J Vet Intern Med 2011;25:446–452

Factors Associated with Adverse Outcomes during parenteral Nutrition Administration in Dogs and Cats

Y. Queau, J.A. Larsen, P.H. Kass, G.S. Glucksman, and A.J. Fascetti

Background: Parenteral nutrition (PN) is increasingly used to support hospitalized dogs and cats. Published assessments of outcome are limited.

Objective: Evaluate type and prevalence of complications and risk factors for death and complications in dogs and cats receiving PN.

Animals: Three hundred and nineteen dogs and 112 cats that received PN at a teaching hospital between 2000 and 2008.

Methods: Retrospective case review. Diagnosis, duration of PN administration, concurrent enteral feeding, death, and mechanical, septic, and metabolic complications were abstracted from medical records. Association of each parameter with complications and death was analyzed by binary logistic regression.

Results: Pancreatitis was the most common diagnosis (109/319 dogs, 34/112 cats), and 137/319 dogs and 51/112 cats died. Dogs and cats received 113 ± 40% and 103 ± 32% of resting energy requirement, respectively. Mechanical (81/319 dogs, 16/112 cats) and septic (20/319 dogs, 6/112 cats) complications were not associated with death ($P > .05$). Hyperglycemia was the most common metabolic complication (96/158 dogs, 31/37 cats). Hypercreatininemia in dogs (8/79) was the only complication associated with death ($P < .01$). Chronic kidney disease in dogs, hepatic lipidosis in cats, and longer duration of inadequate caloric intake before PN in both species were negatively associated with survival ($P < .05$). Factors positively associated with survival included longer duration of PN administration in both species, enteral feeding in cats with any disease, and enteral feeding in dogs with respiratory disease ($P < .05$).

Conclusions and Clinical Importance: PN can be effectively used to provide the energy requirements of most critically ill dogs and cats. Most complications accompanying PN administration do not affect survival.

Key words: Critical care; Hyperglycemia; Intravenous feeding; Retrospective.

Parenteral nutrition (PN) is indicated for dogs and cats unable to consume or tolerate adequate amounts of enteral nutrients for a prolonged period of time. PN is typically a mixture of a fat emulsion, dextrose, and amino acid solutions. Electrolytes, B vitamins, and trace minerals are sometimes added. Solutions are usually administered initially at a fraction of the goal rate and gradually increased based on the animal's response, although this is variable among clinicians. PN has historically been referred to as total (TPN) when covering 100% of the nutrient and calorie needs, and as partial when providing only a fraction of requirements.[1] In small animals, PN solutions are rarely formulated to provide all essential nutrients. PN is delivered into a central vein (central parenteral nutrition [CPN]) or a peripheral vein (peripheral parenteral nutrition [PPN]); therefore the currently recommended terms are CPN and PPN.[2] The osmolarity of PPN admixtures is usually modified by diluting the solution with sterile water or decreasing the amount of dextrose in order to prevent thrombophlebitis. In most cases, this also lowers the caloric density of these solutions.

Abbreviations:

CPN	central parenteral nutrition
ME	metabolizable energy
OR	odds ratio
PN	parenteral nutrition
PPN	peripheral parenteral nutrition
RBC	red blood cells
RER	resting energy requirement

Although the benefit of PN in human patients is controversial and current guidelines favor enteral nutrition when possible,[3] PN decreases the risk of death when early enteral nutrition cannot be initiated[4] and might have benefits in specific conditions.[5] Limited data assessing the use of PN in hospitalized dogs and cats are available.[6–10] In these studies, PN was associated with various metabolic changes, including hyperglycemia, which was the most common, followed by electrolyte disturbances and hyperlipidemia. Mechanical and septic complications occurred less frequently but interfered with PN delivery. Based on these studies, PN is considered relatively safe to use in small animals, and recommendations have been made for monitoring of potential complications and intervention.[1,11] However, methods of PN administration varied across studies as well as complication categorization and incidence.

The objectives of this study were to evaluate the complication types and incidences occurring in a large number of dogs and cats during PN administration and

From the William R. Pritchard Veterinary Medical Teaching Hospital (Queau, Glucksman), Department of Molecular Biosciences (Larsen, Fascetti), and the Department of Population Health and Reproduction (Kass), School of Veterinary Medicine, University of California, Davis, CA. This study was done at the Veterinary Medical Teaching Hospital, School of Veterinary Medicine, University of California, Davis, CA.

Corresponding author: Andrea J. Fascetti, VMD, PhD, DACVIM, DACVN, Department of Molecular Biosciences, School of Veterinary Medicine, University of California, Davis, CA 95616; e-mail: ajfascetti@ucdavis.edu

Submitted August 9, 2010; Revised February 1, 2011; Accepted February 16, 2011.

10.1111/j.1939-1676.2011.0714.x

to determine the associations of animal and PN variables with mechanical, septic, and metabolic complications and hospital outcome (discharge or death including euthanasia). Changes in nutritional management and occurrence of complications within the period of time studied were also analyzed. We hypothesized that PN can be used effectively to deliver the energy requirement of critically ill animals without increased risk of death, and that complications associated with its delivery decreased with experience gained over the 9-year study period.

Materials and Methods

Data Collection

The database of the William R. Pritchard Veterinary Medical Teaching Hospital (VMTH) was used to identify dogs and cats that received PN for at least 12 hours between January 1, 2000 and December 31, 2008. When an animal received PN at 2 different visits, only the 1st occurrence was included.

All medical records were reviewed by a single clinician (Y.Q.). Signalment (age, sex, and breed) was retrieved, and diagnoses reported by the primary clinicians in the medical records were retrospectively categorized as follows: acute kidney injury, chronic kidney disease, pancreatitis, esophagitis, gastroenteritis, hepatopathy, hepatic lipidosis (cats only), diabetes mellitus or keto-acidosis, cardiovascular disease, respiratory disease, neurologic disease, oncologic disease (regardless of the organ system affected) and other (including trauma, skin disease, etc.). Body weight and body condition score[12,13] at presentation and during the first 96 hours of PN administration were recorded. When available, objective weight history was recorded. The durations of anorexia and inadequate caloric intake for the periods before admission and during hospitalization were retrieved. Intake was deemed inadequate when decreased appetite and vomiting were documented.

The following data related to PN administration were recorded: PN type (CPN, PPN), catheter type and location, time between admission and PN initiation, durations of PN administration and hospitalization, time to increase PN to goal rate, characteristics of the PN formula (energy distribution among protein, fat, and carbohydrate, caloric density, potassium content), calories provided by PN at goal rate (expressed as a percentage of the resting energy requirement [%RER]), and concurrent intravenous administration of fluids. All PN formulas included 20% lipid emulsification,[a] 8.5% amino acid solution,[b,c] 50% dextrose,[d] B-vitamin complex,[e] and sometimes potassium chloride[f] or potassium phosphate.[g] For CPN, 7 standard formulas with predetermined caloric distributions were available to the clinicians (4 formulas for dogs and 3 formulas for cats), and provided either maintenance or restricted amounts of amino acids. In these standard formulas, protein ranged from 7 to 18% metabolizable energy (ME) in dogs and 13 to 23% ME in cats, fat ranged from 42 to 54% ME in dogs and 38 to 54% ME in cats, and carbohydrate ranged from 28 to 48% ME in dogs and 23 to 45% ME in cats. Potassium concentration ranged from 0 to 39.4 mEq/L. The PN composition was customized for all PPN cases or for animals receiving CPN when one of the standard formulas was not appropriate. Concurrent voluntary or assisted enteral feeding during the first 96 hours of PN administration was recorded.

Complications that developed during PN administration were classified as mechanical, septic, or metabolic. Mechanical complications referred to catheter dislodgement or occlusion, leakage or damage of administration lines, and equipment failures necessitating temporary or definitive disruption of PN. Septic complications were characterized by catheter site inflammation in animals with fever or neutrophilia unrelated to the primary disease, or by positive bacterial culture of the catheter or blood. Metabolic complications were defined as biochemical or hematologic variables that were low or normal before PN administration and subsequently became higher than normal at least once during the first 96 hours of PN administration (complication classified as "hyper"), or as variables that were high or normal at PN initiation and subsequently became lower than normal (complication classified as "hypo"). Values were classified as normal, hyper, or hypo relative to the VMTH laboratory reference ranges. Data from animals that received hemodialysis during PN administration were excluded.

The serum concentrations of the following variables were recorded before PN administration and at 24, 48, and 96 hours after PN initiation: glucose, urea, creatinine, albumin, total and ionized calcium, phosphorus, sodium, potassium, chloride, bicarbonate, and triglycerides. Serum glucose concentration was also recorded at 12 hours after PN initiation when available. Glucose concentrations were determined either by automated chemistry analyzers or by portable glucose meters. For all other parameters, there were insufficient data for analysis. The occurrence of gross serum lipemia and the use of insulin during PN administration were noted. Hematocrit, red blood cells (RBC), white blood cells, neutrophil, lymphocyte, and platelet counts were recorded at similar time points as for biochemical variables. When the maximal rate for PN administration was reached, the relative change (expressed as a %) of each variable compared with its value before PN initiation was calculated. Outcome (discharge or death including euthanasia) was recorded.

Statistical Analyses

Microsoft Excel[h] was used for descriptive statistics (mean, median, standard deviation, incidence proportions). The denominators used to calculate proportions corresponded to the number of animals for which the data were available, and differed for each variable. The Shapiro-Wilk test was used to analyze continuous data for normality. Unless specified otherwise, the continuous data are presented as mean $\pm$ SD.

Comparisons in continuous measures between 2 groups were made with either a Student's *t*-test or a Wilcoxon-Mann-Whitney test. A paired *t*-test was used to compare changes in continuous dependent variables within individuals over 2 time points. Chi-square tests of homogeneity were used to compare the distribution of categorical dependent variables between groups. Logistic regression was used to compare the odds of binary outcomes (hospital outcome, occurrence of a given complication) as a function of antecedent potential risk factors. Results are reported as odds ratios (OR) and 95% confidence intervals (95% CI). The effect of time (year) was assessed by linear regression for continuous variables and logistic regression for binary outcome variables. *P*-values $<.05$ were considered significant.

Results

Population

Three hundred and nineteen dogs and 112 cats were included in the study (Table 1). Seventy-nine percent of dogs and 75% of cats were diagnosed with more than 1 disease (Table 1). Mixed breed dogs were the most represented (20%), followed by Labrador Retrievers (8%), Dachshunds (6%), and Golden Retrievers (6%). Domestic Shorthaired cats were the most common (65%), followed by Domestic Longhaired cats (15%), Domestic Mediumhaired cats (7%), and Siamese (7%). Other breeds each accounted for $<5\%$ of the population. Weight loss was documented by objective weight history

Table 1. Characteristics of the population receiving PN.

	Dogs (n = 319)	Cats (n = 112)
Age (years; mean ± SD)	7.9 ± 4.14	9.7 ± 4.40
Sex (n; Male, Female)	M = 162, F = 157	M = 65, F = 47
Weight (kg; mean ± SD)	18.8 ± 13.73	4.9 ± 1.62
BCS (median [range])	5 [1–9]	5 [1–9]
Most common diagnoses		
Pancreatitis	109 (34%)	34 (30%)
Gastroenteritis	87 (27%)	25 (22%)
Hepatopathy[a]	60 (18%)	26 (23%)
Hepatic lipidosis	0 (0%)	21 (19%)
Acute kidney injury	80 (25%)	12 (11%)
Chronic kidney disease	35 (11%)	13 (12%)
Respiratory disease	106 (33%)	18 (16%)
Cardiovascular disease	54 (17%)	13 (12%)
Neurologic disease	34 (11%)	13 (12%)
Oncologic disease	41 (13%)	15 (13%)
Diabetes mellitus[b]	17 (5%)	12 (11%)

BCS, body condition score.
[a]Except hepatic lipidosis.
[b]Includes animals with keto-acidosis.

in 52/319 dogs (16%) and 16/112 cats (14%). The durations of inadequate intake and anorexia before PN are reported in Table 2.

PN Parameters

Duration of hospitalization, PN administration and hospitalization before PN initiation, and time needed to reach maximal infusion rate are reported (Table 2). Catheter information was not available for 11 dogs. Jugular catheters were the most commonly used (225/308 dogs, and 98/112 cats), followed by centrally placed saphenous catheters (80/308 dogs and 14/112 cats). Cephalic and femoral veins were uncommonly used in dogs (2/308 and 1/308, respectively), and not used in cats. Triple lumen catheters were predominant in both species (285/305 dogs and 97/110 cats). Other types of catheters used were single (11 dogs and 6 cats), double (3 dogs and 7 cats), and quadruple lumen (6 dogs and 0 cats).

A majority of animals (276/319 dogs [87] and 101/112 cats [90]) received one of the standard CPN solutions, with 27% of dogs and 4% of cats receiving a protein restricted formula (Table 3). The remainder received customized CPN or PPN formulas. The majority of animals (253/312 dogs [81%]; 66/105 cats [63%]) received at least their RER. In both species, the amount of energy provided by PN decreased during the 9-year study period ($P < .001$). Weight decreased slightly after 96 hours of PN administration ($-0.2 \pm 6.8\%$ in 130 dogs and $-0.9 \pm 10.3\%$ in 64 cats), which was significant in dogs ($P < .05$) but not cats.

In 125/319 dogs (39%) and 54/110 cats (49%), concurrent enteral feeding was initiated or continued during the first 96 hours of PN administration. It could not be confirmed in 2 cats. In both species, this proportion increased during the 9-year study period ($P < .05$). Oral caloric intake was not consistently quantified in the medical records.

Three hundred and four out of 319 dogs (95%) and 105/112 cats (94%) received concomitant intravenous administration of fluids. Among those, 280/304 dogs received crystalloids and 58/304 received colloids (with 45 receiving both types of fluids). Likewise, 104/105 cats received crystalloids and 10/105 received colloids (with 9 receiving both).

Complications

Mechanical complications occurred in 81/319 dogs (25%) and 16/112 cats (14%) at median times of 48 and 68 hours after PN initiation, respectively. In dogs only, there was a higher risk of mechanical complication when a saphenous catheter was used to deliver PN compared with a jugular catheter (OR 2.69 [1.50–4.81]; $P < .001$). Septic complications occurred in 20/319 dogs (6%) and 6/112 cats (5%) at median times of 72 and 67 hours, respectively. Dogs had a higher risk of developing a septic complication when receiving PPN compared with CPN (OR 5.89 [1.24–22.53]; $P < .05$). Blood or catheter tips were cultured in 13/20 dogs, with positive results in 6 dogs, revealing the following microorganisms: *Escherichia coli* (3), *Serratia marcescens* (3), *Staphylococcus intermedius* (1), and *Pseudomonas aeruginosa* (1). For 2 of the dogs, 2 organisms were identified. Likewise, cultures were submitted in 3/6 cats and positive in 2: *Enteroccocus faecalis* was isolated from 1 catheter culture and *Pasteurella multocida* from 1 blood culture. The remaining animals developed a fever with local inflammation at the site of the catheter, a leukocytosis with left shift or both that were not attributed to another cause. The incidence rates of mechanical and septic complications did not change during the 9-year study period in dogs ($P = .58$ and .14, respectively) or in cats ($P = .79$ and .71, respectively).

Table 2. Duration (hours) of variables related to PN administration in dogs (n = 319) and cats (n = 112).

	Dogs			Cats		
Duration (hours) of	Mean ± SD	Median	Range	Mean ± SD	Median	Range
Hospitalization	247 ± 159.3	214	32–1096	194 ± 118.3	173	23–599
Hospitalization before PN	83 ± 82.4	72	0–984	58 ± 51.2	48	3–240
Inadequate caloric intake before PN	164 ± 124.6	144	0–972	183 ± 165.5	120	20–720
Anorexia before PN	100 ± 87.3	84	0–672	92 ± 108.5	72	0–720
PN administration before reaching PN goal rate	16 ± 13.0	12	0–86	18 ± 15.2	13	0–69
PN administration	107 ± 82.1	93	3–548	96 ± 79.1	80	14–429

Table 3. Distribution of PN categories and energy provided.

	Dogs (n = 319)		Cats (n = 112)	
	CPN	PPN	CPN	PPN
n (%)	303 (95)	16 (5)	107 (96)	5 (4)
Caloric density (kcal/mL)	1.13 ± 0.15	0.74 ± 0.27*	0.96 ± 0.10	0.62 ± 0.06*
Energy provided at goal rate (% RER)	115 ± 40	73 ± 32*	103 ± 34	84 ± 24

Results are expressed as mean ± SD.
*Value significantly different from CPN ($P < .05$).

All cats and 315/319 dogs (99%) had at least 1 abnormal serum biochemical value before PN administration (Table 4). For the animals that were hyperglycemic before PN initiation, serum glucose concentrations were 144 ± 35.9 and 179 ± 33.9 mg/dL for dogs and cats, respectively. Among nondiabetic animals that were normo or hypoglycemic before PN, 96/158 dogs (61%) and 31/37 cats (84%) developed hyperglycemia during the first 96 hours of PN administration. Serum glucose concentration was 146 ± 32.6 mg/dL in dogs and 213 ± 69.8 mg/dL in cats when hyperglycemia was first recognized after PN initiation, and the maximal concentration observed was 347 mg/dL in dogs and 489 mg/dL in cats. The increase in serum glucose concentration was lower in animals that were hyperglycemic before PN (+10 ± 28.5% in dogs and +32 ± 38.2% in cats) compared with those that were normo- or hypoglycemic before PN (+44 ± 55.3% in dogs and +82 ± 56.4% in cats; animals receiving insulin excluded) ($P < .01$).

In animals that developed hyperglycemia within 24 hours of starting PN, it resolved without insulin by 96 hours in 50/85 dogs (59%), but only 2/20 cats (10%). Insulin was used in 2/96 nondiabetic dogs (2%) and 11/31 nondiabetic cats (35%) that became hyperglycemic during PN. Insulin administration did not restore normoglycemia in either species. The mean time to increase PN to maximal rate was shorter in dogs that developed hyperglycemia than in dogs that did not (14.0 ± 11.2 versus 16.2 ± 11.2 hours, respectively; $P < .05$).

The development of metabolic complications was not associated with the composition or the amount of PN provided in either species, except for hyponatremia in cats, which was more likely to develop when the amount of energy delivered (in %RER) increased (OR 1.19 [1.01–1.44] for every 10% RER increase; $P < .05$) (Table 4).

Gross serum lipemia was recognized in 77/319 dogs (24%) and 26/112 cats (23%), at respective median times of 30 and 21 hours after starting PN. In dogs only, the fat content of the PN formula (in %ME) was negatively associated with the incidence of gross serum lipemia (OR 0.97 [0.94–0.99]; $P < .05$). Serum triglycerides were measured in 43 dogs (21 of which also had gross serum lipemia): 4/43 dogs had a value measured before PN initiation only, 25/43 dogs had a value measured during PN but not prior, and 14/43 had values measured both before and during PN. Among the 39 dogs that had a value measured during PN, it was elevated in 24 dogs (62%). Among the 14 dogs that had values measured both before and after PN, 8/14 were hypertriglyceridemic at both time points and 1/14 developed hypertriglyceridemia after an initial normal value. Concurrent enteral feeding occurred in 8/24 dogs that developed or remained hypertriglyceridemic during PN. Only 3 cats had serum triglycerides measured after PN initiation and all were elevated, and these animals were also fed enterally.

The most common hematologic complications that developed within 96 hours of PN initiation were a low RBC count (17/24 dogs; 71% and 1/3 cats; 33%), neutrophilic leukocytosis (17/31 dogs; 55% and 4/8 cats; 50%), lymphopenia (14/38 dogs; 37% and 3/6 cats; 50%), and thrombocytopenia (11/59 dogs; 19% and 3/8 cats; 38%). These abnormalities were also predominant before PN,

Table 4. Number of animals with the most frequent biochemical abnormalities before and during PN administration.[a]

	Dogs		Cats	
	Before PN	During PN	Before PN	During PN
Hyperglycemia[b]	26% (55/213)	61% (96/158)	56% (48/85)	84% (31/37)
Hypoalbuminemia	91% (100/110)	90% (9/10)	40% (16/40)	25% (6/24)
Hyponatremia	28% (57/206)	34% (50/149)	54% (42/78)	56% (20/36)
Hypokalemia	53% (109/206)	39% (38/97)	51% (39/76)	51% (19/37)
Hyperbicarbonatemia	18% (37/206)	30% (51/169)	53% (31/58)	56% (15/27)
Hypochloridemia	10% (18/181)	13% (22/163)	51% (30/59)	35% (10/29)
Hypocalcemia (iCa)	22% (32/144)	26% (29/112)	0% (0/37)	3% (1/37)
Hypophosphatemia	12% (13/110)	9% (9/97)	19% (6/31)	28% (7/25)

[a]Denominators correspond to the animals for which data were available. For abnormal values developing during PN, the denominator corresponds to animals that did not present with this abnormality before PN initiation.
[b]Diabetic animals excluded.

occurring in >50% of both dogs and cats, except for thrombocytopenia, which was present in 38% of dogs.

Outcomes and Prognostic Indicators

Death (including euthanasia) occurred in 137/319 (43%) dogs and 34/112 (46%) cats, with no significant change during the 9-year study period for either species ($P = .75$ for dogs and $P = .90$ for cats). Neither the development of hyperglycemia nor the relative change in blood glucose was associated with death in either species (Table 5). The only metabolic complication found to be a risk factor for death was the development of hypercreatininemia in dogs (8/79; 10%) ($P < .01$), which was independent of the association between CKD and death. In these 8 dogs, serum creatinine increased from 1.1 ± 0.4 mg/dL before PN to 2.0 ± 0.4 mg/dL during PN (reference range 0.5–1.6 mg/dL).

Discussion

This study of a large population of hospitalized dogs and cats confirmed that PN can be used to provide the energy needs of most animals. Despite the frequent occurrence of various complications, most did not significantly affect hospital outcome. Pancreatitis was the most common diagnosis in both dogs and cats in this study, similar to previous studies.[7–9] This is likely because vomiting and anorexia, commonly associated with this condition[14,15] preclude enteral feeding. In contrast to other studies,[6,8,10] respiratory disease was frequent in dogs receiving PN, probably because of the common use of mechanical ventilation with continuous anesthesia in our institution. As this disease was also associated with a worse prognosis in dogs, it could in part explain the higher mortality rate observed in our dogs (43%) compared with studies at other institutions (30–31%).[6,8] However, animal populations should be compared with caution because of the inherent variability in diagnosis categorizations. As our study was retrospective, reliance upon clinical diagnoses assigned by the primary clinicians was necessary, leading to possible misclassifications.

The provision of at least RER was achieved in 81% of dogs and 63% of cats. The amount of calories delivered by PN significantly decreased during the 9-year study period. This likely reflected the consideration of growing evidence in the human[16] and veterinary literature[10] that overfeeding might increase the incidence of metabolic complications, and that the energy requirement of most hospitalized human patients is closer to RER.[17] On average, CPN provided more energy than PPN in dogs but this was not observed in cats, perhaps because of the small number of cats receiving PPN in our study or the lower number of calories (in %RER) provided to cats on CPN compared with dogs. Regardless, delivery of full RER was achieved with PPN in 6/16 dogs and 3/5 cats. The osmolarity of peripherally administered solutions was kept lower than CPN (data not shown), but the caloric density of these solutions was not always less. This was achieved by increasing the lipid component at the expense of dextrose rather than diluting the solution with water.

Despite being effective at supplying energy, PN was nonetheless accompanied by various complications. Mechanical complications occurred less frequently than reported previously in the same hospital[7,9] (25 versus 37% previously in dogs; 14 versus 21% previously in cats), and was also lower than reported at other institutions[6,10] (28–46%). Catheter placement could partly account for this difference. The risk of mechanical complication was higher for dogs with catheters inserted in the saphenous vein compared with the jugular vein, regardless of whether they ended centrally or peripherally. Jugular catheters, placed in an area of lower motion and less accessible to the animal, should therefore be preferred over saphenous catheters to administer PN. The animal's behavior or activity level might also play a role as suggested by the higher incidence rate in dogs than in cats.

The incidence of septic complications in dogs (6%) and cats (5%) was similar to previous reports in this hospital (7% in dogs and 8% in cats).[7,9] A septic complication was diagnosed based on culture in only 8/26 animals. Therefore, the incidence of septic complications might have been overestimated because of our liberal inclusion criteria. However, as cultures were not submitted in every case, some septic complications might have remained undetected. It is interesting that PPN was a risk factor for this complication in dogs in our study despite reports of lower incidence rates of all types of complications for PPN compared with CPN.[1] This emphasizes the importance of strict aseptic techniques when compounding a PN solution, as

Table 5. Parameters associated with death in dogs and cats receiving PN by bivariate analysis.

Correlation with Death	Odds Ratio[a]	95% CI	*P* Value
Dogs			
Concurrent enteral feeding in dogs with respiratory disease	0.11	0.02–0.71	<.05
Lymphopenia before PN	0.35	0.13–0.88	<.05
Duration of PN (hours)	0.993	0.990–0.997	<.001
Duration of anorexia before PN (hours)	1.006	1.001–1.011	<.05
Chronic kidney disease	2.17	1.39–3.81	<.05
Respiratory disease	2.30	1.06–4.45	<.001
Hypernatremia before PN	4.14	1.56–11.97	<.01
Development of hypercreatininemia	15.95	2.36–∞	<.01
Cats			
Concurrent enteral feeding	0.10	0.05–0.27	<.001
Duration of PN (hours)	0.993	0.987–0.999	<.05
Duration of hospitalization (hours)	0.994	0.991–0.998	<.01
Duration of inadequate caloric intake before PN (hours)	1.003	1.000–1.007	<.05
Hepatic lipidosis	5.12	1.72–15.22	<.01
Hyperchloridemia before PN	6.25	1.04–47.33	<.05

[a]A value < 1.0 for the odds ratio indicates that the parameter is negatively associated with death (ie, associated with a higher survival rate) and inversely for a value >1.0.

well as when placing and maintaining the PN administration line, regardless of placement site. Septic complications were not associated with a higher risk of death, but they represent a potential threat for debilitated animals, and they always led to the interruption of PN administration in our study.

Metabolic complications were predominant overall, as reported previously.[6–10] Hyperglycemia was a predominant complication in nondiabetic animals, with a higher frequency (61% of dogs, 84% of cats) than previously reported with CPN or PPN in the veterinary literature (15–47%),[6–10] perhaps because of our methodology and criteria for categorizing metabolic complications. The use of portable glucose meters in some cases could also have led to inaccuracies in blood glucose measurements, especially at high concentrations.[18–20] Hyperglycemia is also common in human patients receiving PN,[21] and might be because of inefficient assimilation of intravenous glucose secondary to inflammatory cytokines and counter-regulatory hormones such as catecholamines, and to increased gluconeogenesis as well as peripheral insulin resistance.[22] In our study, many nondiabetic animals (26% of dogs and 56% of cats) were hyperglycemic at the time of PN initiation. This has also been reported in another study,[23] where 54% of nondiabetic cats admitted to the intensive care unit had a blood glucose >180 mg/dL. In cats, acute stress related to hospitalization could also contribute to hyperglycemia[24] and should be considered when assessing this finding during PN.

The administration of PN to hyperglycemic animals resulted in a further rise in blood glucose by 10% in dogs and 32% in cats on average. However, for normoglycemic animals, neither the amount of dextrose in the PN formula nor the amount of calories delivered were risk factors for this complication, in accordance with some human studies.[25,26] More importantly, our study did not find hyperglycemia to be a risk factor for death in either dogs or cats receiving PN, in agreement with most previous PN studies in small animals.[7,8,10] Only 1 study[9] found that cats that developed hyperglycemia during PN had a worse prognosis. This discrepancy could be because of differences in complication definitions, as the previous authors classified cats as hyperglycemic when serum glucose increased by ≥ 100 mg/dL irrespective of the initial value.[9] Alternatively, the frequent use of insulin in cats in our study might have blunted or prevented progression of hyperglycemia despite being unsuccessful at restoring normoglycemia. Unfortunately, the low number of animals as well as the variability in the type, dose and frequency of insulin administration precluded further investigation of this effect. The rationale for tight glycemic control in human patients receiving PN reflects that hyperglycemia has been found to be a negative prognostic indicator,[27–29] but similar recommendations for small animals receiving PN are not warranted without more data.

Many other metabolic complications were observed in this study, but none were risk factors for death, except for the development of hypercreatininemia in dogs independently of CKD. Despite being strongly associated with a negative outcome as reported in hospitalized humans,[30] this complication only affected a small number of animals (8 dogs), making the role of PN difficult to interpret in the context of many other confounding factors.

Survival was higher when assisted or voluntary enteral nutrition occurred during the first 96 hours of PN administration in all cats regardless of their disease, and in dogs with respiratory disease. This might reflect those animals with less severe diseases and a better prognosis, which were more likely to eat voluntarily (dogs under ventilation were less likely to be fed enterally), or it might be a benefit provided by early enteral feeding per se. Survival was also higher with longer durations of PN administration, which is likely biased by animals that died sooner and therefore received PN for a shorter period. Because of the retrospective nature of this study, a cause-and-effect relationship for either observation cannot be established. The increasing proportion during the 9-year study period of animals fed enterally during PN reflects the broader use of ''trickle feeding'' to supply a small proportion of the daily calories enterally, with the goal of maintaining intestinal barrier function and motility. This practice is supported by both the human[31–34] and veterinary[35] literature, and further research is needed to define the benefits and risks of concurrent enteral feeding in critically ill dogs and cats.

In conclusion, this study of the largest case series of dogs and cats receiving PN supports that this feeding approach can adequately meet the RER for many critically ill animals. This study confirmed that PN is frequently accompanied by various complications but rejected the hypothesis that its routine use would reduce their nature and prevalence in our hospital population over time. While hyperglycemia and the other complications were not associated with an increased risk for death, they can interfere with PN administration and should be prevented when possible. Consideration should be given to the use of a jugular catheter in dogs to reduce mechanical complications and concurrent enteral feeding in appropriate animals to improve outcome. Prospective studies are needed to determine the potential benefits of PN in dogs and cats, especially when compared with early enteral nutrition.

Footnotes

[a] Intralipid 20% IV Fat Emulsion, Fresenius Kabi, Uppsala, Sweden and Baxter Healthcare Corporation, Deerfield, IL

[b] Travasol 8.5% with or without electrolytes, Baxter Healthcare Corporation

[c] Aminosyn II 8.5% Sulfite-Free without electrolytes, Hospira Inc, Lake Forest, IL

[d] Dextrose 50% solution, Vedco Inc, Saint-Joseph, MO

[e] Vitamin B Complex Injection, Vedco Inc

[f] Potassium Chloride for Inj. Concentrate USP, Hospira Inc

[g] Potassium Phosphates Injection USP, American Regent Inc, Shirley, NY

[h] Microsoft Office Excel 2003, Microsoft Corporation, Redmont, WA

Acknowledgment

Dr Queau is supported by an educational grant from Royal Canin.

References

1. Chan DL. Parenteral nutritional support. In: Ettinger SJ, Feldman EC, eds. textbook of Veterinary Internal Medicine: Diseases of the Dog and the Cat, 7th ed. St Louis, MO: Elsevier Saunders; 2010:701–707.

2. Teitelbaum D, Guenter P, Howell WH, et al. Definition of terms, style, and conventions used in A.S.P.E.N. guidelines and standards. Nutr Clin Pract 2005;20:281–285.

3. Bozzetti F, Forbes A. The ESPEN clinical practice guidelines on parenteral nutrition: Present status and perspectives for future research. Clin Nutr 2009;28:359–364.

4. Simpson F, Doig GS. Parenteral vs. enteral nutrition in the critically ill patient: A meta-analysis of trials using the intention to treat principle. Intensive Care Med 2005;31:12–23.

5. Smoke A, Delegge MH. Chyle leaks: Consensus on management? Nutr Clin Pract 2008;23:529–532.

6. Lippert AC, Fulton RB Jr, Parr AM. A retrospective study of the use of total parenteral nutrition in dogs and cats. J Vet Intern Med 1993;7:52–64.

7. Reuter JD, Marks SL, Rogers QR, et al. Use of total parenteral nutrition in dogs: 209 cases (1988–1995). J Vet Emerg Crit Care 1998;8:201–213.

8. Chan DL, Freeman LM, Labato MA, et al. Retrospective evaluation of partial parenteral nutrition in dogs and cats. J Vet Intern Med 2002;16:440–445.

9. Pyle SC, Marks SL, Kass PH. Evaluation of complications and prognostic factors associated with administration of total parenteral nutrition in cats: 75 cases (1994–2001). J Am Vet Med Assoc 2004;225:242–250.

10. Crabb SE, Freeman LM, Chan DL, et al. Retrospective evaluation of total parenteral nutrition in cats: 40 cases (1991–2003). J Vet Emerg Crit Care 2006;16:S21–S26.

11. Freeman LM, Chan DL. Total parenteral nutrition. In: DiBartola SP, ed. Fluid, Electrolyte and Acid-Base Disorders in Small Animal Practice, 3rd ed. London: Saunders; 2005:584–601.

12. Laflamme D. Development and validation of a body condition score system for cats: A clinical tool. Feline Pract 1997;25: 13–18.

13. Laflamme D. Development and validation of a body condition score system for dogs. Canine Pract 1997;22:10–15.

14. Steiner JM. Canine pancreatic disease. In: Ettinger SJ, Feldman EJ, eds. Textbook of Veterinary Internal Medicine, 7th ed. London: Saunders; 2010:1695–1704.

15. Washabau RJ. Feline pancreatic disease. In: Ettinger SJ, Feldman EJ, eds. Textbook of Veterinary Internal Medicine, 7th ed. London: Saunders; 2010:1704–1709.

16. Klein CJ, Stanek GS, Wiles CE III. Overfeeding macronutrients to critically ill adults: Metabolic complications. J Am Diet Assoc 1998;98:795–806.

17. Miles JM. Energy expenditure in hospitalized patients: Implications for nutritional support. Mayo Clin Proc 2006;81:809–816.

18. Wess G, Reusch C. Evaluation of five portable blood glucose meters for use in dogs. J Am Vet Med Assoc 2000;216:203–209.

19. Cohen TA, Nelson RW, Kass PH, et al. Evaluation of six portable blood glucose meters for measuring blood glucose concentration in dogs. J Am Vet Med Assoc 2009;235:276–280.

20. Johnson BM, Fry MM, Flatland B, et al. Comparison of a human portable blood glucose meter, veterinary portable blood glucose meter, and automated chemistry analyzer for measurement of blood glucose concentrations in dogs. J Am Vet Med Assoc 2009;235:1309–1313.

21. Kumar PR, Crotty P, Raman M. Hyperglycemia in hospitalized patients receiving parental nutrition is associated with increased morbidity and mortality: A review. Gastroenterol Res Pract 2011;pii: 760720. PubMedPMID: 20811546.

22. Digman C, Borto D, Nasraway SA Jr. Hyperglycemia in the critically ill. Nutr Clin Care 2005;8:93–101.

23. Chan DL, Freeman LM, Rozanski EA, et al. Alterations in carbohydrate metabolism in critically ill cats. J Vet Emerg Crit Care 2006;16:S7–S13.

24. Rand JS, Kinnaird E, Baglioni A, et al. Acute stress hyperglycemia in cats is associated with struggling and increased concentrations of lactate and norepinephrine. J Vet Intern Med 2002;16:123–132.

25. McCowen KC, Friel C, Sternberg J, et al. Hypocaloric total parenteral nutrition: Effectiveness in prevention of hyperglycemia and infectious complications—a randomized clinical trial. Crit Care Med 2000;28:3606–3611.

26. Sheean P, Braunschweig C. The incidence and impact of dextrose dose on hyperglycemia from parenteral nutrition (PN) exposure in hematopoietic stem cell transplant (HSCT) recipients. J Parenter Enteral Nutr 2006;30:345–350.

27. Cheung NW, Napier B, Zaccaria C, et al. Hyperglycemia is associated with adverse outcomes in patients receiving total parenteral nutrition. Diabetes Care 2005;28:2367–2371.

28. Lin LY, Lin HC, Lee PC, et al. Hyperglycemia correlates with outcomes in patients receiving total parenteral nutrition. Am J Med Sci 2007;333:261–265.

29. Sarkisian S, Fenton TR, Shaheen AA, et al. Parenteral nutrition-associated hyperglycemia in noncritically ill inpatients is associated with higher mortality. Can J Gastroenterol 2010; 24:453–457.

30. Uchino S, Bellomo R, Bagshaw SM, et al. Transient azotaemia is associated with a high risk of death in hospitalized patients. Nephrol Dial Transplant 2010;25:1833–1839.

31. Windsor AC, Kanwar S, Li AG, et al. Compared with parenteral nutrition, enteral feeding attenuates the acute phase response and improves disease severity in acute pancreatitis. Gut 1998;42:431–435.

32. Braga M, Gianotti L, Gentilini O, et al. Feeding the gut early after digestive surgery: Results of a nine-year experience. Clin Nutr 2002;21:59–65.

33. Gupta R, Patel K, Calder PC, et al. A randomised clinical trial to assess the effect of total enteral and total parenteral nutritional support on metabolic, inflammatory and oxidative markers in patients with predicted severe acute pancreatitis (APACHE II > or = 6). Pancreatology 2003;3:406–413.

34. Louie BE, Noseworthy T, Hailey D, et al. 2004 MacLean-Mueller prize enteral or parenteral nutrition for severe pancreatitis: A randomized controlled trial and health technology assessment. Can J Surg 2005;48:298–306.

35. Qin HL, Su ZD, Hu LG, et al. Effect of early intrajejunal nutrition on pancreatic pathological features and gut barrier function in dogs with acute pancreatitis. Clin Nutr 2002;21:469–473.