# Long-term outcome of cats and dogs with acute kidney injury treated with intermittent hemodialysis: 135 cases (1997–2010)

Adam E. Eatroff, DVM, DACVIM; Cathy E. Langston, DVM, DACVIM;
Serge Chalhoub, DVM, DACVIM; Karen Poeppel; Eleonora Mitelberg

**Objective**—To determine the long-term outcome for small animal patients with acute kidney injury (AKI) treated with intermittent hemodialysis (IHD).

**Design**—Retrospective case series.

**Animals**—42 cats and 93 dogs treated with IHD for AKI.

**Procedures**—Medical records of cats and dogs treated with IHD for AKI from January 1997 to October 2010 were reviewed. Standard methods of survival analysis with Kaplan-Meier product limit curves were used. The log-rank, Mann-Whitney, and Kruskal-Wallis tests were used to determine whether outcome, number of IHD treatments, or duration of hospitalization was different when dogs and cats were classified according to specific variables.

**Results**—The overall survival rate at the time of hospital discharge was 50% (21/42) for cats and 53% (49/93) for dogs. The overall survival rate 30 days after hospital discharge was 48% (20/42) for cats and 42% (39/93) for dogs. The overall survival rate 365 days after hospital discharge was 38% (16/42) for cats and 33% (31/93) for dogs. For all-cause mortality, the median survival time was 7 days (95% confidence interval, 0 to 835 days) for cats and 9 days (95% confidence interval, 0 to 55 days) for dogs.

**Conclusions and Clinical Relevance**—Cats and dogs with AKI treated with IHD have survival rates similar to those of human patients. Although there was a high mortality rate prior to hospital discharge, those patients that survived to discharge had a high probability of long-term survival. (*J Am Vet Med Assoc* 2012;241:1471–1478)

In veterinary medicine, renal replacement therapies have been used to improve the quality of life and extend the survival of patients with both AKI and CKD. Renal replacement therapies include extracorporeal techniques (hemodialysis and hemofiltration) as well as intracorporeal techniques (peritoneal dialysis and renal transplantation). In clinical veterinary medicine, extracorporeal renal replacement therapies have begun to play an increasingly important role in the treatment of AKI, as evidenced by the growing number of case reports, case series, and review articles describing use of IHD and continuous renal replacement therapy in small animals.[1–21] The use of peritoneal dialysis for the control of uremic complications accompanying AKI has also been well documented in the veterinary literature, but these reports[22–28] describe notable adverse effects. Kidney transplantation has also been shown to have a variable success rate and a high incidence of prominent adverse effects.[29–31] Furthermore, renal transplantation may not be necessary in cats and dogs that are able to recover from AKI. Extracorporeal renal replacement therapies have thus emerged as an alternative to peritoneal dialysis and renal transplantation in veterinary medicine. Intermittent hemodialysis is a form of extracorporeal renal replacement therapy that uses the principle of diffusion to remove uremic toxins from the blood through a semipermeable membrane. Diffusion is also used in IHD to normalize the electrolyte and acid-base composition of uremic blood. In veterinary medicine, IHD is indicated to treat the uremic complications of AKI associated with ureteral obstructions, infectious diseases, ingestion of nephrotoxicants, and other miscellaneous renal insults. In the context of these clinical scenarios, IHD has been used to prevent clinical deterioration prior to renal recovery, as the renal insult is addressed and measures are taken to optimize the probability of a return to adequate renal function. Whereas IHD is effective for reducing potentially fatal uremic complications associated with AKI and allowing time for renal recovery, the cost of such treatment may be

**Abbreviations**

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| AKI | Acute kidney injury |
| CI | Confidence interval |
| CKD | Chronic kidney disease |
| IHD | Intermittent hemodialysis |
| IQR | Interquartile range |
| IRIS | International Renal Interest Society |

From the Bobst Hospital, The Animal Medical Center, 510 E 62nd St, New York, NY 10065 (Eatroff, Langston, Poeppel); the Department of Veterinary Clinical and Diagnostic Sciences, Faculty of Veterinary Medicine, University of Calgary, Calgary, AB, T2N 426, Canada (Chalhoub); and the Coral Springs Animal Hospital, 2160 University Dr, Coral Springs, FL 33071 (Mitelberg).

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Address correspondence to Dr. Eatroff (adam.eatroff@amcny.org).

prohibitive for many owners. Therefore, both pet owners and veterinarians may benefit from knowledge regarding the long-term outcome for dogs and cats with AKI that are treated with IHD, as well as from knowledge of factors that may be associated with a better or a worse prognosis or a higher cost of treatment.

Recently, a clinical scoring system was developed to predict the likelihood of survival for 30 days or longer after hospital discharge for dogs with AKI that were treated with IHD. This study[32] reported that approximately 47% (86/182) of dogs survived and were independent of IHD for at least 30 days after hospital discharge. Another study[4] evaluating outcome in cats undergoing IHD for treatment of various types of kidney dysfunction reported a survival rate of 9 of 15 patients for those with AKI and no obvious preexisting CKD. Of the 9 surviving cats, all were alive at the time of last contact, which was a mean ± SD of 12 ± 9 months after hospital discharge.[4] Aside from these reports, we are unaware of any studies evaluating the long-term survival and outcome of cats and dogs with AKI treated with IHD.

The primary purpose of the study reported here was to determine the long-term outcome, defined as a survival time of 365 days or longer, of cats and dogs treated with IHD for AKI. As a secondary objective, we sought to examine whether any variables that influenced survival time could be identified.

## Materials and Methods

**Case selection**—Medical records of cats and dogs that were treated with IHD at the Bobst Hospital of the Animal Medical Center between January 1997 and October 2010 were considered eligible for inclusion and reviewed by one of the authors (AEE). Cases with a diagnosis of AKI were included. Cases were excluded if stage II or higher CKD, as defined by the IRIS staging system (**Appendix**),[33] was documented in the medical records prior to evaluation for AKI. Cases were also excluded if a diagnosis of CKD was made on the basis of clinical signs associated with uremia present for longer than 4 weeks prior to initial evaluation or if a clinical diagnosis of end stage renal disease was made prior to or during the course of treatment with IHD. Additional exclusion criteria included treatment with IHD as a blood purification treatment for an acute intoxication, the absence of a complete medical record, the use of continuous renal replacement therapy in addition to IHD, a concurrent diagnosis of neoplasia, and renal transplantation immediately following IHD. For patients that had more than 1 episode of AKI treated with IHD, only the first episode was evaluated in this study.

**Medical records review and follow-up**—Data retrieved from the medical records of cats and dogs in this study included date of admission to the hospital, signalment, weight, etiology of AKI (if known), number of IHD treatments administered, any additional treatments administered that directly addressed the causes of AKI, duration of hospitalization, survival time from hospital discharge, discharge status from hospital (alive or dead), cause of death (renal vs nonrenal), and whether death was the result of euthanasia. Additional data collected from cats and dogs surviving 365 days or longer included the lowest serum or plasma creatinine concentration between 30 and 90 days after the last IHD treatment. Etiologies for AKI were divided into the following categories: infectious, miscellaneous, obstructive, toxic, and unknown. When the exact date of death was not available, the first day of the month of death was used. For long-term survivors, when data pertaining to serum or plasma creatinine concentrations and outcome (survival time and cause of death) were not available in the hospital medical record, this information was obtained by a combination of requests for medical records from referring veterinarians and telephone questionnaires administered to owners. During telephone questionnaires, owners were asked to provide the following information: the status of the patient (alive or deceased) and the date and cause of death, if the patient was deceased. On the basis of the medical records of the Bobst Hospital, medical records provided by the referring veterinarians, and telephone questionnaires administered to the owners, the cause of death was classified as definitely not, possibly, probably, or definitely renal related. Cats and dogs classified in the first or second category were considered to have died from a nonrenal event. Cats and dogs classified in the third or fourth category were considered to have died from a renal-related event. For those patients for which no information regarding category of death was available, the cause of death was assumed to be renal related.

**Statistical analysis**—Separate analyses were performed for the 42 cats and 93 dogs. Descriptive statistics with frequency (%) for categorical variables and median values with IQRs and complete ranges for continuous variables were used to summarize the data. The survival rate was calculated at the time of hospital discharge, at 30 days following hospital discharge, and at 365 days following hospital discharge. Overall survival time (time until death from any cause) and renal-related survival time (time until death from renal-related causes only) for cats and dogs were determined by computing Kaplan-Meier product limit curves, and median survival times were reported with their corresponding 95% CI.[34] Greenwood's[35] formula was used to calculate the SE. In cases in which death had not yet occurred, the case was considered censored at the number of days from hospital discharge to the last follow-up. The comparison of different groups of cats and dogs (ie, sex, etiology, weight, age, number of treatments, serum or plasma creatinine concentration 30 to 90 days after the last IHD treatment, and duration of hospitalization) and survival time was accomplished with the same standard methods of survival analysis as described above, where group was the stratification variable. Cats and dogs were classified on the basis of their respective serum or plasma creatinine concentrations by means of criteria matching those used by the IRIS staging system. All other variables were categorized by quartiles. These groups were compared with the log-rank test. To determine whether there was a difference in the number of treatments or hospitalization time among different etiologies of AKI (obstructive vs nonobstructive for cats and infectious vs toxic vs unknown vs miscellaneous for dogs), the Mann-Whitney test was used for cats and the Kruskal-Wallis test was used for dogs. A result was considered significant at a

value of $P < 0.05$. All statistical analyses were performed with a commercial software program.[a]

## Results

Two hundred thirteen cases were eligible for inclusion. Seventy-eight cases were excluded because of the following reasons: a diagnosis of CKD (23 cats and 30 dogs), the use of IHD as a blood purification therapy for an acute intoxication (1 cat and 8 dogs), the absence of a complete medical record (2 cats and 7 dogs), the use of continuous renal replacement therapy as an additional renal replacement therapy (3 cats and 1 dog), a concurrent diagnosis of neoplasia (1 cat and 1 dog), and a renal transplant performed immediately following the last IHD treatment (1 cat).

One hundred thirty-five cases (42 cats and 93 dogs) were thus included in the study. Rounding of numbers to the nearest integer caused some percentages not to sum to 100%. Two cats each had 2 episodes of AKI treated with IHD. Two dogs had initial episodes of AKI treated with IHD and were subsequently treated with IHD for CKD. Of the 42 cats included, 17 (40%) were castrated males, 2 (5%) were sexually intact males, 22 (52%) were spayed females, and 1 (2%) was a sexually intact female. The median age and body weight of the cats were 7.0 years (IQR, 4.4 to 9.0 years; range, 0.6 to 13.1 years) and 5.2 kg (11.4 lb; IQR, 4.2 to 5.7 kg [9.2 to 12.5 lb]; range, 2.3 to 11.6 kg [5.1 to 25.5 lb]), respectively. Of the 42 cats, there were 27 (64%) domestic shorthairs, 4 (10%) Siamese, 2 (5%) Persians, 2 (5%) Maine Coons, 2 Himalayans (5%), and 1 (2%) each of Abyssinian, American Shorthair, Ragdoll, domestic longhair, and Tonkinese. Of the 93 dogs, 30 (32%) were castrated males, 21 (23%) were sexually intact males, 37 (40%) were spayed females, and 5 (5%) were sexually intact females. The median age and body weight of the dogs was 7.0 years (IQR, 4.8 to 8.9 years; range, 0.3 to 14.6 years) and 24.3 kg (53.5 lb; IQR, 11.0 to 37.0 kg [24.2 to 81.4 lb]; range, 2.5 to 76.1 kg [5.5 to 167.4 lb]), respectively. There were 38 different breeds of dogs represented. The most common breeds included Labrador Retrievers (18/93 [19%]), mixed-breed dogs (16/93 [17%]), and Golden Retrievers (7/93 [8%]).

An obstructive etiology for AKI was identified in 18 of 42 (43%) cats. Seventeen of these 18 cats had ureteral obstructions, and 1 of 18 had a urethral obstruction. The etiology of AKI was unknown in 10 of 42 (24%) cats, toxic in 8 of 42 (19%) cats, miscellaneous in 4 of 42 (10%) cats, and infectious in 2 of 42 (5%) cats. The 4 miscellaneous etiologies were ischemia associated with anesthesia (2 cases), renal infarction, and uroabdomen. For statistical purposes, etiologies were compared as obstructive versus nonobstructive (including unknown, toxic, miscellaneous, and infectious etiologies) for cats. For dogs, the etiology was unknown in 43 of 93 (46%) of the cases. The etiology was infectious in 21 of 93 (23%) cases, toxic in 20 of 93 (22%) cases, and miscellaneous in 9 of 93 (10%) cases. The 9 miscellaneous etiologies were protein-losing nephropathy (5 cases), sepsis (3), and rhabdomyolysis secondary to heatstroke (1). There were no obstructive etiologies of AKI in the canine cohort.

The median duration of hospitalization was 8 days (IQR, 4 to 12 days; range, 1 to 23 days) for cats and 9 days (IQR, 4 to 15 days; range, 1 to 45 days) for dogs. The median number of IHD treatments administered to cats was 3 (IQR, 2 to 5 treatments; range, 1 to 34 treatments). For dogs, the median number of IHD treatments was 4 (IQR, 2 to 8 treatments; range, 1 to 52 treatments). The interval between IHD treatments varied from 1 to 3 days and was determined on the basis of daily clinical assessment. Six of 42 (14%) cats and 21 of 93 (23%) dogs in our study received a treatment specifically intended to arrest or reverse the cause of AKI, in addition to IHD. Five of the 18 cats diagnosed with obstructive urinary disease underwent surgical correction of the obstruction. The remaining cat was treated with antimicrobials for presumptive concurrent pyelonephritis. All 21 dogs with infectious disease (leptospirosis or pyelonephritis) were treated with antimicrobials. The patients that did not receive a treatment specifically related to the etiology of their AKI were treated with supportive care, including IHD, until renal recovery was sufficient for IHD independence or death occurred.

The overall survival rate at the time of hospital discharge was 50% (21/42) for cats and 53% (49/93) for dogs. The 30-day overall survival rate from the time of hospital discharge was 48% (20/42) for cats and 42% (39/93) for dogs. The 365-day overall survival rate from the time of hospital discharge was 38% (16/42) for cats and 33% (31/93) for dogs. Three of 42 (7%) cats and 21 of 93 (23%) dogs continued to receive IHD treatments for a period of time after they were discharged from the Animal Medical Center. The 3 cats received 3, 5, and 26 outpatient treatments for 4, 10, and 91 days, respectively. Two of the 3 and 1 of the 3 cats survived 30 days and 365 days or longer, respectively, following hospital discharge. The median number of outpatient treatments administered to the 21 dogs was 5 (IQR, 2 to 20 treatments; range, 1 to 43 treatments) over a median of 16 days (IQR, 5 to 48 days; range, 1 to 100 days). Fourteen of 21 (67%) and 10 of 21 (48%) dogs treated with IHD as outpatients survived for 30 days and 365 days or longer, respectively, following hospital discharge.

When all causes of death were taken into account, the median survival time from hospital discharge was 7 days (95% CI, 0 to 835 days) for cats and 9 days (95% CI, 0 to 55 days) for dogs, as depicted by Kaplan-Meier survival curves (**Figure 1**). When only renal-related causes of death were taken into account, the median survival time from discharge was 7 days (95% CI, 0 to 1,476 days) for cats and 7 days (95% CI, 0 to 55 days) for dogs. At the end of the study period, 10 of 42 (24%) cats and 15 of 93 (16%) dogs were still alive and therefore censored in survival analysis. Sixteen of 42 (38%) cats and 36 of 93 (39%) dogs died, and 16 of 42 (38%) cats and 40 of 93 (43%) dogs were euthanized during the study period. The cause of death or reason for euthanasia was renal related in 29 of 32 (91%) cats and 67 of 76 (88%) dogs.

For cats, sex, age, weight, and the number of IHD treatments administered were not associated with overall or renal-related survival time. However, an obstructive etiology for AKI was significantly associated with a longer overall survival time (but not renal-related survival time) versus all

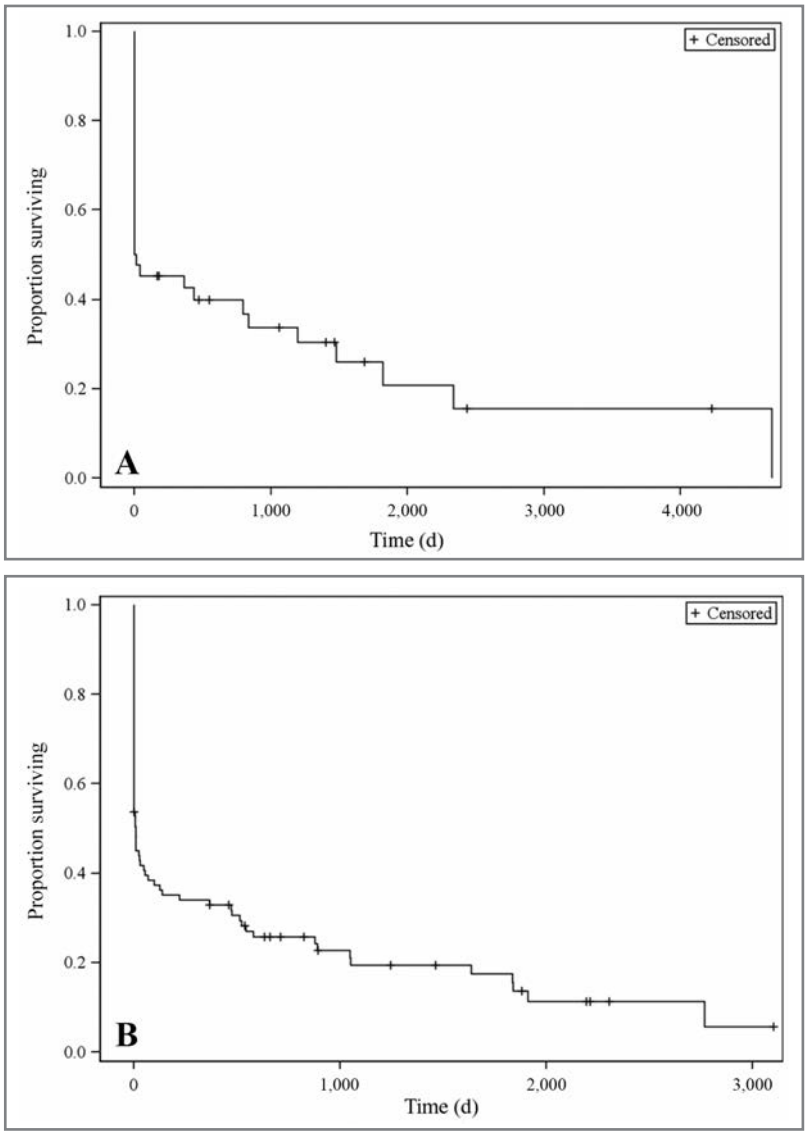


Figure 1—Kaplan-Meier survival curves depicting all causes of death from the time of discharge for cats (A) and dogs (B) treated with IHD for AKI.

other etiologies grouped together ($P = 0.03$). The median overall survival time for obstructive etiologies was 835 days (95% CI, 0 to 2,335 days). Whereas cats with an obstructive etiology had a smaller number of IHD treatments, there was no difference in length of hospitalization between obstructive and nonobstructive etiologies. The length of hospitalization was, however, positively associated with longer overall and renal-related survival times ($P < 0.01$). For the 16 cats surviving 365 days or longer, and with serum or plasma creatinine concentrations available within the 30- to 90-day period following the last IHD treatment, a lower IRIS stage was associated with a longer overall survival time from discharge ($P < 0.01$), but IRIS stage was not associated with renal-related survival time. The median creatinine concentration within the 30- to 90-day period following the last IHD treatment was 2 mg/dL (IQR, 1.7 to 2.8 mg/dL; range, 1 to 5.7 mg/dL [feline reference range, 0.8 to 2.3 mg/dL]). Of the 4 cats with stage I disease, 2 cats lived for 1,196 and 4,667 days, and 2 cats were censored at 1,060 days and 4,225 days. The median overall survival time for cats with stage II disease (9 cats) was not reached. There were 2 cats with stage III disease that survived for 363 days and 1,820 days, and an additional cat with stage III disease that was censored at 166 days. The 1 cat with stage IV disease survived for 438 days.

For dogs, sex, age, weight, and the number of IHD treatments administered were not associated with overall or renal-related survival time. Furthermore, there was no difference in the number of IHD treatments administered or the length of hospitalization, when the various etiologies of AKI were compared. However, the median overall and renal-related survival times were significantly longer for infectious etiologies as compared with all other etiologies ($P < 0.01$). The median overall survival time for infectious etiologies was 533 days (95% CI, 125 to 1,913 days), and the median renal-related survival time could not be determined because of the high proportion of survivors in the infectious etiology group. Also, the survival rate at the time of hospital discharge was 90% (19/21) for the dogs with an infectious etiology. For toxic and unknown etiologies, the median overall and renal-related survival times were 0 days, and for the miscellaneous etiologies, the median overall and renal-related survival times were 9 days (95% CI, 0 to 1,051 days) and 0 days (95% CI, 0 to 10 days), respectively. The duration of hospitalization was positively associated with longer overall and renal-related survival times ($P < 0.01$). For the 25 dogs surviving 365 days or longer and with serum or plasma creatinine concentrations available within the 30- to 90-day period following the last IHD treatment, a lower IRIS stage was associated with a longer overall survival time from discharge ($P < 0.01$), but IRIS stage was not associated with renal-related survival. The median creatinine concentration within the 30- to 90-day period following the last IHD treatment was 1.8 mg/dL (IQR, 1.3 to 2.6 mg/dL; range, 1 to 4.9 mg/dL [canine reference range, 0.4 to 1.8 mg/dL]). The median overall survival times for dogs with stage I, II, or III disease were 1,913 days (the lower confidence limit was 1,638 days, but the upper confidence limit could not be determined in this sample), 2,768 days (95% CI, 1,051 to 2,768 days), and 878 days (95% CI, 367 to 1,048 days), respectively. There were no dogs with stage IV disease that survived 365 days or longer.

## Discussion

In the present study, cats and dogs with a diagnosis of AKI that were treated with IHD had survival rates similar to those reported for human patients treated with either IHD or continual renal replacement theory, in which the survival rate to hospital discharge or at 30

days following initiation of treatment varies from 31% to 63% and the 365-day survival rate varies from 21% to 37.6%.[36–42] Although there was a high mortality rate prior to hospital discharge for the veterinary patients in the present study, those patients that survived to discharge had a high likelihood of long-term survival. Our study demonstrated survival rates to hospital discharge of 50% (21/42) and 53% (49/93) and 365-day survival rates of 38% (16/42) and 33% (31/93) for cats and dogs, respectively. These data provide owners and veterinarians with previously unavailable long-term prognostic information specific to veterinary patients with AKI for which IHD is deemed necessary.

The low survival rate to hospital discharge in our study is similar to results of previous retrospective studies[43,44] evaluating AKI in cats and dogs, the majority of which were not treated with IHD. In the human literature, when patients with AKI who did not undergo renal replacement therapy are compared with those who were treated with renal replacement therapy, a higher mortality rate has been demonstrated for the latter group.[37,38] This difference in mortality rate is likely related to an increased severity of renal dysfunction and the presence of comorbid conditions. Although the presence of comorbid conditions is frequently noted in veterinary patients with AKI, it is difficult to objectively identify and classify these conditions because the clinical signs and clinicopathologic abnormalities for these concurrent problems often overlap with those of AKI. Nonetheless, it is likely that comorbid conditions such as pancreatitis and volume overload, regardless of whether they were sequelae of the etiologic agent of AKI, uremia, or complications resulting from IHD, influenced the outcome in our cohorts of cats and dogs. Despite the existence of these comorbid conditions, cats and dogs treated with AKI achieved a similar survival rate in the present study, compared with results of previous retrospective studies,[43,44] suggesting (but not demonstrating) a survival benefit for IHD in patients with severe AKI.

Although the signalment for both cats and dogs in our study varied, the age, sex, breed, and weight were similar to previous studies[4,32,43,44] evaluating cats and dogs with AKI that were treated with IHD. We evaluated both age and weight as factors that might influence survival, but neither of the 2 variables was associated with either absolute or renal-related survival. In the human literature, multiple studies[36,39,45,46] have demonstrated a negative impact of age on long-term survival of human patients with AKI treated with extracorporeal renal replacement therapies. Furthermore, a recent meta-analysis of 17 human studies evaluating AKI (12 of which used dependence on renal replacement therapy as a criterion for the definition of AKI) determined that an older age, defined as > 65 years, was associated with a decreased probability of recovery of renal function.[47] A possible explanation for the discrepancy between our findings and those of the human literature is that older human patients with AKI are frequently suffering from severe, preexisting, extrarenal disease. In the human literature, the majority of AKI cases reported are hospital acquired[48,49] in which the median age is significantly higher than the rest of the intensive care unit population.[50] These patients are frequently admitted to the intensive care unit for an extrarenal disease, but during the course of the hospital stay, AKI develops as a sequela to the disease for which they are being hospitalized (eg, sepsis) or as a consequence of a diagnostic or therapeutic procedure performed for the purposes of treating the extrarenal disease (eg, radiocontrast nephropathy). One of the most common diseases predisposing human patients to AKI is sepsis, which occurs more frequently in the elderly and has a higher mortality rate in elderly patients.[51,52] In our study, there were only 4 animals with AKI secondary to a preexisting, extrarenal disease (3 dogs with sepsis and 1 dog with heatstroke), suggesting that the majority of patients with AKI in our study experienced a renal insult in the absence of notable, preexisting, extrarenal disease. Furthermore, our exclusion criteria were designed to eliminate patients with preexisting CKD and neoplasia, both of which are diseases frequently encountered in older animals. Therefore, our exclusion criteria may have eliminated older animals with preexisting comorbidities that may have influenced outcome. An additional factor that may have influenced our results is owners' decisions to forego IHD and elect euthanasia for patients with preexisting, extrarenal disease. It is also possible that the small number of cases included in our study precluded the detection of an association between age and outcome of AKI treated with IHD.

The categories of etiologies and their distribution for dogs with AKI treated with IHD were similar to a previous study by Segev et al.[32] However, for cats, the distribution of etiologies was different than that reported by Langston et al.[4] In Langston's study of 29 cats, the etiology of AKI was most frequently toxic (34% of cases). In our cohort of cats, obstructive urinary disease was the most common etiology, accounting for 43% (18/42) of the cases. An obstructive etiology, regardless of whether surgical intervention was pursued, was associated with a longer overall survival time than all of the other etiologies grouped together. Of the 18 cats with obstructive urinary disease, 5 underwent surgery to resolve the obstruction in addition to IHD, whereas 13 cats did not have surgical intervention. Eight of the 13 cats that did not undergo surgery survived 365 days or longer past discharge, and all 8 of these cats had a degree of renal recovery sufficient for discontinuation of IHD prior to hospital discharge, demonstrating that feline obstructive urinary disease (particularly ureteral obstructions) can resolve spontaneously with medical care only (eg, IV fluid therapy and diuretic administration). Cats with obstructive etiologies for AKI also underwent significantly fewer IHD treatments than all of the other etiologies grouped together. These results show that, in select cases, recovery from obstructive urinary disease is possible without surgical intervention and also underscore the pivotal role that IHD plays in stabilizing severe AKI due to obstruction and allowing sufficient time for renal recovery with or without surgical intervention. Owners whose cats are suffering from AKI with an obstructive etiology may benefit from the knowledge that the prognosis is likely better for these patients and that the expense associated with the number of IHD treatments may be less.

For dogs, an infectious etiology (either leptospirosis or pyelonephritis), when compared with each other etiology for AKI, was associated with a high survival rate at the time of hospital discharge and longer overall and renal-related survival times. However, no association between etiology and the number of IHD treatments was demonstrated. Whereas multiple studies[53–59] exist documenting a variable survival rate for dogs with AKI associated with leptospirosis that are not treated with IHD, our findings are in agreement with those of Adin and Cowgill,[21] who also demonstrated a high survival rate at hospital discharge (12/14) for dogs with leptospirosis treated with IHD. As with the dogs in our study, the dogs in that study[21] that were treated with IHD likely had more severe clinical manifestations of uremia than those patients with leptospirosis that were not treated with IHD. Despite this fact, Adin and Cowgill[21] demonstrated a similar survival rate for dogs with leptospirosis treated with IHD, compared with the survival rate of those treated with conventional medical treatment (18/22), suggesting a survival benefit for IHD in patients with severe forms of leptospirosis. The knowledge that this etiology has a favorable prognosis in patients with severe AKI requiring IHD, despite the fact that the number of IHD treatments, hospitalization times, and associated financial costs may equal or exceed those associated with other etiologies of AKI, may be of benefit to dog owners who must decide whether to pursue IHD.

In the present study, the 365-day survival rate for cats and dogs was 38% (16/42) and 33% (31/93), respectively. Despite the fact that the majority of long-term survivors (both cats and dogs) had evidence of persistent renal dysfunction following episodes of AKI, all but 1 cat and all dogs were classified as IRIS stage III or lower. Additionally, 11 of 13 cats and 13 of 22 dogs had serum or plasma creatinine concentrations corresponding to IRIS stage II or lower. The large number of cats and dogs with mild or moderate azotemia is consistent with human studies evaluating long-term outcome of patients with AKI treated with extracorporeal renal replacement therapy. In these studies, percentages of surviving patients independent of extracorporeal renal replacement therapy at the time of hospital discharge range from 68% to 95%.[36,39,40,46,60–63] In our study, 18 of 21 (86%) cats and 28 of 49 (57%) dogs were independent of IHD at the time of hospital discharge. The remaining cats and dogs received additional IHD treatments for a variable time period following hospital discharge, until renal recovery was sufficient to discontinue IHD or death or euthanasia occurred. All animals in our study that survived 365 days or longer were eventually independent of IHD. These findings in both the human literature and our study demonstrate that renal function recovers to a level compatible with an acceptable quality of life in most long-term survivors of AKI and that this recovery occurs in the majority of patients by the time of hospital discharge. For those patients that required ongoing IHD treatments following hospital discharge, the 365-day survival rate was similar to the overall population of patients with AKI treated with IHD, suggesting that the need for ongoing IHD treatments following discharge is unlikely to affect long-term outcome.

For both cats and dogs, IRIS stage at 30 to 90 days after discontinuation of IHD was inversely associated with survival. This association was limited to overall survival, rather than renal-related survival. We speculated that an association between serum or plasma creatinine concentrations and renal-related survival could not be demonstrated because only 4 of 16 cats and 7 of 31 dogs in our study that were long-term survivors died of renal-related causes, and this small number precluded demonstration of a significant relationship. The negative association between serum or plasma creatinine concentration and survival time in cats with CKD has been documented previously.[64–66] Boyd et al[65] utilized the IRIS stages to classify cats with CKD and reported median overall survival times of 1,151 days for cats with stage IIb CKD (serum creatinine concentration > 2.3 mg/dL and ≤ 2.8 mg/dL), 659 days for cats with stage III CKD, and 35 days for cats with stage IV CKD. When comparing survival times on the basis of IRIS stage within the 30- to 90-day period following the last IHD treatment in our study with survival times in the study by Boyd,[65] the median survival times for each IRIS stage were longer in our study. One possible explanation for this discrepancy is the nature of the renal insult in each study. Boyd's study[65] evaluated stable and euhydrated cats with naturally occurring CKD. The most common histopathologic lesion of feline CKD is tubulointerstitial nephritis, which may progress to fibrosis.[67] However, we are unaware of any data that describe the histopathologic lesions of cats with residual kidney dysfunction following AKI. Although there are no means of definitively determining whether cats in our study had underlying CKD undetectable by routine biochemical testing prior to an acute insult, it is probable that many cats in our study did not have underlying renal dysfunction prior to the onset of AKI. Therefore, in many cats, the underlying disease processes responsible for the azotemia documented from 30 to 90 days after the last IHD treatment in our study are likely to be entirely different from the disease process or processes responsible for the CKD described in the study[65] by Boyd.

The present study was limited in several respects, including the retrospective rather than prospective design. It is possible that, because of the frequent absence of prior laboratory data, cases that should have been excluded because of the presence of preexisting CKD were included in the study. The inclusion of these cases may have had a substantial negative effect on survival time. These cases were intended to be excluded from analysis because of the likelihood that patients with preexisting CKD would have a shorter survival time independent of the influence of AKI. Follow-up for both cats and dogs was not consistent; consequently, several data points for serum or plasma creatinine concentrations in samples collected from 30 to 90 days after the last IHD treatment were missing. Some animals were censored at the last date of contact if they were still alive or if the owners or referring veterinarian could not be reached for determination of survival status and serum or plasma creatinine concentrations. Censorship and euthanasia of patients likely resulted in underestimation of survival time. Additionally, due to the limited number of cases available for inclusion, as evidenced by the large number of wide 95% CI for reported survival times, the study was underpowered to detect variables that may have influenced survival.

The timing of serum or plasma creatinine measurement at 30 to 90 days after the last IHD treatment may have impacted our results, as renal function may have been in flux during this period on the basis of reports of renal recovery occurring during periods as long as 6 months.[54] However, renal function was subjectively judged to be either stable or improving in all cases, so the association between serum or plasma creatinine concentration and survival likely represented a worst-case scenario in regard to residual renal function. To minimize the possibility of a dynamic state of renal function, the IRIS staging system is based on plasma creatinine concentrations assessed on at least 2 occasions in a stable patient. Because multiple serum or plasma creatinine concentrations were not available for the examined time period in our study, it was impossible to fulfill the requirements for proper IRIS staging. Nonetheless, we believe that the use of the IRIS staging system for classifying the degree of azotemia is still acceptable, as it has been used to characterize single measurements of serum or plasma creatinine concentrations in previous feline studies[64–66] and has shown prognostic value in these studies.

Lastly, the variety of etiologies responsible for AKI among the cats and dogs may have been a confounding factor in our study. As has been demonstrated previously, the etiology of AKI affects short-term outcome in cats and dogs.[4,32,43,44] Owners of patients with AKI that was due to an etiology associated with increased short-term mortality or low probability of renal recovery may have been more inclined to choose euthanasia during hospitalization or during outpatient IHD treatments, respectively.

Despite these limitations, our findings suggested that cats and dogs treated with IHD for AKI have outcomes similar to those in human medicine. Variables that predicted overall survival were the etiology of AKI (obstructive for cats and infectious for dogs) and the IRIS stage within the 30- to 90-day period following the last IHD treatment for both cats and dogs. These data will provide useful information for referring veterinarians and specialists when counseling an owner on whether IHD is an appropriate choice for the patient.

a. SAS, version 9.2, SAS Institute Inc, Cary, NC.

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## Appendix

The IRIS system for staging CKD on the basis of blood creatinine concentration.

| | Creatinine (mg/dL) | |
|---|---|---|
| **Stage** | **Cats** | **Dogs** |
| I | < 1.6 | < 1.4 |
| II | 1.6–2.8 | 1.4–2 |
| III | 2.9–5 | 2.1–5 |
| IV | > 5 | > 5 |