Use of continuous renal replacement therapy for treatment of dogs and cats with acute or acute-on-chronic renal failure: 33 cases (2002–2006)

Shenandoah H. Diehl, DVM, DACVECC and Ravi Seshadri, DVM, DABVP, DACVECC

Abstract

Objective: To describe the indications, clinical features, outcomes and complications associated with use of continuous renal replacement therapy (CRRT) in 17 client-owned dogs and 16 client-owned cats with acute or acute-on-chronic renal failure refractory to aggressive medical management.

Series summary: Twenty-nine percent of dogs and 44% of cats had evidence of pre-existing chronic kidney disease (CKD). Median duration of CRRT was 16.3 hours (range 0.3–83.0 hours) in dogs and 11.5 hours (range 1.0–35.5 hours) in cats. Median canine blood urea nitrogen (BUN) improved from 41.0 mmol/L (115.0 mg/dL) to 11.8 mmol/L (33.0 mg/dL) and creatinine from 636.5 mmol/L (7.2 mg/dL) to 274 mmol/L (3.1 mg/dL). Median feline BUN improved from 46.4 mmol/L (130 mg/dL) to 13.9 mmol/L (39.0 mg/dL) and creatinine from 1069.6 mmol/L (12.1 mg/dL) to 291.7 mmol/L (3.3 mg/dL). Metabolic acidosis resolved in 80% of affected dogs and 71% of affected cats. Hyperkalemia resolved in 100% of affected dogs and 88% of affected cats. Complications noted with CRRT included iatrogenic hypokalemia, iatrogenic metabolic alkalosis, clinical hypocalcemia, total hypercalcemia, filter clotting, anemia, hypothermia, and neurologic complications. Forty-one percent of dogs and 44% of cats survived to discharge. No dogs and only 1 cat developed newly diagnosed CKD.

New or unique information provided: CRRT can be a viable option for the management of acute or acute-on-chronic renal failure in dogs and cats that are refractory to aggressive medical management. The frequency of complications associated with CRRT in this study warrants further experience with this modality before its widespread use can be recommended.

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Introduction

Acute renal failure (ARF) is a potentially life-threatening disease in dogs and cats. ARF-induced changes in metabolic state and fluid balance may cause life-threatening arrhythmias, hypertension, vasculitis, hypervolemia, interstitial fluid retention, gastrointestinal bleeding, oliguria, and anuria. These abnormalities may lead to respiratory and circulatory collapse and damage to other organ systems. Standard ARF management includes removal of the inciting cause, IV fluid therapy, use of osmotic and chemical diuretic agents, medical management of acid–base and electrolyte abnormalities,

correction of fluid volume irregularities and uremic signs, and nutritional and cardiovascular support.[1] Despite aggressive intervention, many ARF patients remain refractory to medical management and succumb to the consequences of uremia before renal recovery can occur.[1] It is well recognized that replacement of renal function can be performed via dialysis while awaiting renal recovery or transplantation. Peritoneal dialysis (PD) and intermittent hemodialysis (IHD) have been successfully used to manage severe uremia due to various disease processes in dogs and cats.[2,3] PD is readily available and less expensive when compared with other modalities. IHD is becoming more readily available but the distance to dialysis centers may render this modality unfeasible for many pet owners. Additionally, many veterinary patients requiring dialytic therapy have concurrent critical illness requiring care within an intensive care setting that may not be equipped with IHD.

From Advanced Critical Care and Internal Medicine, Tustin, CA.

Address correspondence and reprint requests to:
Dr. Shenandoah H. Diehl, Advanced Critical Care and Internal Medicine, 3021 Edinger Avenue, Tustin, CA 92780.
E-mail: hishenandoah@gmail.com

Continuous renal replacement therapy (CRRT) is an emerging therapy that has been investigated in veterinary medicine for the treatment of ARF and can be utilized within the intensive care unit (ICU) setting.[a,4] CRRT is a dialytic therapy that is continuously administered 24 hr/day rather than on an intermittent basis.[5] Depending on the machine, extracorporeal circuit (ECC) and mode prescribed, CRRT may use the principles of convection, diffusion, or both to achieve clearance of solutes and excess body fluid. In humans, CRRT has been effective in treating a number of life-threatening conditions including ARF.[6,7] Two recent reviews of the indications for, and the biophysical principles related to, CRRT have been published.[4,8] Although standardized CRRT prescriptions and protocols have arisen in the human ICU setting, similar protocols have not been established in veterinary medicine. CRRT is currently being utilized in only a few veterinary settings where experience is limited. There are reports in the veterinary literature on the management of 1 client-owned cat with ARF due to suspected lily toxicity, 4 dogs with induced experimental ARF and 1 client-owned dog with naturally occurring ARF.[a,4] The purpose of this report is to describe the use of CRRT in the treatment of ARF and acute-on-chronic renal failure (AOCRF), secondary to various disease processes, in a series of dogs and cats.

Materials and Methods

Criteria for case selection

Medical records of patients that received CRRT for ARF or AOCRF at Advanced Critical Care and Internal Medicine between February 2002 and April 2006 were reviewed. The criteria for inclusion in the study were patients that received standard medical therapy for ARF or AOCRF as described below. When medical management failed to improve clinical status, interventional management options including PD, IHD, and CRRT were discussed with the owners. The owners of all patients enrolled in this study elected CRRT in conjunction with standard medical care.

Case management and CRRT technique

All patients were initially treated with IV fluid therapy with or without the administration of chemical diuretics, osmotic diuretics, or vasopressor agents. Despite appropriate therapy including adequate restoration of perfusion parameters and resolution of dehydration, all patients had either worsening of, or lack of significant improvement in, blood urea nitrogen (BUN) and serum creatinine concentration. A subset of the cases also exhibited concurrent non-responsive hyperkalemia, evidence of fluid overload, and anuria.

Following owner consent, a temporary central venous dual-lumen hemodialysis catheter[b] was placed in each patient utilizing systemic or local (or both) analgesia alone or in combination with general anesthesia. The largest diameter catheter that could reasonably be placed was selected, based on patient weight and jugular vein size. Size 8 Fr catheters were placed in all cats and catheters ranging in size from 8 to 14.5 Fr were placed in dogs. Catheters were preferentially inserted into the right external jugular vein. The left external jugular vein was used when right jugular vein placement was not possible. The distal tip of the catheter was advanced to the level of the right atrium when possible or the cranial vena cava when catheter length precluded atrial placement. Thoracic radiography was used to confirm appropriate catheter tip location. Ultrasound-guided needle[c] biopsy and histopathology of the kidney were performed when owners consented.

Continuous venovenous hemodiafiltration (CVVHDF) was initiated using a combination of convective and diffusive solute clearance with ultrafiltration. The dialysis machine[d] utilized ECCs with integrated AN69 (acrylonitrile/sodium methallyl sulfonate) hemodialyzer filters.[e] ECCs[e] with a priming volume of 50 mL were used for all patients weighing 10 kg or less. ECCs[e] with a priming volume of 84 mL were used for dogs weighing between 10 and 30 kg. ECCs[e] with a priming volume of 107 mL were used for all dogs weighing >30 kg, with the exception of 1 dog weighing 60 kg in which an ECC with a priming volume of 84 mL was utilized due to unavailability of an ECC with 107 mL prime volume. The ECC was primed with 0.9% sodium chloride.[f] Commercially available balanced electrolyte dialysate solutions were used. A solution containing 140 mEq/L sodium, 5 mEq/L potassium, 98 mEq/L chloride, 3 mEq/L magnesium, 27 mEq/L acetate, and 23 mEq/L gluconate was used before February 2005.[g] A solution containing 140 mEq/L sodium, 2 mEq/L potassium, 108 mEq/L chloride, 1 mEq/L magnesium, 3 mEq/L lactate, and 32 mEq/L bicarbonate was used, thereafter.[h] Regional citrate anticoagulation (RCA) of the ECC was performed using 4.0% sodium citrate solution[i] administered at the level of the blood access line to remove ionized calcium from blood within the circuit. Calcium chloride (0.8%) solution[j] was administered at the level of the blood return line to replace patient ionized calcium. Balanced isotonic crystalloid pre-filter replacement solution was used. The specific composition of replacement fluid selected was based on patient pre-CRRT laboratory values and included either balanced alkalinizing isotonic crystalloids[g,k] or 0.9% sodium chloride. Initial extracorporeal flow rates were based on a human pediatric CRRT protocol[l] and included blood flow rate of 2–5 mL/kg/min,

dialysate flow rate of $1150 \, mL/m^2/hr$, sodium citrate solution rate of 1.5 times the blood flow value (in mL/hr), calcium chloride solution rate of 0.4 times the sodium citrate flow value (in mL/hr), replacement fluid rate of $0–250 \, mL/hr$ and net ultrafiltration rate of $1–2 \, mL/kg/hr$ depending on patient fluid balance at the time of initiation of CRRT.

Paired venous blood samples were obtained hourly, or more frequently, if indicated, from the ECC and a patient central IV catheter. These samples were analyzed for ionized calcium levels using point-of-care analyzers.[m,n] Adjustments to citrate and calcium rates were made to maintain the extracorporeal ionized calcium $<0.4 \, mmol/L$ (1.6 mg/dL) and patient ionized calcium between 1.1 and $1.4 \, mmol/L$ (4.4–5.6 mg/dL). Ultrafiltration rate was adjusted based on clinician assessment of patient fluid balance status. The access and return lines of the ECC were reversed if considered indicated by inadequate blood flow from the catheter access port. Heat support was provided via an in-line IV fluid line warmer,[o] internal cage heat support,[p] and external circulating air heater.[q] Supplemental therapy was administered at the discretion of the attending clinician.

Patient monitoring during CRRT included rectal temperature, pulse rate, and systolic blood pressure (SBP) using a Doppler blood pressure device.[r] Urine output (UOP) was monitored via an indwelling urinary catheter and closed collection system. Urine samples were submitted for culture and antibiotic sensitivity if not previously obtained. Patient BUN, serum creatinine, central venous acid–base, electrolyte, and hematocrit values were obtained on an hourly basis using point-of-care analyzers.[m,n] Additional labwork was performed at the discretion of the attending clinician.

CRRT was continued until renal biochemical values had normalized and uremic complications had resolved. Post-CRRT supportive therapy was prescribed at the discretion of the attending clinician. CRRT was reinstituted in patients whose renal function remained inadequate on post-CRRT support.

Extraction of data from medical records

The following information was collected from each medical record: signalment; concurrent disease processes; body weight on presentation; historical evidence of CKD; duration of therapy before referral; duration of therapy following referral but before initiation of CRRT; significant abnormalities in pre-treatment labwork (complete blood count, chemistry panel, electrolytes, acid–base values, urinalysis, urine culture/sensitivity); indications for CRRT; dialysis catheter size; dialysis filter size; dialysis prescription and duration of dialysis; change in BUN, creatinine, sodium, potassium, ionized

and total calcium, and hematocrit concentrations during CRRT; complications, duration of therapy following CRRT but before discharge; patient outcome; and results of renal histopathology. The incidence of ARF and AOCRF in dogs and cats in the ICU population during the study period was determined by a computerized database search.

Statistical methods

Descriptive statistics were performed and results reported as median and range. When laboratory values were reported to be above the analyzer's detectable range, the high limit of the analyzer range was used in calculations and figures.

Results

Demographics

Seventeen dogs were treated with CRRT and included 9 spayed female, 1 intact female, 4 neutered male, and 3 intact male dogs. Breeds represented include Labrador Retriever ($n = 4$), Shetland Sheepdog ($n = 3$), German Shepherd Dog ($n = 2$), and 1 each of American Eskimo, Scottish Terrier, Staffordshire Terrier, Brittany Spaniel, Miniature Bull Terrier, Newfoundland, Jack Russell Terrier, and mixed breed dog. Median age at presentation was 88 months (range 6–194 months). Median body weight at presentation was 26.55 kg (range 10.68–60.00 kg).

Sixteen cats were treated with CRRT. This group included 12 neutered male and 4 spayed female cats. Breeds represented include Domestic Shorthair ($n = 12$), Domestic Longhair ($n = 1$), Maine Coon ($n = 2$), and Tonkinese ($n = 1$). Median age at presentation was 109 months (range 14–194 months). Median body weight at presentation was 5.57 kg (range 2.84–6.45 kg).

Indications for renal replacement therapy (RRT) in dogs included inadequate improvement of azotemia ($n = 17$) with concurrent evidence of fluid overload ($n = 4$) or anuria ($n = 1$). In cats, RRT was indicated due to inadequate improvement of azotemia ($n = 16$) with concurrent evidence of fluid overload ($n = 7$) and nonresponsive hyperkalemia ($n = 2$).

The incidence of ARF and AOCRF in our facility's ICU population during the study period was 1.12% and 0.56%, respectively (1.68% combined) for dogs (243 ARF, 122 AOCRF, total cases 21,692) and 1.35% and 1.74%, respectively (3.11% combined) for cats (104 ARF, 133 AOCRF, total cases 7,627). The 17 dogs treated with CRRT represented 4.66% of all dogs with ARF or AOCRF combined and the 16 cats treated with CRRT represented 6.75% of all cats with ARF or AOCRF combined.
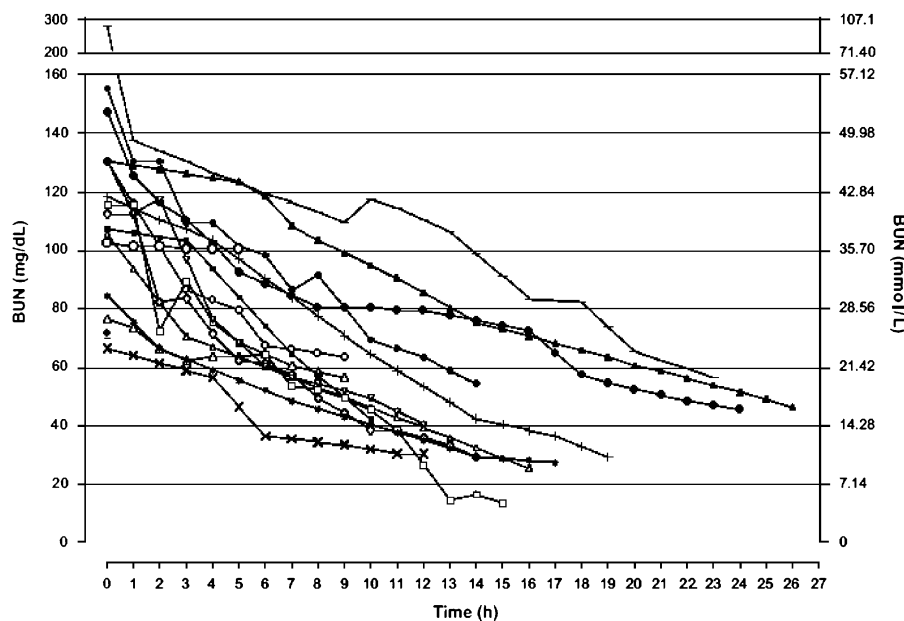
Figure 1: Canine blood urea nitrogen concentration *versus* duration of continuous renal replacement therapy. Each line represents 1 patient's data. Symbols in this figure have been randomly assigned to patients and are not consistent between figures.

Evaluation before CRRT

Median duration of medical therapy at a referring veterinary facility before presentation was 39 hours (range 0–168 hours) in dogs and 49 hours (range 0–104 hours) in cats. Median duration of therapy from admission to our facility to initiation of CRRT was 5.5 hours (range 0.5–97.0 hours) in dogs and 5.0 hours (range 1.5–34.5 hours) in cats. Median duration of CRRT in dogs was 16.3 hours (range 0.3–83.0 hours) and in cats was 11.5 hours (range 1.0–35.5 hours).

Common abnormalities in pre-CRRT labwork reflecting the renal component of each patient's illness are reported in sections below. Remaining laboratory changes did not affect the course of CRRT. Urine culture was positive for *Escherichia coli* in 2 dogs, *Streptococcus canis* in 1 dog, and *Enterococcus faecalis* in 1 dog. Urine culture was positive for *Escherichia coli* in 1 cat. No patients were diagnosed with leptospirosis. Inconsistently reported UOP measurements prevented useful conclusions regarding UOP.

Physiologic changes associated with CRRT

BUN/creatinine: Pre-CRRT BUN results were above the analyzer's readable range in 5 dogs and 3 cats. In these cases, the analyzer's high limit (46.4 mmol/L [130.0 mg/dL]) was used in pre-CRRT calculations and in figures. Three dogs and 2 cats died before collection of recheck labwork after initiation of CRRT. All remaining patients showed improvement in the degree of azotemia with CRRT, as shown in Figures 1–4.

BUN in dogs improved from a pre-CRRT median of 41.1 mmol/L (115.0 mg/dL) (range 23.6–100.0 mmol/L [66.0–281.0 mg/dL]) to a post-treatment median of 11.8 mmol/L (33.0 mg/dL) (range 4.3–22.5 mmol/L [12.0–63.0 mg/dL]). The median creatinine in dogs decreased from 636.5 mmol/L (7.2 mg/dL) (range 247.5–1290.6 mmol/L [2.8–14.6 mg/dL]) to 274.0 mmol/L (3.1 mg/dL) (range 159–397.8 mmol/L [1.8–4.5 mg/dL]) following CRRT treatment. BUN in cats improved from a median of 46.4 mmol/L (130.0 mg/dL) (range 25.3–92.4 mmol/L [71.0–259.0 mg/dL]) to 13.9 mmol/L (39.0 mg/dL) (range 7.9–40.7 mmol/L [22.0–114.0 mg/dL]) following CRRT treatment. The median creatinine in cats decreased from 1069.6 mmol/L (12.1 mg/dL) (range 415.5–1900.6 mmol/L [4.7–21.5 mg/dL]) to 291.7 mmol/L (3.3 mg/dL) (range 132.6–786.7 mmol/L [1.5–8.9 mg/dL]) following CRRT treatment.

Potassium

Two dogs demonstrated hyperkalemia at the initiation of CRRT. The potassium normalized in 1 dog (from 6.30 to 4.92 mEq/L; reference interval 4.0–5.6 mEq/L) and hypokalemia developed in the other (from 5.61 mEq/L to a nadir of 2.87 mEq/L) during CRRT. Intradialytic iatrogenic hyperkalemia (6.18 mEq/L) due to excessive IV fluid potassium chloride supplementation[s] occurred in 1 dog that was normokalemic prior to CRRT. The potassium in this dog normalized (4.78 mEq/L) during CRRT with decreased IV fluid potassium supplementation. Intradialytic hypokalemia occurred in 12 dogs
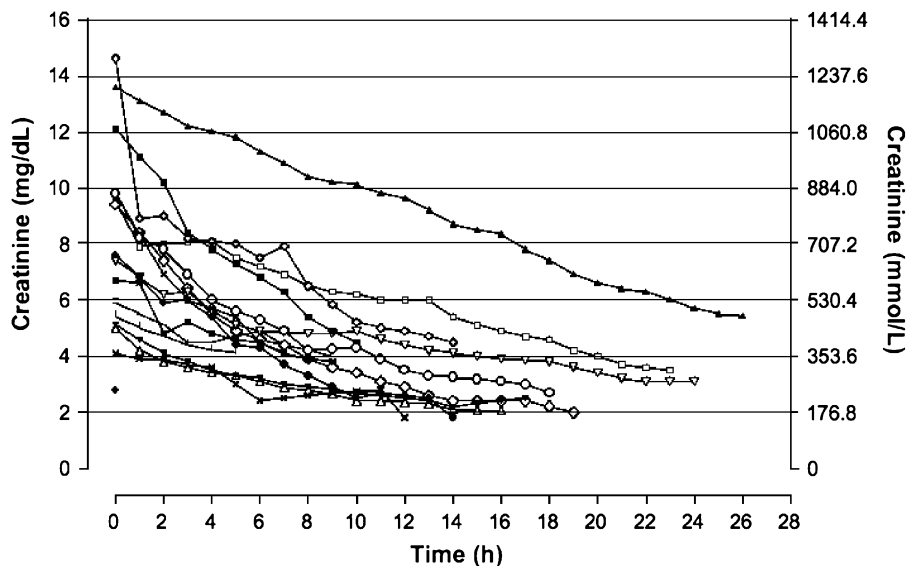
Figure 2: Canine serum creatinine concentration *versus* duration of continuous renal replacement therapy. Each line represents 1 patient's data. Symbols in this figure have been randomly assigned to patients and are not consistent between figures.

(median nadir 3.14 mEq/L, range 2.41–3.37 mEq/L). With increased potassium supplementation, hypokalemia worsened in 1 dog (from 2.86 to 2.41 mEq/L), persisted in 7 dogs (median 3.35 mEq/L, range 2.83–3.94 mEq/L) and resolved in 3 dogs (4.24, 4.80, and 4.92 mEq/L).

Nine cats demonstrated hyperkalemia (median 6.96 mEq/L, range 5.50–8.67 mEq/L; reference interval 3.9–5.3 mEq/L) at the initiation of CRRT. Two of these cats showed persistent hyperkalemia despite aggressive therapy before CRRT (potassium increasing from 8.00 to 8.21 mEq/L over 2.5 days of therapy in 1 cat and decreasing from 8.70 to 7.55 mEq/L over 21 hours of therapy in the other). Hyperkalemia resolved in 7 cats (median 4.41 mEq/L, range 3.34–5.30 mEq/L) and improved but persisted in one cat (from 6.70 to 6.20 mEq/L) during CRRT. One hyperkalemic cat died before a recheck potassium value could be obtained. Intradialytic hyperkalemia due to excessive IV fluid potassium supplementation occurred in 3 cats (median 6.15 mEq/L,
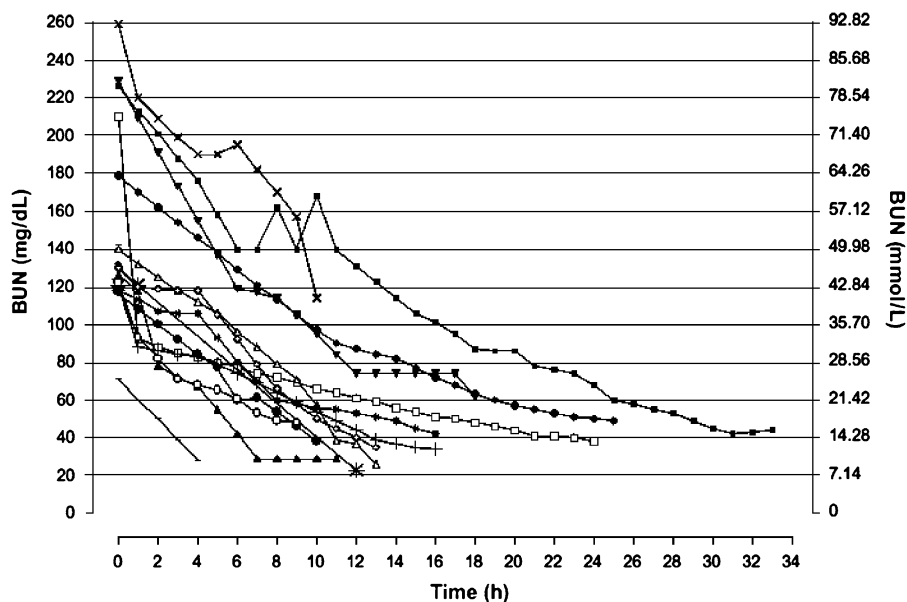

Figure 3: Feline blood urea nitrogen concentration *versus* duration of continuous renal replacement therapy. Each line represents 1 patient's data. Symbols in this figure have been randomly assigned to patients and are not consistent between figures.

Figure 4: Feline serum creatinine concentration *versus* duration of continuous renal replacement therapy. Each line represents 1 patient's data. Symbols in this figure have been randomly assigned to patients and are not consistent between figures.
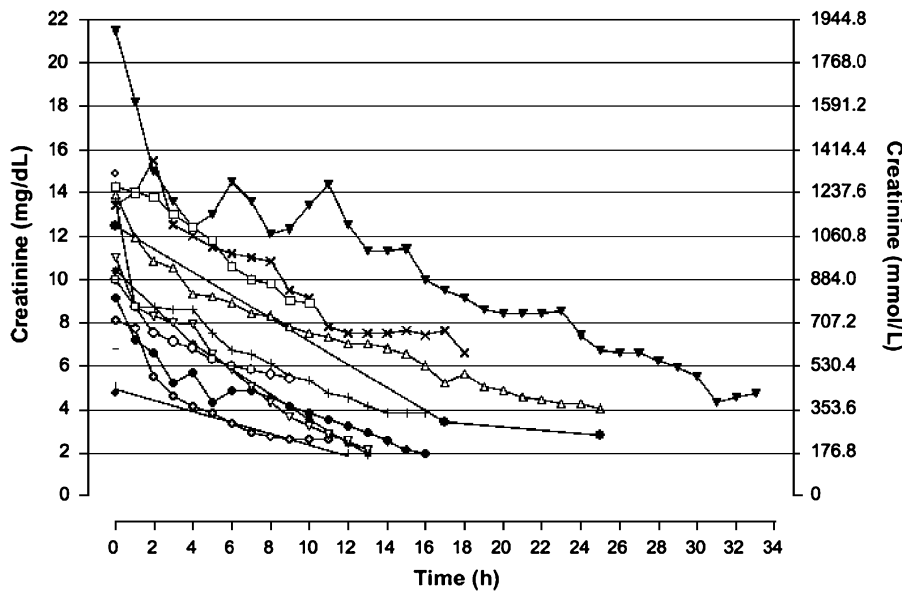
range 5.55–6.55 mEq/L). The potassium normalized (3.92, 4.01, and 5.2 mEq/L) in all cats with a decrease in IV fluid potassium supplementation. Intradialytic hypokalemia occurred in 7 cats (median nadir 2.97 mEq/L, range 2.20–3.15 mEq/L). All 7 cats were normokalemic before CRRT. Hypokalemia improved but persisted in all 7 cats (median 3.10 mEq/L, range 2.69–3.32 mEq/L) during CRRT.

Sodium
One cat presented with evidence of chronic hypernatremia (4 day duration) before CRRT. This cat had rapid lowering of sodium concentration (from 171 to 166 mEq/L; reference interval 147–156 mEq/L) during the initial 1.5 hours of CRRT. This cat developed central nervous system (CNS) signs and seizures and died despite resuscitation efforts following cardiorespiratory arrest. The concurrent drop in BUN could not be calculated in this cat because it died before a recheck BUN was measured. Iatrogenic hypernatremia (163, 161, and 166 mEq/L) developed in 3 cats. All were normonatremic before CRRT but were receiving IV 50% dextrose[t] (2 cats) or IV mannitol[u] therapy (2 cats). The iatrogenic hypernatremia resolved in 1 cat with IV 5% dextrose in water[v] and improved but persisted in the remaining cats (from 163 to 157 mEq/L and from 166 to 156 mEq/L). None of these 3 cats received a hypernatric dialysate, replacement solution, medication, or infusion.

Calcium
Total calcium values were reported in 9 dogs during CRRT. Four dogs that had normal total calcium values within the reference interval of 2.1–3.1 mmol/L (8.2–12.4 mg/dL) before CRRT developed iatrogenic total hypercalcemia (median 4.2 mmol/L [16.7 mg/dL], range 3.3–5.3 mmol/L [13.4–21.2 mg/dL]) during CRRT. Two additional dogs had total hypercalcemia before CRRT that increased (from 3.1 to 4.7 mmol/L [12.5–18.9 mg/dL] and from 3.2 to 5.2 mmol/L [12.7–21.0 mg/dL]) during CRRT. One hypercalcemic dog was euthanized during CRRT before a recheck calcium value was measured. Hypercalcemia had improved in 1 dog 18 hours post-CRRT (from 3.9 to 3.2 mmol/L [15.5–12.9 mg/dL]) and in 1 dog 20 hours post-CRRT (from 5.3 to 3.1 mmol/L [21.2–12.5 mg/dL]). The remaining 3 dogs did not have the value rechecked before discharge. The total calcium value had normalized in all surviving dogs at the time of first recheck between 3 and 8 days after discharge.

Total calcium values were reported in 3 cats during CRRT. Two cats had normal total calcium values within the reference interval of 2.0–2.9 mmol/L (8.2–11.8 mg/dL) before CRRT but developed iatrogenic hypercalcemia (4.0 mmol/L [16.0 mg/dL] and 4.5 mmol/L [18.2 mg/dL]) during CRRT. One hypercalcemic cat was euthanized before a recheck calcium value was measured. Total calcium value had normalized in the other cat by the time of recheck 11 days later.

Ionized calcium values were reported in 15 dogs during CRRT. Ionized hypocalcemia occurred in all 15

dogs (median nadir 0.66 mmol/L [2.65 mg/dL], range 0.34–0.95 mmol/L [1.36–3.81 mg/dL]; reference interval 1.12–1.40 mmol/L [4.49–5.61 mg/dL]). Four dogs had clinical signs consistent with ionized hypocalcemia as demonstrated by muscle fasciculations ($n = 3$) and severe muscle tremors ($n = 1$). The median ionized calcium nadir for clinically affected dogs was 0.68 mmol/L (2.73 mg/dL) (range 0.34–0.74 mmol/L [1.36–2.97 mg/dL]). One mildly affected dog was not treated for the hypocalcemia and remained symptomatic throughout therapy. Complete resolution of signs was observed in the remaining 3 dogs after treatment with an increased rate of IV calcium chloride and administration of IV calcium gluconate.[w]

Ionized calcium values were reported in 13 cats during CRRT. Ionized hypocalcemia occurred in all of the 13 cats (median nadir 0.56 mmol/L [2.24 mg/dL], range 0.34–0.82 mmol/L [1.36–3.29 mg/dL]; reference interval 1.12–1.42 mmol/L [4.49–5.69 mg/dL]). Four cats were clinical for the ionized hypocalcemia demonstrated by muscle fasciculations ($n = 3$) and tachypnea with shallow respirations ($n = 1$). The ionized calcium nadir was unavailable in 2 of these cats and was 0.37 mmol/L (1.48 mg/dL) and 0.83 mmol/L (3.33 mg/dL) in the others. Complete resolution of signs was observed in all cats after treatment with an increased rate of IV calcium chloride ($n = 3$) and administration of IV calcium gluconate ($n = 2$).

Acid–base balance

Venous acid–base values were reported in 16 dogs during CRRT. Ten had metabolic acidosis before CRRT (median bicarbonate 15.6 mEq/L, range 10.9–17.2 mEq/L; reference interval 20.8–24.2 mEq/L). With CRRT, acidosis resolved in 8 dogs (80% of affected dogs) (median bicarbonate 23.1 mEq/L, range 22.5–31.2 mEq/L) and improved but persisted in 2 dogs (bicarbonate from 15.6 to 18.3 mEq/L and from 15.8 to 16.4 mEq/L). Five dogs developed iatrogenic metabolic alkalosis during CRRT (median bicarbonate 30.1 mEq/L, range 20.5–31.2 mEq/L) that resolved over time without specific therapy. Three of these dogs had normal acid-base parameters before CRRT (bicarbonate; 22.4, 23.2, and 23.7 mEq/L) and 2 had metabolic acidosis before CRRT (bicarbonate; 16.0 and 17.2 mEq/L).

Venous acid-base values were reported in all cats during CRRT. Fourteen had metabolic acidosis before CRRT (median bicarbonate 14.4 mEq/L, range 10.0–17.6 mEq/L; reference interval 18.0–23.2 mEq/L). While on CRRT, acidosis resolved in 10 cats (71% of affected cats) (median bicarbonate 25.6 mEq/L, range 20.3–33.0 mEq/L), improved but persisted in 1 cat (bicarbonate from 13.0 to 17.0 mEq/L), showed no significant change in 1 cat (bicarbonate from 12.0 to 12.0 mEq/L

during 1.4 hours of CRRT before death), and worsened in 1 cat (bicarbonate from 15.0 to 11.9 mEq/L). Four cats developed iatrogenic metabolic alkalosis during CRRT (median bicarbonate 30.5 mEq/L, range 26.2–30.8 mEq/L). One of these cats had normal acid–base values (bicarbonate 21.9 mEq/L) before CRRT and 3 had metabolic acidosis (11.1, 14.4, and 17.6 mEq/L) before CRRT. In all surviving cats, the metabolic alkalosis resolved over time without specific therapy.

Hematologic

Transfusion of 1 U of packed red blood cells (PRBCs) was required in each of 4 dogs due to blood loss anemia following hemodialyzer filter clotting. Five units of PRBCs were required due to blood loss anemia following hemodialyzer filter clotting in 4 cats.

Blood pressure

Blood pressure readings were reported in 15 dogs during CRRT with hypotension developing in 2 dogs (Doppler SBP value of 53 and 56 mmHg). These dogs were previously normotensive (106 and 112 mmHg). One of these dogs died due to cardiorespiratory arrest at the time of documented hypotension. The hypotension resolved in the remaining dog and SBP stabilized between 112 and 152 mmHg without specific intervention. Blood pressure readings were reported in 12 cats during CRRT. One cat had been normotensive (SBP 120 mmHg) before CRRT and developed hypotension (SBP 65 mmHg) during CRRT. This cat died due to cardiorespiratory arrest at the time of documented hypotension.

Thermoregulation

Ten dogs experienced hypothermia (median 36.1 °C [97.0 °F], range 35.5–37.1 °C [96.0–98.7 °F]; reference interval 37.7–39.2 °C [100.0–102.5 °F]) during CRRT. Two dogs remained hypothermic during CRRT (35.5 and 36.1 °C [96.0 and 97.0 °F]) despite initiation of thermal support with active warming. Hypothermia resolved in the remaining dogs with thermal support measures. All 15 cats for which rectal temperature readings were reported experienced hypothermia (median 34.9 °C [94.9 °F], range 32.7–37.1 °C [90.9–98.9 °F]; reference interval 37.7–39.2 °C [100.0–102.5 °F]). Eight cats remained hypothermic during CRRT (median 35.5 °C [96.0 °F], range 33.0–36.7 °C [91.4–98.1 °F]) despite active warming. Hypothermia resolved in the remaining cats with thermal support.

Central nervous system

One dog exhibited CNS signs including twitching and vocalization during CRRT that responded to IV man-

nitol therapy. Three cats exhibited CNS signs during CRRT. The first cat developed nystagmus, head tremors, and facial fasciculations. Signs resolved with a single IV mannitol bolus. The second cat developed hyperexcitable behavior, twitching, and anxiety. Signs resolved spontaneously within 48 hours without specific intervention. The third cat presented with an 8-year history of seizures and developed progressive obtundation, convulsions, and became comatose and died following cardiorespiratory arrest despite resuscitation efforts. Review of the medical record did not identify the definitive cause of CNS signs in any of these patients. The drop in BUN from initiation of CRRT to the exact onset of neurologic signs was not able to be determined based on medical record review, but the average hourly urea reduction ratio (URR), defined as [(pre-dialysis BUN – post-dialysis BUN)/pre-dialysis BUN]/[time interval (h)] $\times$ 100%, was 6.1% in the dog (BUN decreased from 43.5 to 10.3 mmol/L [122–29 mg/dL] over 12.5 hours), 2.6% in the first cat (BUN decreased from 80.7 to 14.3 mmol/L [226–40 mg/dL] over 31.5 hours), 9.2% in the second cat (BUN decreased from 72.8 to 9.3 mmol/L [204–26 mg/dL] over 9.5 hours) and 4.8% in the third cat (BUN decreased from 57.8 to 12.1 mmol/L [162–34 mg/dL] over 16.5 hours).

ECC

A total of 9 hemodialyzer filters failed in 6 dogs due to clot formation. In 2 of these dogs, citrate infusion was inadvertently started over 2 minutes after CRRT was initiated. In all events of filter clotting in dogs, the peak ECC ionized calcium concentration exceeded the target range with a median of 0.80 mmol/L (3.21 mg/dL) (range 0.54–1.45 mmol/L [2.16–5.81 mg/dL]). A total of 9 filters failed due to clotting in 7 cats. In all events of filter clotting in cats, the peak ECC ionized calcium exceeded the target range with a median of 0.56 mmol/L (2.24 mg/dL) (range 0.45–0.81 mmol/L [1.80–3.24 mg/dL]). Four dogs experienced dialysis catheter clotting concurrent with filter clotting that necessitated replacement of the catheter.

Outcome and survival

Six of 17 (35%) dogs and 7 of 16 (44%) cats completed their CRRT session as planned. The remaining patients were discontinued from CRRT prematurely due to poor prognosis (1 cat), filter clotting with owners unwilling to restart CRRT (4 dogs and 2 cats), death (4 dogs and 4 cats) or humane euthanasia (3 dogs, and 2 cats). Median duration of CRRT in dogs was 16.3 hours (range 0.3–83.0 hours) and in cats was 11.5 hours (range 1.0–35.5 hours). The median duration of therapy from termination of CRRT to discharge in dogs was 2.7 days (range

1.8–7.0 days) and in cats was 3.0 days (range 0.56–4.1 days). Seven of 17 dogs (41%) survived to discharge, 6 of 17 (35%) died (4 during CRRT and 2 after), and 4 of 17 (24%) were euthanized (3 during CRRT and 1 after). Of the dogs that survived to discharge, all had azotemia at the time of discharge with median BUN of 26.8 mmol/L [75.0 mg/dL] (range 13.0–31.1 mmol/L [35.0–87.0 mg/dL]) and median creatinine of 433.2 mmol/L (4.9 mg/dL) (range 221.0–574.6 mmol/L [2.5–6.5 mg/dL]). At the time of recheck within 2 weeks after discharge, 3 dogs (43% of 7 surviving dogs, 18% of all study dogs) had BUN and creatinine values within the reported reference range while 4 (57% of 7 surviving dogs, 24% of all study dogs) remained azotemic. In the subpopulation of persistently azotemic dogs, median recheck BUN was 10.7 mmol/L (30.0 mg/dL) (range 2.5–72.8 mmol/L [7.0–204.0 mg/dL]) and median recheck creatinine was 389.0 mmol/L (4.4 mg/dL) (range 88.4–769.1 mmol/L [1.0–8.7 mg/dL]).

All 4 dogs that were azotemic at recheck had a previous history of CKD. Renal histopathology was performed in 3 of these dogs revealing evidence of moderate ($n = 1$) or severe ($n = 2$) chronic kidney disease (CKD) in addition to an acute insult. These dogs included those with pancreatitis ($n = 1$), pancreatitis with concurrent *Streptococcus* spp. urinary tract infection ($n = 1$), prednisone administration with concurrent radiation therapy ($n = 1$) and non steroidal anti-inflammatory drug administration with concurrent cisplatin chemotherapy ($n = 1$, renal biopsy declined). The dog in which biopsy was declined had historical biochemical and ultrasonographic evidence of CKD before CRRT. The 3 dogs that had complete resolution of azotemia included those with severe dog bite wounds and histopathologic diagnosis of acute tubular nephrosis due pigment nephropathy ($n = 1$), acute pancreatitis with histopathologic diagnosis of acute tubular necrosis ($n = 1$) and aspirin administration with concurrent dehydration due to field trial exercises ($n = 1$, renal biopsy declined).

Seven of 16 (44%) cats survived to discharge, 5 of 16 (31%) died (4 during CRRT and 1 after) and 4 of 16 (25%) were euthanized (2 during CRRT and 2 after). Of the 7 cats that survived to discharge, 2 had azotemia and 5 had BUN and creatinine values within the reported reference range at the time of discharge. Median BUN at discharge was 10.0 mmol/L (28.0 mg/dL) (range 5.4–35.7 mmol/L [15.0–100.0 mg/dL]) and median creatinine was 194.5 mmol/L [2.2 mg/dL] (range 123.8–707.2 mmol/L [1.4–8.0 mg/dL]). At the time of recheck 2–12 weeks after discharge, 1 cat had been euthanized without recheck labwork being performed, 5 cats had BUN and creatinine values within the reported reference range and 1 cat remained azotemic

with a BUN greater than the reference range of the analyzer (46.4 mmol/L [130 mg/dL]) and a creatinine of 468.5 mmol/L (5.3 mg/dL). The cats that had complete resolution of azotemia were those with presumed lily toxicity and histopathologic diagnosis of moderate acute tubular necrosis ($n = 1$) and urethral obstruction ($n = 4$, renal biopsy declined). The cat that remained persistently azotemic had no historical, biochemical, or ultrasonographic evidence of CKD before CRRT. Renal biopsy was declined and ARF of unknown etiology was diagnosed.

Select subpopulations were evaluated with respect to outcome. There was an 80% (4/5 cats) survival in the subpopulation of cats with prolonged urethral obstruction. None of the 4 surviving cats was azotemic on recheck evaluation. Survival was 20% (1/5 dogs) in the subpopulation of dogs with hospital-acquired ARF. The surviving dog (with pigment nephropathy, as reported above) demonstrated normal renal function on recheck evaluation. Survival was 100% (3/3 dogs) in the subpopulation of dogs that developed ARF or AOCRF concurrent with pancreatitis. One had normal renal values on recheck evaluation and 2 maintained levels of azotemia similar to those documented before their acute-on-chronic insult. When evaluating only patients with ARF (without evidence of pre-existing CKD), survival was 42% (5/12) in dogs and 67% (6/9) in cats. When evaluating only patients with pre-existing CKD (based on historical, biochemical, or ultrasonographic evidence of CKD before CRRT; or histopathologic evidence of CKD; or both), survival was 60% (3/5) in dogs and 14% (1/7) in cats.

Discussion

CRRT is becoming more popular in human ICUs as a means of providing renal replacement and in some geographic regions has replaced IHD as the method of choice for RRT in ARF.[9] Specific advantages of CRRT over IHD proposed in the human literature include improved hemodynamic tolerance due to slower ultrafiltration, improved fluid balance, ability to provide unlimited nutrition, and improved control of azotemia, electrolyte and acid-base derangements.[10] Despite these specific advantages, human prospective studies comparing outcome with IHD *versus* CRRT in ARF provide insufficient data to afford one modality a clear advantage over the other.[11–14] A summary of results of recent comparisons has been published.[10] Given the availability of CRRT equipment in veterinary medicine and reports of similar outcome with CRRT and IHD in human ARF patients, the current study aimed to investigate the application of CRRT in veterinary ICU patients with ARF and AOCRF.

The incidence of ARF in human medicine remains high at 1–25% of critically ill patients.[15] Recent increases in reported incidence may be attributed to the development of multi organ dysfunction in patients who previously would not have survived to develop this complication.[16] While the current study has provided information on the incidence of ARF and AOCRF in our ICU population, it is unknown whether an upward trend has occurred over time. Mortality for humans with ARF in the ICU is 30–70% despite the early and aggressive application of RRT.[16–17] While the veterinary literature lacks the same statistically powered conclusions as those in human medicine, several studies provide useful information regarding outcome in dogs and cats with renal failure. In a 2002 study of 80 dogs with ARF due to various etiologies that were treated with conventional management, survival was 20%.[x] In a 1989 study of 25 dogs with ARF or AOCRF that failed conventional management and required PD, survival was 24%.[18] When IHD was used from 1993 to 2003 in 124 dogs with ARF of various etiologies, all of which failed traditional management for ARF, an overall survival rate of 42% was observed.[y] When IHD was used in 119 cats with acute uremia of various etiologies, a 52% survival was achieved.[z] A proportion of surviving dogs and cats develop CKD following therapy for ARF but not all studies report this outcome variable. A summary of clinical studies detailing survival statistics in both dogs and cats with ARF has recently been published.[19]

Overall survival rates in our population are similar to previous reports of patients with similar population characteristics requiring dialytic therapy by PD or IHD. The subpopulation of cats with urethral obstruction showed an 80% survival in our study, which is similar to previously reported survival rate of 75% in 44 cats with an obstructive etiology of acute azotemia.[z] Hospital-acquired ARF carried a 20% survival rate in our study, which contained only 5 dogs in this subpopulation. A 1996 study of 29 dogs with hospital-acquired ARF reported a survival rate of 38%.[20] While only 1 cat in the present study developed newly documented CKD, the preservation of renal function in the patients with ARF is encouraging.

Figures 1 through 4 illustrate the gradual reduction in BUN and creatinine during CRRT with resolution of azotemia in patients that were dialyzed for a sufficient duration. The reported post-CRRT BUN and creatinine values include data for patients that were discontinued from CRRT before achieving criteria for therapy termination. These values, therefore, do not reflect the full potential for CRRT to control azotemia.

Each of the complications reported in the present study has been described with human CRRT.[21] Early

filter clotting, patient death, or owner decision to prematurely terminate CRRT or euthanize the pet contributed to inadequate duration of CRRT to completely resolve azotemia. Development of a consistent patient and owner selection process and a protocol that minimizes complications may reduce the frequency of early termination of therapy and may allow the full benefits of properly executed CRRT to be evaluated.

Complications related to dialysate prescription warrant modification of the current protocol. The protocol utilized in the majority of cases used a dialysate with a relatively low potassium concentration (2.0 mEq/L). Hypokalemia was a frequent complication in the current population, occurring in 71% of dogs and 47% of cats that had intra-dialytic potassium values reported. A dialysate with a higher potassium concentration or additional supplementation should be employed in normokalemic or hypokalemic patients to help prevent this complication.

The rapid decrease in sodium in the cat with chronic hypernatremia and CNS signs indicated that CRRT has the potential to exceed the commonly accepted safe sodium correction rate of 0.5 mEq/L/hr if the dialysate sodium concentration is not tailored to the individual patient. Although it is unclear whether the drop in sodium with CRRT was the cause of death in this patient, a dialysate containing a higher sodium content may have prevented this complication. The development of hypernatremia in 3 cats was also noted in the study and was not explained by review of the medical records. Because a hypernatric dialysate, medication, or supplemental fluid was not administered to any of these cats, free water loss was suspected although was not documented in the medical record. Hypernatremia has been reported with ARF, CKD, and the administration of osmotic diuretics.[22] An osmotic diuretic was administered in all 3 of the affected cats. Urine electrolyte measurement may have been useful in explaining the hypernatremia but was not performed.

Metabolic acidosis resolved in a large number of affected patients (80% of dogs and 71% of cats) with CRRT. An increase in the duration of CRRT is expected to gradually resolve the acidosis in the remaining patients, similar to the gradual reduction in BUN and creatinine over time. In our study, supplemental bicarbonate appeared to increase the risk for development of metabolic alkalosis. An increase in dialysate bicarbonate concentration beyond standard recommendations appears to be warranted only if a lack of acidosis improvement is noted over time.

Hypercalcemia is a well-described complication of RCA in human CRRT.[23] The ratio between total calcium and ionized calcium is termed 'citrate gap.' As citrate is infused into the ECC, it binds to ionized calcium and sequesters it, rendering it unable to support coagulation of the extracorporeal blood. The citrate-ionized calcium complexes then enter the patient's bloodstream along with the calcium replacement delivered to the patient to maintain patient ionized calcium concentration. The result is patient ionized hypocalcemia with a concurrently elevated total patient calcium (measured as both citrate-bound and free ionized calcium). As the citrate is metabolized over time to bicarbonate by the liver, the bound ionized calcium is released and the total hypercalcemia resolves but metabolic alkalosis may develop. The metabolic alkalosis observed in the current study was not severe in any case and resolved following discontinuation of CRRT. Utilization of a lower citrate flow rate, or a dialysate with a lower concentration of bicarbonate, or both, may reduce the frequency of this complication. A non-citrate anticoagulant protocol may prevent this complication altogether.

Heparin-based protocols entirely avoid this complication as well as the potential complication of perivascular necrosis following accidental extravasation of calcium chloride. Concerns for necrosis may be severe enough in some cases to warrant the use of calcium gluconate instead of calcium chloride in RCA protocols in veterinary medicine. Heparin-based protocols have been utilized extensively in veterinary IHD[3] and are being utilized currently in CRRT protocols at other facilities. The main complication encountered with heparin-based protocols is the increased risk of bleeding associated with the systemic anticoagulation.[23] There is not enough evidence available even in the human literature to afford 1 protocol a clear advantage over the other; however, RCA leads to decreased bleeding events than heparin-based anticoagulation protocols in patients with bleeding tendencies.[23] Complications related to the anticoagulant protocol used included clinical hypocalcemia, total hypercalcemia, metabolic alkalosis, and filter clotting, all of which are described in the human literature.[23] Human RCA protocols dictate specific adjustment of the sodium citrate and calcium replacement rate based on serial evaluations of patient and ECC ionized calcium concentrations. Adjustment of CRRT prescriptions made in the present study were guided by serial ionized calcium values but were not protocol based. The excessively high ionized ECC calcium is the most likely factor contributing to filter clotting. The excessively low patient ionized calcium led to frequent clinical hypocalcemia. There is clearly a need for protocol-based adjustment of these rates to maintain these values within the target range and therefore reduce these complication rates.

The low frequency of hypotension observed in the current study may be related to the relatively slow rate of fluid removal and solute shifts utilized during CRRT.

Although not utilized in the present study, the administration of colloid solutions to prime the ECC may help to prevent initial drops in SBP. Although the cause of death was unclear in 2 hypotensive patients that died during CRRT, hypotension likely played a significant role. The pre-emptive use of colloid solutions during ECC priming and a standardized protocol incorporating the use of central venous pressure measurements and pressor agent administration during CRRT may have prevented this complication.

Significant hypothermia during CRRT was prolonged despite active warming techniques. Results suggest that pre-emptive heat support may be warranted to help prevent this complication. The dialysis machine utilized during this study did not have an active warming mechanism, although active warming is available on most currently available machines. The addition of approximately 50 mL to the ECC renders this option unfeasible in cats or small dogs, but this device may be considered for larger patients. Passive IV fluid bag warming covers and active circulating warm air IV line warmers are available for additional warming but were not utilized.

When anticoagulation of the ECC fails and filter clotting occurs, the blood within the entire ECC must be discarded. This contributes to the development of blood loss anemia. The frequency of blood transfusions related to filter clotting in the present study suggests that additional strategies must be developed to further prolong filter life. ECC ionized calcium values associated with clotted filters were excessive and improvements in the RCA protocol must be made to better maintain the ionized calcium value within the target range. In addition, an increased pre-filter replacement fluid rate (to dilute blood before reaching the filter) or a change to a heparin-based or other anticoagulant protocol may prolong filter life. If increased citrate is utilized, increased calcium replacement may be required to prevent clinical hypocalcemia and the bicarbonate concentration of the dialysate must be modified to help minimize the risk of metabolic alkalosis.

The CNS signs observed in our study may have been due to ionized hypocalcemia, cerebral infarct, cerebral vasospasm, cerebral hypoxia, systemic hypertension, intracranial hemorrhage, or dialysis disequilibrium syndrome (DDS), along with other less likely possibilities. DDS has been described in detail and is believed to occur as a result of an excessively rapid lowering of solutes (most importantly urea) from the extracellular fluid relative to the intracellular space.[24] This results in a fluid shift into the intracellular compartment and cerebral edema, which may cause CNS signs. The URR is used as a measure of the efficiency of the dialysis session in IHD and corresponds to the change in BUN over

the entire session divided by the pre-IHD BUN. While the standard recommendation for human IHD is a URR of >70% for CKD patients,[25] shorter or less efficient sessions are utilized in patients with severe azotemia to help prevent the development of DDS by limiting solute shifts. In veterinary IHD, URRs of up to 85% or greater are common in CRF patients but may lead to DDS in patients with severe azotemia.[26] In patients with BUN values >53.6 mmol/L [150 mg/dL], it has been recommended that the URR of the IHD session be limited to 25–40%[27] or 30–50%.[28] An alternative recommendation in humans is to target a URR no >10% in patients weighing <10 kg with BUN values >89.3 mmol/L [250 mg/dL].[29] Because of a much lower solute reduction rate with CRRT than with IHD, there are no similar guidelines for human CRRT, and DDS has never been reported in CRRT in critically ill humans.[29] Based on this information, it is very unlikely that the CNS signs in the dog and 3 cats reported here were due to DDS. Coagulopathy causing intracranial hemorrhage is rarely reported in humans with RCA and is therefore also an unlikely cause of the CNS signs in our patients. Imaging of the brain was not performed in the present study but would be required to reach a definitive diagnosis. The improvement in some patients following mannitol therapy does not rule out nor confirm any of the differential diagnoses that were under consideration.

In the current study, each individual patient received CRRT following failure to respond to aggressive traditional management. These patients represent a subpopulation of patients with severe renal injury. In many cases, CRRT was delayed for hours to many days after the diagnosis of ARF or AOCRF due to owner or clinician preference and thus may represent poor candidates for CRRT. The incidence of induction of CKD was 6% in cats in the present study while no dogs developed CKD. Numerous human publications have shown that earlier intervention with RRT yields improved survival, and some publications report decreased progression to CKD with earlier intervention.[30] In light of these findings, it does not seem prudent to delay initiation of RRT until the global consequences of uremia further compromise patient stability and lead to multiorgan injury. The Acute Dialysis Quality Initiative has established a recommended definition for ARF in humans in efforts to help guide the timing of initiation of RRT.[31] Perhaps a paradigm shift in veterinary medicine, using human outcome data as a surrogate for large veterinary studies that are currently lacking, may allow us to intervene earlier and assess whether an improved outcome can be achieved using earlier intervention. While the use of CRRT in 4.66% canine admissions and 6.75% of feline admissions with ARF or AOCRF may be

considered excessive or unwarranted, this value would be considered inappropriately low compared with human guidelines for initiation of RRT.[30]

One limitation of the present study is its small patient population that prevented trends in outcome from being powered for statistical significance. Larger studies will be required to define variables that may independently affect outcome. While the study population is considered a suitable cross-section of our ICU patient population, it may differ significantly from populations in non-specialty practices and in other geographic or socioeconomic regions and results must be interpreted accordingly. Given the retrospective nature of the study, the incompleteness of medical records prevented evaluation of certain parameters that may have influenced outcome, such as UOP and total dose of dialysis delivered. In future well-designed prospective clinical studies, these parameters and others thought to potentially influence outcome may be critically evaluated. In addition, several potential benefits of CRRT proposed in the human literature were not explored in the present study but may be critically evaluated. These include, but are not limited to, removal of dialyzable drugs or ingested toxins and clearance of mediators of sepsis and molecules contributing to encephalopathy in hepatic failure.[6,7]

The results of the present study have provided information on the safety and utility of CRRT in dogs and cats with ARF and AOCRF in the ICU. The incidence of the numerous reported complications may be reduced with improved protocols and improved experience with this technology, as has been observed over time with human CRRT. The optimum CRRT prescription for veterinary patients with ARF or AOCRF remains unclear, just as the optimum prescription for IHD in ARF was unclear <2 decades ago before extensive work by the pioneers of veterinary hemodialysis. The details of the cases presented here provide a starting point from which further research into CRRT may be developed. Improved protocols that reduce the complication rate must be evaluated before CRRT can be recommended for widespread use.

Acknowledgements

Footnotes

a Park J, Youn H, Park S, Hwang C. Application of continuous renal replacement therapy (CRRT) for acute renal failure in dogs (abstract). *J Vet Intern Med* 2006;20:787.
b HemoCath, MedComp Inc., Harleysville, PA.
c Super Core Biopsy Needle, Jorgensen Laboratories Inc., Loveland, CO.
d Cobe Prisma, Gambro Renal Care Products Inc., Lakewood, CO.
e Prisma M10 PRE Set, M60 PRE Set and M100 PRE Set, Hospira Inc.
f 0.9% Sodium chloride, Hospira Inc.
g Plasmalyte-A, Travenol Laboratories, Deerfield, IL.
h PrismaSate BK2/0, Gambro Renal Products, Daytona Beach, FL.
i Anticoagulant sodium citrate solution, Baxter Healthcare Corporation, Fenwal Division, Deerfield, IL.
j 10% calcium chloride, American Pharmaceutical Partners Inc., Los Angeles, CA.
k Normosol-R, CEVA Laboratories, Overland Park, KA.
l The Children's Hospital of Alabama, Division of Pediatric Nephrology and Transplantation, Pediatric Hemodiafiltration Order Sheet.
m Stat Profile Critical Care Xpres, NOVA Biomedical, Waltham, MA.
n I-Stat Portable Clinical Analyzer, I-Stat Corp., East Windsor, NJ.
o Tempcare Veterinary Fluid Warmer, Elltec Co. Ltd, Nagoya, Japan.
p ICU Model 200H, Snyder Mfg. Company, Centennial, CO.
q Bair Hugger Model 550, Arizant Healthcare, Eden Prairie, MN.
r Doppler Ultrasonic Flow Detector Model 811-B, Parks Medical Electronics, Aloha, OR.
s Potassium chloride, Phoenix Pharmaceutical Inc., St. Joseph MO.
t Dextrose 50% solution, Phoenix Pharmaceutical Inc.
u Mannitol 20%, Phoenix Pharmaceutical Inc.
v 5% Dextrose in Water, Hospira Inc.
w Calcium gluconate, Abraxis Pharmaceutical Products, Schaumburg, IL.
x Forrester SD, McMillan NS, Ward DL. Retrospective evaluation of acute renal failure in dogs (abstract). *J Vet Intern Med* 2002;16:354.
y Francey T, Cowgill LD. Use of hemodialysis for the management of ARF in the dog: 124 cases (1990–2001) (abstract). *J Vet Intern Med* 2002;16:352.
z Pantaleo V, Francey T, Fischer JR, Cowgill LD. Application of hemodialysis for the management of acute uremia in cats: 119 cases (1993–2003) (abstract). *J Vet Intern Med* 2004;18:418.

References

1. Cowgill LD, Francey T. Acute uremia, In: Ettinger SJ, Feldman EC. eds. Textbook of Veterinary Internal Medicine, Vol. 2, 6th edn. St. Louis, MO: Elsevier Inc.; 2005, pp. 1731–1751.
2. Labato MA, Ross LA. Peritoneal dialysis, In: DiBartola SP. ed. Fluid, Electrolyte, and Acid-Base Disorders in Small Animal Practice, 3rd edn. St. Louis, MO: Elsevier Inc.; 2006, pp. 635–649.
3. Cowgill LD, Francey T. Hemodialysis, In: DiBartola SP. ed. Fluid, Electrolyte, and Acid–Base Disorders in Small Animal Practice, 3rd edn. St. Louis, MO: Elsevier Inc.; 2006, pp. 650–677.
4. Landerville AJ, Seshadri R. Utilization of continuous renal replacement therapy in a case of feline acute renal failure. J Vet Emerg Crit Care 2004; 14(4):278–286.
5. Bellomo R, Ronco C, Mehta RL. Nomenclature for continuous renal replacement therapies. Am J Kidney Dis 1996; 28(5, Suppl. 3):S2–S7.
6. Dirkes S, Hodge K. Continuous renal replacement therapy in the adult intensive care unit – History and current trends. Crit Care Nurse 2007; 27(2):61–80.
7. Meyer MM. Renal replacement therapies. Crit Care Clin 2000; 16(1):29–56.
8. Ronco C, Bellomo R, Wratten ML, et al. Future technology for continuous renal replacement therapies. Am J Kidney Dis 1996; 28(5, Suppl. 3):S121–S129.
9. Uchino. The epidemiology of acute renal failure in the world. Curr Opin Crit Care 2006; 12:538–543.
10. Chanchairujira T, Mehta RL. Continuous dialysis therapeutic techniques, In: Henrich WL. ed. Principles and Practice of Dialysis. Philadelphia, PA: Lippincott Williams & Wilkins; 2004, pp. 162–180.
11. Swartz RD, Messana JM, Orzol S, et al. Comparing continuous hemofiltration with hemodialysis in patients with severe acute renal failure. Am J Kidney Dis 1999; 34:424–432.
12. Jakob SM, Frey FJ, Uehlinger DE. Does continuous renal replacement therapy favorably influence the outcome of patients? Nephrol Dial Transpl 1996; 11:1250–1255.
13. Mehta RL, McDonald B, Gabbai FB, et al. A randomized clinical trial of continuous versus intermittent dialysis for acute renal failure. Kidney Int 2001; 60:1154–1163.

14. Kellum JA, Angus DC, Johnson JP, et al. Continuous versus intermittent renal replacement therapy: a meta-analysis. Intensive Care Med 2002; 28:29–37.

15. Bellomo R. Defining, quantifying, and classifying acute renal failure. Crit Care Clin 2005; 21:223–237.

16. Manns M, Sigler MH, Teehan BP. Continuous renal replacement therapies: an update. Am J Kidney Dis 1998; 32(2):185–207.

17. Kierdorf HP, Seiberth HG. Continuous renal replacement therapies versus intermittent hemodialysis in acute renal failure: what do we know? Am J Kidney Dis 1996; 28(5, Suppl. 3):S90–S96.

18. Crisp MS, Chew DJ, DiBartola SP, et al. Peritoneal dialysis in dogs and cats: 27 cases (1976–1987). J Am Vet Med Assoc 1989; 195:1262–1266.

19. Francey T. Outcome of dogs and cats treated with hemodialysis, In: Langston C. ed. Proceedings of Advanced Renal Therapies Symposium. New York, NY: Animal Medical Center; 2006, CD-ROM.

20. Behrend EN, Grauer GF, Mani I, et al. Hospital-acquired acute renal failure in dogs: 29 cases (1983–1992). J Am Vet Med Assoc 1996; 208(4):537–541.

21. Ronco C, Bellomo R. Complications with continuous renal replacement therapy. Am J Kidney Dis 1996; 28(5, Suppl. 3):S100–S104.

22. Dibartola SP. Disorders of Sodium and Water: hypernatremia and hyponatremia, In: DiBartola SP. ed. Fluid, Electrolyte, and Acid–Base Disorders in Small Animal Practice, 3rd edn. St. Louis, MO: Elsevier Inc.; 2006, pp. 47–79.

23. Davenport A. Problems with anticoagulation for continuous renal replacement therapies, In: Lameire N, Mehta R. eds. Complications of Dialysis. New York, NY: Marcel Dekker Inc.; 2000, pp. 215–268.

24. Nissenson AR, Fine RN. Clinical Dialysis, 4th edn. New York, NY: McGraw-Hill Medical Publishing Division; 2005, pp. 253–254.

25. National Kidney Foundation. KDOQI Clinical practice guidelines for hemodialysis adequacy, Update 2006. Am J Kidney Dis 2006; 48(S1):S2–S90.

26. Cowgill LD, Langston CE. Role of hemodialysis in the management of dogs and cats with renal failure. Vet Clin Small Anim 1996; 26:1347–1378.

27. Cowgill LD. Blood purification: application of hemodialysis and hemoperfusion in uremic animals, In: Otto C. ed. Proceedings of ACVECC Postgraduate Course 2002: The Critical Kidney. San Antonio, TX: ACVECC; 2002, p. 40.

28. Fischer JR, Pantaleo V, Francey T, et al. Veterinary hemodialysis: advances in management and technology. Vet Clin Small Anim 2004; 34:935–967.

29. Bagshaw SM, Peets AD, Hameed M, et al. Dialysis disequilibrium syndrome: brain death following hemodialysis for metabolic acidosis and acute renal failure – A case report. BMC Nephrol 2004; 5:9.

30. Palevsky PM. Renal replacement therapy I: indications and timing. Crit Care Clin 2005; 21:347–355.

31. Bellomo R, Ronco C, Kellum JA, et al. Acute renal failure – definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care 2004; 8(4):R204–R212.