in 6 of 12 (50%) of these cats. Median renal pelvis dilation was 2.7 mm (range, 1.0 to 10 mm). Ureteral dilation was present in 9 of 20 (45%) cats, and the dilation was unilateral in 6 of 9 (67%) of these cats. Ureteral dilation was distal in 2 of 9 cats and proximal in 8 of 9 cats, with 1 cat being counted in each group due to identification of left distal ureteral dilation and right proximal ureteral dilation. Median ureteral dilation was 2.4 mm (range, 1.6 to 8.3 mm). Echogenic material was present in the renal pelvis of 4 kidneys (3 cats). The renal pelvis measurements of these kidneys were 10.9, 9.9, 6.6, and 6.6 mm. In cats with pyelectasia but without echogenic material (9/12 cats), two renal pelvis measurements were 6.7 mm and another measured 3.7 mm, but the remaining (7/12 cats) were ≤3 mm. A single cat was rechecked with abdominal ultrasound 6 days after the initial study. The left renal pelvis of this cat originally measured 9.9 mm and, upon reevaluation, was 3 mm. Pyelectasia and ureteral dilation were not more common in cats with a previous diagnosis of CKD compared to those without a previous diagnosis of CKD (P = .168 and P > .999, respectively). There was evidence of retroperitoneal disease in 5 of 20 (25%) cats, with the tissue around the kidneys being described as hyperechoic with or without the presence of mild retroperitoneal effusion.

### Microbiological data and antimicrobial therapy

A total of 38 bacterial isolates were cultured from 32 positive aerobic urine cultures from these cats with suspected APN (Figure 1). As expected, *E. coli* was the most common isolated urinary pathogen, representing 34 of 38 (89%) isolates. Of the 33 *E. coli* isolates with available susceptibility testing, all were resistant to ampicillin and amoxicillin-clavulanate based on the feline plasma MIC breakpoint (Table 4). Antimicrobials were used empirically in 28 of 32 (88%) cases. An antimicrobial was prescribed following urine culture results in 3 cases. The remaining case was euthanized prior to starting antimicrobial therapy. A potentiated penicillin (ampicillin-sulbactam, n = 13; amoxicillin-clavulanate, 5) was the most...
common class prescribed empirically, followed by a fluoroquinolone (pradofloxacin, 8; enrofloxacin, 4; Figure 2). Following availability of urine culture and susceptibility results, there was a change in antimicrobial therapy in 11 of 28 (39%) cases. Median duration of antimicrobial therapy was prescribed for ≤ 14 days; however, 2 of these 3 cats were lost to follow-up shortly after hospital discharge.

Outcome

One cat was euthanized within 24 hours of initial presentation and was censored from outcome analysis. Of the remaining 31 cats, 29 (94%) survived to discharge. The 2 cats that were euthanized prior to discharge had an initial IRIS AKI grade of V. One was treated with ampicillin-sulbactam and the other with enrofloxacin. Following discharge, 24 cats were documented to be alive at 1 month. An additional cat was euthanized 6 days after discharge due to progressive azotemia, and this cat had an initial IRIS AKI grade of IV and was treated with a combination of ampicillin-sulbactam and pradofloxacin initially and discharged with only pradofloxacin. The other 4 cats were lost to follow-up. Fourteen cats had documentation of their serum creatinine between 2 and 4 weeks after discharge. The median creatinine at recheck for these cats was 3.05 mg/dL (range, 1.7 to 6.3 mg/dL) compared to 3.25 mg/dL (2 to 9.2 mg/dL) at presentation. Only 7 cats had documentation of their serum creatinine between 2 and 3 months after discharge. The median creatinine at this time point was 1.9 mg/dL (1.6 to 5 mg/dL).

Survival information for 3 months following discharge was available for 20 cats. Most of the cohort was lost to follow-up after this timeframe. The all-cause case mortality rate was 6 of 20 (30%) by 3 months. The cause of death was determined to be renal related in 4 of the cases, including the 2 cats that did not survive to discharge, the cat with progressive azotemia euthanized 6 days after discharge, and 1 cat with persistent clinical signs and progressive azotemia euthanized 70 days after discharge. The cause of death was undetermined in the other

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Table 4—Urinary *Escherichia coli* isolates with susceptibility testing from cats described in Table 1 with their associated minimum inhibitory concentrations (MICs) for the classes of antibiotic used in the treatment of this cohort. All urine samples were collected via cystocentesis, and Clinical and Laboratory Standards Institute (CLSI) breakpoints were used to determine the percent susceptible to the selected antibiotics.

<table>
<thead>
<tr>
<th>Class</th>
<th>Antimicrobial</th>
<th>MIC frequency (µg/mL)</th>
<th>MIC breakpoint (µg/mL)</th>
<th>Percent susceptible</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>Ampicillin</td>
<td>&gt; 1 (n = 20) ≤ 2 (n = 9) ≤ 4 (n = 2) ≤ 16 (n = 1) ≥ 32 (n = 1)</td>
<td>≤ 0.25²</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Amoxi-clav</td>
<td>≤ 0.25/0.12²</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Cephalosporin (first gen)</td>
<td>Cephalexin</td>
<td>4 (n = 14) ≤ 8 (n = 4)</td>
<td>≤ 2³</td>
<td>91</td>
</tr>
<tr>
<td>Cephalosporin (second gen)</td>
<td>Cefpodoxime</td>
<td>≤ 1 (n = 22)</td>
<td>≤ 2⁴ ≤ 2 (n = 9)</td>
<td>92</td>
</tr>
<tr>
<td>Fluoroquinolone</td>
<td>Enrofloxacin</td>
<td>&gt; 16 (n = 2) ≤ 0.25 (n = 29) ≤ 2 (n = 1)</td>
<td>≤ 0.5²</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td>Marbofloxacin</td>
<td>≤ 0.5 (n = 29) ≤ 2 (n = 1)</td>
<td>≤ 1²</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td>Orbifloxacin¹</td>
<td>≤ 1 (n = 15)</td>
<td>≤ 12</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Pradofloxacin²</td>
<td>≤ 0.25 (n = 15)</td>
<td>≤ 0.25⁵</td>
<td>100</td>
</tr>
</tbody>
</table>

¹Antimicrobials added to Kansas State University Veterinary Health Center panel January 2016. Orbifloxacin and pradofloxacin were not tested on all isolates. ²CLSI breakpoint, feline skin and soft tissue. ³CLSI breakpoint, canine skin and soft tissue. ⁴CLSI breakpoint, canine wound, abscess, and urinary tract. ⁵CLSI breakpoint, feline respiratory, skin, and soft tissue.

Figure 2—Flow diagram of empirical and pathogen-directed antibiotic therapies prescribed in cats described in Figure 1. Pathogen-directed prescriptions were the antibiotics prescribed once bacterial culture and antibiotic susceptibility testing were completed. APN = Acute pyelonephritis. FQ = Fluoroquinolone. Gen = Generation.

The cats in this study were older (median age, 15 years) and mostly female, which is similar to what is reported with cats diagnosed with a lower urinary tract infection.\(^8,11,12,23\) Approximately half of the cats were previously diagnosed with CKD, supporting the notion that APN is a common cause of acute-on-chronic kidney disease.\(^3\) Clinical signs were relatively nonspecific, and findings of fever and abdominal pain were uncommonly identified, which is similar to a previous report.\(^24\)

Microscopic bacteriuria was found in most cats (84%) in this study, with pyuria documented to a lesser degree (56%). These results were consistent with another recent retrospective study.\(^18\) As previously reported, urine sediment examination may be a helpful predictor of whether an aerobic bacterial urine culture will be positive. This information may aid in the decision to start empirical antimicrobial therapy while urine culture results are pending. However, a urine culture remains the gold standard in cats with AKI when APN is a differential diagnosis. Despite a lack of microscopic bacteriuria in some of the cats in this cohort, all met the criteria set for a clinical diagnosis of APN. It is possible that microscopic bacteriuria may have been missed by the individual evaluating the urine sediment. Bacterial counts from urine collected from the urinary bladder may be lower with feline pyelonephritis\(^18\) but all the E coli isolates from this study were \(\geq\) 10,000 CFUs/mL. The clinical signs in the 4 cats without microscopic bacteriuria were vomiting (n = 3), anorexia (3), lethargy (3), stranguria (3), and hematuria (2).

There were no specific ultrasound findings found in all cases in this study. A previous diagnosis of CKD and ultrasonographic findings of pyelectasia and ureteral dilation were relatively common in this study, but there was no association found between CKD and pyelectasia or ureteral dilation. There is considerable overlap in renal pelvic and ureteral dilation in stable CKD cats and cats with a clinical diagnosis of pyelonephritis;\(^2,27\) so it is difficult to draw conclusions regarding these parameters in this study. Although uncommon, some of the cats in this study had echogenic material in the renal pelvis or evidence of retroperitoneal disease, which could increase suspicion for APN.\(^25\) We excluded cats that were definitively diagnosed and treated for a ureteral obstruction.
These cats were diagnosed with a ureteral obstruction from ureterolithiasis and had a subcutaneous bypass device placed. Four of the cats in this study had renal pelvis dilation > 6 mm. We suspected this was due to pyonephrosis and elected not to exclude them, but it is difficult to definitively rule out that they had a ureteral obstruction from another etiology or to know whether the main cause of the azotemia was pyonephrosis that was nonresponsive to medical therapy. Three of these cats had echogenic material in the renal pelvis identified on ultrasound. One cat had a renal pelvis that measured 9.9 mm, which decreased to 3 mm 6 days later. The initial serum creatinine for this cat was 2.8 mg/dL, and approximately 1 month after discharge from the hospital, the serum creatinine for this cat was 2.3 mg/dL. Another cat with a renal pelvis of 6.6 mm had an initial creatinine of 2.1 mg/dL but was lost to follow-up. The third cat had a renal pelvis that measured 10 mm. The initial creatinine was 3.0 mg/dL, and at 1 month after discharge, the creatinine was 3.4 mg/dL. The cat without echogenic material in the renal pelvis measured 6.7 mm. The creatinine for this cat was initially 2.9 mg/dL and had decreased to 1 mg/dL approximately 1 month after discharge.

*E coli* was the most common bacteria cultured from urine of cats with a clinical diagnosis of APN in this study. This finding is similar with what is reported from the urine cultures of cats with lower urinary tract infections. It is also consistent with a recent report of cats with AKI, which is the only other manuscript to our knowledge that describes the pathogens found with feline upper urinary tract infections.

Empirical antimicrobial therapy was initiated in most cases in this study, and ampicillin-sulbactam was used most frequently. Susceptibility to amoxicillin-clavulanate is typically used to predict susceptibility to ampicillin-sulbactam. At the time of this study, all *E coli* isolates at KSUVHC were considered resistant to amoxicillin-clavulanate according to the Clinical and Laboratory Standards Institute feline MIC breakpoint of ≤ 0.25/0.12 μg/mL for both urine and skin or soft tissue isolates. As a consequence, all the urinary *E coli* isolates at KSUVHC were considered resistant to amoxicillin-clavulanate according to the plasma MIC breakpoint, and the 90th percentile of the MIC was 4 μg/mL. However, recently the Clinical and Laboratory Standards Institute has updated the urine-specific MIC breakpoint of amoxicillin-clavulanate to ≤ 8/4 μg/mL based on urine amoxicillin and clavulanate concentrations in nonazotemic cats using a dose of 12.5 mg/kg, PO, every 12 hours. The authors caution practitioners to interpret results using plasma MIC breakpoints since pyelonephritis is a tissue infection. If the microbiology laboratory is unaware that pyelonephritis is of concern, it is likely that urine-specific MIC breakpoints will be applied, and inappropriate antimicrobial selection may occur based on the laboratory interpretation. The low end of the test range was set at 2 μg/mL for ampicillin and amoxicillin-clavulanate for the microbiology laboratory at UWVC, precluding susceptibility interpretation. Standardization among microbiology laborato-
tories and further studies are needed to determine whether higher doses of amoxicillin-clavulanate or ampicillin-sulbactam could be alternative antimicrobial therapeutic options for feline APN. It is important to note that aminopenicillin pharmacokinetics are altered in dogs and cats with azotemia. It is unknown whether some of these differences could lead to treatment failure. Additionally, the change in metabolism of this medication can lead to an increase in frequency of drug side effects in cats.

Empirical antimicrobial therapy using a fluoroquinolone or third-generation cephalosporin when APN is suspected is recommended by the International Society of Companion Animal Infectious Diseases while awaiting urine culture and susceptibility results based on bacterial species prevalence in dogs. Although these would be appropriate choices for the regions in this study, restraint on their use as initial therapy for all cases of AKI while urine culture results are pending should be employed given the increase in resistance seen in small animal uropathogens. Enrofloxacin is the most commonly utilized injectable fluoroquinolone in cats, but acute diffuse retinal degeneration is a known dose-dependent adverse effect for this species. Recently, clearance of this drug has been shown to be similar among cats with normal and varying degrees of reduced renal function after a single dose. The effects of cumulative dosing in the azotemic feline population have yet to be determined. Consequently, the most appropriate dosing regimen for cats with APN that are treated in the hospital with multiple doses is not known. None of the cats of this study were reported to have developed retinotoxicity, but only 4 cats received enrofloxacin for a median of 3.5 days (range, 2 to 5 days). Pradofloxacin was preferentially prescribed at 1 institution (KSUVHC), likely due to evidence that cats may tolerate higher-than-recommended doses and its availability as an oral suspension. The IV route is recommended for sick veterinary patients with APN, but this strategy might not lead to better outcomes in people. Given the heterogeneity of treatments in this cohort, recommendations on fluoroquinolone route and type unfortunately cannot be made. Antimicrobial treatment duration was prolonged in this cohort, likely based on previous recommendations. Currently, shorter courses (10 to 14 days) are recommended based on human guidelines; however, studies evaluating the most appropriate duration of therapy in small animal patients are still needed.

The all-cause mortality rate by 3 months in this study was 30%. Survival for this etiology of AKI appears to be better than what is previously reported when all causes of AKI in cats are considered. This mortality rate is consistent with a meta-analysis of case series showing a higher survival rate in 22 cats with an infectious cause of AKI compared to cats with a noninfectious cause. The markers of glomerular filtration rate (creatinine, BUN, and phosphorus) at presentation were all higher in nonsurvivors compared with survivors, which may reflect the severity of renal injury. The initial IRIS AKI grade was not found to be predictive of survival in this study (P =
.054), but the small sample size may have weakened statistical analysis.

There are several limitations to this study. As a case series of cats with APN, findings and interpretations should be made in the context of a lack of a comparative group. Due to the retrospective nature of the study, case management was not standardized, and some data were missing from the medical record, including patients lost to follow-up, which likely precluded identification and assessment of important information. The diagnosis of APN was putative, as none of the cats had pyelocentesis performed; however, bacterial culture of urine obtained by pyelocentesis may not necessarily be superior to culture of urine obtained by cystocentesis. Alternatively, it is possible that cats with a lower urinary tract infection that had a different cause of AKI were included in this study. The population in this study was relatively small, so statistical comparisons may have been underpowered to detect differences. Many of the cats had 1 or more concurrent diseases, and it is difficult to determine whether the presenting clinical signs are from APN or another active disease process since they are nonspecific. However, these signs were reported by the clients to have developed acutely, so we believe that most of them are likely related to APN. Additionally, test range and antimicrobials included in the susceptibility panel were not consistent between the 2 microbiology laboratories as well as within each laboratory over time.

In conclusion, cats with suspected APN in the geographic regions included in this study have *E coli* as the predominant bacterial species cultured from urine, and a fluoroquinolone or third-generation cephalosporin would be reasonable empirical treatment options based on in vitro susceptibility data. Older female cats with underlying CKD compose the most common population given the clinical diagnosis of APN. Survival in our study cohort was better than what has previously been reported for all-cause mortality with feline AKI.

**Acknowledgments**

The authors would like to thank Desiree Rivera for assistance in initiating the review of our University of Wisconsin-Madison Veterinary Care feline urine culture data set to help in the identification of cats with acute pyelonephritis.

**Disclosures**

The authors have nothing to disclose. No AI-assisted technologies were used in the generation of this manuscript.

**Funding**

The authors have nothing to disclose.

**References**


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**Supplementary Materials**

Supplementary materials are posted online at the journal website: avmajournals.avma.org