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Retrospective evaluation of the impact of early enteral nutrition on clinical outcomes in dogs with pancreatitis: 34 cases (2010–2013)

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Abstract

Objective – To evaluate the effect of early enteral nutritional therapy on time to return to voluntary intake, maximum food consumption, incidence of gastrointestinal intolerance (GI), and total hospitalization time for dogs with acute pancreatitis.
Design and Setting – Retrospective analysis of dogs with pancreatitis at a veterinary teaching hospital between 2010 and 2013.
Animals – Thirty-four client-owned dogs diagnosed with acute or acute-on-chronic pancreatitis.
Procedures and Interventions – Medical records of dogs evaluated for inappetence, anorexia, and GI for which a diagnosis of pancreatitis was recorded were reviewed. The time to initiation of food offerings since hospitalization were recorded in addition to signalment, historical medical conditions, chief complaint, physical examination findings, diagnostic results, treatments provided, timing of food offering (within 48 h of hospitalization, early feeding group (EFG) versus delayed feeding group (DFG), diet therapy (low fat versus high fat), caloric intake (% resting energy requirement), incidence of GI (%), and length of hospitalization (LOH) (days). A Clinical Severity Index Score (CSIS) was determined for each patient.
Measurements and Main Results – Dogs in the EFG demonstrated a decreased time to return of voluntary intake (2.1 days, EFG versus 2.7 days, DFG; $P = 0.05$) and time (days) to maximum intake (3, EFG versus 3.4 DFG) as compared to the DFG dogs. The DFG exhibited more GI versus EFG irrespective of CSIS grouping (60% versus 26%, $P = 0.04$). A CSIS ≥ 7 was associated with prolonged LOH ($P = 0.004$); however, time to initiation of feeding and diet selection did not impact LOH ($P = 0.8$).
Conclusions and Clinical Relevance – Results of the study suggested that feeding within 48 hours of hospitalization for canine pancreatitis has a positive impact on return to voluntary intake and decreases the frequency of GI in these patients, independent of CSIS. The traditional protocol of withholding food during hospitalization may not be necessary nor yield the most benefit for patient recovery; subsequently early enteral refeeding should be considered.

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Keywords: canine, gastrointestinal intolerance, nutritional support

Abbreviations

AP	acute pancreatitis
cPLI	canine pancreatic lipase immunoreactivity
CSIS	Clinical Severity Index Score
DFG	delayed feeding group
EFG	early feeding group
EN	enteral nutrition
FE	feeding events
GI	gastrointestinal intolerance
LOH	length of hospitalization
NPO	nothing per os
RER	resting energy requirement

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SAP severe acute pancreatitis
US ultrasonographic

Introduction

Pancreatitis is the most common disease of the exocrine pancreas in dogs.[1] Pancreatitis may be acute or chronic although the difference is largely histological and not necessarily clinical.[1–3] Although most episodes are mild and self-limiting, some cases present with anorexia, depression, abdominal pain, and vomiting accompanied by signs of dehydration and shock. In such cases, a diagnosis of severe acute pancreatitis (SAP) is strongly supported if positive immunoassay (eg, canine pancreatic lipase immunoreactivity [cPLI]) results are coupled with ultrasonographic (US) changes consistent with pancreatic inflammation, or increased catalytic assay values (eg, amylase and lipase) and there is development of local complications or distant organ failure.[4–7] The reported mortality rate in dogs with SAP ranges from 27 to 58% with surviving animals usually requiring intensive treatment and hospitalization.[4]

The traditional therapy for SAP is largely supportive with emphasis on analgesia, maintenance of fluid and electrolyte balance, and antiemetic therapy while the pancreas is "rested" by withholding food.[8,9] However, this approach is complicated due to increased metabolic demands, substantial protein catabolism, gut-derived inflammation, and potential bacterial translocation ultimately resulting in the development of systemic inflammatory response syndrome or sepsis.[9] In people, there have been numerous clinical trials performed demonstrating the benefit of decreased inflammatory complications associated with early enteral nutrition (EN) when compared with parenteral nutrition for treatment of acute pancreatitis (AP).[10–17] In veterinary medicine, early EN has been demonstrated to improve clinical outcomes in both parvoviral infections and septic peritonitis, a response that has been attributed to reduced catabolism, prevention of protein-energy malnutrition, improved integrity of epithelial tight junctions, and overall decreased intestinal inflammation.[18,19] Although studies prospectively evaluating tolerance of enteral feeding in veterinary patients with AP are limited, there is growing evidence supporting the benefits of early EN in this population. A recent small pilot study of dogs with AP demonstrated no exacerbation in signs of pain or vomiting in the enterally fed group when compared to the parenterally fed group.[10,20] However, there are no trials in veterinary medicine comparing early EN to the traditional therapy of nothing per os (NPO) in AP.[9,10] Therefore, optimal nutritional management of AP in dogs remains unclear and warrants further research.

The primary purpose of this case series was to evaluate the effect of nutritional therapy provided early (ie, within 48 h of presentation), on time to the return to voluntary intake, maximum consumption, incidence of gastrointestinal intolerance (GI), and total length of hospitalization (LOH) as compared to those treated NPO. Our hypothesis was that the provision of early EN therapy to patients diagnosed with AP would result in decreased time to voluntary intake; increased or no difference in maximum consumption of resting energy requirement (RER) calories; decreased or no difference to incidence of GI; and decreased total LOH compared to patients treated NPO for the first 48 hours of hospitalization. Additionally, we evaluated the potential impact of clinical severity index score (CSIS), dietary fat level, and concurrent drug therapy on incidence of adverse GI events with successful re-feeding in these patients.

Materials and Methods

Records of dogs that were evaluated for inappetence, anorexia, vomiting, or regurgitation and for which a diagnosis of pancreatitis was recorded over a 4-year period from 2010 through 2013 at a university veterinary teaching hospital were eligible for inclusion. Records were considered for inclusion if a reasonable diagnosis of acute or acute-on-chronic pancreatitis was achieved by a combination of 2 of the 3 following diagnostic results: positive immunoassay (quantitative cPLI), consistent increase in catalytic assays (amylase and lipase), or compatible US changes. A cut-off of amylase and lipase activity at a minimum of 3 times the high end of reference interval was considered consistent with pancreatitis.[5,7] A positive US diagnosis was established if compatible US changes resulted in a diagnosis of pancreatitis as noted in the final report dictated by a Diplomate of the American College of Veterinary Radiology. Records were excluded if the period of hospitalization was < 48 hours, the patient had preexisting diabetes mellitus, exocrine pancreatic insufficiency, concurrent diabetic ketoacidosis, or was euthanized for nonmedical reasons. Records where the % RER could not be determined due to incomplete reporting of patient caloric intake were also excluded.

A standardized data sheet was used to record the following information for each animal: signalment, body weight and body condition score, RER, known predisposing factor(s), comorbidities, results of diagnostics performed, serum chemistry (specifically serum amylase and lipase concentrations), cPLI, interpretation of abdominal ultrasound, treatments provided, days until nutrition therapy offered since admission, daily nutrition therapy offerings including specific diet and fat

content (ie, low, <3 g fat/100 kcal or high, >3 g fat/100 kcal), days until return to voluntary intake based upon the time that food was first offered (defined as consuming a minimum of 5% RER), daily voluntary intake (% RER), incidence of GI including time relation to a recent meal offering if applicable (vomiting or regurgitation – [yes versus no]), and LOH. Dogs in whom feeding was initiated within the first 48 hours of hospitalization were included in the early feeding group (EFG), while dogs in whom feeding was initiated sometime after 48 hours of hospitalization were included in the delayed feeding group (DFG). Return to voluntary intake was defined as consuming a minimum of 5% RER. RER was determined by the exponential allometric equation, current body weight in kilograms$^{0.75}$ × 70.[23] A tolerant feeding event (FE) was associated with no GI, whereas an intolerant FE was associated with GI within 3 hours of food consumption.

A CSIS was assigned for each enrolled patient on a standardized data sheet.[2] The original 24-point scale described by Mansfield et al was utilized in this study not to predict outcome but rather apply a retrospective objective scoring system in order to group cases of similar severity (Table 1). Five variables (endocrine, hepatic, renal, hematopoietic, and local complications) were not shown to be statistically significant when using the scale to predict outcome and thus were subsequently excluded by Mansfield et al from their revised clinical severity index 10-point scale. However, it is the authors' opinion that exclusion of these variables would reduce stratification of disease severity in the analysis groups. Furthermore, the inclusion of the aforementioned variables would not affect the statistical power of the current study. Therefore, the original 24-point scale was utilized.

Statistical methods

All statistical analyses were performed in standard statistical software.[a] Descriptive statistics were calculated, with continuous data reported as means, medians, and ranges and categorical data reported as frequencies. Nonparametric Wilcoxon two-sample tests were run to compare continuous variables across categorical groupings. Chi-square tests were used to evaluate relationships between two categorical variables, unless sample sizes were low. In those instances, Fisher's exact test was used. Logistic regression was used to evaluate the impact of multiple variables on one categorical response variable. Exact binomial confidence intervals were calculated for proportions of interest. All *P* values were compared to a cut-off value of 0.05.

Results

Four hundred and forty-two dogs were treated for suspected acute or acute-on-chronic pancreatitis during the study period and were eligible for inclusion. Four hundred and eight dogs were excluded (86 were not hospitalized for a minimum of 48 h, 54 had preexisting diabetes mellitus, 16 were diagnosed with diabetic ketoacidosis at presentation, 111 did not meet the burden of diagnostic inclusion, and 141 did not have sufficient reporting of diet or voluntary intake throughout hospitalization). Thirty-four dogs treated for acute or acute-on-chronic pancreatitis during the study period were eligible (Table 2). Breeds represented included Yorkshire Terrier ($n = 7$ [21%]), Labrador Retriever (5 [15%]), Australian Shepherd (2 [6%]), and Miniature Schnauzer (2 [6%]). Another 18 breeds were represented with 1 dog each.

Twelve dogs (35%) were identified to have one or more of the following predisposing factors with the following incidence: steroid use (7), obesity (5), dietary indiscretion (4), hypertriglyceridemia (2), abdominal surgery (1), or hypotension/ischemic insult (1). No identifiable predisposing causes were noted at the time of treatment nor retrospectively in the remaining cases (65%) and were therefore deemed idiopathic, consistent with previously published veterinary literature.[21,22] (Table 2).

As the veterinary teaching hospital is a tertiary referral center, cases referred for treatment are often accompanied by complex medical histories or have one or more comorbidities identified during their hospitalization period. Twenty-four dogs (71%) had one or more of the following concurrent diseases with the following incidence: chronic kidney disease (6), untreated seizures (3), neoplasia located outside of the gastrointestinal tract (3), immune mediated hemolytic anemia (2), immune-mediated polyarthropathy (2), protein losing enteropathy (2), hypothyroidism (2), primary thrombocytopenia (1), intervertebral disc disease (1), pyoderma (1), inflammatory bowel disease (1), eosinophilic lymphadenitis/pharyngitis (1), heartworm disease (1), and urinary incontinence (1). No comorbidities were identified in 29% of the population (Table 2).

The severity and intensive management requirements of each case were stratified according to the original published CSIS system for AP in dogs. Twenty-four (71%) dogs were in the first quartile scoring ≤6. The remaining (10 [29%]) were within the second quartile score ≥7 to ≤12. Although no dogs in this study were score >12, scores 13–24 represent the third and fourth quartiles. Of the 34 dogs included in this study, 34 (100%) survived to discharge; however, 1 dog represented to the hospital 48 hours post discharge for recrudescence of clinical signs (ie, anorexia, fever, and nausea demonstrated by ptyalism) and was subsequently euthanized. An

Table 1: Factors associated with various body systems that were assessed initially as part of a Clinical Severity Index Score for acute pancreatitis in dogs (potential maximum total of 24 points)

System	Finding	Point allocation
Endocrine	No abnormalities	0
	Preexisting diabetes mellitus	1
	Diabetic ketoacidosis	2
Hepatic	No abnormalities	0
	≥2.5-fold increase (compared with upper limit of reference range) in at least 2 of the following:	
	Serum alkaline phosphatase, alanine transferase, and aspartate aminotransferase activities	1
	≥5-fold increase (compared with upper limit of reference range in at least 2 of the following: Serum alkaline phosphatase, alanine transferase, and aspartate aminotransferase activities	2
	Extrahepatic bile duct obstruction	3
Renal	No abnormalities	0
	Azotemia (≤1.5-fold increase [compared with upper limit of reference range] in serum urea and creatinine concentration)	1
	Anuria or azotemia (≥1.5-fold increase [compared with upper limit of reference range] in serum urea and creatinine concentration)	2
Hematopoietic	No abnormalities	0
	WBC count $\geq 20.0 \times 10^9$ cells/L or $\leq 4.0 \times 10^9$ cells/L, with ≤10% band neutrophils	1
	WBC count $\geq 20.0 \times 10^9$ cells/L or $\leq 4.0 \times 10^9$ cells/L, neutrophil count $\leq 1.0 \times 10^9$ cells/L, or ≥10% band neutrophils	2
	Clinicopathologic evidence of hypercoagulability or coagulation abnormalities	3
	Clinical evidence of disseminated intravascular coagulation or bleeding diathesis	4
Local complications	No abnormalities	0
	Peritonitis extending beyond peripancreatic area	1
	Pseudocyst or other acute fluid accumulation	2
	Pancreatic abscess	3
Cardiac	No abnormalities	0
	<60 ventricular premature complexes/24-hour period or heart rate >180 beats/min	1
	Paroxysmal or sustained ventricular tachycardia	2
Respiratory	No abnormalities	0
	Clinical evidence of dyspnea or tachypnea (>40 breaths/min)	1
	Clinical evidence of pneumonia or acute respiratory distress syndrome	2
Intestinal integrity	No abnormalities	0
	Intestinal sounds not detected during >3 auscultations in 24-hour period	1
	Hematochezia, melena, or regurgitation	2
	No enteral food intake for >3 days	3
	No enteral food intake for >3 days and at least 2 of the following: Hematochezia, melena, and regurgitation	4
Vascular forces	No abnormalities	0
	Systolic arterial blood pressure <60 or >180 mm Hg or serum albumin concentration <18 g/L	1
	Systolic arterial blood pressure <60 or >180 mm Hg and serum albumin concentration <18 g/L	2

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additional dog represented to the hospital 72 hours post discharge for persistent anorexia and was readmitted.

Data analysis is reported based on the timing (early or delayed) of offering food for the following points of interest: (1) the time to return to voluntary eating, (2) the maximum caloric intake per day during hospitalization, (3) the incidence of GI, and (4) LOH. Additional factors with possible impact on these 4 major interest points were likewise evaluated. Study populations included in the analysis were as follows:

(1) *All dogs* ($n = 34$); regardless of clinical severity score, assisted fed and not assisted fed.
(2) *Nonassisted fed dogs only* ($n = 27$). Included dogs that were limited to voluntary intake only throughout their hospitalization regardless of clinical severity score.
(3) *Assisted fed dogs only* ($n = 7$). Included dogs that were assisted fed via a nasoesophageal tube at some point in their hospitalization regardless of clinical severity score. No other enteral assisted feeding device or

Table 2: Baseline characteristics of 34 dogs with acute pancreatitis

Characteristic	Value		
	Early feeding group ($n = 19$)	**Delayed feeding group ($n = 15$)**	**Total population ($n = 34$)**
Age (y)	9.7 ± 4.0	8.7 ± 3.5	9.2 ± 3.8
Sex and neuter status			
Sexually intact female	0	0	0
Neutered female	14 (74)	9 (60)	23 (68)
Neutered male	5 (26)	5 (33)	10 (29)
Sexually intact male	0	1 (7)	1 (3)
BCS (0–9 scale)	5 ± 1.5	6 ± 1	5 ± 1.5
Known predisposing factor			
Yes	6 (32)	6 (40)	12 (35)
No	13 (68)	9 (60)	22 (65)
Concurrent/preexisting disease			
Yes	17 (89)	7 (47)	24 (71)
No	2 (11)	8 (53)	10 (29)
Clinical Severity Index Score	5 ± 4	5 ± 2	5 ± 3
0–6	11 (58)	13 (87)	24 (71)
7–12	8 (42)	2 (13)	10 (29)
>12	No animals met this criterion		

Values reported are mean ± SD or number of dogs (%).
BCS, body condition score.

parenteral feeding was utilized in this population. Analysis was performed on their voluntary intake only.

(4) *Clinical severity, all dogs* ($n = 34$) with a CSIS of ≤6 ($n = 24$) and ≥7 to ≤12 ($n = 10$).

Study populations were then subclassified into EFG, those who were offered food for voluntary intake early (ie, within 48 h of admittance to the hospital) or DFG (ie, those who were held NPO for a minimum of 48 h from admittance to the hospital). All dogs included in this study presented with an average of 3.1 days of anorexia preceding hospitalization (median 2.5 days, range 0–7) based upon history obtained at the time of intake. Dogs in the EFG had an average of 3 days of anorexia preceding hospitalization (median 2.5 days, range 0–7). Dogs within the DFG had an average of 3.3 days of anorexia preceding hospitalization (median 3 days, range 1–7).

Time to return to voluntary intake

In this population of dogs ($n = 34$), 19 (56%) were in the EFG versus 15 (44%) in the DFG (Table 3). The EFG dogs showed a significantly reduced time to return to voluntary intake as compared to dogs in the DFG (mean of 2.1 days versus 2.7 days, respectively; $P = 0.05$). Average mean time to maximum calorie intake was 3.0 days since initial food offerings in the EFG and 3.4 days in the DFG dogs (Table 3). Seven dogs were assisted fed at some point in their hospitalization with 4 in the EFG and 3 in the DFG. The small sample size of this subpopulation limited statistical analyses. There was no difference detected ($P = 0.44$) in mean time to return to voluntary intake between the feeding groups based on CSIS (≤6 versus ≥7 to ≤12).

Gastrointestinal intolerance

In this population of dogs, significantly more dogs in the DFG experienced GI (60%), defined as either regurgitation or vomiting, when compared to the EFG dogs (26%; $P = 0.04$) (Table 3). These 9 (60%) DFG dogs experienced the majority (71%) of their intolerance events when either being managed NPO or refusing to eat, while the remaining GI occurred when they consumed up to 66% RER. The mean dietary fat content (gram/100 kcal basis) of DFG dogs exhibiting GI was 3.6 (mode 5.4), and 3.3 (mode 2.9) for DFG dogs with no GI; however, dietary fat content appeared not to have impacted incidence of GI (Table 3). Five (26%) of the EFG dogs experienced GI, with the majority (61%) of GI occurring while refusing to eat, and the remainder of incidences noted when dogs consumed up to 66% RER. The mean dietary fat content in diets consumed by EFG dogs with and without GI was 4.2 (mode 5.4), and 3.2 (mode 1.8) grams fat/100 kcal, respectively (Table 3).

The data were likewise evaluated based on successful feeding events (FE), defined as the animal consuming a minimum of 5% RER. A tolerant FE was associated with no GI, whereas an intolerant FE was associated

Table 3: Time to return to voluntary intake, animals experiencing gastrointestinal intolerance, and total hospitalization time (days) for 34 dogs who were fed within the first 48 hours (EFG) or who were NPO for at least the first 48 hours (DFG)

	Population				
	EFG		DFG		
Variable	No. of dogs*	Value	No. of dogs*	Value	*P* value§
Time to return to voluntary intake (day consumed ≥5% RER) all dogs ($n = 34$)	19 (56)	2.1 (1)†	15 (44)	2.7 (3)†	0.05
Nonassisted fed dogs ($n = 27$)	15 (56)	1.6 (1)†	12 (44)	3.3 (3)†	0.03
Assisted fed dogs ($n = 7$)	4 (57)	4 (5)†	3 (43)	5 (6)†	
Time to reach maximum intake (day maximum calories consumed) all dogs ($n = 34$)		3 (3)†		3.4 (3)†	
Animals experiencing gastrointestinal intolerance (GI) ($n = 14$)	5 (26)		9 (60)		0.04
Nonassisted fed dogs	4 (21)		6 (40)		
Assisted fed dogs	1 (6)		3 (20)		
Dietary fat content (g/100 kcal) when GI was observed		4.2 (5.4)‡		3.6 (5.4)‡	
Dietary fat content (g/100 kcal) when GI was not observed		3.2 (1.8)‡		3.3 (2.9)‡	
Incidents of observed GI and narcotics ($n = 11$)	6(55)		5(45)		0.76
Dietary fat content ≤3 g/100 kcal, no narcotics/narcotics	2(33)/0(0)		2(40)/0(0)		
Dietary fat content ≥3 g/100 kcal, no narcotics/narcotics	3(50)/1(17)		2(40)/1(20)		
Length of hospitalization (days)	19 (56)	6 (5)†	15 (44)	5.1 (5)†	0.8

*Number of dogs (% of total population).
†The mean number of days (median day).
‡The mean dietary fat level (mode).
§*P*-values represent the means; where no *P*-value is provided, statistics were not available.

with GI. Utilizing a logistic regression model, the timing of feeding (EFG versus DFG, $P = 0.116$) coupled with dietary fat content (low vs. high, $P = 0.099$) had no impact on the incidence of GI during successful FE ($P = 0.188$). It is worth noting that 25.9% of the FE that used a high dietary fat content had associated GI, whereas 11.8% of FE that used a low dietary fat content diet had associated GI ($P = 0.153$).

Though approximately half of all GI in DFG and EFG dogs (47% and 54%, respectively) occurred while receiving narcotics for analgesia, the delivery of narcotic drugs during successful FE had no impact on incidence of adverse GI events ($P = 0.556$). The risk of GI across narcotic use within a high dietary level of fat was not significant ($P = 0.756$).

Incidence of GI in the nonassisted DFG dog population (40%) accounted for over half of the all dog DFG population experiencing intolerance (60%). The 3 DFG dogs that were assisted fed experienced GI at some point in their hospitalization; however, none occurred after initiating assisted feedings. Incidence of GI in the nonassisted EFG dog population (21%) was similar to the all dog EFG population (26%). Only 1 of the 4 dogs in the EFG dog that were assisted fed experienced GI at some point in their hospitalization; however, this incident occurred prior to initiating assisted feedings (Table 3).

There was no significant difference detected on the incidence of GI based upon the CSIS ($P = 1.00$) and no significant impact on GI between the EFG and DFG dogs with similar severity scores.

Total hospitalization time

Early or delayed feeding did not significantly impact LOH for the all, nonassisted fed, or assisted fed dog populations ($P = 0.8$; $P = 0.6$; $P = 0.6$, respectively, Table 3).

LOH (days) was significantly increased ($P = 0.004$) for cases with severity scores ≥7 to ≤12 (mean 8; median 7) as compared to those with scores ≤6 (mean 4.9; median 4.4). However, there was no significant impact on LOH between EFG and DFG dogs with similar clinical severity scores.

Maximum consumption

Table 4 summarizes the maximum voluntary consumption (% RER) for all groups based on EFG versus DFG and CSIS. Fourteen percent of DFG dogs failed to consume >5% of their RER throughout their hospitalization as compared to 5% of the EFG dogs. Fifty-three percent of DFG dogs consumed >33% RER, with 75% and 25% of these dogs being categorized as CSIS ≤ 6 and ≥7 to ≤12, respectively. Sixty-three percent of EFG dogs had a maximum voluntary intake of >33% RER, with 58% and 42% of these dogs being categorized as CSIS ≤ 6 and ≥7 to ≤12, respectively.

Discussion

Historically, the protocol for treating AP was to "rest" the pancreas in an effort to avoid the impetus for

Table 4: Voluntary maximum consumption for both the early and delayed feeding groups with subcategories of nonassisted and assisted fed based on Clinical Severity Index Score (CSIS)

	Voluntary maximum consumption as percent RER*			
Population	**0%–5%**	**>5%–33%**	**>33–66%**	**>66%**
Early feeding group				
All animals ($n = 19$)	1 (5)	6 (32)	7 (37)	5 (26)
CSIS ≤ 6 ($n = 11$)	0 (0)	4 (36)	5 (46)	2 (18)
CSIS ≥ 7 ($n = 8$)	1 (12)	2 (25)	2 (25)	3 (38)
Nonassisted fed ($n = 15$)	0 (0)	4 (27)	6 (40)	5 (33)
CSIS ≤ 6 ($n = 9$)	0 (0)	2 (22)	5 (56)	2 (22)
CSIS ≥ 7 ($n = 6$)	0 (0)	2 (33)	1 (17)	3 (50)
Assisted fed† ($n = 4$)	1 (25)	2 (50)	1 (25)	0 (0)
CSIS ≤ 6 ($n = 2$)	0 (0)	2 (100)	0 (0)	0 (0)
CSIS ≥ 7 ($n = 2$)	1 (50)	0 (0)	1 (50)	0 (0)
Delayed feeding group				
All animals ($n = 15$)	2 (14)	5 (33)	5 (33)	3 (20)
CSIS ≤ 6 ($n = 13$)	2 (15)	5 (39)	3 (23)	3 (23)
CSIS ≥ 7 ($n = 2$)	0 (0)	0 (0)	2 (100)	0 (0)
Nonassisted fed ($n = 12$)	2 (17)	2 (17)	5 (12)	3 (25)
CSIS ≤ 6 ($n = 10$)	2 (20)	2 (20)	3 (30)	3 (30)
CSIS ≥ 7 ($n = 2$)	0 (0)	2 (100)	0 (0)	0 (0)
Assisted fed† ($n = 3$)	0 (0)	3 (100)	0 (0)	0 (0)
CSIS ≤ 6 ($n = 3$)	0 (0)	3 (100)	0 (0)	0 (0)
CSIS ≥ 7 ($n = 0$)	No animals met this criterion			

*Values reported are number of dogs and (%) categorical population.

†Values represent voluntary consumption only of these dogs, despite feeding tube in place.

pancreatic exocrine stimulation that would ultimately result in autodigestion and potential worsening of the disease process. However, this has not been proven in dogs and several studies have suggested that there is minimal to no negative pancreatic feedback in dogs when provided nutrition in both the duodenum and jejunum.[10,25–27] It is the authors' observation that most patients are brought to veterinarians for evaluation after clinical signs of inappetence, anorexia, or GI fail to resolve on their own, and subsequent diet change(s) occurring over several successive days have had little or no impact. The ideal duration of fasting has not been identified in human or veterinary literature, and may likely be patient-severity dependent if required at all. In fact, further imposed anorexia may be counterproductive to overall gastrointestinal health as avoidance of EN has been correlated to increased gut permeability, bacterial or endotoxin translocation, and immunosuppression.[1,4,8–11] Additionally, the gut itself may either start or contribute to the systemic inflammatory response in AP.[24]

The present study of dogs treated for acute or acute-on-chronic pancreatitis found that the dogs that were held NPO for a minimum of 48 hours from admission to the hospital experienced significantly more days of GI throughout their hospitalization period. Additionally, a greater percentage of these dogs ultimately consumed a considerably smaller percentage of RER than those dogs that had been offered food starting at the time of hospital admittance. However, there was not a statistically significant difference in GI incidence in dogs scoring ≤6 or ≥7 on the CSIS throughout the hospitalization period.

As the average days of anorexia in all groups preceding hospitalization was 3 days, this finding suggests that the period of anorexia prior to hospitalization may be sufficient to "rest" the pancreas according to traditional dogma and that further imposed food restriction while hospitalized is unwarranted. Studies including dogs with both experimentally induced and naturally occurring AP report benefit from nutritional support implemented within 48 hours of admission or immediately if ≥5 days of anorexia, defined as consuming <66% of RER, is present.[9,10,31] Early nutritional intervention becomes more important with increasing severity of disease.[1] When voluntary intake is insufficient to meet daily caloric intake goals, a more effective method of nutritional support therapy is required. Assisted feeding provides an efficient means of facilitating nutritional support and is generally well tolerated.

The present study found a significant difference in return to voluntary intake, defined as consuming >5% RER related to the timing of initiating food offerings. This difference was not affected by degree of severity of disease. Not only did the EFG dogs return to voluntary intake more quickly when food was introduced ($P = 0.05$) but they also reached their maximum

voluntary intake faster than the DFG dogs. This likely could be a positive influence on voluntary intake as the presence of intraluminal nutrients may stimulate central hunger impulses via complex neurologic signaling pathways.[27,28]

In the present study the sample size for evaluating the impact of assisted feeding was too small to allow for statistical evaluation of this group alone. However, all dogs that were assisted fed in the DFG resumed voluntary intake while hospitalized, whereas 17% of dogs in the DFG group that were not assisted fed remained anorexic throughout the hospitalization period. Moreover, none of the assisted fed dogs in the DFG experienced GI after the initiation of assisted feeding. This may imply that assisted feeding is likely beneficial in patients who are experiencing prolonged anorexia (≥5 days from the start of clinical signs) in regards to returning to voluntary intake and may have a tendency to positively impact the frequency of GI. However, prospective, randomized, controlled studies are necessary to determine definitive association and clinical significance.

Historically, when selecting the diet to implement enteral feeding it has been generally recommended to select a highly digestible diet designed for patients with gastrointestinal disease. Avoidance of a diet with a moderate to moderately high-fat content (>3 g/100 kcal) has been the long-standing recommendation; however, in one study of healthy dogs, there was no significant difference in measureable pancreatic secretions in dogs fed variable fat content.[28] This raises the question of whether feeding a low-fat diet is essential in the management of AP.[4,9,28] Review of the study data for both the early and delayed feeding groups indicated higher dietary fat content (g/100 kcal basis) was associated with GI as compared to no GI (3.6 versus 3.3 DFG; 4.2 versus 3.2 EFG), though statistical analysis of these data was not possible. When evaluated based on successful FE rather than number of dogs, a lower percentage (11.8%) of the FE with concurrent GI was noted when dogs consumed a diet with low dietary fat content as compared to dogs consuming a diet with high dietary fat content (25.9%). Contrary to these observational data, logistic regression analysis indicates that dietary fat level had no statistical impact on incidence of GI (ie, regurgitation or vomiting), which is the hallmark clinical concern with managing the canine AP patient.

There was not an impact on LOH on any group in relation to the timing of implementation of nutritional therapy. The only factor that had a significant impact on LOH in the present study was a CSIS > 7. In people, patients that tolerated early EN had a decreased duration of care and ultimately cost of hospitalization.[29] Unlike human counterparts, the timing of discharge in veterinary medicine can be influenced by limitation of owner finances. Therefore, future prospective studies to determine the impact of enteral nutritional therapy provided within 48 hours of hospitalization on duration of care and ultimately cost of hospitalization of dogs with acute or acute-on-chronic pancreatitis with a CSIS score ≥7 is needed.

The present study had a number of limitations, notably the retrospective nature and small sample size. Prior to 2012, recording of volume consumed of the prescribed nutritional therapy in an objective manner was not a standardized practice at our teaching hospital and resulted in the exclusion of a number of cases that would otherwise have met the inclusion criteria. Treatment protocol differences in clinician therapeutic preferences were minimal as all cases received antiemetic therapy (maropitant,[b] ondansetron,[c] or metoclopramide[d]) and analgesia (fentanyl[e]) within published dosage ranges.[25] No case was prescribed a known appetite stimulant. One case received an injection of a corticosteroid (dexamethasone[f]) within published dosage ranges for anti-inflammatory purposes.[25] All cases received at least one dose of an antimicrobial (ampicillin sulbactam[g] or metronidazole[h]) within published dosage ranges[25] and crystalloid fluid therapy to meet maintenance requirements and correct any identified hypovolemia and electrolyte disturbances. A small number of cases received plasma or a colloid solution[i] for oncotic support. Although statistical evaluation was not performed, given the similarity of therapeutic approach of all cases independent of primary clinician, the author feels this limitation had minimal impact on study findings. Though we attempted to highlight the potential impact of dietary fat on study outcomes, dietary fat intake was not part of the inclusion or exclusion criteria of this retrospective study design, and focused statistical analysis associated with fat content influencing the primary study outcomes was not warranted. Future research to identify the impact of early, low-fat nutritional therapy on systemic and specific pancreatic biomarkers of inflammation and clinical outcome may well benefit optimization of the nutrient profile for refeeding these patients.

The traditional nutrition support protocol of prolonged NPO for the management of dogs diagnosed with AP should be challenged based on studies that report the benefits of early nutrition support for human pancreatitis patients. Our study of dogs, with naturally occurring pancreatitis, supports the human studies in that time to implementation of a feeding plan had a positive impact on return to voluntary intake. Offering food within the first 48 hours of hospital admission for AP was associated with a significantly faster return to voluntary intake and a reduction in the number of dogs exhibiting GI. These findings were independent of the CSIS of

the patient, although dogs with a CSIS ≥7 did have a significantly prolonged LOH. Overall, the findings in this study population indicate that early enteral feeding is associated with a lower incidence of GI, suggesting a relevant benefit to this nutritional approach in the management of naturally occurring canine pancreatitis. Based on our findings we do not feel the approach of managing dogs with pancreatitis with periods of NPO is justified. Moreover, early refeeding was not associated with adverse complications in these patients.

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Footnotes

[a] SAS, Version 9.3; Cary, NC.
[b] Maropitant citrate (Cerenia), Zoetis, Florham Park, NJ.
[c] Ondansetron HCl (Zofran), GlaxoSmithKline, Durham, NC.
[d] Metoclopramide HCl (Reglan), Wyeth-Ayerst, Madison, WI.
[e] Fentanyl (Sublimaze), Akorn, Lake Forest, IL.
[f] Dexamethasone injection (azium solution), Schering-Plough, Kenilworth, NJ.
[g] Ampicillin Sodium/Sulbactam Sodium (Unasyn), Pfizer, New York, NY.
[h] Metronidazaole Injection (generic), B. Braun. Bethlehem, PA.
[i] Tetrastarch Injection (Voluven), Pfizer.

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