Evaluation of Serum Feline Pancreatic Lipase Immunoreactivity and Helical Computed Tomography versus Conventional Testing for the Diagnosis of Feline Pancreatitis


Serum feline trypsinogen-like immunoreactivity (fTLI) concentrations and abdominal ultrasound have facilitated the noninvasive diagnosis of pancreatitis in cats, but low sensitivities (33% and 20–35%, respectively) have been reported. A radioimmunoassay has been validated to measure feline pancreatic lipase immunoreactivity (fPLI), but the assay’s sensitivity and specificity have not been established. In human beings, the sensitivity of computed tomography (CT) is high (75–90%), but in a study of 10 cats, only 2 had CT changes suggestive of pancreatitis. We prospectively evaluated these diagnostic tests in cats with and without pancreatitis. In all cats, serum was obtained for fTLI and fPLI concentrations, and pancreatic ultrasound images and biopsies were acquired. Serum fPLI concentrations (P<.0001) and ultrasound findings (P=.0073) were significantly different between healthy cats and cats with pancreatitis. Serum fTLI concentrations (P=.15) and CT measurements (P=.18) were not significantly different between the groups. The sensitivity of fTLI in cats with moderate to severe pancreatitis was 80%, and the specificity in healthy cats was 75%. Feline PLI concentrations were both sensitive in cats with moderate to severe pancreatitis (100%) and specific in the healthy cats (100%). Abdominal ultrasound was both sensitive in cats with moderate to severe pancreatitis (80%) and specific in healthy cats (88%). The high sensitivities of fPLI and abdominal ultrasound suggest that these tests should play an important role in the noninvasive diagnosis of feline pancreatitis. As suggested by a previous study, pancreatic CT is not a useful diagnostic test for feline pancreatitis.

Key words: Cats; Computed tomography; Histopathology; Pancreas; Trypsinogen-like immunoreactivity.

Despite the establishment of pancreatitis as a relatively common and important disease in cats, the antemortem diagnosis of this disease remains challenging. The vague and nonspecific history of anorexia, lethargy, and weight loss and clinicopathologic findings of increased liver enzyme activities or hyperbilirubinemia that could easily be attributed to hepatic dysfunction in the absence of pancreatitis frequently delay the diagnosis of this elusive disease. Furthermore, historical findings of vomiting and abdominal pain that are commonly reported in humans and dogs with pancreatitis, are less commonly reported in the cat. The diagnosis is further complicated by the observation that serum activities of amylase and lipase, biological markers that are widely considered helpful for detecting pancreatic inflammation in humans, have been shown to lack sensitivity and specificity for pancreatitis in the cat. Abdominal radiographs, although readily available and easy to perform, are considered nonspecific for the diagnoses of pancreatitis in cats.

Validation of an ELISA for measurement of serum trypsinogen-like immunoreactivity (fTLI) concentration has facilitated the noninvasive diagnosis of pancreatitis in cats. However, implementation of a cut-off value of 100 μg/L for the assay resulted in a suboptimal sensitivity of 33% and specificity of <80%. Feline pancreatic lipase recently has been purified from harvested whole pancreatic tissue for development of an immunoassay for the measurement of feline pancreatic lipase. A radioimmunoassay for the measurement of feline pancreatic lipase immunoreactivity (fPLI) in serum recently has been developed and validated in 30 healthy cats, but the sensitivity and specificity of this assay have not been established in cats with spontaneous disease (Steiner, Wilson, and Williams, unpublished data). The sensitivity of the recently developed canine pancreatic lipase immunoreactivity assay (cPLI) has been determined to be 82% in 11 dogs with biopsy-proven pancreatitis in contrast to a sensitivity of 36% for the canine trypsinogen-like immunoreactivity (cTLI) assay.

In humans, the overall sensitivity of computed tomography (CT) in establishing a diagnosis of pancreatitis is 75–90%, with a specificity of ≥85%. In a single report evaluating the use of contrast-enhanced CT for the diagnosis of histologically confirmed canine pancreatitis, 14 of 22 dogs (64%) had pathologic changes observed on CT. There has only been 1 published study evaluating the use of contrast-enhanced CT for the diagnosis of feline pancreatitis to date. In that study, only 2 of 10 cats with histologically confirmed pancreatitis had evidence of pancreatic changes on CT. In 2 recent studies in young healthy cats with biopsy-proven normal pancreatic histology, the anatomic and densitometric values of the normal pancreas were established. In these studies, the pancreas was identified on pre- and postcontrast CT studies with considerable postcontrast enhancement of pancreatic tissue.

Ultrasonographic changes associated with pancreatitis in cats have been well characterized and include dilatation of the gall bladder and common bile duct, regional peritoneal
effusion, a hypoechoic pancreas with hyperechoic peripancreatic fat, and thickening of gastric and duodenal walls. The pancreatic ultrasonographic findings in 20 clinically normal cats have been reported and were in agreement with a previous report that the normal feline pancreas can be visualized by ultrasonography. In previous reports, the sensitivity of abdominal ultrasound for the diagnosis of pancreatitis was determined to be 20% and 35%.

The goal of this study was to compare the clinical performance of new diagnostic tests of pancreatitis (serum fTLI concentration and contrast-enhanced CT) with that of more traditional tests for pancreatitis (serum fPLI concentration and abdominal ultrasound) in cats with mild to severe pancreatitis and in cats without pancreatitis.

Materials and Methods

Animals

Symptomatic Cats. Client-owned cats (21) with clinical signs consistent with pancreatitis (eg, anorexia, lethargy, vomiting, diarrhea, weight loss) were evaluated at the University of California, Davis, Veterinary Medical Teaching Hospital (UCD-VMTH) between August 2001 and December 2002. Symptomatic cats were only included in the study if all diagnostic procedures were deemed in the best interest of the patient by the clinician, anesthetist, and surgeon in charge of the animal and with owner consent.

Apparently Healthy Control Cats. Eight cats from an animal shelter without clinical signs also were evaluated at UCD-VMTH during the same time period. All healthy cats had no known history of gastrointestinal disease and underwent the same evaluation as did the symptomatic cats. The University of California Care and Use Committee approved studies in the healthy shelter cats.

A complete history, physical examination, CBC, serum biochemistry, and urinalysis were obtained. Serum was obtained for fTLI and fPLI concentrations and pancreatic ultrasound images were acquired ≥12 hours before laparotomy or postmortem examination in all cats. Helical contrast-enhanced pancreatic CT studies were acquired immediately before laparotomy in 11 of 21 (52%) of the symptomatic cats and in 8 of 8 (100%) healthy cats. All 29 cats had pancreatic biopsies obtained by abdominal exploratory laparotomy in 20 cats (17 symptomatic, 3 healthy) and by postmortem examination in 9 cats (4 symptomatic, 5 healthy). Left and right pancreatic limb biopsies were obtained in 17 of 21 (81%) of the symptomatic cats and in all of the healthy cats. The gross appearance of the pancreas was evaluated by the attending surgeon, pathologist, or investigator (MAF) in 19 of 21 (90%) of the symptomatic cats. Abnormalities in color (erythema), texture (cobble stone appearance), edema, nodularity, size (enlarged), and surrounding mesentery (erythematous) were noted. Intestinal, hepatic, and mesenteric lymph node biopsies were obtained in all healthy cats and (as clinically warranted) in 19 of 21 (90%), 20 of 21 (95%), and 12 of 21 (57%) of the symptomatic cats, respectively.

Determination of Serum fTLI and fPLI Concentrations

Serum was batched and stored at −70°C before mailing on dry ice to Texas A&M University Gastrointestinal (GI) Laboratory for analysis. Serum fTLI and fPLI concentrations were determined separately by radioimmunoassay validated for use in the cat (Steiner, Wilson, and Williams, unpublished data). The reference range for serum fTLI was 12–82 μg/L, with concentrations ≥100 μg/L being considered diagnostic of pancreatitis. The reference range for fPLI was 2.0–6.8 μg/L, with concentrations ≥10 μg/L considered diagnostic of pancreatitis. The reported intra-assay variability for fTLI is 3.0–9.4% and interassay variability is 4.0–8.2%. For fPLI, the coefficients of variation of 4 different serum samples were 10.1, 4.5, 2.2, and 3.9% for intra-assay variability and 24.4, 15.8, 16.6, and 21.3% for interassay variability.

Abdominal Ultrasound Imaging

Twenty-six of 29 (90%) pancreatic ultrasound studies were performed with the use of 1 ultrasound system. Three healthy cats were examined with a similar ultrasound system. A minimum of 120 seconds of continuous images were acquired and stored on videotape. A board-certified radiologist (EJH) reviewed all videotaped pancreatic ultrasound images in a blinded fashion. For transabdominal pancreatic ultrasound, the following criteria were considered normal: visualization of the majority of the pancreas, smooth borders seen in both the longitudinal and transverse imaging planes, and relatively isoechoic pancreas compared with surrounding fat and mesentery. The following criteria were assigned a single point: increase in the size of the gland, enhanced visualization of the pancreatic duct or the common bile duct, irregular contour to the gland in either the transverse or longitudinal imaging plane, hypoechoic parenchyma of the pancreas, and increased echogenicity of the surrounding mesentery. A total score ≥1 was considered consistent with pancreatitis, with a maximum score of 5 assigned.

Computed Tomography Imaging

With the cats under general anesthesia, contiguous 3-mm transaxial images were acquired from the dome of the diaphragm to the caudal flexure of the duodenum with the use of a single breath-hold helical acquisition while respiration was suspended with an inflation pressure of 15 cm H2O. Images were acquired in helical mode with a standard abdominal reconstruction algorithm, 140 kVp, and a field of view consistent with the largest diameter of the abdomen. After anatomical localization of the pancreas on precontrast images, a postcontrast study of the pancreas was acquired immediately after IV administration of ionic iodinated contrast medium at a dosage of 880 mg I/kg BW. For the postcontrast study, the field of view was reduced to 1 mm to improve out-of-plane resolution. All images were electronically stored as DICOM (Digital Imaging and Communications in Medicine) images. A board-certified radiologist (ERW) reviewed all CT images in a blinded fashion with an image workstation and commercially available software. Quantitative image analysis included determination of largest cross-sectional linear dimensions of the left and right limbs of the pancreas with electronic calipers and determination of pre- and postcontrast pancreatic parenchymal density by operator-defined region of interest analysis. The pancreas also was characterized in terms of shape or margin definition, tissue homogeneity, and pattern of postcontrast enhancement. The following were considered normal criteria: a pancreas with uniform density, mild lobulated margin, and uniform contrast enhancement. The following criteria were consistent with pancreatitis: pancreatic enlargement, mixed density, irregular margin, and mixed contrast enhancement. Because the left limb of the pancreas was consistently imaged, pancreatic enlargement was assessed by comparing the diameter of the left limb of the healthy cats to that of the symptomatic cats.

Histologic Evaluation

Pancreatic biopsies from the left or right limb were obtained by a ligature technique. The surgeon collected a piece of pancreas from the distal portion of the left or right limb if the pancreas appeared grossly normal. An incisional biopsy was obtained from any grossly abnormal site. For pancreatic biopsies obtained by postmortem examination, samples were acquired within 30 minutes of death, and the entire pancreas was removed and serial sections of its entire length were taken. A minimum of 3 sections from each pancreatic division
(left and right limb and body) was obtained, with 0.5 cm between sections and with greater numbers of sections obtained with larger pancreases. Biopsy samples were immersion-fixed in 10% neutral buffered formalin and processed routinely for paraffin embedding; 4-μm-thick sections were stained with hematoxylin-eosin. All pancreatic histopathology samples were reviewed and scored in a blinded fashion by a board-certified pathologist (HEVDC). All sections of the same pancreatic division were arranged on 1 slide, considered as 1 representative section for that particular pancreatic division, and received 1 cumulative score in the grading system.

A semiquantitative histopathology grading scheme was established that reflected the severity of acute and chronic pancreatic lesions. The grading system was based on a point system for 2 criteria in acute pancreatitis (AP; neutrophilic inflammation and edema or saponification of mesenteric fat) and 3 criteria in chronic pancreatitis (CP; lymphocytic inflammation, interstitial fibrosis, and cystic acinar degeneration). Cats with pancreatic neoplasia were excluded.

**Chronic Pancreatitis** The absence of lymphocytes or focal small nests of lymphocytes were considered normal and assigned 0 points, a mild lymphocytic inflammatory infiltrate (involving a maximum of 25% of the pancreatic parenchyma) was assigned 1 point, moderate lymphocytic inflammation (affecting <50% of the parenchyma) was assigned 2 points, and severe lymphocytic inflammation (affecting >50% of the pancreatic parenchyma) was assigned 3 points. The absence of interstitial fibrosis was assigned 0 points, mild thickening of the septa or multifocal areas of mild interstitial fibrosis was assigned 1 point, moderate thickening of most septa was assigned 2 points, and marked thickening of septa by fibrous tissues or dissection of fibrous tissue into the lobules was assigned 3 points. The absence of cystic acinar degeneration was assigned 0 points. If present, points were assigned on the basis of the number of cystic structures: 3 cysts (1 point), 3–5 cysts (2 points), and ≥6 cysts (3 points).

**Acute Pancreatitis** The grading for interstitial neutrophilic inflammation was similar to that for lymphocytic inflammation, except 0 points were only given if no neutrophils were present. The absence of interstitial edema or mesenteric fat necrosis was assigned 0 points, 1 point was assigned if these features were present in <25% of the parenchyma (mild), 2 points were assigned if these features were present in 25–50% of the parenchyma (moderate), and 3 points were assigned if these features were present in >50% of the parenchyma (severe).

The sum of the points for each criterion in AP and CP was calculated, with maximum scores of 6 and 9, respectively. A cumulative score of 0 points was assigned for normal pancreatic histology and absence of AP and CP. The following cumulative point scores were considered consistent with acute pancreatitis in which 2 criteria were evaluated: mild (1–2 total points), moderate (3–4), and severe (5–6). The following cumulative point scores were considered consistent with chronic pancreatitis in which 3 criteria were evaluated: mild (1–3 total points), moderate (4–6), and severe (7–9).

The histopathology grade (mild, moderate, or severe) from all slides reviewed was based on the highest cumulative score from the multiple biopsies reviewed for a single patient. In all patients with pancreatitis, evidence of pancreatitis was present on multiple slides from a single biopsy or in multiple biopsy samples. On the basis of the grading scores for acute and chronic pancreatitis, the pancreatic lesions could be placed in the Hill and Van Winkle classification system of acute neutrophilic pancreatitis (AP only), chronic nonsuppurative pancreatitis (CP only), and chronic active pancreatitis (AP and CP present).

**Statistical Analysis**

On the basis of historical information (symptomatic or healthy) and histopathologic grade (normal, mild, moderate, or severe pancreatitis), all cats were assigned to 1 of the following groups: healthy cats with normal pancreas; symptomatic cats with normal pancreas; or symptomatic cats with mild, moderate, or severe pancreatitis. The histopathologic grades of moderate and severe pancreatitis were considered a single group for statistical purposes because of the small number of cats in each group considered separately. Statistical analysis was not performed on the symptomatic cats with normal pancreas because sample size (n = 3) was too small for comparison purposes. Presenting complaints; physical examination findings; selected hematologic, serum biochemistry, and urinalysis results; serum fTLI and fPLI concentrations; abdominal ultrasound grades; and CT measurements were compared among the groups of cats. For continuous response data, the Jonckheere-Terpstra test for ordinal categories was used, and for categorical response data, the Kruskal-Wallis analysis of variance was used.

Five cats had CP (1 by postmortem examination, 4 by laparotomy) that was deemed moderate to severe in nature. For these 5 cats, the mean cumulative point score for AP of the left limb was 4.8 (median 5, range 3–6) and for the right limb was 5 (median 4, range 4–7). CP was evident in biopsy samples obtained from both the right and left limb in all cats. All 5 cats also had evidence of moderate to severe AP in at least 1 limb. The mean cumulative point score for AP of the left limb was 2 (median 2, range 0–5) and for the right limb was 3 (median 3, range 0–6). No statistical differences were noted for histopathologic grade between the left and right limb for CP or AP (P = 1.0 and .44, respectively).

Thirteen cats had CP (4 by postmortem examination, 9 by laparotomy) that was deemed mild in nature. For these 13 cats, the mean cumulative point score for CP of the left limb was 1.7 (median 2, range 0–3) and for the right limb was 1.3 (median 1, range 0–3). CP was evident in biopsy samples obtained from both the right and left limbs when acquired in 5 of 9 cats. Three cats in this group had evidence of mild AP in at least 1 limb. The mean cumulative point score for AP for the left and right limb was 0.2 (median 0; ranges 0–1 and 0–2, respectively). No cat had an AP or CP histopathology grade greater than 2 or 3, respectively. No statistical differences were noted for the histopathologic grade between the left and right limb for CP or AP (P = .78 and 1.0, respectively).

Three cats that presented with clinical signs consistent with pancreatitis had no evidence of AP, CP, or pancreatic neoplasia on histopathology (1 by postmortem examination, 2 by laparotomy). These 3 cats were diagnosed with moderate intestinal inflammation with mild hepatitis; T-cell...
lymphoma of the intestines, liver, and mesenteric lymph node; and mild intestinal inflammation with severe lipodis-
sis. The 8 healthy cats had no evidence of abnormal pancreatic histopathology or neoplasia.

The 21 client-owned cats had clinical signs consistent with pancreatitis (eg, anorexia, lethargy, vomiting, diarrhea, weight loss), and 8 apparently healthy cats had no abnormal clinical signs (Table 1). Significant differences were noted between the healthy cats and the cats with mild and mod-erate to severe pancreatitis for anorexia (P = .0039), vom-iting (P = .018), and weight loss (P = .037). Physical examination findings of abdominal pain, dehydration, cran-nial abdominal mass effect, icterus, and body condition sco-re' are summarized in Table 1 and were not significantly different among groups. Selected CBC, serum biochemistry results, and urine specific gravity results are summarized in Table 2. One cat in the mild pancreatitis group that pre-sented for euthanasia did not have samples submitted for CBC, serum biochemistry, or urinalysis. Significant differ-ences in hematologic, biochemical, and urine analysis variables were not detected among groups except for serum albumin and urine specific gravity. Serum albumin concentra-tions were significantly different between healthy cats, cats with mild pancreatitis, and cats with moderate to severe pancreatitis (P = .0048). Cats with moderate to severe pan-creatitis were significantly more likely to be hypoalbumin-emic compared with healthy cats (P = .013) and cats with mild pancreatitis (P = .0048). Urine specific gravity was significantly different among the 3 groups (P = .0009). Compared with healthy cats, cats with mild pancreatitis had significantly less concentrated urine (P = .0006) and cats with moderate to severe pancreatitis approached significan-ce for this difference (P = .055). The potential effect of prior fluid therapy on serum albumin concentration and urine specific gravity in symptomatic cats was not evalu-at ed.

Mean serum fTLI and fPLI concentrations, cumulative abdominal ultrasound score, and mean cross-sectional di-ameter of the left limb of the pancreas measured by CT are summarized in Table 3. Individual data points for serum fTLI and fPLI concentrations are presented in Figures 1, 2, respectively. Serum fTLI concentrations were not signifi-cantly different between the healthy cats and cats with mild and moderate to severe pancreatitis (P = .15). Serum fPLI concentrations were significantly different among all 3 groups (P < .0001), between healthy cats and cats with moderate to severe pancreatitis (P = .0016), between healthy cats and cats with mild pancreatitis (P = .030), and between cats with mild pancreatitis and those with mod-erate to severe pancreatitis (P = .0005). Abdominal ultra-sound scores were significantly lower in healthy cats com-pared with cats with mild and moderate to severe pancre-atitis (P = .0073), but CT measurements were not signifi-cantly different among these same groups (P = .18). Four of 5 (80%) cats with moderate to severe pancreatitis and 6 of 11 (55%) cats with mild pancreatitis had at least 1 gross abnormality (eg, pancreatic erythema, cobble stone appearance, edema, nodularity, enlargement, erythematous surrounding mesentery) noted by the attending surgeon, pathologist, or investigator (MAF) that was consistent with pancreatitis. Of the 3 symptomatic cats without pancreatitis, 2 had mild pancreatic texture irregularity, or edematous appearance was noted.

Intestinal, hepatic, and mesenteric lymph node abnor-malities were characterized in 15 of 19 (79%), 17 of 20 (85%), and 8 of 12 (67%) of the symptomatic cats, re-spectively. In the 5 cats with moderate to severe pancreatitis, 3 cats had histologic evidence of mild to moderate intestinal inflammation, and 1 cat was diagnosed with intestinal T-cell lymphoma. Three cats were diagnosed with mild to moderate hepatic inflammation, and 1 cat was diagnosed with lipodisosis and cholangitis. Mild histiocytic lymph node inflammation was noted in 2 cats and lymphangiectasia was identified in 1 of 4 cats from this group.

In the cats with mild pancreatitis, mild to moderate in-testinal inflammation was noted in 7 cats, intestinal T-cell lymphoma in 2 cats, intestinal adenocarcinoma in 1 cat, and severe ulcerative gastritis in 1 of 11 cats. Mild to moderate hepatic inflammation was noted in 7 cats, lipodisosis in 2 cats, biliary adenocarcinoma and cholangitis in 2 cats individu-ally, and severe lymphocytic cholangiohepatitis and mastocytosis in 1 of 12 cats in this group. Lymph node pa-

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**Table 1.** Clinical signs and physical exam findings in healthy and symptomatic cats.

<table>
<thead>
<tr>
<th>Histologic Groups</th>
<th>Healthy with Normal Pancreas (n = 8)</th>
<th>Symptomatic with Normal Pancreas (n = 3)</th>
<th>Mild Pancreatitis (n = 13)</th>
<th>Moderate to Severe Pancreatitis (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical signs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Vomiting</td>
<td>0</td>
<td>2</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Anorexia</td>
<td>0</td>
<td>3</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>Weight loss</td>
<td>0</td>
<td>3</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Lethargy</td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Physical exam</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Dehydration</td>
<td>0</td>
<td>1</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Cranial abd mass</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Icterus</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>BCS</td>
<td>4.6</td>
<td>4.3</td>
<td>5.1</td>
<td>3.6</td>
</tr>
</tbody>
</table>

n, number of cats in each category; BCS, body condition score as mean and range.
Table 2. Selected CBC, serum biochemical analysis, and urine specific gravity results in healthy and symptomatic cats.

<table>
<thead>
<tr>
<th>Histologic Groups</th>
<th>Healthy with Normal Pancreas (n = 8)</th>
<th>Symptomatic with Normal Pancreas (n = 3)</th>
<th>Mild Pancreatitis (n = 12)</th>
<th>Moderate to Severe Pancreatitis (n = 5)</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCT (%)</td>
<td>31.5 (22.3–41.3)</td>
<td>28.6 (23.1–38.0)</td>
<td>34.4 (16.9–46.9)</td>
<td>27.7 (23.8–40.2)</td>
<td>30–50</td>
</tr>
<tr>
<td>WBC (cell/μL)</td>
<td>14,582 (2,770–41,890)</td>
<td>11,503 (5,603–18,190)</td>
<td>20,345 (8,870–43,700)</td>
<td>20,318 (10,240–44,010)</td>
<td>4,500–14,000</td>
</tr>
<tr>
<td>Platelets (×10^9/μL)</td>
<td>305 (291–481)</td>
<td>415 (193–549)</td>
<td>359 (206–772)</td>
<td>186 (28–250)</td>
<td>180–500</td>
</tr>
<tr>
<td>Calcium (mg/dL)</td>
<td>9.4 (7.5–11.5)</td>
<td>9.3 (7.7–11.6)</td>
<td>9.5 (8.4–10.6)</td>
<td>10.6 (7.8–18)</td>
<td>9.4–11.4</td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
<td>24.8 (14–32)</td>
<td>29.7 (13–44)</td>
<td>21.7 (9–64)</td>
<td>21.8 (17–26)</td>
<td>18–33</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>1.14 (0.9–1.4)</td>
<td>1.20 (0.4–2)</td>
<td>1.28 (0.6–1.9)</td>
<td>1.02 (0.6–1.3)</td>
<td>1.1–2.2</td>
</tr>
<tr>
<td>Glucose (g/dL)</td>
<td>115 (75–162)</td>
<td>100 (90–117)</td>
<td>193 (90–478)</td>
<td>172 (67–298)</td>
<td>73–134</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>4.3 (2.9–6)</td>
<td>4.2 (2.4–5.7)</td>
<td>4.2 (2.5–6.5)</td>
<td>4.1 (3.1–6)</td>
<td>2.9–5.3</td>
</tr>
<tr>
<td>Globulin (g/dL)</td>
<td>2.5 (1.7–3.1)</td>
<td>2.3 (1.8–3.2)</td>
<td>2.5 (2.0–3.3)</td>
<td>1.8 (1.5–2.2)</td>
<td>1.9–3.9</td>
</tr>
<tr>
<td>Total bilirubin (mg/dL)</td>
<td>0.2 (0.1–0.4)</td>
<td>2.2 (0.1–6.4)</td>
<td>3.3 (0.1–15.3)</td>
<td>2.3 (0.1–7.3)</td>
<td>0–0.2</td>
</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
<td>124 (55–153)</td>
<td>149 (109–197)</td>
<td>189 (94–532)</td>
<td>137 (79–219)</td>
<td>89–258</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>17 (5–51)</td>
<td>257 (7–742)</td>
<td>92 (3–366)</td>
<td>49 (6–138)</td>
<td>12–46</td>
</tr>
<tr>
<td>ALP (U/L)</td>
<td>20 (7–40)</td>
<td>101 (17–255)</td>
<td>156 (8–904)</td>
<td>45 (6–98)</td>
<td>14–71</td>
</tr>
<tr>
<td>GGT (U/L)</td>
<td>1.8 (0–6)</td>
<td>1 (0–2)</td>
<td>3.1 (0–19)</td>
<td>0.8 (0–2)</td>
<td>0–4</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>59 (17–123)</td>
<td>308 (40–816)</td>
<td>235 (13–1,536)</td>
<td>67 (23–196)</td>
<td>28–106</td>
</tr>
<tr>
<td>USG</td>
<td>1.058 (1.050–1.076)</td>
<td>1.044 (1.033–1.051)</td>
<td>1.024 (1.010–1.041)</td>
<td>1.032 (1.010–1.058)</td>
<td>1.010–1.060</td>
</tr>
</tbody>
</table>

HCT, hematocrit; WBC, white blood cell count; BUN, blood urea nitrogen; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, gamma glutamyl transpeptidase; ALT, alanine aminotransferase; USG, urine specific gravity.

Table 3. Serologic and imaging results (mean, range of scores) in healthy and symptomatic cats.

<table>
<thead>
<tr>
<th>Histologic Groups</th>
<th>Healthy with Normal Pancreas</th>
<th>Symptomatic with Normal Pancreas</th>
<th>Mild Pancreatitis</th>
<th>Moderate to Severe Pancreatitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>fTLI</td>
<td>86.6 (26.4–202.4)</td>
<td>70.9 (58.7–92.1)</td>
<td>65.0 (28.5–102.8)</td>
<td>237.0 (50.6–364.5)</td>
</tr>
<tr>
<td>fPLI</td>
<td>5.5 (2.4–7.5)</td>
<td>11.4 (5.5–19.6)</td>
<td>15.9 (4.9–68.5)</td>
<td>167.9 (48.9–460.3)</td>
</tr>
<tr>
<td>AUS score</td>
<td>0.13 (0–1)</td>
<td>0.07 (0–1)</td>
<td>0.77 (0–2)</td>
<td>2.2 (0–5)</td>
</tr>
<tr>
<td>CT csd</td>
<td>0.7 (0.5–0.9)</td>
<td>1.0 (0.9–1.1)</td>
<td>0.7 (0.5–0.8)</td>
<td>2.3 (1.0–4.8)</td>
</tr>
</tbody>
</table>

fTLI, feline trypsinogen-like immunoreactivity concentrations; fPLI, feline pancreatic lipase immunoreactivity; AUS score, abdominal ultrasound total score; CT csd, cross-sectional diameter of left limb of pancreas measured by computed tomography.
Results of this study identified a similar signalment and similar clinical signs, physical examination findings, and hematologic abnormalities for the cats with pancreatitis, as did previous reports. Similar to previous studies, fTLI concentrations did not correlate strongly with a diagnosis of feline pancreatitis. Feline PLI concentrations were sensitive in the moderate to severe pancreatitis group and specific in healthy cats. In contrast to other reports, abdominal ultrasound was both sensitive in cats with moderate to severe pancreatitis and specific in healthy cats, but the specificity was unacceptably low (33%) in the 3 symptomatic cats without histologic evidence of pancreatitis. Similar to a previous report in cats and dogs, and in contrast to the findings in humans, contrast-enhanced CT was not a useful diagnostic test for pancreatitis in cats in this study.

Our attempt in this study was to separate cats into clinically defined groups (no pancreatic pathology, mild pancreatitis, and moderate to severe pancreatitis) with histopathology as the "gold standard" for classification. Two issues were addressed in an attempt to consistently obtain an accurate histopathologic diagnosis for each cat. Because pancreatitis can occur multifocally, all cats that had pancreatic tissue acquired by postmortem examination (10 of 29, 34%) had their entire pancreas removed, and serial sections of the pancreas (left and right limbs and body) were evaluated. For cats that had pancreatic biopsies obtained by laparotomy (19 of 29, 66%), the distal right and left limb of the pancreas was biopsied in 15 of 19 cats (79%) in an attempt to maximize the potential of obtaining a representative histopathologic sample. The histopathology grade (normal, mild, moderate to severe) was compared with the highest cumulative point score of all biopsies reviewed for a single cat, would have potentially been affected in 2 cats with moderate to severe pancreatitis and 4 cats with mild pancreatitis if a single pancreatic biopsy had been obtained. The higher grade was noted in the right limb of both cats with moderate to severe pancreatitis and was evenly divided (2 right, 2 left) for cats with mild pancreatitis. Despite this finding, there was no statistical difference in histopathology grade between the right and left limbs. Finally, in 1 cat, pancreatic lesions were noted during laparotomy.
in the body and proximal aspect of the left limb of the pancreas, and the surgeon obtained a biopsy from that site.

The 2nd issue addressed was methodology in histopathologic evaluation. Several classification systems for pancreatic inflammatory diseases have been proposed in human medicine, and Hill and Van Winkle described 1 for feline pancreatitis. Although histopathology is used to some extent in many of these classification systems, a grading system of the histopathologic lesions that is based on the combination of individual scores for different aspects of the lesions has not been described to date. To reliably evaluate the pancreatic lesions of the cats in this study, an objective grading system for lesions suggestive of AP and CP was described in the classification system by Hill and Van Winkle, was used. A board certified pathologist (HEVDC), who was blinded to the historical and clinical findings, graded all pancreatic biopsies. AP was always consistent with the condition described as acute suppurative pancreatitis in the Hill and Van Winkle classification system. Cats with acute necrotizing pancreatitis, as described by Hill and Van Winkle, were not found, possibly because of the type of clinical cases selected for this study. Eight of 18 (44%) cats in this study had evidence of AP and CP, which is consistent with the findings of Hill and Van Winkle. Ten cats in the mild pancreatitis group had histologic evidence of CP only. This group of cats most closely correlates with the Hill and Van Winkle classification of chronic nonsuppurative pancreatitis.

With the use of a cut-off value of 100 μg/L, the sensitivity of fTLI was higher (80%) for the moderate to severe pancreatitis cats and lower (8%) for the mild pancreatitis cats compared with the previously reported sensitivity of 33%.

Considering all cats, the low sensitivity for fTLI of cats compared with the previously reported sensitivity of pancreatitis cats and lower (8%) for the mild pancreatitis was higher (80%) for the moderate to severe pancreatitis group. Although the radiologist was blinded to historical and clinical findings, each cat in this study had an extensive and thorough videotaped ultrasound evaluation of the pancreas. This evaluation was potentially more extensive than previous retrospective ultrasound studies in which the pancreas was evaluated during a routine abdominal ultrasound procedure and was not a focus for the ultrasound study. In addition, if a patient did not permit an extensive study, a study was repeated after anesthetic premedication was administered in preparation for abdominal exploratory surgery. In addition, the presence of concurrent extrapancreatic disorders, including intestinal and hepatobiliary disease, might have influenced the ultrasonographic features used for diagnosing pancreatitis. For example, the enhanced visualization of the common bile duct in a cat with hepatobiliary disease and pancreatitis might have been more likely a result of hepatobiliary disease and not pancreatitis. Other possible explanations for these differences include advancements in ultrasound technology and radiologist skill levels. The suboptimal specificity of abdominal ultrasound for the symptomatic cats without pancreatitis (33%) should be interpreted with caution because only 3 cats were in this group. It is highly unlikely that pancreatitis was missed, because 1 of the 3 cats had a postmortem examination with serial sections of the entire pancreas for histologic evaluation and the other 2 cats had laparotomies performed during which both limbs of the pancreas were biopsied. Nevertheless, the overall specificity (73%) would probably have decreased if more symptomatic cats without pancreatitis were studied.

Contrast-enhanced CT allowed visualization of the pancreas in 18 of 19 (95%) cats in this study, in contrast to a previous study in which visualization of the feline pancreas by CT was considered difficult and not possible without IV administration of contrast medium. Differences in cross-section diameter, contours, enhancement, and pre- and post-contrast density were not noted between normal and symptomatic groups. Differences were noted in cats with marked enlargement of the pancreas, but this was not a consistent finding. In addition, measurement of pancreatic size is affected by positioning of the patient and pancreas and can create discrepancies in patient-to-patient measurements. These findings are consistent with those of Gerhardt et al, and provide further evidence for the lack of support for the use of current CT technology in the diagnosis of pancreatitis in cats.

Pancreatitis in cats often is associated with diseases in other organs, such as the liver (eg, hepatic lipidosis, cholangiohepatitis, cholangitis) and intestine (eg, inflammatory bowel disease). In one study, 5 of 13 (38%) cats with he-
pathic lipodosis were noted to have acute pancreatitis. In a separate study, 5 of 36 (14%) cats with lymphocytic portal hepatitis and 7 of 18 (39%) with cholangiohepatitis had inflammatory bowel disease and mild pancreatitis. In 1 additional study, 2 of 5 cats (40%) were reported to have chronic interstitial pancreatitis associated with cholangitis. In the study reported here, a lower number of cats with pancreatitis had lipodosis (19%), with higher numbers having intestinal (63%) and hepatic inflammation (75%). Possible explanations for these findings include earlier surgical intervention before development of lipodosis, a larger number of intestinal biopsies obtained per patient (on average 1 gastric, duodenal, jejunal, and ileal biopsy) that increased the diagnostic yield, and the inclusion of patients with mild intestinal and hepatic inflammation. The clinical importance of mild pancreatitis in cats with severe concurrent disorders needs to be considered because cats might have been presented because of their concurrent disease. In addition, although fPLI is specific for the feline pancreas, concurrent diseases could affect serum fPLI concentrations, and additional studies evaluating fPLI in cats with concurrent disorders are warranted.

A marked difference was noted between the ages for the symptomatic (mean 11.3, median 11 years) and healthy cats (mean 3.1, median 2 years). Selecting healthy shelter cats led to a younger population of cats compared with the symptomatic hospital population. Ideally, an age-matched group would have been preferable for comparison purposes. Although significant differences were found with fPLI and abdominal ultrasound between the study groups, caution should be considered when interpreting these results. Potential limiting factors include the small sample size of the cats with moderate to severe pancreatitis, the marked differences in age between the healthy cat and the symptomatic cats, and the limitations of procuring a representative pancreatic biopsy in all cats.

The high sensitivities of fPLI and abdominal ultrasound suggest that these tests should play a crucial role in the noninvasive diagnosis of pancreatitis in cats. Pancreatic CT is not a useful diagnostic test in cats with pancreatitis. Additional studies are needed to further evaluate the use of fPLI and abdominal ultrasound in a larger population of cats with AP and CP that is mild, moderate, and severe in nature. In addition, although fPLI and ultrasound are specific in healthy cats, studies evaluating these tests in clinically symptomatic cats with normal pancreatic histology are needed. Because of the small number of cats in this subgroup and their clinical importance, this population of cats, in particular, needs additional study.

### Footnotes

* f HDI 3000 Ultrasound system and C4-7 MHz linear probe, Philips Medical Systems, Bothell, WA
* g HDI 3000 Ultrasound system and C4-7 MHz linear probe, Philips Medical Systems, Bothell, WA
* h HiSpeed FX/i CT scanner, General Electric Medical Systems, Milwaukee, WI
* i Conray 400, Mallinkrodt Inc, St Louis, MO
* j eFilm, Merge-eFilm, Milwaukee, WI
* k StatXact, Cytel Software Corporation, Cambridge, MA

### References


