Early nutritional support is associated with decreased length of hospitalization in dogs with septic peritonitis: A retrospective study of 45 cases (2000–2009)

Debra T. Liu, DVM; Dorothy C. Brown, DVM, MSCE, DACVS and Deborah C. Silverstein, DVM, DACVECC

Abstract

Objective – To determine whether the timing and route of nutritional support strategy affect length of hospitalization in dogs with naturally occurring septic peritonitis.

Design – Retrospective study encompassing cases from 2000 to 2009.

Setting – University teaching hospital.

Animals – Forty-five dogs that survived septic peritonitis.

Interventions – None.

Measurements and Main Results – Nutritional strategy for each dog was categorized as either enteral nutrition (EN: free choice voluntary eating or assisted tube feeding) or central parenteral nutrition (CPN). Early nutritional support was defined as consistent caloric intake initiated within 24 hours postoperatively. Consistent caloric intake occurring after 24 hours was defined as delayed nutritional support. Data reflective of nutritional status included body condition score, serum albumin concentration, and duration of inappetence before and during hospitalization. Body weight change from the beginning to the end of hospitalization was calculated. A modified Survival Prediction Index 2 score was calculated for each dog at admission. Additional clinical data recorded for comparison of illness severity included indicators of severe inflammation (eg, presence of toxic changes in neutrophils and immature neutrophils), coagulopathy (eg, prolonged prothrombin time and activated partial thromboplastin time), the use of vasopressors and blood transfusions, and presence of concurrent illnesses. Nutrition-related complications were classified as mechanical, metabolic, or septic complications. Multivariate linear regression analyses were used to determine the relationship of nutritional strategy with hospitalization length, while considering the presence of nutrition-related complications, the nutritional status- and illness severity-related variables. While controlling for other variables, dogs that received early nutrition had significantly shorter hospitalization length (by 1.6 days). No statistically significant association was found between route of nutrition and hospitalization length. The presence of concurrent illnesses and nutrition-related metabolic complications were also associated with longer hospitalization length (by 2.1 and 2.4 days, respectively).

Conclusions – Early nutritional support in dogs with septic peritonitis is associated with a shorter hospitalization length.

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Keywords: canine, enteral nutrition, intensive care unit, malnutrition, parenteral nutrition, sepsis

Abbreviations

aPTT	activated partial thromboplastic time
BCS	body condition score
CPN	central parenteral nutrition
EN	enteral nutrition
LOH	length of hospitalization
MODS	multiple organ dysfunction syndrome
PN	parenteral nutrition

PT   prothrombin time
SPI2   survival prediction index 2

Introduction

The importance of nutrition in critically ill animals is increasingly being recognized.[1–3] Evidence to guide clinical decisions regarding the optimal nutritional strategy is however sparse. There have been 2 veterinary clinical studies comparing different nutritional strategies within a specific disease process for canine parvo viral infection and hemorrhagic gastroenteritis.[4,5] To the authors' knowledge, the effects on clinical outcome of different nutritional strategies in dogs with septic peritonitis have not been examined previously.

Dogs with septic peritonitis are often critically ill, and predisposed to malnutrition from elevated stress hormones and cytokines accelerating catabolism to fuel the immune system and other vital organs.[6] The mortality rates for dogs with septic peritonitis are reported as high as 70% in dogs with multiple organ system dysfunction syndrome (MODS) and 25% in dogs without MODS, underscoring a wide spectrum of disease severity.[7] Clinical signs associated with septic peritonitis include vomiting, regurgitation, and abdominal pain, all of which negatively impact appetite and the ability to tolerate enteral feeding. Although a functional gastrointestinal tract is present in most of these dogs postoperatively, many dogs remain inappetent and nauseated due to ongoing peritonitis and opioid-induced ileus. Recumbency may also place these dogs at risk for aspiration pneumonia. Consequently, the timing and route of nutritional support are often discussed in the postoperative period.

The optimal time frame, or acceptable delay prior to commencement of nutritional support has not been defined in critically ill animals, and it may be dissimilar for different disease processes and various routes of nutrition delivery. Enteral nutrition (EN) is generally recommended first for its beneficial effect on the integrity of gut mucosa.[4] When EN is not feasible due to poor tolerance related to clinical signs listed above, vasopressor-dependent hypotension or lack of expertise for nasojejunal tube placement, parenteral nutrition (PN) is an alternative approach to ensure adequate nutritional intake. However, there are concerns for its effects on cytokine production, hormonal release, and immunosuppression.[8,9] Therefore, the goal of this study is to investigate the effect of timing and route of nutritional support on length of hospitalization (LOH) in dogs that survived septic peritonitis. Markers of nutritional status, illness severity, and nutrition-related complications were also evaluated for their potential association with LOH. The null hypothesis is that timing and route of nutrition do not influence LOH in dogs that survive septic peritonitis.

PN may be delivered into a central vein (central PN) or a peripheral vein (peripheral PN). Central PN was previously referred to as "total parenteral nutrition," which implied that it met all caloric and nutrient needs of the animal.[10,11] Because the exact protein-caloric and micronutrient requirements of critically ill dogs are unknown, central PN is the preferred term and is used in this report.

Materials and Methods

Study design and data collection

A retrospective review of medical records for dogs diagnosed with septic peritonitis from 2000 to 2009 was performed. The diagnosis of septic peritonitis was based on the presence of intracellular bacteria in the peritoneal fluid, positive culture result of the peritoneal fluid, or confirmation of the contaminant source during exploratory surgery. Only dogs that survived to discharge were included. Dogs with incomplete medical records or that received no nutritional support during hospitalization were excluded.

Information retrieved included the signalment and total days of hospitalization. For each dog, the nutritional support method was categorized as either EN or CPN. For the purpose of this study, EN was defined as assisted tube feeding or free choice voluntary eating. The standard procedure in this hospital is to offer a variety of food 2–4 times a day to all animals that are not vomiting or regurgitating. Examples of common diets offered include commercial canine diets (Hill's Prescription Diet i/d Canine, Purina Veterinary Diets Therapeutic canine formulas EN Gastroenteric, Iams Veterinary Formulas Intestinal Low-Residue/Canine, Hill's Prescription Diet k/d Canine, Pro Plan Canine Formulas Chicken and Rice Entrée Classic, Pro Plan Canine Formulas Shredded Blend Lamb and Rice Formula), boiled rice and chicken, chicken baby food, and sandwich meat (ham and turkey). The decision to place a feeding tube was made by the primary clinician based on the individual dog's clinical condition and owner consent. Days of consistent voluntary food consumption (recorded as single or multiple "+" signs on the treatment sheet ≥3 times a day) or tube feeding (successful feeding ≥3 times a day without vomiting or regurgitation) were recorded. Exact caloric food intake was not quantified. Dogs that received CPN at any time point were allocated to the CPN group and the number of days CPN was administrated was noted. Instrumentations used for nutrition delivery (eg, jugular catheter, peripherally inserted central catheter, gastrostomy tube, jejunostomy tube) were recorded.

PN in our hospital is employed only for dogs intolerant of enteral feeding and our standard CPN protocol is outlined below for dogs. CPN is used far more commonly for critical ill animals in our hospital than peripheral PN. A central line placed in an aseptic manner is required and one lumen is dedicated solely for PN administration. Freshly formulated PN is prepared daily and the PN glass bottles and administration lines are replaced in a sterile fashion daily. Canine caloric requirements are calculated based on the following formula: resting energy requirement (RER) = 70 × (body weight in kilogram)$^{0.75}$ or RER = 30 × (body weight in kilogram) + 70.[10] Fifty percent of RER is delivered on the first day of CPN and the full RER is provided thereafter. Fifteen to 25% of targeted calories are provided as protein (Aminosyn 8.5%)[a] for dogs based on the protein deficit and ongoing losses. The remainder of calories is delivered equally as dextrose (50% dextrose)[b] and lipid (Intralipid 20%).[c] Zinc is supplemented at 1 μg/kcal provided. Potassium phosphate is added at 8 mM/1,000 kcal provided. Two milliliters of vitamin B complex[d] per liter of PN is added as well. Transition to oral feeding is facilitated as soon as possible. The rate of CPN administration is weaned gradually over 12–24 hours once the dog eats or tolerates tube feeding well for 24 hours. For hypoglycemic dogs, the standard protocol for additional dextrose supplementation in our hospital aims to maintain the blood glucose concentration between 3.9 and 7.2 mmol/L (70–130 mg/dL), except when managing diabetic animals requiring insulin therapy.

For the purpose of this study, early nutritional support was defined as either CPN or EN with consistent caloric intake that occurred within 24 hours after surgery. Delayed nutritional support was defined as failure to achieve positive caloric intake (either EN or CPN) within 24 hours postoperatively.

In order to evaluate the dogs' nutritional statuses, albumin concentration,[3] body condition score (BCS),[12] days of inappetence before hospitalization, days of no caloric intake during hospitalization, and body weight at admission and discharge were recorded. BCS was determined by the admitting veterinarian and final-year veterinary student. A 5-point scale[12] based on the physical examination findings was used as follows: (1) very thin; (2) underweight; (3) ideal; (4) over weight; (5) obese.

The severity of illness was evaluated by a standardized modified model of Survival Prediction Index (SPI2) score[13] and several commonly used clinical parameters, including the presence of immature neutrophils or a left shift, toxic changes observed in neutrophils,[14] prolonged prothrombin time (PT), prolonged activated partial thromboplastic time (aPTT), vasopressor dependence to maintain a systolic blood pressure above 90 mm Hg (as measured by noninvasive Doppler or oscillometric methods) during hospitalization, the use of blood transfusion, and the presence of concurrent illnesses. The SPI2 is a mathematical formula developed to score disease severity objectively based on clinical data of the dog within 24 hours of hospital admission. The score ranges from 0 to 1. A lower score is associated with more severe disease and higher risk of fatality.[13] The SPI2 score was calculated for each dog based on the following formula.

$$\text{Logit } P = 0.3273$$
$$+ (0.0108 \times \text{mean arterial blood pressure})$$
$$- (0.0102 \times \text{respiratory rate})$$
$$- (0.2183 \times \text{creatinine}) + (0.0164 \times \text{PCV})$$
$$+ (0.3553 \times \text{albumin}) - (0.1184 \times \text{age})$$
$$- (0.8069 \times \text{medical vs. surgical status}^*)$$

$$P(\text{SPI}) = e^{\text{logit } P}/(1 + e^{\text{logit } P}),$$

*medical vs. surgical status is a dichotomous variable (medical = 1, surgical = 0)

Concurrent illnesses included primary dysfunction of the major body systems, including cardiac diseases documented by echocardiography, pulmonary disorders documented by chest radiographs, renal failure (persistent azotemia despite adequate hydration), hepatic failure (documented clinical signs of hepatic encephalopathy and increased ammonia concentration), endocrine, neurological, gastrointestinal, and immune-mediated hematological disorders. Ophthalmic, dermatological, and noninfectious orthopedic or reproductive disorders were excluded (eg, cataracts, cruciate ligament tear, arthritis, cryptorchidism).

The presence of nutrition-related complications was recorded. Complications related to PN and EN administration were divided into mechanical, metabolic, and septic categories. Mechanical complications were identified as any kind of catheter or tube complication leading to the temporary or permanent interruption of nutritional delivery (eg, thrombosis, dislodgement, leakage, clogging). Septic complications were defined as an infected catheter or feeding tube site based on clinical suspicion or positive culture from the catheter tip, CPN solution, or blood. Metabolic complications were determined by evaluating biochemical data in accordance with the normal reference ranges. The occurrence of metabolic complications was defined as 1 or more of the following, which either developed or worsened during the time of positive caloric intake: hypokalemia ($K < 3.4$ mmol/L); hyperglycemia (glucose > 7.8 mmol/L [140

mg/dL]); hypomagnesemia (total Mg < 0.74 mmol/L [<1.8 mg/dL]); hypophosphatemia (P <0.91 mmol/L [2.8 mg/dL]); lipemia.

Statistical analysis

Descriptive statistics were calculated. Normally distributed variables were expressed as means and standard deviations, while those not normally distributed were expressed as medians and ranges. Categorical variables were expressed as frequencies and percentages. Linear regression analyses for LOH was performed to evaluate associations with age, route of nutrition (EN versus CPN), timing of nutrition (early versus delayed nutrition support), albumin concentration, BCS, weight change, days of inappetence prior to admission, days in the hospital with no caloric intake, total days of zero to minimal caloric intake (the sum of previous 2 variables), SPI2 score, the presence of toxic changes, the presence of a left shift, the presence of concurrent illnesses, use of blood products, use of vasopressors, the presence of prolonged PT, the presence of prolonged aPTT, and the presence of nutrition-related complications (mechanical, metabolic, and septic complications).

For the regression model, 2-way interactions among the main effects were investigated. Univariate analysis was performed and variables with a value of $P < 0.20$ were evaluated in a multivariable model. A given variable was retained in the multivariable model when the value of P for that variable was ≤ 0.05. All analyses, including graphical analyses to evaluate model assumptions, were performed by use of commercial software.[e]

Results

One hundred and fifty-nine dogs with septic peritonitis were identified, and of these 45 dogs were enrolled in the study. Of the 114 dogs excluded, 73 dogs were euthanized at the time of diagnosis, 32 dogs died or were euthanized despite treatment, and 9 surviving dogs were excluded due to zero caloric intake prior to being discharged from the hospital. The median age was 4 years (range: 0.3–13 years). Ten intact males, 14 castrated males, 5 intact females, and 16 spayed female dogs were included. The study population included 13 mixed breed dogs, 6 Labrador Retrievers, 4 German Shepherds, 3 Rottweilers, 2 Boxers, 2 Doberman Pinschers, 2 Golden Retrievers, and one of each for the 13 other pure breeds. Causes of septic peritonitis are listed in Table 1.

Twelve dogs received consistent nutrition starting within 24 hours postoperatively (27%) and the remaining 33 dogs received delayed nutritional support. Thirty-two dogs received EN (71%); 13 dogs received CPN (29%). Among the 12 dogs that received early nutrition, 4 dogs received CPN and 8 dogs received EN. Among the 33

Table 1: Etiology of septic peritonitis in 45 study dogs

Cause of septic peritonitis	Number of dogs affected
Gastrointestinal foreign body obstruction	13
Intestinal neoplasia	1
Gastrointestinal ulceration and perforation	1
Gastric dilation and volvulus	2
Dehiscence from prior gastrointestinal surgery	3
Dehiscence post-ovariohysterectomy	5
Prostatic abscesses	2
Pyometra	3
Bladder rupture from urethral obstruction and urinary tract infection	3
Hepatic abscesses	1
Gall bladder rupture	2
Trauma	2
Other*	7

*Other causes in which $n = 1$ include scrotal hernia, intussusception, gastrostomy tube septic complication, bite wounds, abscessed splenic tumor, and surgical sponges in the abdomen. In one dog with a positive culture of abdominal fluid, the source of abdominal sepsis could not be identified at surgery.

dogs that received delayed nutrition, 9 dogs received CPN and 24 dogs received EN. The average duration of hospitalization was 6.7 ± 2.6 days. CPN was delivered to 10 dogs via jugular triple lumen catheter and 3 dogs via peripherally inserted central catheter introduced through the lateral saphenous vein. Gastrostomy tube was placed in 4 dogs; only 1 of those dogs was successfully fed via the gastrotomy tube. Gastrostomy tube was used for gastric decompression only in the 3 other dogs due to severe ileus, vomiting, regurgitation, and large quantities of gastric residual volumes. Of these latter 3 dogs, 2 dogs received CPN and 1 dog started to eat on its own 48 hours postoperatively as the ileus and vomiting resolved.

The mean serum albumin concentration was 25.0 ± 8.0 g/L (2.5 ± 0.8 g/dL). The median BCS was 3 out of 5 (range: 1–5). The median weight change during hospitalization was +0.4 kg (range: −2 to +4.8 kg). The median duration of inappetence prior to admission was 3 days (range: 0–19 days). The median duration of no caloric intake in the hospital was 2 days (range: 0–8 days). The median duration for total days of minimal to no caloric intake since the onset of illness was 6 days (range: 0–21 days).

The mean SPI2 of the 45 study dogs was 0.84 (range: 0.521–0.959). Toxic changes in the neutrophils were present in 30 dogs (67%); a left shift was present in 31 dogs (69%). Twenty-five dogs had both toxic changes in the neutrophils and a left shift. Seven dogs had prolonged PT (16%); 17 dogs had prolonged aPTT (38%). Twenty-two dogs received blood transfusions (49%).

Fifteen dogs developed vasopressor-dependent hypotension during hospitalization (33%). Concurrent illnesses were present in 7 dogs (16%), including aspiration pneumonia ($n = 3$), chronic valvular disease ($n = 2$), immune-mediated thrombocytopenia ($n = 1$), and inflammatory bowel disease ($n = 1$).

Nineteen dogs developed nutrition-related metabolic complications (42%). Hypomagenesemia and hypokalemia were the most common type of metabolic complications related to nutrition, occurring in 33% and 20% of the study population, respectively. Five dogs (11%) had transient hyperglycemic episodes and none of them required insulin therapy. Hypophosphatemia occurred in 5 dogs (11%). No dogs developed lipemia due to nutritional support. Twelve dogs developed more than 1 type of metabolic complications (27%). Hyperglycemia, hypokalemia, and hypomagnesemia occurred both in dogs fed enterally and in dogs fed parenterally. Hypophosphatemia occurred only in dogs fed parenterally.

Three dogs developed nutrition-related septic complication (7%). Purulent discharge developed at the entry site of the jugular triple lumen catheter in 1 dog, for which the catheter was removed. Two other cases of septic complication involved gastric leakage around the gastrostomy tube, requiring surgery to decontaminate the abdomen. One dog developed a mechanical complication: leakage from the jugular triple lumen catheter was found and the catheter was removed thereafter.

For linear regression analysis, 14 variables were identified on univariate analysis as eligible for inclusion in the model with P value <0.20: age, route of nutrition (EN versus CPN), timing of nutrition (early versus delayed nutritional support), albumin concentration, days in the hospital with no caloric intake, SPI2 score, the presence of toxic changes in neutrophils, the presence of a left shift, the presence of concurrent illnesses, use of blood transfusions, use of vasopressors, prolonged PT, the presence of nutrition-related metabolic complications, and the presence of nutrition-related septic complication. Three variables remained significant in the final model: the timing of the nutritional support, the presence of concurrent illnesses, and the presence of nutrition-related metabolic complications. Controlling for the presence of concurrent illnesses and nutrition-related metabolic complications, dogs receiving early nutritional support were hospitalized 1.6 fewer days than dogs receiving delayed nutrition (95% CI 0.1–3.0 days; $P = 0.037$). Controlling for the timing of nutrition and the presence of nutrition-related metabolic complications, dogs with concurrent illnesses were hospitalized 2.1 more days than dogs without concurrent illnesses (95% CI 0.3–3.9 days; $P = 0.022$). Controlling for the timing of nutrition and the presence of concurrent illnesses, dogs with nutrition-related

metabolic complications were hospitalized 2.4 more days than dogs without metabolic complications (95% CI 1.1–3.8 days; $P = 0.001$).

Discussion

While many studies focus on the negative impacts of malnutrition, few studies have specifically investigated the effects of early versus delayed nutritional support in critically ill animals. This retrospective study documents that early nutrition, within 24 hours postoperatively, is associated with a shorter LOH (by 1.6 days) in dogs with septic peritonitis when compared to delayed nutrition. The timing of the nutrition may therefore play a role in the clinical course of recovery in critically ill animals.

In septic dogs, the activation of local or systemic inflammatory response and the release of stress hormones (eg, catecholamines, glucagon, cortisol) result in a sustained hypermetabolic state characterized by profound catabolism.[6] If the hypermetabolic state continues without intervention, immunosuppression, depletion of nutrients at the tissue and cellular level, organ failure, and death may eventually ensue. The mechanism by which early nutrition decreases LOH in dogs with septic peritonitis is not well understood. Potential theories include hormonal modulation attenuating the hypermetabolic response,[15] preservation of hepatic antioxidant defense,[16–18] and prevention of protein-caloric malnutrition and its complications. Additionally, EN maintains gastrointestinal barrier function[4] and is associated with improved blood flow to the gastrointestinal tract, liver,[19] and kidneys.[20] Previously, Mohr et al[4] analyzed the beneficial effects of early nutrition in dogs with parvoviral infection and found faster clinical improvement in dogs for which EN was instituted within 12 hours of admission.[4] In another investigation of partial PN use, LOH was also correlated with the timing of nutrition.[21] Together with our present study, these findings provide evidence that consistent enforcement of early nutrition contributes to faster recovery in certain critically ill animals.

We analyzed 20 nutrition- and illness severity-related variables in this study. In addition to the timing of nutrition, 2 other variables were also associated with LOH, including the presence of concurrent illnesses and nutrition-related metabolic complications. In dogs with septic peritonitis, multiple organ failure is unfortunately common and it is associated with a higher mortality.[7] Understandably, the presence of concurrent illnesses correlates to a longer LOH (by 2.1 days).

For the nutrition-related metabolic complications, there are likely multiple causes. Hyperglycemia may be secondary to nutritional support or a manifestation of

sepsis from increased gluconeogenesis and insulin resistance. Decreased serum concentrations of magnesium, phosphorus, and potassium may be associated with transcellular shifts or total body depletion of these ions secondary to refeeding syndrome, acid-base imbalances, or gastrointestinal losses. Therefore, the association of these metabolic complications with longer LOH (by 2.4 days) may be due to these affected dogs being more severely ill or in a worse nutritional state compared to those without metabolic complications. Nutrition was not discontinued in any dogs from this study based on these metabolic complications. Instead, these dogs received electrolyte supplementations as needed.

There are several limitations in this study to be considered. One is the small number of dogs in the study, which may have prevented detection of significant effects by other variables. In addition, due to the retrospective nature of this study, exact enteral caloric intake could not be quantified. Dogs from this study either received CPN or ate voluntarily, except for 1 dog that was fed via a gastrostomy tube. It is unknown whether the results would be different if all dogs were given equivalent caloric support using either EN or CPN support. Nonsurvivors were excluded in this study to avoid the bias associated with humane euthanasia. However, some dogs may have been discharged prematurely according to the owner's wishes, and some dogs may have died following discharge. Finally, many other metabolic and acid-base disturbances reported previously in dogs and cats receiving PN were not included in this study, including hypoglycemia, hypercalcemia, hypocalcemia, hyperkalemia, hypernatremia, hyponatremia, hyperchloremia, hypochloremia, hypoproteinemia, hyperbilirubinemia, hypermagnesemia, hyperphosphatemia, increased serum alkaline phosphatase concentration, azotemia, metabolic acidosis, and metabolic alkalosis.[21–23] The causal relationships of PN to these derangements in dogs and cats are difficult to prove, since the animals suffered from a variety of different diseases in these studies. Therefore, only the 5 biochemical parameters with direct pathophysiological relationships to nutritional support were reported in this study.

To our knowledge, this is the first study to demonstrate a clinical advantage of early nutrition in dogs with septic peritonitis. Future prospective studies that quantify caloric intake when evaluating different nutritional strategies and their effect on outcome are indicated in order to establish better nutritional support guidelines for critically ill animals. The use of jejunostomy or nasojejunostomy tubes in dogs affected by septic peritonitis also warrants further evaluation.

Footnotes

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