Survival in Cats with Naturally Occurring Chronic Kidney Disease (2000–2002)

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Background: Duration of survival of cats with naturally occurring chronic kidney disease (CKD) is poorly characterized.

Hypothesis: Stage of kidney disease based on serum creatinine concentration (SCr) at the time of diagnosis and after correction of prerenal azotemia is strongly associated with duration of survival in cats.

Animals: Two hundred and eleven client-owned cats with naturally occurring CKD evaluated between April 2000 and January 2002.

Methods: Retrospective case review of 733 cats with SCr > 2.3 mg/dL. Examination of the medical records identified 211 cats that met all other inclusion and exclusion criteria for this study. Clinical characteristics, clinicopathologic data, and survival times were extracted from the medical record. Owners and referring veterinarians were contacted by phone to obtain follow-up if it was not documented in the record. Kaplan-Meier survival curves were performed to determine survival times for International Renal Interest Society (IRIS) stage both at diagnosis and at baseline (ie, after correction of prerenal azotemia).

Results: Median survival for cats in IRIS stage IIb at the time of diagnosis was 1,151 days (range 2–3,107), and was longer than survival in stage III (median 778, range 22–2,100) or stage IV (median 103, range 1–1,920) (*P*-value < .0001). *P*-value for effect of stage at diagnosis was < .0001.

Conclusions and Clinical Importance: IRIS stage of CKD based on serum creatinine at the time of diagnosis is strongly predictive of survival in cats with naturally occurring CKD.

Key words: Cats; Chronic kidney disease; Creatinine; IRIS staging system; Survival.

Chronic kidney disease (CKD) affects 1.6–20% of all cats at some point during their lifetime.[1,2] The prevalence of CKD increases with age and up to 31% of cats over 15 years old are affected.[3] Because of the unpredictable progression of CKD and the variable presentation of the disease, few studies have been performed evaluating long-term survival in these cats. One study out of 2 1st-opinion clinics in London divided cats into 3 categories to determine survival: compensated kidney disease (no clinical signs), uremic cats, and end-stage renal failure.[4] Survival data were presented for 60 cats. Cats in the compensated group (n = 15) had a mean survival of 397 days, although 9 of 15 compensated cats were still alive. The 9 cats that were still alive at the time of publication had a mean survival of 1,272 days and 2 further cats were lost to follow-up. Uremic cats (n = 39) had a mean survival of 313 days, with 3 living at the time of publication and 6 lost to follow-up. All cats determined to have end-stage renal failure (n = 26) died < 21 days after diagnosis, with a mean survival of 3 days. Twenty of these cases did not respond to IV fluid therapy and the remaining 6 owners refused treatment. In another study performed at a tertiary care facility, survival data were available for 52 cats.[5] Mean survival in these cats was 36 days, and ranged from 1 to 420 days. Sixty-seven percent of the cats in this study had a creatinine of ≥3.7 mg/dL, and 10 of these cats

had renal lymphosarcoma. A more recent study documented survival in cats with CKD using a modification of the International Renal Interest Society's (IRIS) classification system.[6,7] Cats were classified into stage I, stage IIa, stage IIb (n = 52), stage III (n = 27), and stage IV (n = 13) CKD based primarily on their serum creatinine concentration (SCr) at the time of diagnosis. Only 50 cats in IRIS stage IIb, stage III, or stage IV had survival data available, and the remaining cats were either still alive or lost to follow-up. However a significant correlation was found between SCr at diagnosis and survival time.

It is widely accepted that most cats diagnosed with stage II or greater CKD will progress to end-stage renal failure, regardless of the inciting cause.[7] However, one of the challenges of treating a cat with kidney disease is the unpredictability with which this progression occurs. Both in naturally occurring and experimentally induced kidney disease, cats have been reported to live with static disease for a variable length of time and then decompensate suddenly.[4,8–10] The primary purpose of this study is to determine the average survival time for a large number of cats from a facility that sees both 1st- and 2nd-opinion cases of CKD, and to determine if the IRIS stage at diagnosis and IRIS stage at baseline based on serum creatinine are associated with survival time.

A secondary goal of this study is to determine if any commonly measured hematologic and clinical variables are accurate predictors of survival time. Managing a cat with CKD requires a substantial emotional and financial commitment from owners. Accurate prognostic information will help veterinarians educate owners, allowing them to make decisions based on realistic expectations of the outcome of this disease process.

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Materials and Methods

Inclusion and Exclusion Criteria

The available records of cats with a SCr > 2.3 mg/dL on a serum chemistry panel performed at the Animal Medical Center between April 29, 2000 and January 22, 2002 were evaluated. Cats with a

SCr > 2.3 mg/dL and a urine specific gravity <1.035 were considered for inclusion in the study. If a urine specific gravity was not available at the time of diagnosis, the record was evaluated for clinical signs attributable to CKD (ie, persistent azotemia, chronic polyuria, and polydipsia, small kidneys on abdominal palpation). If 1 or more of these signs were present with a SCr > 2.3 mg/dL, cats were considered for inclusion in the study.

Cats with acute azotemia that resolved after IV fluid therapy were considered to have acute renal failure and were excluded from the study. Cats with postrenal causes of azotemia were excluded; however, cats with azotemia persisting after resolution of the post-renal disorder were included. Although extensive evaluation was not performed on all cats, cats known to have hyperthyroidism, diabetes mellitus, or diseases known to affect renal function were excluded, as were cats with previously documented congestive heart failure or with evidence of malignancy at the time of diagnosis of CKD. Cats with any extra-renal disease causing an expected survival time of <3 months were excluded. Cats were required to have a minimum of physical examination and serum chemistry panel performed. Whenever possible, a CBC, serum thyroxine concentration, and urinalysis were also evaluated. Results of further testing such as radiography, ultrasonography, echocardiography, and infectious disease monitoring were evaluated if they were available.

Data Collection

For each cat, the date of diagnosis of CKD was identified from the medical record and was determined to be the 1st date that the SCr was consistently >2.3 mg/dL, with the previously mentioned additional criteria. A SCr >2.3 mg/dL that returned to normal without fluid therapy was not considered a diagnosis of CKD. If the diagnosis was made during a uremic crisis requiring hospitalization, the 1st recheck data performed as an outpatient (preferred), or the last data set before discharge were recorded and considered to be the baseline SCr. This was done to eliminate the effects of dehydration on SCr. If a cat was administered fluids SC at the time of diagnosis and the subsequent serum creatinine values decreased, the baseline creatinine was considered the 1st recorded creatinine after initiation of fluid therapy. If a cat was not admitted to the hospital for fluid therapy at the time of 1st diagnosis, the stage and SCr at diagnosis were also considered the stage and SCr at the time of baseline (ie, the "baseline" creatinine). If an animal died or was euthanized in the hospital, the cat was not considered to have reached baseline and was not included in the survival calculations from baseline. If the chemistry panel that was performed during the study period was not the 1st chemistry panel available, the date of diagnosis was considered the 1st date that azotemia was documented.

For each cat, the date of birth, breed, and sex were recorded. The number of cats in each breed was calculated and compared with the hospital population of cats from April 29, 2000 to January 22, 2002. The mean age of the current study population was calculated and compared with the hospital population of the same time period. In addition, the number of cats in each stage that were hospitalized was calculated, as well as the mean and median number of days of hospitalization. The number and percentage of animals that were euthanized was calculated and reported as well.

Clinicopathologic data were recorded for each cat at the time of diagnosis, including concentrations of blood urea nitrogen (BUN), serum creatinine, phosphorus, potassium, calcium, albumin, and bicarbonate, and hematocrit or PCV if available. The baseline body weight (defined as the last recorded body weight before the diagnosis of CKD, the weight at diagnosis, or the greatest consistent body weight after diagnosis) was recorded; with the greatest consistent measure being recorded when more than 1 option was available in the medical record. The 1st date at which the weight was consistently decreased from the baseline weight was recorded, in addition to the date that the body weight had decreased by at least 25% below the baseline weight. Consistent weight loss was considered the date at which the cat's weight was less than the baseline weight and continued to decrease at available subsequent visits. The 1st date the hematocrit or PCV was below 25% without evidence of blood loss was recorded. Also recorded was the 1st date of administration of blood products (whole blood, packed red blood cell, or oxyglobin transfusion) if the cause of the anemia was not suspected to be blood loss, as well as the date of initiation of erythropoietin therapy. The date of clinical decompensation was determined for each cat if possible using criteria described below. The date of initiation of regular SC fluid therapy (2 times per week or greater) was recorded.

Cats were followed to death or until lost to follow-up (no cats were known to be alive at the end of the follow-up period [November 2007]). The date of death was recorded for each cat. The reason for death or euthanasia was classified as renal (eg, uremia, anemia of CKD, hypertension), probably renal, possibly renal, and not renal (eg, neoplasia, infectious disease, congestive heart failure). Death was considered probably renal if cats died or were euthanized because of clinical signs that were likely caused by uremia such as anorexia, emaciation, and/or vomiting with no recorded evidence of nonrenal disease. Possibly renal was used to categorize death if clinical signs were unknown, not consistent with uremia, or if another disease process was suspected. Cats whose reason for death was unclear were placed in the category of "possibly renal." For Kaplan-Meier survival analysis, definitely renal and probably renal were combined into 1 category known as renal, and possibly renal and nonrenal were combined into 1 category called nonrenal. Cats that died of nonrenal disease were censored at the time of death. Cats that developed another disease after enrollment (eg, neoplasia, diabetes mellitus) were followed to death and included in all analyses. In cases that did not have a recorded date of death, the referring veterinarian, owner, or both were contacted to try to determine an exact or approximate date of death. If an owner was able to provide only the month of death, the date of death was recorded as the 1st day of that month. If a date of death could not be obtained, cats were excluded from analysis.

Staging of CKD

The staging system for classifying cats with CKD proposed by the IRIS was used with slight modifications, to categorize cats according to their stage of CKD at the time of diagnosis or baseline.[6] In the IRIS classification scheme, cats in stage I have renal insufficiency but not renal failure and are not included in this study. IRIS stage II encompasses cats with creatinine concentrations between 1.6 and 2.8 mg/dL. Because a creatinine concentration above 2.3 (the upper limit of the reference range for the laboratory used by the Animal Medical Center) was required for inclusion into this study, a modification was incorporated into the staging system. Cats were divided into the following groups based on their baseline SCr: stage IIb = SCr > 2.3–2.8 mg/dL; stage III = SCr 2.9–5.0 mg/dL; stage IV = SCr > 5.0 mg/dL.

The IRIS substages of blood pressure and proteinuria were not included in our staging system. Because of the retrospective nature of this study, these 2 variables were inconsistently available for the cats evaluated.

Statistical Methods

Survival data were calculated separately by Kaplan-Meier survival curves for each group of staged cats to determine if the stage of kidney disease at the time of diagnosis was predictive of life expectancy. Survival was calculated from the following dates: diagnosis and baseline (further subcategorized according to stage of disease: stage IIb, stage III, or stage IV), SCr > 4.0 mg/dL, SCr > 5.0 mg/dL, initial weight loss, ≥ 25% weight loss from baseline, anemia (hematocrit or PCV < 25%), intervention for anemia (transfusion or erythropoietin administration), clinical decompensation, and ini-

tiation of SC fluid therapy. A log-rank test was used to compare survival from the points of diagnosis versus baseline for each IRIS stage separately (ie, stage IIb was compared with stage III, stage IIb was compared with stage IV, and stage III was compared with stage IV), to determine if survival times were significantly different between stages. All survival data are reported as median with 95% confidence interval in brackets unless otherwise specified, because of the nonparametric nature of the data. Hazard ratios (HRs) were calculated using a Cox proportional hazard model (multivariate model), to determine whether the individual clinicopathologic variables were predictive of survival, and are presented with the 95% confidence interval. No prior screening of the individual clinicopathologic variables was conducted. Collinearity of clinicopathologic variables was assessed if potentially correlated variables produced statistically significant HR. Clinicopathologic variables were evaluated from the time of diagnosis rather than baseline, to determine whether or not hospitalization would likely be beneficial for these cats. The program used for all statistical analysis was SAS version 9.[a]

Clinical decompensation was considered to be the point at which renal transplantation would have been recommended. This point of decompensation was determined even if conditions that might preclude transplantation were present such as owner unwillingness, fractious demeanor, pyelonephritis, or concurrent neoplasia. This point of clinical decompensation was retrospectively determined by global assessment by 1 of 2 clinicians (LMB or CL), taking into account a combination of SCr level, presence or absence of appetite, nutritional status, presence of anemia, and signs of uremia.

Results

Of the 9,446 serum chemistry panels performed between April 29, 2000 and January 22, 2002, 733 records were available from cats that had a serum creatinine > 2.3 mg/dL. The remainder of cats either had a serum creatinine ≤ 2.3 mg/dL or their records could not be located. Cats were excluded for having prerenal azotemia (81 cats), postrenal azotemia (34 cats), acute renal failure (35 cats), or another undetermined cause of azotemia that was not consistent with CKD (61 cats). An additional 311 cats were excluded for other reasons including an incomplete record, significant extra-renal disease, or a lack of follow-up (ie, the date of death could not be ascertained). Two hundred and eleven cats were identified for inclusion into the study.

Of the 211 cats, the most common breed was domestic shorthair (68%). Other breeds included Siamese (10%), Persian (6.6%), Abyssinian (4%), and Himalayan (3%). Other breeds that were represented by <2% included American Short Hair, Birman, Burmese, domestic longhair, exotic shorthair, Korat, Maine Coon, Manx, Russian Blue, Scottish Fold, and Tonkinese. Siamese, Persian, and Abyssinian breeds were overrepresented compared with the hospital population. In the hospital population during the same time period, Siamese represented 3.6%, Persians represented 3%, and Abyssinians represented 1.5% of the total number of cats seen (n = 13,012 cats). In the present study, there were 101 spayed female, 2 intact female, 101 castrated male, and 2 intact male cats. Reproductive status was not recorded in 1 female and 4 male cats. The mean age for all cats at the time of diagnosis was 12.8 (SD 4.4) years. Mean age for

Table 1. Survival of cats based on stage of CKD at the time of diagnosis.

Stage at Diagnosis	Number of Cats	Percentage of Cats	Survival Median (95% CI)
IIb	78	37	1,151[a] (1,014, 1,565)
III	69	33	778[b] (445, 910)
IV	64	30	103[c] (37, 216)

Survival times with different superscript letters are significantly different, P < .001 by log-rank test.

CKD, chronic kidney disease.

all the cats seen in the hospital population during the same time period was 8.8 years.

At the time of diagnosis, 37% of cats (n = 78) were identified as having stage IIb kidney disease, 33% of cats (n = 69) had stage III kidney disease, and 30% of cats (n = 64) had stage IV kidney disease (Table 1). Median survival for cats in stage IV at diagnosis was 103 (37, 216) days, versus median survival for cats in stage IV at baseline, which was only 35 (21, 99) days. Thirty percent (19/64) of cats in stage IV at the time of diagnosis were actually categorized in a lower stage after the prerenal component of their azotemia was corrected with fluid therapy. Survival data for cats based on stage at baseline is presented in Table 2. P-value for effect of stage on survival was < .0001. Thirty-nine cats were hospitalized at the time of diagnosis. One cat in stage IIb CKD, 8 cats in stage III CKD, and 30 cats in stage IV CKD were hospitalized. The median number of days of hospitalization for cats in all stages was 5 days (range 3–12), and the mean number of days was 5.9 (SD 1.97). Median overall survival time of all cats in the study from the time of diagnosis was 771 (651, 910) days. A Kaplan-Meier survival curve based on stage at diagnosis is presented in Figure 1. A Kaplan-Meier survival curve based on stage at baseline is presented in Figure 2. Seventy-five percent of all cats were euthanized (n = 158) and 25% of these cats died of natural causes (n = 53).

One hundred and twenty-one cats developed anemia before death (Table 3). Median survival from the point of anemia development to death was 100 (65, 186) days. Out of the remaining 90 cats, 44 did not develop anemia before death, and 46 did not have a PCV or hematocrit recorded within the 3 months before death. Forty-two cats underwent intervention for their anemia. The median survival time for these cats from the point of intervention was 25 (6, 74) days.

Table 2. Survival (in days) of cats based on stage of CKD determined after correction of prerenal azotemia.

Stage at Baseline	Number of Cats	Percentage of Cats	Survival Median (95% CI)
IIb	82	39.4	1,151[a] (1,014, 1,565)
III	84	40.3	679[b] (445, 910)
IV	42	20.2	35[c] (21, 99)

Survival times with different superscript letters are significantly different, P < .001 by log-rank test.
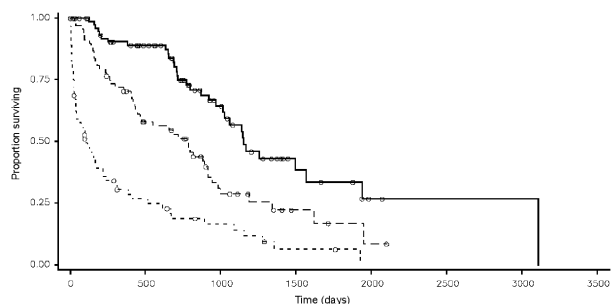
CKD, chronic kidney disease.

Fig 1. Kaplan-Meier survival curve of cats with CKD, based on stage at diagnosis (open circles denote censored observations). Stage IIb (n=78) is represented by a solid black line, stage III (n=69) is a hatched line, and stage IV (n=64) is a dotted line.

Sustained weight loss was present in 142 cats before death, with a median survival time of 401 (233, 601) days from the point weight loss 1st occurred. Twenty-two cats did not have sustained weight loss before death, and for 47 of the cats, it is unknown whether or not weight loss was present. The use of enteral feeding tubes was not recorded, but they were infrequently used during the study period. Eighty-one cats lost > 25% of their baseline body weight with a median survival time of 83 (56, 194) days from the point that 25% weight loss was documented. Seventy-two cats did not lose 25% of their body weight before death, and it is unknown whether the remaining 58 cats lost > 25% of their body weight before death.

Median survival from the point of SC fluid administration (n = 142 cats) was 273 (175, 424) days. Forty-three cats were not receiving SC fluids and it is unknown whether the remaining 26 cats received SC fluids before death.

One hundred and forty-five cats had a documented SCr value > 4.0 mg/dL before death. Median survival of these cats from the point that their SCr became > 4.0 mg/dL was 123 (81, 193) days. For 35 cats, this information was not available, and the remaining 31 cats had a SCr < 4.0 mg/dL at the time of death. Ninety-eight cats had a documented SCr > 5.0 mg/dL before death. Median survival in these cats was 44 (32, 97) days.

One hundred and thirty-five cats were determined to have reached the point of clinical decompensation as defined above before their death, with a median survival of 40 (31, 64) days from decompensation to death. Whether
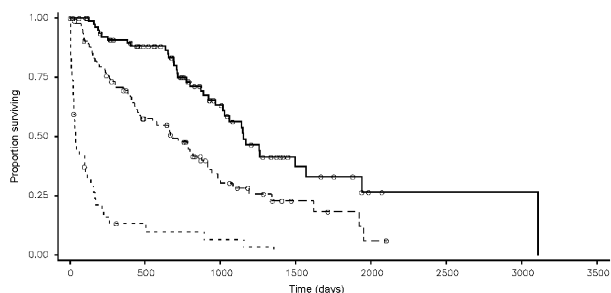

Fig 2. Kaplan-Meier survival curve of cats with CKD, based on stage at baseline (open circles denote censored observations). Stage IIb (n=82) is represented by a solid black line, stage III (n=84) is a hatched line, and stage IV (n=42) is a dotted line.

Table 3. Survival time from onset of criteria.

Criteria	Number of Cats	Survival Median (95% CI)
Diagnosis	211	771 (651, 910)
Weight loss	142	401 (233, 601)
Start of SC fluids	142	273 (175, 424)
Creatinine > 4.0 mg/dL	145	123 (81, 193)
Anemia (PCV < 25%)	121	100 (65, 186)
>25% weight loss	81	83 (56, 194)
Creatinine > 5.0 mg/dL	98	44 (32, 97)
Clinical decompensation	135	40 (31, 64)
Anemia intervention	42	25 (6, 74)

Survival was calculated from the time of diagnosis of CKD, the point of consistent weight loss, the initiation of SC fluids (whether before or following any hospital admission), the 1st time that the creatinine was consistently > 4.0 mg/dL, the time that anemia was 1st present, the time that > 25% of the initial weight was lost, the 1st time that creatinine was consistently > 5.0 mg/dL, the point of clinical decompensation, and the time of intervention for anemia.

CKD, chronic kidney disease.

decompensation was reached is unknown in 54 cats, and the remaining 22 cats did not reach a point of clinical decompensation before their death.

Each clinicopathologic variable was evaluated at the time of diagnosis to determine if it was predictive of survival (Table 4). Age at diagnosis, albumin, BUN, creatinine, calcium, bicarbonate, potassium, and hematocrit were not found to be predictive of survival in the multivariate model. The only clinicopathologic variable that was predictive of survival was serum phosphorus (P = .0043). The HR was 1.179 (1.053, 1.320). For each 1 U increase in the blood level of phosphorus, there is an 11.8% increase in the risk of death.

Discussion

The results of this study indicate that IRIS stage of kidney disease, based on SCr at the time of diagnosis and baseline, is strongly associated with survival in cats. This is in contrast to a study of 80 cats in 1998 that found the

Table 4. Hazard ratios were calculated using Cox proportional hazard model (multivariate model).

Variable	P-Value	Hazard Ratio (95% CI)
Age at diagnosis	.5794	1.016 (0.960, 1.075)
Albumin	.9926	0.996 (0.472, 2.102)
BUN	.2074	1.005 (0.997, 1.013)
Creatinine	.7131	0.980 (0.883, 1.089)
Calcium	.5329	0.922 (0.715, 1.189)
Phosphorus	**.0043**	**1.179 (1.053, 1.320)**
Bicarbonate	.1967	0.955 (0.891, 1.024)
Potassium	.8337	1.039 (0.725, 1.490)
PCV	.4103	0.981 (0.939, 1.026)

The only clinicopathologic variable that is associated with survival is serum phosphorus concentration (P = .0043).

BUN, blood urea nitrogen. Results in bold were found to be statistically significant.

SCr concentration at the time of diagnosis to be a poor predictor of survival time in uremic cats.[4] However, a more recent study comparing cats that survived versus cats that did not survive for >1 month from diagnosis found that cats with a higher creatinine at diagnosis were more likely to die of kidney disease within the 1st month.[11] SCr was also significantly associated with survival in a prospective study that found an increased SCr to be associated with a shorter survival time.[12] In the current study, duration of survival based on stage at diagnosis was not dramatically different from duration of survival based on stage at baseline for stage IIb or stage III. However, in cats classified with stage IV CKD at the time of diagnosis, median survival time was 103 days, whereas cats categorized in stage IV CKD at the time of baseline had a median survival time of only 35 days. It is likely that the prerenal component of azotemia in several of the cats caused them to be initially categorized in a more advanced stage. The prerenal component of azotemia is rapidly reversible with fluid therapy. The survival times of cats categorized as stage IV after diuresis (ie, at baseline) more closely parallel the survival times of previously reported cats in stage IV.[7]

The median survival time of 2.1 years (771 days) from the time of diagnosis for all cats analyzed, regardless of stage, is similar to previous reports in the literature.[7,13,14] The data indicate that cats that were diagnosed early in the disease (ie, stage IIb) can live up to 8.5 years from baseline, with a median of 3.15 (1,151 days) years. The median life expectancy for cats diagnosed in stage III kidney disease at baseline was 1.86 years (679 days), with some surviving up to 5.75 years. Cats determined to be in stage IV kidney disease at baseline had the worst prognosis, with a median survival of only 1.16 months (35 days). These results are also similar to the recent study evaluating survival of 50 cats with CKD based on IRIS stage at diagnosis.[7] In the previous study, survival times of cats in stage IIb kidney disease were reported as 1.4 years (504 days) in normotensive cats, but only 187 days in stage IIb cats with hypertension. Stage III cats had a reported survival time of 154 days (normotensive cats) and 281 days (hypertensive cats). Cats in stage IV were found to have a survival time of 57 days (normotensive cats) and 21 days (hypertensive cats). Although the results are similar, a direct comparison is difficult because of the fact that blood pressure was not routinely analyzed in cats in the present study. In the present study, the median survival of cats in stage IIb was 1,151 days regardless of whether they were staged at diagnosis or baseline, whereas cats in stage III at diagnosis lived a median of 778 days versus cats in stage III at baseline that lived a median of 679 days. Median survival was significantly different between stages from both diagnosis and baseline (P-value < .001).

Secondary objectives of this study included determining the median survival time of these cats from certain clinical benchmarks, and determining if there is 1 parameter that can consistently predict at what point an animal will die from its kidney disease. This information would be valuable to determine the ideal time to perform renal transplantation. Different institutions use varied subjec-tive and objective parameters to determine when to initiate the pretransplant evaluation, which may take 2–4 weeks to complete. Anemia, weight loss, and progressive azotemia in the face of medical management have all been suggested as potential indications for the ideal time to recommend a renal transplant.[15–19] One study found that weight loss was the most reliable indicator of clinical deterioration in cats with CKD.[9] Of the 135 cats in our study that reached clinical decompensation, median survival time was 40 days from the time of clinical decompensation. However, one of the limitations of this study was that the point of clinical decompensation was decided in a retrospective manner. Evaluation of cats at predetermined intervals may allow a more accurate determination of clinical decompensation.

Recommending transplantation when a cat has exceeded a baseline creatinine of 4.0 mg/dL has also been suggested.[18,19] Median survival time in this study was 123 days once the creatinine exceeded 4.0 mg/dL. In another study, cats that developed a SCr > 4.5 mg/dL died within 5–63 days, and typically presented 3 weeks after the increase in creatinine with dehydration and complete anorexia.[9] In our study, the median survival time from the point a cat reached stage IV (SCr > 5.0 mg/dL) was 44 days. The present study was not designed to identify a definitive marker to determine the best point for a renal transplant. The decision must still be based on a multitude of factors, but it is the authors' opinion that a conversation with owners about transplantation should be undertaken proactively when the cat is in stage III kidney disease rather than waiting until the cat reaches stage IV disease or clinical decompensation.

In the multivariate analysis, age, albumin, BUN, creatinine, calcium, bicarbonate, potassium, and hematocrit were not found to be predictive of an increased risk of death. A low albumin concentration has previously been identified as a negative prognostic indicator in acute renal failure in cats, and in CKD in people.[20,21] Hypoalbuminemia is likely multifactorial and may be a marker for inflammation and malnutrition, rather than being a causal factor. Because we only analyzed the albumin at the time of diagnosis in these cats, we do not know if their albumin decreased as the disease progressed. It is also possible that because we analyzed the albumin at the time of diagnosis, some cats had a falsely elevated albumin level because of dehydration. In future studies, it may be valuable to follow the albumin throughout the course of disease to determine if albumin is predictive of survival in cats with CKD. In the present study, phosphorus was the only clinicopathologic parameter that was associated with an increased risk of death. Similar to our results, a study of 50 cats in Japan also found that higher phosphorus was associated with a higher risk of death within 1 month. However, in contrast to the present study they found that a higher SCr, BUN, and a lower PCV were associated with an increased risk of death. They also found that potassium and bicarbonate were not predictive of an increased risk of death, and albumin and calcium were not evaluated.[11] In previous studies, hematocrit was found to be negatively correlated to SCr,[22] but hematocrit was not significant in the multivariate

analysis in the present study (eg, anemia was not a significant predictor of an increased risk of death). A potential explanation for these findings is that a lower hematocrit is a marker of more severe kidney disease rather than a cause of shortened survival. Our results differ from a study of 39 cats symptomatic for CKD, in which anemic cats had shorter survival times compared with the group as a whole.[4] However, 30% of the anemic cats in the present study received some therapy specific for anemia which may have affected outcome. Again, because of the decision to evaluate these variables from diagnosis, the hematocrit may have been falsely elevated in cats that were dehydrated at the time of diagnosis. Hematocrit was also found to be associated with shorter survival times in another study of survival in cats with CKD.[12] That study also found that increased SCr, phosphate, and urea concentrations were associated with shorter survival times, of which only the increases in phosphorus are supported by the findings of the current study. Although the findings of this study differ from several recent studies, because of the fact that each variable was only calculated from the time of diagnosis, the clinical use of these parameters as predictors of prognosis is still unknown. Based on the results of the current study, an increased phosphorus concentration at the time of diagnosis is a significant predictor of an increased risk of death. Although IRIS stage alone is predictive of survival, actual SCr values, when considered in a model including additional clinicopathologic variables, is not a significant predictor of survival.

Survival was calculated from the point of intervention for anemia and the administration of SC fluids. It is difficult to make solid conclusions for either of these parameters. Only 42 of the 121 anemic cats underwent intervention for anemia and many factors were likely involved in this decision, including owner finances and the experience or comfort level of the primary care veterinarians. Similarly, the decision to put a cat on SC fluids was not standardized, with some cats receiving fluid therapy beginning shortly after diagnosis regardless of hydration status and presence of uremic symptoms. Other cats did not receive fluid therapy until uremic symptoms were severe. It is possible that if all cats were started at a predetermined point in the course of their disease (ie, inability to maintain clinical hydration) this parameter would prove to be more prognostic of survival.

Clinically relevant kidney disease can be detected in the absence of azotemia. For example, proteinuria is a predictor of progressive renal damage.[7,12] Although commonly used, SCr is not a precise indicator of glomerular filtration rate, and in early kidney disease, small changes in creatinine may represent large changes in GFR.[23] Although recognition of early stages of CKD is important to allow early institution of measures to slow progression (eg, dietary therapy), we chose to limit this study to cats with a SCr exceeding the reference range, a commonly used criteria for diagnosing CKD. Because of the retrospective nature of this report, GFR measurement, urine protein concentration, and renal imaging studies were not routinely available, and we did not attempt to include cats with CKD before the onset of azotemia.

There are several limitations of this retrospective study. Therapy for these cats was not standardized and was at the discretion of the attending clinician. However, the results are representative of community practice, where treatment for kidney disease is not standardized among primary veterinarians, or even specialists. The decision of when to begin certain therapies and interventions is one that is made using a combination of factors based on the patient, owner and veterinarian. The IRIS staging system takes into account the presence of proteinuria and hypertension. While treated hypertension has not been shown to affect survival in cats, proteinuria has been shown to affect survival.[7,11,12] Cats with a urine protein/creatinine ratio (UPC) over 0.4 have a 4 times higher risk of death compared with cats with a UPC < 0.2.[7] In another study, an increased UPC was the most likely variable to be associated with increased mortality in cats with CKD.[11] Unfortunately, because of the retrospective nature of this study, the presence or absence of hypertension and proteinuria was not consistently evaluated. For this reason, we chose to not include either in the analysis.

Euthanasia is almost always a confounding factor in veterinary studies. Different owners have different perceptions of quality of life, based on their life experiences and their culture. Other reasons may contribute to the decision to euthanize, possibly unrelated to quality of life of the animal. Some of the cats in this study were undoubtedly euthanized prematurely, either for financial reasons or because of the intense time commitment that may have been required by the owner. It is possible that some of these cats would have survived longer or recovered from a uremic episode if they had not been euthanized prematurely for nonmedical reasons. In the present study, 75% of cats were euthanized. Survival times would have likely been longer if all cats had been allowed to die of natural causes. An additional limitation of this study is that cats were excluded from the study if follow-up was not available. We do not feel that this biased the results, as live cats were followed to the point of death and included in all survival analyses. However, more cats could potentially have been included in the analysis if lack of follow-up was not used as an exclusion criterion.

The present study supports that SCr concentration at the time of baseline is strongly predictive of survival in cats with naturally occurring CKD. This study also showed that for each 1 U increase in the phosphorus level at the time of diagnosis, there is an 11.8% increase in the risk of death. Potassium, calcium hematocrit, bicarbonate, albumin, BUN, and SCr were not significant predictors of death. Survival analysis of results from both diagnosis and baseline suggests that many cats have a prerenal component to their azotemia at the time of 1st diagnosis that is rapidly reversible with fluid therapy. We speculate that staging cats at the time of baseline, rather than diagnosis allows us to eliminate the prerenal component and may more closely represent the correct stage of disease and the prognosis for survival.

Footnote

Acknowledgment

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