Association between chronic azotemic kidney disease and the severity of periodontal disease in dogs

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Abstract
Naturally occurring periodontal disease affects >75% of dogs and has been associated with cardiac lesions and presumptive endocarditis. However, the relationships between periodontal disease and chronic kidney disease (CKD) in dogs have not been studied. In a retrospective longitudinal study the incidence of azotemic CKD was compared between a cohort of 164,706 dogs with periodontal disease and a cohort of age-matched dogs with no periodontal disease from a national primary care practice. These dogs contributed 415,971 dog-years of follow-up from 2002 to 2008. Hazard ratios and 95% confidence intervals from Cox regression were used to compare the incidence of azotemic CKD in dogs with stage 1, 2, or 3/4 periodontal disease to dogs with no periodontal disease. The hazard ratio for azotemic CKD increased with increasing severity of periodontal disease (stage 1 hazard ratio = 1.8, 95% confidence interval: 1.6, 2.1; stage 2 hazard ratio = 2.0, 95% confidence interval: 1.7, 2.3; stage 3/4 hazard ratio = 2.7, 95% confidence interval: 2.3, 3.0; \( P \) trend = <0.0001) after adjustment for age, gender, neuter status, breed, body weight, number of hospital visits, and dental procedures. Increasing severity of periodontal disease was also associated with serum creatinine >1.4 mg/dl and blood urea nitrogen >36 mg/dl, independent of a veterinarian’s clinical diagnosis of CKD.

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1. Introduction
Chronic kidney disease (CKD) is a common human medical condition that has been associated with cardiovascular disease, premature mortality, decreased quality of life, and increased health-care costs (Foley et al., 2005). Using data from the National Health and Nutrition Survey (NHANES) for 1999–2004, the Centers for Disease Control and Prevention reported that 16.8% of people in the United States aged ≥20 years had CKD, an increase of 15.9% from the 1988 to 1994 NHANES III (Saydah et al., 2007). Untreated CKD may progress to end-stage renal disease requiring dialysis or kidney transplantation. The prevalence of end-stage renal disease has steadily increased over the past 25 years with >100,000 new cases reported in 2002, and a nationwide prevalence of 431,284 patients undergoing dialysis treatment or renal transplant (Collins et al., 2005).

Risk factors for CKD were identified in a study of 11,955 persons ≥18 years of age surveyed as part of NHANES III. Adults with periodontal disease (7.5%), were 4.5-times (confidence interval CI: 3.02, 6.71) more likely to have CKD than those with no periodontal disease while edentulous adults were 11-times (CI: 6.86, 17.20) more likely to have CKD (Fisher and Taylor, 2009). In addition, a cross-sectional
study of 5537 middle aged–black and white men from the Atherosclerosis Risk in Communities Study demonstrated a similar association between periodontal disease and renal insufficiency after adjustment for concurrent demographic and cardiovascular risk factors (Kshirsagar et al., 2005). However, the authors appropriately noted that a prospective study is needed to determine the causal nature of the observed relationship between periodontal disease and CKD, as both of these conditions are characterized by local and systemic inflammation.

Large epidemiological studies of periodontal disease in dogs are now possible due to nationwide veterinary practices that use electronic health records. For example, a recent study of approximately 120,000 pet dogs with periodontal disease and an age-matched cohort without periodontal disease was conducted using the electronic health records of the largest private veterinary practice in North America (Glickman et al., 2009). In this study the records of pet dogs were reviewed for up to five years to determine the incidence of cardiovascular diseases. Significant associations were found between the severity of periodontal disease and subsequent presumptive diagnoses of cardiovascular diseases including endocarditis, but not between the stage of periodontal disease and common non-cardiovascular-related infectious and non-infectious conditions. However, the findings of this study were questioned by specialists in veterinary cardiology (Peddle and Sleeper, 2009) who noted that the results were inconsistent with the findings of a previous published clinical study (Peddle et al., 2009).

In the present retrospective longitudinal study the hypothesis was tested that an increasing severity of periodontal disease was associated with increased incidence of azotemic CKD over time.

2. Materials and methods

2.1. Data source

Banfield the Pet Hospital operates >750 privately owned, full-service, primary-care veterinary hospitals in 43 states that see approximately 115,000 separately accessorized dog and cat office visits each week. Banfield uses proprietary practice management software to create electronic health records that are uploaded nightly to a central database and stored in Oracle format (Oracle Database, Redwood Shores, CA). All medical records of dogs from 2002 to 2008 were reviewed for this study.

2.2. Periodontal cohort selection

Two cohorts of dogs were created for this study; one had a diagnosis of periodontal disease and the other had no diagnosis of periodontal disease or clinical exam findings suggestive of periodontal disease. Dogs were selected for the periodontal cohort when they had a diagnosis of periodontal disease stage 1, 2, or 3/4 during the years 2002–2008. First, all dogs with a diagnosis of periodontal disease stage 3/4 were selected and the date of their first diagnosis of stage 3/4 periodontal disease was set as the entry date into the study. Then, all dogs with a diagnosis of periodontal disease stage 2 were selected in the same manner, provided they had never had a diagnosis of periodontal disease stage 3/4. Finally, all dogs with a diagnosis of periodontal disease stage 1 were selected, provided they never had a diagnosis of periodontal disease stage 2 or 3/4. Dogs with periodontal disease were not included if there were missing or inconsistent data (e.g. birth date after death date) or the stage of periodontal disease was not recorded, there were no follow-up visits after the date of diagnosis of periodontal disease, or they were >15 years of age.

Banfield veterinarians had electronic access in their hospital to descriptions and photographs that illustrated the clinical stages of periodontal disease. Stage 1 periodontal disease was characterized by acute gingival inflammation with no loss of gingival attachment. Stage 2 was characterized by chronic gingivitis and up to 25% dental attachment loss or alveolar bone loss; periodontal pockets may exist. Stage 3/4 periodontal disease was characterized by up to 50% dental attachment or alveolar bone loss with periodontal pockets and possible gingival recession and root exposure. At the time of this study, Banfield veterinarians were not asked to evaluate pre-specified teeth or distinguish between stage 3 and stage 4 periodontal disease, and radiographs were not required for specific staging.

2.3. Non-periodontal cohort selection

A non-periodontal disease cohort for the years 2002–2008 was created by identification of dogs that never had a diagnosis of periodontal disease or any of the following examination findings suggestive of periodontal disease including gingival recession, gingivitis, infected pockets or receding gingiva. Non-periodontal cohort dogs were frequency matched to periodontal cohort dogs based on year of visit and age. A random sample of non-periodontal dogs was selected from each calendar year and 3-month age group so as to mimic the proportion of periodontal dogs with stage 1, 2, or 3/4 periodontal disease. For dogs >13 years old, 6-month age groups were used for frequency matching, because of small sample sizes. After forming the potential non-periodontal cohort in each age category, a single non-periodontal cohort was randomly selected, with each dog in an age-calendar year group having the same probability of being selected; the total number of dogs without periodontal disease was therefore equivalent to the total number of dogs with periodontal disease. Similar to the periodontal cohort, dogs in the non-periodontal cohort were excluded if data was missing or inconsistent, no follow-up visits after the selection date had occurred, or if they were >15 years of age.

2.4. Assessment of azotemic CKD

Serum BUN and creatinine concentrations were identified in the medical records for all dogs at all time points in which they were recorded following the initial date of entry into the study. Criteria for a diagnosis of azotemic CKD were a serum creatinine concentration >1.4 mg/dl and a concurrent diagnosis code of ‘chronic renal failure’. If more than one such diagnosis was recorded for a dog,
only the date of the first diagnosis of azotemic CKD was used in the analysis. Dogs were excluded from data analysis if prior to entry into the study they had a diagnosis of chronic renal failure, or if serum creatinine was above the reference range. Dogs with azotemic CKD were further subdivided into three severity groups using serum creatinine concentrations recommended by the International Renal Interest Society (IRIS). These three groups (corresponding to IRIS Stages II–IV) were serum creatinine concentrations of 1.4–2.0 mg/dl, 2.1–5.0 mg/dl, or >5.0 mg/dl, respectively. Further IRIS subclassification based on urine protein-to-creatinine ratio and blood pressure was not possible in the present study due to the large number of dogs with insufficient data.

2.5. Data analysis

The incidence of azotemic CKD per 1000 dog-years was calculated for dogs without evidence of periodontal disease and separately for dogs with periodontal disease based on stage (stage 1, 2, or 3/4). Multivariate Cox proportional hazards regression models were constructed by stepwise selection using the PHREG procedure in SAS (SAS Institute, Inc., Cary, NC). Selection models for each dependent variable included periodontal disease stage (1, 2, 3/4), neuter status (yes, no), pure breed (yes, no), gender (male, female), age in years (0 < 2, 2 to <4, 4 to <6, 6 to <8, 8 to <10, 10+), weight in kilograms (0 to <4.5, 4.5 to <13.6, 13.6 to <22.7, 22.7 to <34.0, 34.0 to <45.5, 45.5+), log hospital visits per month, and having had at least one dental procedure (yes, no) performed at Banfield, including cleaning with or without extractions, at any time following entry into the study. Body weight was available for approximately 68% of all hospital visits; body weight was estimated for visits in which weight was not recorded using a previously described statistical method (Glickman et al., 2009). This weight estimation procedure using data from Banfield medical records resulted in a high correlation between actual and estimated weights (r² = 0.97). The variables gender, neuter status, breed, and number of hospital visits during the follow-up period, number of months of follow-up and dental treatment were entered into all Cox regression models to control for potential confounding, regardless of statistical significance. Age and weight were selected on the basis of statistical significance (P < 0.01) by use of a stepwise procedure.

The follow-up period began on January 1, 2002 and ended on December 31, 2008; the last hospital visit was the right censoring date for hazard modeling. The same criteria used to select dogs to calculate incidence rates of outcome events were also used to select dogs for inclusion in Cox proportional hazard models. Multiplicative interactions in final models were tested by multiplication of the two variables in question and inclusion of the main effect and interaction terms in the final model. For all hazard ratios (HR), 2-sided P values and 95% confidence intervals (CI) are reported. Survival curves were calculated and graphed using fitted Cox proportional hazard models. The estimated survival probabilities were plotted against the number of days of follow-up.

3. Results

The periodontal cohort consisted of 164,706 dogs of which 60,870 had stage 1 disease, 57,150 had stage 2 disease, and 46,686 had stage 3/4 disease (Table 1). These dogs were frequency matched based on year of diagnosis and age to 164,706 dogs with no history of periodontal disease. Dogs enrolled from 721 different Banfield hospitals from 2002 to 2008 contributed 415,971 cumulative dog-years of observation. The median number of days of follow-up for dogs with stage 1, stage 2, and stage 3/4 periodontal disease was 368, 372, and 339, respectively; it was 376 days for dogs with no history of periodontal disease and the distribution of follow-up time was similar for all groups (Fig. 1). The mean (median) age and weight, and proportion of dogs by gender, neuter status, and breed in each cohort were calculated (Table 2). Given the relatively large number of dogs in each group, statistically significant differences between groups by age, weight, gender, neuter status, and breed were not reported, because they were small and often clinically irrelevant. The mean age of dogs increased and the mean weight of dogs decreased with increasing severity of periodontal disease. The proportion of dogs that had a
The risk of a diagnosis of azotemic CKD in dogs, irrespective of the magnitude of increase in serum creatinine concentration, increased significantly with increasing severity of periodontal disease (Table 3). The HR for azotemic CKD was 2.66 (CI: 2.35, 3.02) in dogs with stage 3/4 periodontal disease as compared with dogs with no history of periodontal disease. The HR for azotemic CKD was slightly lower for neutered (HR 0.89; CI: 0.79, 1.02) versus intact dogs, and for dogs that had a dental procedure performed during the study period (HR 0.77; CI: 0.69, 0.85). Breed (mixed versus purebred) was not associated with the HR for azotemic CKD. The HR for azotemic CKD increased with increasing age, and was highest in dogs with body weight <4.5 kg.

Increasing severity of periodontal disease was significantly associated with increasing blood urea nitrogen and serum creatinine concentrations, regardless of IRIS Stage of azotemic CKD (Table 4 and Figs. 2 and 3). The HR for azotemic CKD dogs when subclassified into IRIS Stages II and III, increased significantly with increasing severity of periodontal disease (Table 4 and Figs. 4–6). The highest HR was for dogs with stage 3/4 periodontal disease with a diagnosis of stage II azotemic CKD (serum creatinine concentration 1.4–2.0 mg/dl) (HR 3.35; CI: 2.48, 4.52).

4. Discussion
In this large retrospective longitudinal study of dogs in a national primary care veterinary practice, the severity of periodontal disease was positively related to the inci-

<table>
<thead>
<tr>
<th>Table 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristics of dogs (n = 329,412) visiting a nationwide primary care veterinary practice that participated in a cohort study from 2002 to 2008 to evaluate relationships between the severity of periodontal disease and the risk of chronic kidney disease.</td>
</tr>
<tr>
<td>Variable</td>
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<tr>
<td></td>
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<tr>
<td>Age (years)</td>
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<td>Weight (kg)</td>
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<td>Variable</td>
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<tr>
<td></td>
</tr>
<tr>
<td>Breed</td>
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<td></td>
</tr>
<tr>
<td>Dental treatment</td>
</tr>
</tbody>
</table>

| a Values may not sum to 100% due to missing data. |
Table 3
Risk of first clinical diagnosis of azotemic chronic kidney disease in a cohort of 329,412 dogs by stage of periodontal disease; hazard ratios were determined using multivariable Cox regression.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
<th>Hazard ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periodontal disease</td>
<td>No periodontal disease Referent</td>
<td>1.80</td>
<td>1.55, 2.08</td>
</tr>
<tr>
<td></td>
<td>Stage 1</td>
<td>1.97</td>
<td>1.72, 2.57</td>
</tr>
<tr>
<td></td>
<td>Stage 2</td>
<td>2.66</td>
<td>2.35, 3.02</td>
</tr>
<tr>
<td>Neutered</td>
<td>No Referent</td>
<td>0.89</td>
<td>0.79, 1.02</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>0.87</td>
<td>0.80, 0.96</td>
</tr>
<tr>
<td>Breed</td>
<td>Pure Referent</td>
<td>1.15</td>
<td>0.93, 1.43</td>
</tr>
<tr>
<td></td>
<td>Mixed</td>
<td>0.93</td>
<td>0.71, 1.20</td>
</tr>
<tr>
<td>Gender</td>
<td>Female Referent</td>
<td>0.87</td>
<td>0.69, 0.85</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>0.93</td>
<td>0.93, 1.43</td>
</tr>
<tr>
<td>Dental treatment</td>
<td>No Referent</td>
<td>0.77</td>
<td>0.69, 0.85</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>0.74</td>
<td>0.62, 0.90</td>
</tr>
<tr>
<td>No. hospital visits</td>
<td></td>
<td>2.76</td>
<td>2.64, 2.89</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0–&lt;2 Referent</td>
<td>1.18</td>
<td>0.65, 2.15</td>
</tr>
<tr>
<td></td>
<td>2–&lt;4</td>
<td>2.09</td>
<td>1.18, 3.71</td>
</tr>
<tr>
<td></td>
<td>4–&lt;6</td>
<td>3.72</td>
<td>2.12, 6.53</td>
</tr>
<tr>
<td></td>
<td>6–&lt;8</td>
<td>6.80</td>
<td>3.89, 11.87</td>
</tr>
<tr>
<td></td>
<td>8–&lt;10</td>
<td>17.84</td>
<td>10.28, 30.96</td>
</tr>
<tr>
<td></td>
<td>10+</td>
<td>17.84</td>
<td>10.28, 30.96</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>&lt;4.5 Referent</td>
<td>0.86</td>
<td>0.75, 0.99</td>
</tr>
<tr>
<td></td>
<td>4.5–&lt;13.6</td>
<td>0.80</td>
<td>0.68, 0.94</td>
</tr>
<tr>
<td></td>
<td>13.6–&lt;22.7</td>
<td>0.79</td>
<td>0.67, 0.93</td>
</tr>
<tr>
<td></td>
<td>22.7–&lt;34.1</td>
<td>0.57</td>
<td>0.46, 0.71</td>
</tr>
<tr>
<td></td>
<td>34.1–&lt;45.5</td>
<td>0.87</td>
<td>0.63, 1.20</td>
</tr>
<tr>
<td></td>
<td>45.5+</td>
<td>0.87</td>
<td>0.63, 1.20</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval.

dence of a clinical diagnosis of azotemic CKD over time. An association of the severity of periodontal disease in dogs with increasing age and decreasing body weight was expected based on previous descriptive studies and may be explained by smaller dogs more often being fed moist commercial foods and table foods by their owners that are more likely to promote dental calculus accumulation compared with dry dog foods (Harvey et al., 1994; Lund et al., 1999). The findings of the present study of dogs are also consistent with a positive association between periodontal disease and CKD in humans (Kshirsagar et al., 2005). However, studies in humans have generally been cross-sectional and therefore, subject to confounding by shared demographic and environmental risk factors for periodontal and renal disease including infection and inflammation (Scannapieco and Panesar, 2008).

The mechanisms by which periodontal disease may increase the risk of CKD are not known. Evidence in humans

Table 4
Risk of first onset of azotemic chronic kidney disease or first elevated laboratory measure of serum creatinine or blood urea concentration in a cohort of 329,412 dogs by stage of periodontal disease; hazard ratios were determined using multivariable Cox regression.

| Outcome                             | No periodontal disease | \begin{tabular}{l} Periodontal disease \\ No. cases \end{tabular} | \begin{tabular}{l} Stage 1 \\
No. cases \\nHazard ratio^a (95% CI) \end{tabular} | \begin{tabular}{l} Stage 2 \\
No. cases \\nHazard ratio^a (95% CI) \end{tabular} | \begin{tabular}{l} Stage 3/4 \\
No. cases \\nHazard ratio^a (95% CI) \end{tabular} | \begin{tabular}{l} P_{trend} \end{tabular} |
<table>
<thead>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic kidney disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine 1.4–2.0 mg/dl</td>
<td>68</td>
<td>60</td>
<td>2.04 (1.43, 2.91)</td>
<td>84</td>
<td>2.15 (1.56, 2.99)</td>
<td>159</td>
</tr>
<tr>
<td>Creatinine 2.0–5.0 mg/dl</td>
<td>240</td>
<td>157</td>
<td>1.66 (1.35, 2.04)</td>
<td>247</td>
<td>1.92 (1.60, 2.30)</td>
<td>381</td>
</tr>
<tr>
<td>Creatinine &gt;5.0 mg/dl</td>
<td>136</td>
<td>95</td>
<td>1.98 (1.52, 2.59)</td>
<td>119</td>
<td>2.05 (1.59, 2.64)</td>
<td>171</td>
</tr>
<tr>
<td>Blood urea nitrogen only&gt;36 mg/dl</td>
<td>2461</td>
<td>1341</td>
<td>1.28 (1.20, 1.38)</td>
<td>1864</td>
<td>1.42 (1.34, 1.51)</td>
<td>2787</td>
</tr>
<tr>
<td>Creatinine only&gt;2.0 mg/dl</td>
<td>1663</td>
<td>912</td>
<td>1.38 (1.27, 1.50)</td>
<td>1142</td>
<td>1.50 (1.39, 1.62)</td>
<td>1421</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval.

^a Adjusted for age, weight, gender, neuter status, dental treatments.
suggests that periodontitis results in subclinical systemic inflammation that promotes atherosclerosis and leads to secondary renal hypoxemia, progressive renal damage, and CKD through localized arterial stenosis and reduced cardiac output (Scannapieco and Panesar, 2008). Inflammatory markers including C-reactive protein and interleukin-6 are increased in most human patients with CKD regardless of etiology (Kalantar-Zadeh, 2007). Furthermore, other non-renal conditions known to induce subclinical systemic inflammation and dyslipidemias such as diabetes and some cardiovascular diseases, have been associated with CKD in epidemiological studies (Weiner and Sarnak, 2004). Interestingly, although periodontal disease severity among dogs in the present study was associated with increasing risk of azotemic CKD, dogs appear to be relatively resistant to development of atherosclerosis, type-2 diabetes, coronary artery disease, and primary systemic hypertension. However, a previous longitudinal study in dogs did report a significant relationship between the severity of periodontal disease and non-specific biomarkers of inflammation such as white blood cell count and the percentage of monocytes in peripheral blood (Glickman et al., 2009). A statistical association between periodontal disease severity and histological lesions in the heart and kidneys of dogs at necropsy has also been reported, but the temporal relationship between these conditions could not be evaluated (DeBowes et al., 1996).

Little has been published on possible associations in dogs between presence and severity of periodontal disease and serum concentrations of biomarkers of inflammation, or on the possible benefits to systemic health of treating periodontal disease, despite the high prevalence of periodontitis in dogs by four years of age (Colmery and Frost, 1986). Of potential practical importance in the present study is the finding that treatment of periodontal disease was associated with a 23% reduction in the risk of azotemic CKD. This is consistent with a recent population based survey of 11,869 men and women that reported a significant association of poor oral hygiene with low grade systemic inflammation (de Oliveira et al., 2010). Because therapy for periodontal disease and the level of oral hygiene provided
for dogs at home by their owners was not standardized in
the present canine study, randomized-controlled trials will
be required to evaluate the effectiveness of periodontal dis-
ease therapy for preventing systemic diseases secondary to
inflammation caused by oral microbial infections.

To our knowledge, the present epidemiological study
involving 415,971 cumulative dog-years of observation
is the largest ever conducted in dogs, but nevertheless
had several limitations. Some of these limitations are
attributable to its retrospective nature and the inability
of the investigators to standardize patient examinations
including uniform staging of periodontal disease (the ex-
posure variable) and the accuracy of diagnosis of azotemic
CKD (the primary outcome variable). Also, the median
number of days of follow-up for dogs in this study was
limited to approximately one year. Longer follow-up will
be required to characterize the full impact of periodontal
disease on kidney function.

With respect to the exposure variable, staging of peri-
odontal disease was clinical in nature and did not require
radiographic confirmation, probing of gingival pocket
depth, or other objective criteria. However, Banfield rou-
tinely provides their veterinarians and dental technicians
with color photographs and descriptions in electronic for-
mat to assist them in determining the stage of periodontal
disease. It was not possible in this study to compare the
clinical stage with the reported examination findings, since
some veterinarians assigned a periodontal disease stage
to a dog but failed to record these examination findings
in the medical record, while other veterinarians recorded
the oral examination findings but failed to document the
periodontal disease stage. Because the staging of peri-
odontal disease was performed prior to a diagnosis of
azotemic CKD, misclassification with regard to the stages
of periodontal disease was likely unbiased. The fact that a
dose–response relationship was detected between increas-
ing severity (stage) of periodontal disease and clinical and
laboratory measures of azotemic CKD, indicates the peri-
odontal scoring system used by Banfield veterinarians was
robust despite the fact that the repeatability of the peri-
odontal scoring system used by Banfield veterinarians at
the time of this study had not been evaluated. Similar
sources of measurement error in staging of periodontal
disease have been reported in large human retrospective
studies (Genco et al., 2002).

Given the retrospective nature of the present study
a diagnosis of azotemic CKD was based on the clinical
judgment of attending veterinarians in conjunction with
an elevated serum creatinine concentration. This could
have led to some misdiagnoses. This approach, however,
is consistent with other studies of naturally-occurring CKD
in dogs (Lund et al., 1999; Cortadellas et al., 2010). The
investigators did not control the number and timing of
serum creatinine tests performed for dogs in either the
periodontal disease cohort or the non-periodontal disease
cohort. We believe it is unlikely however, that dogs with
acute kidney injury or severe pre- or post-renal azotemia
would have been evaluated and misdiagnosed by Ban-
field veterinarians as having CKD. The investigators did not
attempt to exclude dogs from the study if they had a con-
current diagnosis of trauma or another disease typically
associated with large increases in serum creatinine of non-
renal origin. Even if some dogs in this study had diseases
associated with acute changes in renal function, it is not
likely to have resulted in differential bias with respect to
an association with severity of periodontal disease. This
large retrospective study of thousands of electronic medi-
cal records highlights the difficulty in conducting detailed
record reviews including medical notes that are typically
stored in free text fields. In such studies one typically uti-
lizes algorithms for disease diagnoses based on physical
exam and laboratory test results as well as standardized
diagnostic codes.

The use of serum creatinine concentrations as the pri-
mary clinico-pathologic criterion of azotemic CKD poses an
additional limitation. The gold standard for documenting
reduced renal function is measurement of glomerular fil-
tration rate, which can be easily and accurately estimated
using serum creatinine concentration and demographic
data in human patients. Glomerular filtration rate (GFR),
however, is not routinely used in veterinary clinical prac-
tice primarily due to practical limitations (i.e. limited
availability of radionucleotide testing sites, requirement
for multiple blood draws, etc.). In addition, it is unclear
whether medical interventions in patients with non-
azotemic CKD (i.e. IRIS Stage I CKD) would be of any benefit
in slowing disease progression and improving prognosis
(Von Hendy-Willson and Pressler, 2010). Since GFR was not
used to identify dogs with reduced renal function, some
dogs classified as not having azotemic CKD could have had
IRIS Stage I disease.

Finally, instructions given to owners by Banfield staff
regarding oral hygiene or dental treatments dogs may have
received at other veterinary hospitals following a diagnosis
of periodontal disease were not evaluated for their associ-
ation with azotemic CKD. At the time of this study, it was
the policy of Banfield veterinarians to provide client edu-
cation regarding oral hygiene and home care to all dog
owners following a diagnosis of periodontal disease, as
well as stage-specific protocols that included dental clean-
ing and systemic administration of antimicrobials for 2–3
weeks for dogs with stage 3/4 disease. Dental treatment of
dogs by Banfield veterinarians most often included dental
cleaning and extractions, all of which were included as a
dental treatment variable in the multivariate Cox propor-
tional hazard models for CKD. However, antimicrobial use
was not considered in the analyses because it could not be
determined whether these drugs were actually adminis-
tered to dogs by their owners. Given these limitations, the
findings only suggest that dental treatment by a veterinar-
ian following a diagnosis of periodontal disease may reduce
the subsequent risk of azotemic CKD in dogs.

5. Conclusion

In conclusion, this study using electronic medical
records revealed significant positive associations between
the severity of periodontal disease and the incidence of
azotemic CKD over time. Additional studies are needed to
evaluate explanatory mechanisms. Epidemiological stud-
ies of dogs could similarly determine if periodontal disease
severity is a risk factor for other systemic diseases associ-
ated with inflammation and what periodontal treatments or prevention strategies are most effective in preventing a decline in kidney function as dogs age.

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**Conflict of interest statement**

None declared by any of the authors.

**References**


