Standard Article
J Vet Intern Med 2018;32:962–966

Computed Tomographic Angiography of the Pancreas in Cats with Chronic Diabetes Mellitus Compared to Normal Cats

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Background: Diabetes mellitus (DM) is a common endocrinopathy in cats. No known diagnostic test or patient characteristic at the time of diagnosis can predict likely disease course, unlike in people in whom computed tomographic angiography (CTA) is used. No published data exist regarding the CTA appearance of the pancreas in cats with DM, and thus, it is unknown what if any CTA variables should be further assessed for associations with pancreatic endocrine function.

Hypothesis/Objectives: A significant difference in pancreatic attenuation, volume, and size will be identified between normal cats and those with chronic DM on CTA.

Animals: Ten healthy control cats and 15 cats with naturally occurring DM present for >12 months.

Methods: Prospective cross-sectional study comparing pancreatic attenuation, enhancement pattern, size, volume, pancreatic volume-to-body weight ratio (V:BW), pancreatic arterial: portal phase ratio (A:P), time-to-arterial enhancement, and time-to-peak portal enhancement on CTA between sedated healthy control cats and those with chronic DM.

Results: The pancreas in cats with chronic DM was significantly larger, had higher volume, higher V:BW, and shorter time-to-peak portal enhancement on CTA when compared to normal cats.

Conclusions and Clinical Importance: Peak portal enhancement time, pancreatic size, pancreatic volume, and V:BW can be used to differentiate normal sedated cats from those with chronic DM by CTA. These variables warrant further investigation to identify possible associations with endocrine function.

Key words: Contrast; Endocrine; Feline; Iodinated.

Diabetes mellitus (DM) is 1 of the most common endocrine diseases in cats affecting up to 1.24% of cats in North America.[1] Cats most commonly develop a condition similar to type-2 DM in people, in which insulin-secreting ability initially is impaired by chronic hyperglycemia, glucotoxicity, and oxidative pancreatic injury.[2] Without rapid control of hyperglycemia, affected patients often permanently lose the ability to secrete insulin as pancreatic beta cells are destroyed and irreversibly replaced by substances such as amyloid.[3] To date, no known single diagnostic test or patient characteristic at the time of diagnosis can predict disease course or diabetic remission potential in affected cats.

In people, computed tomography (CT) is the most common imaging modality used to assess patients for pancreatic disease, including pancreatitis and neoplasia.[4–6] In addition, it has been used to evaluate pancreatic endocrine function and predict which patients will become diabetic after pancreatectomy.[7] Computed tomographic variables such as larger pancreatic volume, larger pancreatic volume/body weight ratio (V:BW), higher arterial phase attenuation, or higher arterial phase-to-portal phase attenuation ratio (A:P) were found in people who did not develop diabetes mellitus after pancreatectomy.[7] Other studies in people have confirmed smaller pancreatic volumes on CT in patients with both type 1 and type 2 DM.[8–10] No reports describe the computed tomographic angiography (CTA) appearance of the pancreas in cats with DM. This information is important not only to assist with differentiation of pancreatic diseases, but also for future scientific investigations into the utility of CTA for assessment of endocrine pancreatic dysfunction.

The purpose of our study was to describe the CTA characteristics of the pancreas in cats with chronic DM and to compare these findings to those of age-matched healthy control cats. Our hypothesis was that there would be significant differences in pancreatic attenuation, volume, and size between healthy cats and those with long-term DM.

Abbreviations:

A:P	arterial phase-to-portal phase attenuation ratio
CT	computed tomography
CTA	computed tomographic angiography
DM	diabetes mellitus
HU	Hounsfield unit
ROI	region of interest
SD	standard deviation
V:BW	volume-to-body weight ratio

Materials and Methods

A prospective cross-sectional study of client-owned diabetic cats referred to the University of Georgia Veterinary Medical Center for study participation and staff-owned healthy cats solicited as a

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This study was carried out at the University of Georgia, College of Veterinary Medicine, Athens, GA 30602.

An abstract of this study was presented at the 2017 ACVR Annual Scientific Conference in Phoenix, AZ.

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Submitted September 24, 2017; Revised October 24, 2017; Accepted November 15, 2017.

DOI: 10.1111/jvim.14899

control population was performed. The study was approved by the University of Georgia Clinical Research Committee, and informed owner consent was obtained for all cats in the study.

Diabetic cats of any age, sex, or breed that had been diagnosed with DM for >1 year and on insulin therapy were enrolled. Additionally, cats free from any signs of systemic illness were recruited from hospital staff as a control population and were age-matched to within 1 year of a diabetic enrollee. Complete history, physical examination, CBC, serum biochemistry, urinalysis, quantitative pancreatic lipase immunoreactivity, and serum total thyroxine concentration were obtained in all cats. In addition, a serum fructosamine concentration was obtained in all diabetic cats. Healthy control cats were excluded from participation if any clinically relevant abnormalities were identified on physical examination or screening laboratory testing. Cats also were excluded if they were considered clinically to be >5% dehydrated on physical examination because they could not be rehydrated properly before performance of CTA.

After enrollment, a catheter was placed in the cephalic vein and each cat sedated by a standardized protocol: butorphanol[a]: 0.3–0.5 mg/kg IV, diazepam[b]: 0.3–0.5 mg/kg IV, and ketamine[c]: 2–5 mg/kg IV. Triple-phase CTA of the pancreas was performed in all sedated cats while in ventral recumbency on the couch of a 64-slice helical CT scanner.[d] Images were acquired using 120 kVp, 200 mAs, and a pitch of 0.8 and reconstructed into 1-mm-thick slice images by an abdominal algorithm. A precontrast CT of the entire abdomen was obtained. A single slice located at the body of the pancreas was identified on the precontrast CT and used for acquisition of the dynamic CT series. Images were acquired every 2 seconds for 44 seconds starting at the time of injection of nonionic iodinated contrast medium[e] at a dosage of 300 mgI/kg. A power injector was used to administer the contrast medium at a rate of 5.0 mL/s. Circular regions of interest (ROI) fitting the luminal size of the aorta and portal vein were used to measure attenuation of the vessels and determine the time-to-arterial enhancement as well as time-to-peak portal enhancement. These delay times were recorded and entered into the CT planning program for acquisition of arterial and portal phases. After another administration of nonionic iodinated contrast medium at 600 mgI/kg with a power injector, aortic and portal phase images of the entire pancreas were acquired. Arterial phase images were acquired in a cranial-to-caudal direction with portal phase images acquired caudal-to-cranial. Scan variables were the same as used in the precontrast study. A delayed-phase CT of the entire abdomen also was obtained 3–5 minutes after the final contrast medium injection. If motion artifact was noted on the delayed-phase images, the scan was repeated until motion was no longer identified. Cats were given IV fluids at a rate of 2.0–2.5 mL/kg/h after contrast medium injection, and heart and respiratory rates were monitored throughout the sedation period.

All images were transferred to a dedicated workstation and viewed by postprocessing viewing software.[f] Studies were anonymized, randomized, and reviewed in a soft-tissue window with the ability to adjust window level and width as desired. Subjective CTA changes were evaluated by consensus of 2 board-certified radiologists (SS, AS) blinded to disease status, with a single board-certified radiologist (SS) making all quantitative measurements. The following CT variables were assessed in all cats: pancreatic attenuation and enhancement pattern, width and height of the pancreatic body; width, height and length of the left and right lobes of the pancreas; pancreatic volume; V:BW; and, A:P.

Pancreatic attenuation was measured and compared in Hounsfield units (HU) by using a circular ROI consistently placed in the body of the pancreas. The A:P of the pancreas was calculated by dividing the mean arterial phase attenuation by the mean portal phase attenuation. The enhancement pattern of the pancreas was subjectively classified as either homogenous or heterogenous on arterial, portal, and delayed-phase images.

Using postcontrast transverse and reformatted dorsal plane images, the width and height of the body of the pancreas and the height, width, and length of the left and right lobes of the pancreas were measured. Electronic calipers were used to average 3 separate measurements for each dimension of the pancreas to account for minor variation in caliper placement. All width and height measurements were obtained perpendicular to the orientation of the pancreas. The width of the body of the pancreas was measured at the level of the pancreatic incisure on dorsal reformatted images. The height of the pancreatic body was measured at its maximum diameter on transverse images. Using dorsally reformatted images, the length of the left and right lobes of the pancreas was measured from the most caudal extent cranially to the level of the pancreatic incisure. Dorsal reformatted images also were used to measure the width of the left and right lobes of the pancreas 6 mm caudal to the pancreatic incisure. The height of the left and right pancreatic lobes was measured on transverse images 6 mm caudal to the pancreatic incisure. Pancreatic volume was measured on transverse postcontrast images by the summation of area technique.[11] The V:BW was calculated for each cat by dividing pancreatic volume by body weight in kilograms.

All statistical analyses were performed by commercially available software.[g] Pancreatic CTA variables were compared between normal and diabetic cats by Student t tests and chi-square tests as appropriate. The folded form F statistic was used to test whether variances were equal between groups. If unequal, Satterthwaite's approximation for degrees of freedom for the Student's t test was used. Significance was set at a threshold of 0.05.

Results

Ten control cats and 17 diabetic cats were enrolled in the study. The control cat group included 3 spayed females and 7 neutered males with a median age of 11 years (range, 6–15 years) and median body weight of 4.5 kg (range, 3.0–5.4 kg). The diabetic cat group included 5 spayed females and 12 neutered males with a median age of 12 years (range, 7–14 years) and body weight of 6.3 kg (range, 4.4–7.7 kg). No significant difference in the proportion of males and females ($P = 0.9742$) or age ($P = 0.3283$) was identified between groups, but diabetic cats had significantly higher body weights ($P = 0.0002$).

Triple-phase CTA was successful in 26 of 27 cats, with the exception being a diabetic cat in which the arterial phase was not but the portal and delayed phases were obtained. Thus, no data were available on this cat for inclusion into assessments of arterial attenuation, enhancement pattern, and A:P. A second delayed postcontrast scan had to be obtained in 9 cats, including 5 control and 4 diabetic cats, because of motion artifact. The mean time-to-arterial enhancement was 6.6 seconds for both control and diabetic cats with standard deviations (SD) of 2.1 and 0.9, respectively ($P = 0.9870$). The mean time-to-peak portal enhancement was significantly different between groups ($P = 0.0006$) at 22 seconds (SD $\pm$ 4.4) in control cats and 16.7 seconds (SD $\pm$ 2.6) in chronic diabetic cats. Mean pancreatic attenuation in both control and diabetic cats is listed in Table 1 with no significant difference identified between groups. In addition, no

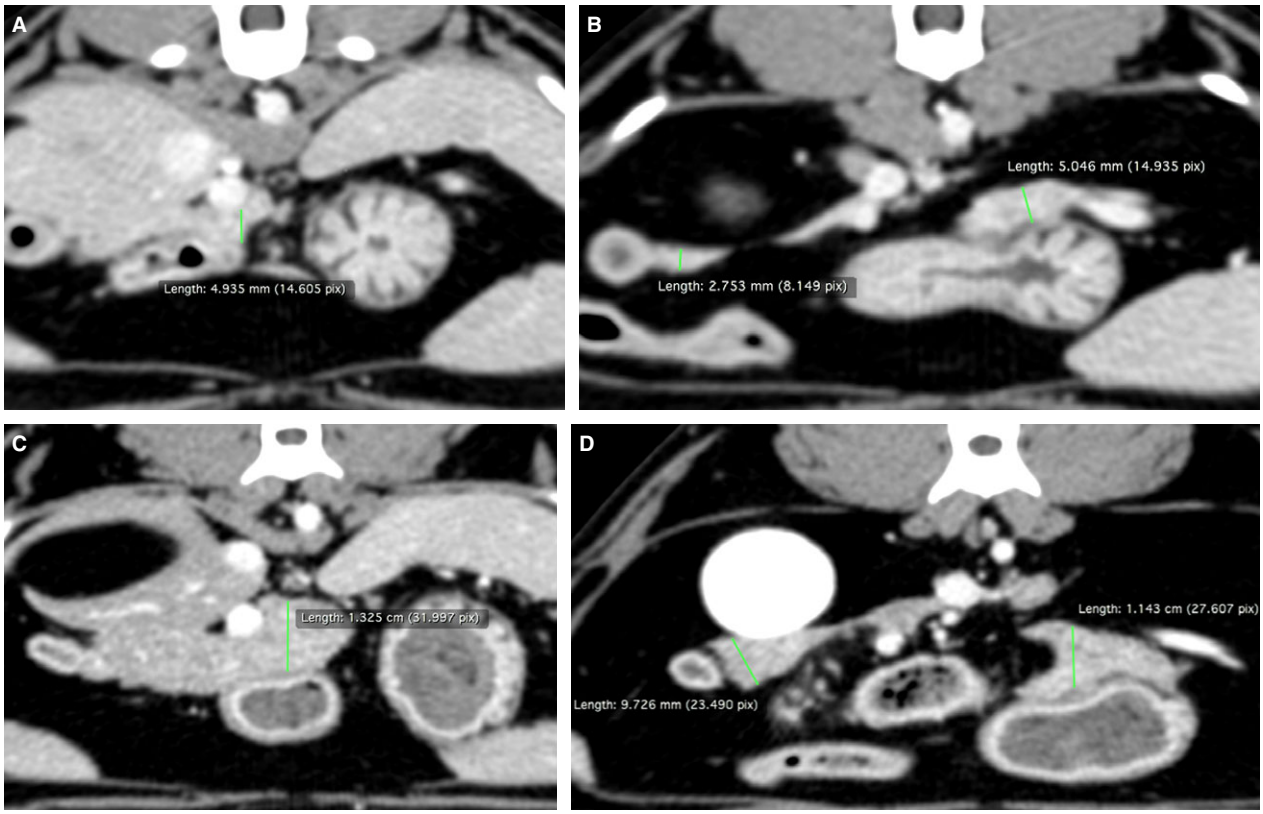

Fig. 1. Transverse delayed-phase CT images at the level of the pancreatic body in a normal (**A**) and diabetic cat (**C**) as well as corresponding images in the same cats 6 mm caudal to the pancreatic incisure demonstrating the thickness of the left and right lobes (**B**—normal, **D**—diabetic). All images are in a soft-tissue window. (window level—40, window width—300).

Table 1. Mean pancreatic CT attenuation in healthy and chronically diabetic cats.

	Healthy			Chronic diabetic			
Phase	n	Mean (HU)	SD	n	Mean (HU)	SD	*P* value
Pre	10	49	6	17	49	7	1.0
Arterial	10	76	7	16	74	10	0.5742
Portal	10	168	15	17	158	32	0.2786
Delayed	10	125	19	17	117	24	0.3981

n, number; SD, standard deviation; HU, Hounsfield units.

significant differences were identified in pancreatic enhancement pattern (Table 2) in arterial, portal, or delayed-phase images between control and diabetic cats. No significant difference ($P = 0.2612$) was noted in A:P with mean A:P of 0.45 (SD $\pm$ 0.04) in control cats and 0.48 (SD $\pm$ 0.11) in diabetic cats. Mean pancreatic size and associated *P* values are listed in Table 3 for both control and chronically diabetic cats. Significant differences were noted between groups in pancreatic volume ($P \leq 0.0001$) and V:BW ($P = 0.0003$). Mean pancreatic volume was 115.14 cm^3 (SD $\pm$ 47.26) in chronically diabetic cats versus 39.93 cm^3 (SD $\pm$ 15.75) in control cats. Mean pancreatic V:BW also was higher in chronically diabetic cats at 19.33 (SD $\pm$ 8.60) compared to 9.29 (SD $\pm$ 3.61) in controls.

Discussion

We identified differences in pancreatic CTA variables between normal cats and those with chronic DM, including peak portal enhancement time, size, volume, and pancreatic V:BW. This baseline information is

Table 2. Pancreatic enhancement pattern in healthy and chronically diabetic cats.

	Healthy			Chronic diabetic			
Phase	n	Homog	Heterog	n	Homog	Heterog	*P* value
Arterial	10	10	0	16	15	1	0.4201
Portal	10	10	0	17	15	2	0.2597
Delayed	10	10	0	17	14	3	0.1588

n, number; Homog, homogenous; Heterog, heterogeneous.

Table 3. Pancreatic size in healthy and chronically diabetic cats on CT.

	Healthy		Chronic diabetic		
Variable	Mean (cm)	SD	Mean (cm)	SD	*P* value
LL height	0.65	0.14	1.00	0.42	0.0041
LL length	6.87	1.99	9.16	1.84	0.0054
LL width	0.88	0.19	1.08	0.29	0.0600
Body height	0.77	0.18	1.15	0.40	0.0026
Body width	1.88	0.39	2.57	0.82	0.0068
RL height	0.43	0.09	0.75	0.32	0.0010
RL length	3.86	1.44	6.67	1.51	0.0001
RL width	0.65	0.17	1.35	0.43	<0.0001

LL, left lobe; RL, right lobe.

important not only for identification and characterization of disease, but also suggests that additional studies are warranted to determine whether these CTA variables can predict the severity of endocrine pancreatic dysfunction in affected cats and the potential for diabetic remission at the time of DM diagnosis. This information could influence initial therapeutic decision-making and better inform client expectations.

The 17 diabetic cats in our study were felt to be representative of the general population of cats with insulin-dependent DM, with the majority being neutered males and relatively older (≥12 years).[1,12] The control population was age-matched to account for any possible acquired age-related changes in pancreatic appearance on CTA. The only difference identified between groups was that DM-affected cats weighed significantly more than did normal control cats. This finding is consistent with previously published reports of increased body weight being a risk factor for DM development.[1,12]

In people, perfusion of the pancreas on CT has been used to assess endocrine and exocrine function as well as to differentiate various diseases.[7,13,14] The CT variables evaluated in these reports included pancreatic attenuation, perfusion, A:P, time-to-peak enhancement intensity, and pancreatic blood volume.[7,13] In people, it has been hypothesized that pancreatic islets with good blood flow have appropriate function[15] and that a more attenuating pancreas has better blood flow and thus endocrine function.[7] Although not statistically significant, pancreatic attenuation of normal control cats in our study was the same or greater in all phases when compared to cats with DM. This potential subtle difference in attenuation may be caused by decreased blood flow, amyloid deposition in the pancreas of cats with DM, or both. However, it is unclear at this point if attenuation differences are associated with pancreatic endocrine function in cats, and thus, further investigations are needed. A significantly shorter time-to-peak portal enhancement (16.7 versus 22 seconds) was identified in cats with DM. Although not assessed in our study, the difference in time-to-peak portal enhancement may be a consequence of differences in heart rates, cardiac stroke volume, or subclinical systemic hypertension associated with DM or secondary to other systemic disease.[16,17] In our study, the body of the pancreas was chosen for assessment of pancreatic attenuation because of its consistent location in the abdomen and close proximity to the liver and spleen. Thus, it is unknown what attenuation values would be found in other areas of the pancreas and whether they might differ from those obtained in the body of the pancreas.

Diabetic cats in our study had a significantly larger left lobe (height and length), right lobe (height, length, and width), and body (height and width) (Figure 1). In addition, overall pancreatic volume was significantly higher in cats with DM. The reason for this finding is unclear, but it may be caused by a combination of the previously reported histopathologic changes in cats with long-term DM, including hydropic degeneration and accumulation of glycogen in islet cells, deposition of amyloid, lymphocytic infiltrates, proliferation of interstitial tissues, and ductal metaplasia of acinar cells.[18–20] This finding differs from people with either type-1 or type-2 DM, who have smaller pancreatic volumes.[8,9] The reason for this difference is unknown, but it may be a result of species differences or potential concurrent disease (such as pancreatitis) in the study cats. Interestingly, 12 of 17 diabetic cats had SPEC pancreatic lipase immune reactivity concentrations above the reference range of 3.5 μg/dL (range, 3.7–50.0), although none had clinical evidence of disease. Histopathology of the pancreas was not performed in our study, and thus, it is unknown what (if any) active concurrent pancreatic diseases were present and what effect (if any), they may have had on pancreatic size and volume. In addition, pancreatic V:BW was higher in diabetic cats. Although diabetic cats weighed significantly more than control cats, this finding suggests that patient weight was not a confounding factor when assessing pancreatic volume.

The primary limitation of our prospective study was the relatively small sample size, which may have prevented identification of a statistically significant difference in CTA variables, such as pancreatic attenuation, between groups. In addition, although a triple-phase CTA was successfully obtained in 26 of 27 cats, a second delayed postcontrast scan had to be acquired in 9 of 27 cats because of motion artifact. The artifact was most commonly the result of respiratory motion. A delayed postcontrast scan of the pancreas free of motion artifact was required for calculation of pancreatic volume, which necessitated the repeat scan. Ultimately, we do not feel the repeated scan was an impediment to overall image acquisition or interpretation. In general, the effects of motion artifact and the ability to acquire a diagnostic scan should always be taken into account, and the scan and sedation or anesthesia protocols adjusted as necessary. Finally, correlating CTA variables with histopathologic findings on pancreatic biopsy samples would have allowed better characterization of the differences found in our study. However, all enrolled cats were client- or staff-owned animals, and the potential risks associated with pancreatic biopsy could not be justified clinically for the purposes of our project.

In conclusion, triple-phase CTA of the pancreas was easily performed in sedated cats. Cats with DM had significantly shorter time-to-peak portal enhancement,

larger pancreas, higher pancreatic volume, and higher pancreatic V:BW on CTA. These CTA variables should be considered when imaging diabetic cats, and further investigations into associations with endocrine dysfunction are warranted.

Footnotes

[a] Torbugesic, Zoetis Inc, Kalamazoo, MI
[b] Diazepam, Hospira Inc, Lake Forest, IL
[c] Ketaset, Zoetis Inc, Kalamazoo, MI
[d] Siemens Somatom sensation, Munich, Germany
[e] Omnipaque 350, GE Healthcare, Princeton, NJ
[f] Osirix v.5.7, Pixmeo, Geneva, Switzerland
[g] SAS V 9.4 Cary, NC

Funding

ACVR Diplomate Research Award.

Acknowledgments

The authors acknowledge Dr. Deborah Keys, PhD, for statistical analysis.

Conflict of Interest Declaration: Authors declare no conflict of interest.

Off-label Antimicrobial Declaration: Authors declare no off-label use of antimicrobials.

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