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Concurrent Diseases and Conditions in Cats with Renal Infarcts

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Background: Renal infarcts identified without definitive association with any specific disease process.

Objective: Determine diseases associated with diagnosis of renal infarcts in cats diagnosed by sonography or necropsy.

Animals: 600 cats underwent abdominal ultrasonography, necropsy, or both at a veterinary medical teaching hospital.

Methods: Information obtained from electronic medical records. Cats classified as having renal infarct present based on results of sonographic evaluation or necropsy. Time-matched case-controls selected from cats that underwent the next scheduled diagnostic procedure.

Results: 309 of 600 cats having diagnosis of renal infarct and 291 time-matched controls. Cats 7–14 years old were 1.6 times (odds ratio, 95% CI: 1.03–2.05, \( P = .03 \)) more likely to have renal infarct than younger cats but no more likely to have renal infarct than older cats (1.4, 0.89–2.25, \( P = .14 \)). All \( P \) < 0.14 are statistically significant. Cats with renal infarcts were 4.5 times (odds ratio, 95% CI: 2.63–7.68, \( P < .001 \)) more likely to have HCM compared to cats without renal infarcts. Cats with renal infarcts were 0.7 times (odds ratio, 95% CI: 0.51–0.99, \( P = .046 \)) less likely to have diagnosis of neoplasia compared to cats without renal infarcts. Cats with diagnosis of hyperthyroidism did not have significant association with having renal infarct. Cats with renal infarcts were 8 times (odds ratio, 95% CI: 2.55–25.40, \( P \leq 0.001 \)) more likely to have diagnosis of distal aortic thromboembolism than cats without renal infarcts.

Conclusions and Clinical Importance: Cats with renal infarcts identified on antemortem examination should be screened for occult cardiomyopathy.

Key words: Abdominal ultrasonography; Cardiomyopathy; Cardiovascular; Kidney; Radiology and diagnostic imaging; Thromboembolism.

Chronic renal infarcts in cats result in hyperechoic wedge-shaped sections of tissue on sonographic examination, caused by disruption of blood flow to a renal pyramid, whereas acute renal infarcts might have decreased or mixed echogenicity. Renal infarcts may develop secondary to a variety of diseases that increase the rate of thrombus formation, which may include hyperthyroidism, neoplasia, and cardiomyopathy. Clinically, the authors have noted the incidental presence of renal infarcts in a number of cats undergoing sonographic evaluation for nonrenal causes. Necropsy is another diagnostic tool which can identify both renal infarcts and the presence of a predisposing disease process.

Kidneys are vulnerable to infarction because of their vascular anatomy. The interlobular arteries which feed the renal lobes have no anastomoses, which increase their susceptibility to ischemic necrosis. In addition, the high percentage of the circulating blood volume directed toward the kidney increases the likelihood for thromboemboli. Coagulation disorders in cats have been identified or suggested with cardiomyopathy, hyperthyroidism, and neoplasia. Hypertrophic cardiomyopathy (HCM), first described more than 35 years ago, is the most common form of heart disease in cats. HCM has a known association with hypercoagulability and thrombus formation, and is commonly associated with congestive heart failure (CHF) and aortic thromboembolism (ATE). A single study has reported the presence of thrombi in other organs of cats diagnosed with ATE, including renal and cerebral thrombosis. As early cardiomyopathy can be an occult disease, the presence of renal infarcts on ultrasound might be a useful and unexpected screening tool.

The purpose of this study was to determine if the ultrasonographic and postmortem identification of renal infarcts in cats with HCM were associated when compared to a time-matched control population of cats without HCM. Our null hypothesis was that cats with HCM had a similar frequency of renal infarcts identified on either ultrasound or necropsy when compared to cats without HCM.

Material and Methods

Criteria for Selection of Cases

Medical records of cats were reviewed retrospectively by searching for any of the following key words as sonographic, clinical, or postmortem diagnoses within the computer database of the Veterinary Medical Teaching Hospital at the University of California, Davis: cardiomyopathy, ATE, or infarct. Cases were selected between the dates of December 1, 1998 and March 1,
2011. Cats that had been diagnosed with a renal infarct either by abdominal ultrasound or necropsy were included as a case in this study. Cases were excluded in which the cat had recently undergone surgery within 4 months or if the cat was less than 1 year of age as renal infarcts were presumed to be a disease found in adult animals\textsuperscript{32} and surgery has a potential to lead to vascular endothelial damage or a disruption of blood flow\textsuperscript{20}.

**Procedures**

Data were extracted from medical records of eligible cases and entered onto a standardized electronic data sheet. For each cat, the following information was collected from the record: signalment, date of visit, presence of HCM, presence of other cardiomyopathy, method of diagnosis of cardiomyopathy, presence of cardiac thrombus, presence of renal infarct or thrombus, presence of distal aortic thrombus, presence of clinical pelvic or thoracic limb ATE, diagnosis of hyperthyroidism, and diagnosis of neoplasia. Cats were categorized as young adult (1–6 years), adult (7–14 years), or geriatric (15–21 years). Cats were categorized as male or female, regardless of reproductive status. HCM and other cardiomyopathies were diagnosed either by echocardiogram or necropsy and histopathology. All abdominal ultrasounds were completed by radiology residents under the direct supervision of ACVR board-certified faculty members. All ultrasound reports were written and approved by a board-certified radiologist immediately after that examination. Premortem diagnosis of HCM was defined by echocardiographic findings including papillary muscle hypertrophy, severe to complete obliteration of the left ventricular lumen at the end of systole, or a thickened left ventricular wall (>6 mm).\textsuperscript{14,17,21,30–32} Echocardiograms were either performed before referral to UC Davis by a board-certified radiologist or board-certified cardiologist, or were completed at UC Davis by a radiology resident and a board-certified cardiologist. Postmortem diagnosis of HCM was based on heart weight to body weight ratio (>6.5 g kg\textsuperscript{-1}), histopathologic evidence of myocyte hypertrophy, and interstitial or interfibrillar fibrosis.\textsuperscript{14–17} Necropsies were performed by residents in the anatomic pathology program, and were directly supervised by board-certified pathologists at the time of the study, review of the histopathology, and completion of the report. Signs to indicate a clinical diagnosis of ATE included 2 or more of the following: pelvic or thoracic limb paresis or paralysis, cyanotic nail beds, toe pads coldness and cool extremities, decreased or absent pulses, contracted and painful limb muscles, and painful vocalization. The presence of hyperthyroidism was defined as a total thyroxine level (T4) increased above the reference range at time of presentation or within the previous 4 months. The presence of neoplasia was defined as antemortem diagnosis at UC Davis or by a referring veterinarian based on cytology or biopsy performed by a veterinary pathologist within 12 months of presentation or postmortem at UC Davis based on necropsy and histopathology. No follow-up was attempted for any of the cats included in the study.

For each case, a time-matched control was assigned, and identical data were collected from their electronic medical record. A time-matched control was assigned by searching the date of the visit of the infarct case and then searching for the next cat closest in time that had received an abdominal ultrasound or necropsy, dependent of the source of diagnosis for the infarct case, restricted to a 1-month window of time. Control cases were eliminated if they showed up in both the ultrasound control group and the necropsy control group, and the next closest case-control was chosen. For 20 cases, a case-control could not be assigned as the next cat with either an ultrasound or a necropsy performed was not found within the 1 month window for controls. Case-controls were not age-matched, breed-matched, or matched by sex.

**Statistical Analysis**

Associations between renal infarct and covariates and other diagnoses of interest were assessed by using the Chi square test or Fisher’s exact test if the expected frequency in 1 more cells was less than 5.\textsuperscript{33} All statistical analyses were performed by using a commercially available computer program.\textsuperscript{4}

**Results**

A total of 600 cases were evaluated with 309 cats identified as having a diagnosis of renal infarct via sonography or necropsy, and 291 cats identified as time-matched controls. Ultrasonography was performed on 375 cats and 240 cats had a necropsy performed, with 13 cats having both.

Breeds included domestic short hair (348), domestic long hair (88), domestic medium hair (59), mixed breed (29), Siamese (21), Maine Coon (14), Persian (13), Himalayan (8), Abyssinian (4), Burmese (2), Bengal (2), Manx (2), Ragdoll (2), Rex (2), Scottish Fold (2), and 1 each of the following breeds: American shorthair, Norwegian Forest Cat, Sphynx, and Tonkinese. One cat’s breed was not identified in the records. Reproductive status was female spayed (253), female intact (10), male neutered (317), male intact (18), and unknown (4). The mean age for all cats was 9.8 years; median was 10 years, ranging from 1 to 21 years of age. Breed, reproductive status, and age of the control group and the case group were comparable.

Nine cats had a renal artery thrombus identified, 2 via ultrasound and 8 via necropsy. All cats with renal arterial thrombosis were also diagnosed with a cardiomyopathy. One hundred and ninety-one cats had a renal infarct identified on abdominal ultrasound, and 118 cats had a renal infarct identified on necropsy. Cats diagnosed with renal infarcts were 4.5 times more likely to have HCM compared to cats without renal infarcts (95% CI: 2.63–7.68, \( P < .001 \)). There was no association between the presence of renal infarct and hyperthyroidism (OR: 1.6, 95% CI: 0.93–2.70, \( P = .088 \)). Cats with renal infarcts were less likely to have a diagnosis of neoplasia compared to cats without renal infarcts (OR: 0.7, 95% CI: 0.51–0.99, \( P = .046 \)).

All cats with cardiac thrombus identified via ultrasound or necropsy had renal infarcts. Cats with renal infarcts were 8.1 times more likely to have a diagnosis of distal ATE than cats without a renal infarct (95% CI: 2.55–25.40, \( P \leq .001 \)). Cats with renal infaracts were 8.4 times more likely to have a pelvic limb ATE than cats without (95% CI: 2.65–26.31, \( P < .001 \)). All cats with thoracic limb ATE on physical examination had renal infarcts.

Age of the cats was associated with the presence of a renal infarct. Cats between the ages of 7 and 14 years were more likely to have a renal infarct, with adult cats being 1.6 times more likely to have a renal infarct compared to young adult cats (95% CI: 1.03–2.15, \( P = .03 \)) but no more likely than geriatric cats (1.4, 95% CI: 0.89–2.25, \( P = .14 \)).
Because age was identified as an effect modifier, stratified analyses were performed where possible. Geriatric cats with renal infarcts were not more likely to have HCM compared to cats without renal infarcts (OR: 2.7, 95% CI: 0.68–11.1, \( P = .10 \)). However, young adult cats and adult cats with renal infarcts were more likely to have HCM than cats without renal infarcts (OR: 4.9, 95% CI: 1.4–18.1, \( P = .004 \) for young adult cats and OR: 4.7, 95% CI: 2.15–11.0, \( P < .001 \) for adult cats).

The identification of distal ATE was significantly associated with the presence of renal infarcts in geriatric cats only (\( P < .001 \)). The relationship between pelvic limb ATE and renal infarcts was not significant when adjusted for age.

When stratified by age, renal infarcts did not have a significant association with hyperthyroidism or neoplasia.

**Discussion**

Renal infarcts were significantly associated with a diagnosis of HCM in cats regardless of the method of diagnosis. Cats with cardiomyopathy are hypercoagulable compared to healthy cats.\(^5\) Hypercoagulability is caused by alterations of at least 1 of the 3 portions of Virchow’s triad.\(^6,9,29\) Cats with HCM may have changes associated with all sections of the triad, with endothelial disruption from dilatation of cardiac chambers (specifically the left atrium), turbulent blood flow or stasis associated with the enlarged atrium, and increased platelet activation all having been described previously.\(^7,9\) This hypercoagulability increases the risks of thromboembolism, as is evident in the increased association between ATE and HCM.\(^8,14,16,23–25,27,28\)

There was not a significant relationship between renal infarcts and hyperthyroidism in this study, similar to previous studies.\(^23,24,27,28\) A systematic review of thyroid dysfunction and effects on coagulation in human medicine identified a prothrombotic state in hyperthyroid patients and a hypocoagulable state in patients with hypothyroidism.\(^34\) Increased risk of hemorrhage has been identified as a potential side effect of methimazole administration in hyperthyroid cats,\(^13\) but hypercoagulability has not been tested in treated or untreated hyperthyroid cats to the best of the authors’ knowledge. Evaluation with thromboelastography may help determine if hyperthyroid cats are hypercoagulable.

Cats diagnosed with neoplasia were less likely to have renal infarcts in this study, which was an unexpected finding. Some neoplasias are associated with a hypercoagulable state in cats, either through disruption of vascular endothelium or physical disruption of blood flow.\(^29\) The lack of association with neoplasia in the face of renal infarcts suggests that neoplasia may not be as likely to cause a hypercoagulable state in cats. In addition, hypercoagulability might only be associated with specific types of neoplasia. As the specific histopathologic diagnosis for neoplasia was not investigated in this study, this avenue of investigation should be considered in the future.

While a recent study identified Ragdoll cats as being predisposed to cortical lesions including renal infarcts, Ragdoll and non-Ragdoll cats may commonly have ultrasonographic abnormal findings.\(^35\) One study identified Ragdoll cats as being overrepresented for the diagnosis of HCM compared to the hospital population.\(^23\) Other studies have identified Persians as a breed more likely to be diagnosed with HCM.\(^16,22\) Because of the relatively low numbers of purebed cats in this study, breed-related renal or cardiac abnormalities were not identified. A study evaluating larger numbers of purebed cats might help determine if breed-related renal or cardiac abnormalities are intertwined.

While renal infarcts occurred more frequently in senior cats than in adult cats, the odds of their presence did not increase as age advanced to that of geriatric cats. If renal infarcts are caused by an underlying hypercoagulable state, such as cardiomyopathy, one can argue that these disease processes are more likely to develop during the middle years than in later years. Another possibility is that geriatric cats which might otherwise have developed a hypercoagulable state because of the presence of cardiomyopathy, have already succumbed to the sequelae of the disease before attaining an age greater than 14 years. Cats with HCM have mean ages of 4.8–5.9 years at the time of diagnosis.\(^14,16,18,20\) With the relatively young age at diagnosis of HCM, and the median survival time ranging from 300 to 1,276 days,\(^14,18,20–22,25\) one can postulate that it would be difficult to find a geriatric cat with HCM, and therefore difficult to find a geriatric cat with a higher risk of a renal infarct.

The loss of a significant association between renal infarcts and cardiac thrombus when stratified by age is likely because of the small numbers of cats in each group with a cardiac thrombus. The significant association of distal ATE with the presence of renal infarcts in geriatric cats only may be caused by an increased odds being driven by age of the cats and not the increased odds of developing a distal ATE. The relationship between both pelvic limb ATE and thoracic limb ATE with renal infarcts lost significance when adjusted for age because of small numbers of ATE being reported in each age group.

This study identified that effects of cardiac-related hypercoagulability may be seen at an earlier stage in the disease process, as evidenced by the increased association of renal infarcts with a diagnosis of HCM. The finding of the even greater association between the presence of renal infarcts and a clinical diagnosis of ATE further indicates that thromboembolic disease can be present before a large aortic thrombus develops. Sustained echocardiographic contrast (SEC) is considered a risk factor for the development of thromboembolic events.\(^30\) Identifying the presence or absence of SEC in the cats identified with HCM might have further solidified the connection between early thrombus formation and cardiomyopathy. Because of its retrospective nature, and the frequent finding of HCM diagnosis being performed by a veterinarian not associated with our institution, SEC presence was not reliably recorded.
Limitations of this study are primarily because of its retrospective nature and method of data collection. When reviewing ultrasound reports and necropsy reports, if no description of an abnormality, such as renal infarct, was written, then it was listed as absent in our data sheet. This raises the potential for a false negative as the abnormality may have been present but not reported. Lack of follow-up on cases may have prevented identification of newly diagnosed hyperthyroidism in cats with the months after sonographic evaluation. Having this information would have helped support or deny the findings of a lack of association between renal infarcts and feline hyperthyroidism. Other sources of bias included less than optimal case-control ratio and diagnoses originating from multiple referral hospitals. A prospective study might help determine if the findings of this study can be repeated and help determine the cause and effect relationship between renal infarcts and HCM.

A recent study identified that over 15% of apparently healthy cats had undiagnosed HCM. This study has identified that cats with renal infarcts identified on abdominal ultrasound have a 4.5 times higher risk of having HCM. It also showed that cats with renal infarcts had an 8-fold risk of having a catastrophic ATE. The effect of treatment of HCM cats with low-dose aspirin or clopidogrel on morbidity or mortality from thrombotic events has been difficult to assess in previous studies. However, as aspirin and clopidogrel have been found to experimentally decrease platelet aggregation, these medications are thought to decrease the risk of hypercoagulability in vivo. By identifying evidence of a thrombotic event through the sonographic diagnosis of a renal infarct, the authors recommend that screening for occult cardiac disease be performed in cats with this finding, as early diagnosis and treatment of HCM may improve survival.

Footnote

a STATA v. 10, StataCorp, College Station, TX

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

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