Associations between dietary factors and pancreatitis in dogs

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Objective—To estimate associations between dietary factors and pancreatitis in dogs.

Design—Retrospective case-control study.

Animals—198 dogs with a clinical diagnosis of pancreatitis and 187 control dogs with a diagnosis of renal failure without clinical evidence of pancreatitis.

Procedures—Information on signalment, weight, body condition, dietary intake, medical history, diagnostic tests performed, concurrent diseases, treatments, duration of hospitalization, and discharge status was extracted from medical records. Information on dietary intake, signalment, weight, and medical, surgical, and environmental history was collected through a telephone questionnaire. Logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals.

Results—On the basis of information extracted from the medical record, ingesting unusual food items (OR, 4.3) increased the odds of pancreatitis. On the basis of information gathered through the telephone questionnaire, ingesting unusual food items (OR, 6.1), ingesting table scraps the week before diagnosis (OR, 2.2) or throughout life (OR, 2.2), and getting into the trash (OR, 13.2) increased the odds of pancreatitis. Multivariable modeling indicated that reporting exposure to ≥ 1 dietary factor during the telephone questionnaire (OR, 2.6), being overweight (OR, 1.3) or neutered (OR, 3.6), previous surgery other than neutering (OR, 21.1), and the interaction between neuter status and previous surgery other than neutering (OR, 0.1) were associated with the odds of pancreatitis.

Conclusions and Clinical Relevance—Results suggested that dietary factors, being neutered, and previous surgery other than neutering increased the odds of pancreatitis in dogs. (*J Am Vet Med Assoc* 2008;233:1425–1431)

Previous claims that certain dietary factors can increase the odds of pancreatitis in dogs have been based mainly on anecdote.[1,2] On the other hand, high-fat diets have been shown experimentally to induce pancreatitis[3] and to increase the severity of experimentally induced pancreatitis[4] in dogs. Diet has also been shown experimentally to affect the concentration of pancreatic enzymes,[5] and in some dogs, the onset of clinical signs of pancreatitis can follow ingestion of fatty foods.[6]

In previous studies[1] of pancreatitis, dietary variables have often been excluded, making it difficult to determine the role of diet in this condition. The purpose of the study reported here therefore was to determine whether specific dietary factors were associated with pancreatitis in dogs.

Materials and Methods

The study was conducted as a retrospective case-control study. The study protocol was reviewed and approved by the Texas A&M University Institutional Review Board.

Case selection—Medical records of the Small Animal Clinic at Texas A&M University were reviewed to identify dogs first examined on an inpatient basis between January 1, 2000, and December 31, 2005, in which a diagnosis of pancreatitis had been made. Dogs were included as case dogs in the present study if history and clinical signs were suggestive of pancreatitis and the diagnosis had been confirmed on the basis of ancillary testing. Because there currently is no definitive test for pancreatitis in dogs, specific testing criteria were not used in the present study to identify dogs with pancreatitis. Rather, dogs were considered to have pancreatitis if the diagnosis had been made by the primary clinician on the basis of various combinations of clinical signs, radiographic findings, ultrasonographic findings, serum cPLI, and histologic findings and if other possible conditions had been ruled out on the basis of results of a CBC and serum biochemical panel. Information was obtained only for the first visit of each case

Abbreviations

BCS	Body condition score
CI	Confidence interval
cPLI	Canine pancreatic lipase immunoreactivity
OR	Odds ratio

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dog, and information for subsequent visits of the same dog was not included. Dogs examined solely on an outpatient basis and dogs with a concurrent illness that was the primary reason for examination were excluded from the present study. This included dogs with acute or chronic renal failure unrelated to pancreatitis, acute intervertebral disk disease, trauma secondary to being hit by a car, esophageal foreign bodies, seizures, and malignant neoplasia.

Control selection—Control dogs consisted of dogs first examined on an inpatient basis at the Small Animal Clinic between January 1, 2000, and December 31, 2005, in which a diagnosis of acute or chronic renal failure of unknown cause was made. Dogs with a concurrent diagnosis of pancreatitis, acute intervertebral disk disease, trauma secondary to being hit by a car, esophageal foreign body, seizures, or malignant neoplasia were excluded from the control group. However, dogs that had a history of pancreatitis that had resolved and that did not have any current indications of pancreatitis were included in the control group.

Control dogs were frequency matched with case dogs on the basis of disease severity. Disease severity categories for case and control dogs consisted of the following: not treated with IV fluids and discharged from the hospital alive, treated with IV fluids and discharged from the hospital alive, and died or euthanatized while hospitalized. For disease severity categories with more control than case dogs, control dogs were randomly selected to equal the number of case dogs. For categories with more case than control dogs, all control dogs were included.

Review of medical records—Information on dietary factors was obtained from the medical records of case and control dogs. Specifically, when available, information was obtained on whether the dog had ingested any table food on a regular basis or had ingested any food items that were unusual for the dog. For this analysis, veterinary-prescribed homemade diets were not considered table food. Proximity of the onset of clinical signs to a holiday was evaluated on the basis of recorded date of admission. Holidays evaluated were those that were expected to be celebrated by most of the population in the referral area and included New Year's Day, Mardi Gras (Fat Tuesday), Easter, Memorial Day, Independence Day, Labor Day, Halloween, Thanksgiving, and Christmas. A dog was considered to have developed clinical signs in conjunction with a holiday if the diagnosis had been made within 7 days after the holiday. For Easter, Thanksgiving, and Christmas, a dog was also considered to have developed clinical signs in conjunction with the holiday if the diagnosis was made on that day because food preparations typically began earlier for these 3 holidays.

Additional information obtained from medical records of dogs included in the study consisted of age at the time of diagnosis, breed, sex, neuter status, body weight, body condition, concurrent diseases, diet, admission date, discharge status, hospitalization time, number of days treated with IV fluids, cPLI at the time of admission, and whether serum obtained at the time of admission was grossly lipemic. Body condition was categorized as underweight, normal, or overweight as determined by the BCS, when available, and comments included in the record, when BCS was not recorded. If body condition had been scored on a 5-point scale, dogs with a BCS < 2.5 were categorized as underweight, dogs with a BCS between 2.5 and 3.5 were categorized as normal, and dogs with a BCS > 3.5 were categorized as overweight. If body condition had been scored on a 9-point scale, dogs with a BCS < 4 were categorized as underweight, dogs with a BCS between 4 and 6 were categorized as normal, and dogs with a BCS > 6 were categorized as overweight. If a BCS or specific comments had not been recorded in the medical record, body condition was categorized by comparing body weight with standard ranges suggested by the American Kennel Club.

Discharge status was recorded as alive, euthanatized, or died. Diet history was extracted from the general entrance questionnaire that clients completed while in the waiting room and from the history sheet that senior veterinary students completed while questioning the owner in the examination room. Dogs in which hypothyroidism was diagnosed while hospitalized and dogs receiving thyroid supplementation at the time of the initial examination were considered to have concurrent hypothyroidism.

Telephone questionnaire—Additional information on dietary factors was obtained through a telephone questionnaire. Owner addresses and telephone numbers were obtained from the medical records of case and control dogs included in the study, and a copy of the telephone questionnaire, a letter of introduction, and an information sheet about the study were mailed to the owners. Packets were sent out every 1 to 2 weeks in batches of 100 from October through November 2006. The order of mailings was randomized so that the investigator conducting telephone interviews was blinded to whether individuals owned a case or control dog. Owners were called beginning 1 week after each set of mailings and asked to participate in the study. For owners who agreed to participate, the interview followed a prearranged script.[a] Three attempts were made to contact each owner. A message was left if an answering machine was reached.

The telephone questionnaire included questions about the dog's signalment, health history, regular diet, housing, and preventative health treatments and about other pets in the household; demographic information regarding the owner was also obtained. Questions regarding 5 dietary factors were included: whether the dog had ingested any unusual food items during the week before admission to the Small Animal Clinic, whether the dog had ingested table scraps during the week before admission, whether the dog routinely ingested table scraps, whether the dog had ingested food items from the trash during the week before admission, and whether the dog had been present at a large gathering with food during the week before admission. Exposure to any combination of these 5 factors was also included in the analysis. Information on ingestion of nonfood items, including foreign bodies, toxins, and owner medications, was excluded. Health history included questions about prescription medications and previous illnesses, traumatic events, and surgeries. Previous surgeries were categorized as neutering, elective surgeries other than neutering (eg, orthopedic, dental, or cosmetic surgery and benign mass removal), and urgent surgeries other than neutering (eg, surgery of the abdominal or pelvic cavity or neoplastic mass removal).

Statistical analysis—The Kolmogorov-Smirnov test was used to determine whether continuous variables, including age, weight, hospitalization time, number of days receiving fluids IV, and serum cPLI, were normally distributed. Because data were not normally distributed, they were summarized as median and range, and the Mann-Whitney *U* test was used to compare values between case and control dogs.

Categoric variables, including sex, neuter status, whether serum was grossly lipemic, concurrent illnesses, referral status, proximity to a holiday, breed, year of diagnosis, body condition, and dietary factors, were summarized as frequencies and compared between case and control groups by use of χ^2 or Fisher exact tests. Crude ORs, 95% CIs, and Pearson χ^2 *P* values were calculated. Adjusted ORs, 95% CIs, and Mantel-Haenszel χ^2 *P* values were calculated after stratification on the basis of disease severity. A difference of ≥ 15% between crude and adjusted ORs was taken to indicate that confounding was meaningful and that stratification needed to be incorporated in the analysis.

Binary logistic regression was used to estimate the association between case-control status and the predictor variables in the study. Bivariable analysis was used to evaluate each variable individually, with variables with *P* values ≤ 0.2 included in subsequent analyses. Although information on inappropriate dietary ingestion was obtained from the medical record, the primary exposure of interest was any inappropriate dietary ingestion as reported during the telephone interview. For each primary exposure of interest, the OR from the bivariable analysis (crude OR) was compared with the OR when evaluated with each other variable individually (adjusted OR). Those variables with a ≥ 15% difference between adjusted and crude ORs were considered confounders.

Multivariable analysis included confounders and those variables with *P* values ≤ 0.20 in bivariable analyses as a starting point for model building. The model building only included data from case and control dogs whose owners participated in the telephone interview, with other dogs excluded because of missing data. Any inappropriate dietary factor as determined during the telephone interview was the primary variable of interest. Backward stepwise analysis based on likelihood ratio tests was used to determine the final main effects model. However, the primary exposure and all variables determined to be confounders were forced into the model. In addition, pairwise interaction terms were created for all variables retained in the main effects model and tested for significance by means of backward stepwise analysis.

Variables extracted from the medical records were compared between owners who did and did not respond to the telephone questionnaire. For continuous variables, the Mann-Whitney *U* test was used to compare values between responders and nonresponders. For categoric variables, the Pearson χ^2 test was used to compare values between responders and nonresponders.

All statistical analyses were performed with commercially available software.[b] Values of $P \leq 0.05$ were considered significant. Exact software[c] was used for bivariable analyses when contingency tables had cells containing 0.

Results

Between January 1, 2000, and December 31, 2005, 265 dogs with pancreatitis and 472 dogs with renal failure were examined at the Small Animal Clinic. Of these, 198 met the inclusion criteria for the case group and 186 met the inclusion criteria for the control group. There were 6 dogs examined during the study period in which both renal failure and pancreatitis were diagnosed, and 5 of these dogs were excluded because the order of disease development could not be determined. The remaining dog was retained in the control group because renal failure was diagnosed prior to the development of pancreatitis. Owners of 114 of the 198 (58%) case dogs and 113 of the 186 (61%) control dogs responded to the telephone questionnaire. Annual diagnosis of pancreatitis was significantly higher during 2004 and 2005 than it was during 2000 to 2003 (OR, 1.8; 95% CI, 1.2 to 2.8; *P* = 0.004).

Body weight, hospitalization time, and number of days treated with fluids IV were significantly different between case and control dogs (**Table 1**). Serum cPLI was not significantly different between case and control dogs, but values were available for only 91 of the case dogs and only 3 of the control dogs. Sex distribution was not significantly different between case and control dogs (**Table 2**); however, the proportion of dogs that were neutered was significantly higher for case than for control dogs.

Disease severity was not identified as a meaningful confounder; therefore, unconditional logistic regression was performed. In bivariable screening, the odds of pancreatitis were significantly higher in Miniature Schnauzers than in dogs of other breeds (OR, 4.1; 95% CI, 1.9 to 9.2; *P* < 0.001), in Yorkshire Terriers than in dogs of other breeds (OR, 4.3; 95% CI, 1.2 to 15.3; *P* = 0.015), and in terriers in general (OR, 2.5; 95% CI, 1.4 to 4.5; *P* = 0.001). Dogs with grossly lipemic serum were 3.9 times (95% CI, 1.9 to 8.1; *P* < 0.001) as likely to have pancreatitis as were dogs without grossly lipemic serum, and dogs with diabetes mellitus were 3.6 times (95% CI, 1.0 to 13.1; *P* = 0.039) as likely to have pancreatitis as were dogs without diabetes mellitus.

Table 1—Comparison of descriptive statistics for 198 dogs with pancreatitis (case dogs) and 186 dogs with renal failure of unknown cause (control dogs) enrolled in a retrospective case-control study of the association between dietary factors and pancreatitis.

Variable	Case dogs	Control dogs	*P* value
Age (y)	8 (0.2–18)	7 (0.2–19)	0.105
Weight (kg)	9.1 (0.5–49.5)	14.8 (0.5–81.8)	0.002
Hospitalization time (d)	3 (1–37)	1 (1–35)	0.003
Duration of IV fluid treatment (d)	2.0 (0–14)	0.5 (0–27)	0.004
Serum cPLI (µg/L)*	333 (2.5–1,351)	148 (134–328)	0.328

Data are given as median (range).
*Values were available for only 91 case and 3 control dogs.

Overweight dogs were 1.9 times (95% CI, 1.2 to 3.0; $P = 0.004$) as likely to have pancreatitis as were dogs that were normal or underweight. Dogs that were reported in the medical record to have had a history of unusual food ingestion, which included ingestion of any food item that the dog did not normally eat, were 4.3 times (95% CI, 1.7 to 10.7; $P = 0.001$) as likely to have pancreatitis as were dogs without any such history.

Bivariable analysis of results of the telephone questionnaire (114 case and 113 control dogs) also identified dietary factors associated with pancreatitis (**Table 3**). Dogs with exposure to ≥ 1 of the 5 dietary factors assessed through the telephone interview (ie, dogs with any inappropriate dietary factor) were 2.9 times (95% CI, 1.7 to 5.0; $P < 0.001$) as likely to have pancreatitis as were dogs without exposure to any of these factors. Compared with dogs without exposure to any of these dietary factors, dogs exposed to 1, 2, or 3 to 5 factors were 2.1 times (95% CI, 0.8 to 5.3), 2.3 times (95% CI, 1.2 to 4.7), and 11.4 times (95% CI, 2.5 to 105.3), respectively, as likely to have pancreatitis. Dogs that had undergone surgery any time previously were 7.2 times (95% CI, 2.9 to 18.0; $P < 0.001$) as likely to have pancreatitis as were dogs that had not undergone surgery previously. Dogs with a history of urgent surgeries other than neutering were 27.5 times (95% CI, > 3.5) as likely and dogs with a history of elective surgery other than neutering were 4.0 times (95% CI, 0.2 to 61.6) as likely to have pancreatitis as were sexually intact dogs that had not undergone surgery previously.

The multivariable logistic regression model included a history of any inappropriate dietary factor as assessed during the telephone interview as the primary exposure of interest. A variable for body condition was retained in the model to control for confounding. The final model included the primary exposure of interest (ie, any inappropriate dietary factor), body condition (overweight vs normal or underweight), year of diagnosis (2000 to 2003 vs 2004 or 2005), any previous surgery other than neutering, neuter status (neutered vs sexually intact), and a term for the interaction between neuter status and previous surgery other than neutering (**Table 4**). The model used only 100 case

Table 2—Results of bivariable analyses of potential associations between pancreatitis and data extracted from medical records for 198 dogs with pancreatitis (case dogs) and 186 dogs with renal failure (control dogs) examined at the Texas A&M University Small Animal Clinic between 2000 and 2005.

Variable	Case dogs*	Control dogs*	OR (95% CI)	*P* value
Terrier group	0.22 (44/198)	0.10 (19/186)	2.5 (1.4–4.5)	0.001
Examined between 2000 and 2003	0.48 (96/198)	0.34 (63/186)	1.8 (1.2–2.8)	0.004
Proximity to a holiday	0.15 (30/198)	0.20 (38/186)	0.7 (0.4–1.2)	0.176
Overweight	0.42 (73/173)	0.27 (48/175)	1.9 (1.2–3.0)	0.004
Ingestion of unusual food items	0.14 (26/185)	0.04 (6/163)	4.3 (1.7–10.9)	0.001
Ingestion of table food	0.58 (108/185)	0.49 (80/163)	1.5 (1.0–2.2)	0.082
Male	0.50 (99/198)	0.48 (89/186)	1.1 (0.7–1.6)	0.674
Neutered	0.85 (168/198)	0.67 (125/186)	2.7 (1.7–4.5)	< 0.001
Spayed female	0.44 (88/198)	0.42 (78/186)	1.1 (0.7–1.7)	0.620
Castrated male	0.40 (80/198)	0.25 (47/186)	2.0 (1.3–3.2)	0.002

*Data are given as proportion of dogs (number of dogs with factor/number of dogs for which information was available).

Table 3—Results of bivariable analyses of potential associations between pancreatitis and data obtained through telephone interviews of owners of 114 dogs with pancreatitis (case dogs) and 113 dogs with renal failure (control dogs) examined at the Texas A&M University Small Animal Clinic between 2000 and 2005.

Variable	Case dogs*	Control dogs*	OR (95% CI)	*P* value
Previous surgery	0.95 (106/112)	0.71 (79/111)	7.2 (2.9–18.0)	< 0.001
Surgery other than neutering	0.37 (41/112)	0.23 (26/111)	1.9 (1.1–3.4)	0.032
Previous surgery in sexually intact dogs	0.53 (8/15)	0.07 (2/30)	16.0 (2.8–92.7)	0.002
Previous surgery† in neutered dogs	0.34 (33/97)	0.30 (24/81)	1.2 (0.6–2.4)	0.532
Ingestion of unusual food items‡	0.22 (25/114)	0.04 (5/113)	6.1 (2.2–16.5)	< 0.001
Ingestion of table scraps‡	0.40 (46/114)	0.24 (27/113)	2.2 (1.2–3.8)	0.008
Ingestion of table scraps on a regular basis	0.39 (44/114)	0.22 (25/113)	2.2 (1.2–4.0)	0.007
Got into trash‡	0.08 (7/114)	0.00 (0/113)	13.2 (> 2.1)	0.003
Present at large gathering with food‡	0.06 (7/114)	0.02 (2/113)	3.6 (0.7–17.9)	0.092

†Other than neutering. ‡During the week prior to admission.
See Table 2 for remainder of key.

Table 4—Results of multivariable logistic regression of associations between various factors and pancreatitis for 100 dogs with pancreatitis (case dogs) and 105 dogs with renal failure (control dogs) examined at the Texas A&M University Small Animal Clinic between 2000 and 2005.

Variable	Parameter estimate	*P* value (Wald)	OR (95% CI)
Any inappropriate dietary factor	0.95	0.004	2.6 (1.4–5.0)
Overweight (vs underweight or normal)	0.24	0.480	1.3 (0.7–2.5)
Examined between 2000 and 2003 (vs 2004 or 2005)	1.2	< 0.001	3.5 (1.9–6.5)
Previous surgery other than neutering	3.1	0.001	21.1 (3.3–133.9)
Neutered (vs sexually intact)	1.3	0.009	3.6 (1.4–9.5)
Interaction between previous surgery and neuter status	–3.0	0.004	0.05 (0.01–0.38)

Table 5—Comparison of descriptive statistics for 227 dogs whose owners responded to a telephone questionnaire regarding potential associations between pancreatitis and dietary factors (responders) and 157 dogs whose owners did not respond (nonresponders).

Variable	Responders	Nonresponders	*P* value
Age (y)	8.0 (0.3–19.0)	7.0 (0.2–18.0)	0.017
Weight (kg)	12.1 (1.4–54.1)	10.2 (0.5–81.8)	0.047
Hospitalization time (d)	2.0 (1–35)	2.0 (1–37)	0.685
Duration of IV fluid treatment (d)	1.0 (0–27)	1.3 (0–14)	0.704
Serum cPLI (µg/L)	352 (2.5–1,262)	232 (15–1,351)	0.429
Overweight	0.33 (70/209)	0.37 (51/139)	0.540
Terrier group	0.17 (38/227)	0.16 (25/157)	0.832
Examined between 2000 and 2003	0.54 (122/227)	0.66 (103/157)	0.020

Data are given as median (range) or as proportion of dogs (number of dogs with factor/number of dogs for which information was available).

and 105 control dogs because of missing values but was considered a good fit for the data on the basis of the Hosmer-Lemeshow statistic ($P = 0.814$).

Among dogs that were sexually intact, those with a history of previous surgery were 21 times (95% CI, 3.3 to 134; $P = 0.001$) as likely to have pancreatitis as were dogs that had never undergone surgery. Among dogs that were neutered, those with a history of previous surgery other than neutering were not significantly (OR, 1.1; 95% CI, 0.52 to 2.2; $P = 0.844$) more likely to have pancreatitis than were dogs without any history of surgery other than neutering. Among dogs without any history of surgery other than neutering, those that were neutered were 3.6 times (95% CI, 1.4 to 9.5; $P = 0.009$) as likely to have pancreatitis as were dogs that were sexually intact. Among dogs with a history of surgery other than neutering, those that were neutered were less likely (OR, 0.19; 95% CI, 0.03 to 1.1; $P = 0.060$) to have pancreatitis than were dogs that were sexually intact.

Median hospitalization time, number of days treated with IV fluids, serum cPLI, body condition, and breed group distribution (terrier group vs other) were not significantly different between responders and nonresponders to the telephone questionnaire (**Table 5**). However, age, weight, and year of diagnosis were significantly different between the 2 groups.

Discussion

Results of the present study suggested that certain dietary factors were significantly associated with pancreatitis in dogs. In particular, both a history of unusual food ingestion in the medical record and a report of any inappropriate dietary factor during the telephone interview were significantly associated with pancreatitis. This suggested that exposure to an unusual food may be important in the pathogenesis of pancreatitis. Of the individual dietary factors examined, getting into the trash the week before admission had the highest relative odds of pancreatitis; however, the upper limit of the 95% CI could not be defined because none of the dogs in the control group were reported to have gotten into the trash the week before admission. The association between pancreatitis and getting into the trash might be due to the types of items dogs are likely to find in the trash. For example, trash can contain lower-quality foodstuffs, including fat trimmings and expired or spoiled food. Feeding table scraps the week before admission and feeding table scraps regularly throughout life were also associated with similar increases in the odds of pancreatitis. Owners that regularly gave their dogs table scraps often continued to do so during the week before admission. Dogs that did not eat table scraps the week before admission but did regularly could have been anorectic because of illness. There were some owners who did not regularly feed table scraps but did so during the week before admission. In these instances, pancreatitis could have developed because the owner fed the dog table scraps or the dog could have developed pancreatitis earlier and the owner began feeding table scraps because of anorexia. On the other hand, a history of ingesting table scraps in the medical record and a report of the dog having been present at a large gathering with food during the week before admission were not significantly associated with increased odds of pancreatitis.

Dietary fat has previously been suggested to cause pancreatitis in dogs.[3,4] A potential problem with the association between dietary factors and pancreatitis is that it is unknown how diet history might have affected the clinical workup for case and control dogs. However, because 80 of 163 (49%) control dogs were noted in their medical records to have received table scraps, it is likely that dietary history was not a major factor in the diagnosis of pancreatitis.

In bivariable analyses in the present study, neutered dogs and castrated male dogs had increased odds for developing pancreatitis. Spayed and neutered dogs may have an increased risk of becoming overweight.[7,8] However, the term for body condition was retained in the multivariable model; thus, confounding associated with body condition was controlled for in this analysis. Surprisingly, spayed female dogs did not have an increased odds of pancreatitis, relative to all other dogs, which contradicts what has been reported in previous studies.[1,2]

Median body weight was significantly different between case and control groups in the present study, with dogs with pancreatitis weighing significantly less than dogs with renal failure. The lower body weight of dogs with pancreatitis could have been due to a predisposition for pancreatitis among smaller dog breeds. Some breeds that have been reported to be at increased risk for pancreatitis in previous studies[1,2] also had an increased odds of pancreatitis in the present study. This included Miniature Schnauzers, Yorkshire Terriers, and terriers as a group. In the present study, however, we did not find an association between the nonsporting breeds, Labrador Retrievers, or Miniature Poodles and odds of pancreatitis, as has been reported elsewhere.[1,2] Breed associations might indicate a genetic predisposition for pancreatitis or could reflect differences in diet, such as a greater likelihood of being fed table scraps, among smaller dogs.[9]

A history of previous surgery was associated with an increased odds of pancreatitis in the present study. This could have been due to exposure to anesthetic agents, trauma to the pancreas during surgery, or hypoperfusion of the pancreas during surgery. Sexually intact dogs with a history of previous surgery had a much higher odds of having pancreatitis than did sexually intact dogs without any such history, whereas neutered dogs with a history of previous surgery (other than neutering) were not more likely to have pancreatitis than were neutered dogs without any history of other surgery. Type of surgery had an effect on the association between pancreatitis and previous surgery in sexually intact dogs, with sexually intact dogs that had previously undergone urgent surgery having higher odds of pancreatitis than sexually intact dogs that had previously undergone elective surgery or had not previously undergone surgery. Thus, neuter status (ie, neutered vs sexually intact) seemed to affect the association between previous surgery and pancreatitis.

In the present study, we also found that the diagnosis of pancreatitis increased from 2000 through 2003 to 2004 through 2005, although the diagnosis of renal failure did not change over the course of the study. The increase in apparent incidence of pancreatitis coincided with the development and validation of the cPLI assay,[10,11] suggesting that it was a reflection of the fact that pancreatitis was easier to diagnose, rather than a true increase in the incidence of pancreatitis. It is also possible that referral patterns from private veterinary hospitals changed over the course of this study. Year of diagnosis was retained in the final multivariable model as a dichotomous variable to control for confounding associated with this variable.

An important weakness of the present study was that dogs were included in the case and control groups on the basis of the clinical diagnosis coded in each dog's medical record. Diagnostic criteria can vary among clinicians, and most case dogs did not have histologic confirmation of the diagnosis. Thus, there was some potential for misclassification. However, we believed that inclusion of only those dogs for which the diagnosis had been confirmed would likely have introduced a bias toward inclusion of only those dogs with the most severe pancreatitis, so that the case group would not have represented all dogs with pancreatitis in general. In contrast, the purpose of the present study was to identify associations between dietary factors and clinical pancreatitis in general. Thus, we believed it was necessary to accept some possibility of nondifferential misclassification. Nondifferential misclassification will bias the results toward the null (ie, ORs of 1),[12] except in the extreme situation when misclassification has a higher probability than correct classification.[13]

Bias can arise in case-control studies such as the present study as a result of selection bias, information bias, and confounding.[14] Selection bias occurs when the individuals chosen for the study are not representative of the population of interest. In a case-control study, the case definition determines the population that is being studied, and selection bias occurs when the control group does not represent the source population from which the cases were selected.[14] In the present study, the control group was selected from the same hospital as the case group and consisted of dogs with an unrelated medical condition expected to have a similar referral pattern as the case group. Referral patterns are known to differ on the basis of the underlying complaint, and this can result in errors.[15,16] Renal failure was chosen as the control disease in the present study because disease severity and frequency of admission to the Small Animal Clinic for dogs with renal failure was expected to be similar to disease severity and frequency of admission for dogs with pancreatitis. Renal failure is also not known to be associated with dietary factors, the primary exposure of interest for pancreatitis. It is impossible to identify a perfect control group, and there were several limitations associated with using dogs with renal failure as the control group. In particular, dogs with renal failure are often fed low-protein, high-fat diets and are often anorexic and thus more likely to receive table foods or high-fat foods than the general referral population. Both of these could falsely decrease the measure of association between certain dietary factors and pancreatitis, hence making it more difficult to identify a significant relationship.

The association between response proportion and selection bias is complex.[17] In general, however, a high response proportion may be important for data validity[18] because a low response proportion could mean that nonresponders were systematically different from responders. This will introduce bias into the study if the exposure of interest is associated with the study subject's willingness to participate.[17] To estimate the effects of potential responder bias on ORs, information concerning nonresponders must be available,[19] and analyses should be performed to determine whether there is evidence of systematic differences between responders and nonresponders that might have led to bias. In the present study, data obtained from the medical records were used to determine whether owners who responded to the telephone questionnaire differed from owners who did not respond. Although only 59% of eligible owners responded to the telephone questionnaire, our analysis did not reveal any important differences between responders and nonresponders. The difference between responders and nonresponders in regard to year of diagnosis was likely due to the fact that it was more difficult to contact owners who had brought their dog to the Small Animal Clinic earlier during the study period.

Recall bias is an important concern in case-control studies, especially when there is a substantial time lag between diagnosis and questionnaire administration. Veterinarians who suspect pancreatitis might question and educate clients more thoroughly on the effects of diet, compared with veterinarians who suspect renal failure. In turn, clients who are more thoroughly questioned about diet at the time of admission may be more likely to remember what their dog was eating around the time of diagnosis. This could have introduced some degree of recall bias among telephone questionnaire participants. If owners of dogs with renal failure did not recall their dogs' eating habits and did not report exposure to dietary factors that occurred, but owners of dogs with pancreatitis did recall their dogs' eating habits and reported exposure to dietary factors, measures of association would be biased away from the null. The validity of the dietary information and the effect of recall bias could not be estimated in the present study. However, because ORs calculated on the basis of data from the medical records (ie, data collected prior to physical examination and diagnostic evaluations) were similar to ORs calculated on the basis of data obtained during the telephone interviews, we believe that any errors in data validity or recall were similar between cases and controls.

There are a number of other limitations to the present study. For example, body condition status was determined on the basis of estimated BCS, notes recorded in the medical record, and reported weight versus breed standards. Body condition scoring has been shown to be highly correlated with other methods of estimating body fat content in dogs,[20] but accuracy would be expected to vary on the basis of experience, and imprecision in assignment of body condition status would likely have resulted in nondifferential misclassification. For this reason, the multivariable model might not have completely controlled for the confounding effects of body condition on other variables of interest; however, the bias would be toward the null. In addition, the present study was not able to investigate the potential effects of dietary supplements on development of pancreatitis, as the number of questions on the questionnaire was limited to increase compliance. However, because the use of supplements has increased during recent years, further studies would be warranted to evaluate the effect of their use on the development of pancreatitis in dogs. Finally, the control group used in the present study meant that we were not able to determine whether dietary factors were related to gastrointestinal tract disease in general or pancreatitis specifically. A new control group incorporating dogs with gastrointestinal tract conditions other than pancreatitis would be necessary to identify dietary factors associated with pancreatitis alone and not other common gastrointestinal tract disorders. The control group used in the present study was a good first step, but further study is necessary to better understand the underlying causes and pathogenesis of pancreatitis in dogs.

a. Copies of the questionnaire are available from the corresponding author on request.
b. SPSS, version 12.0.1 for Windows, SPSS Inc, Chicago, Ill.
c. LogXact, version 7, Cytel Inc, Cambridge, Mass.

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