
Ilaria Lippi, DVM, PhD; Grazia Guidi, DVM, PhD; Veronica Marchetti, DVM, PhD; Rosalba Tognetti, DVM, PhD; Valentina Meucci, ChemPharmD, PhD

Objective—To investigate serum calcium-phosphorus concentration product (sCaPP) as a predictor of mortality rate in dogs with chronic kidney disease (CKD).

Design—Retrospective case-control study.

Animals—31 dogs with definitive CKD and 35 apparently healthy dogs.

Procedures—All dogs had been referred for nephrological consultation between December 2008 and December 2010. Dogs with CKD had stable disease for ≥3 months. On the basis of glomerular filtration rate < 60 mL/min/m², 13 of the 35 apparently healthy dogs were subsequently classified as having early CKD. Disease stage among dogs was determined on the basis of plasma creatinine concentration as follows: stage 1, <123.7 µmol/L (n = 13); stage 2, 123.7 to 176.8 µmol/L (7); stage 3, 185.6 to 442 µmol/L (13); or stage 4, >442 µmol/L (11). For each dog, serum concentrations of ionized and total calcium and phosphorus were evaluated once; the latter 2 variables were used to determine sCaPP.

Results—The sCaPP differed significantly between the 22 healthy dogs and dogs with stage 3 or stage 4 CKD. The proportion of dogs with sCaPP > 70 mg²/dL² increased with stage of disease. Mortality rate among the 24 dogs with sCaPP > 70 mg²/dL² was higher than that among the 42 dogs with sCaPP ≤ 70 mg²/dL². Dogs with sCaPP > 70 mg²/dL² had a comparatively lower survival rate, and risk of death was 4.2 times as high as risk for dogs with sCaPP ≤ 70 mg²/dL².

Conclusions and Clinical Relevance—For dogs with CKD, sCaPP > 70 mg²/dL² appeared to be a negative prognostic indicator, which was not influenced by the concomitant serum concentrations of phosphorus and total or ionized calcium. (J Am Vet Med Assoc 2014;245:1135–1140)

Hyperphosphatemia has been associated with decreased survival rate and severe morbidity in dogs and cats with CKD. Plasma phosphorus concentration has been documented as a predictor for progression of CKD in cats, with a 41% increase in the risk of disease progression for every increase of 1 mg/dL. Clinical signs of secondary renal hyperparathyroidism, such as bone demineralization, soft tissue calcification, renal osteodystrophy, and metastatic calcifications, have been reported for both dogs and cats. In particular, metastatic calcifications in the paws have been suggested to develop when sCaPP is > 70 mg²/dL². In humans, sCaPP can be accurately determined from measurements of serum phosphorus concentration and either total or ionized calcium concentration and provides a clinically relevant means of estimating cardiovascular risk associated with CKD. Bone disorders and mineral disorders represent interrelated serum biochemical, bone, and vasculature abnormalities often associated with CKD.

High sCaPP is associated with a major risk of ectopic calcifications that can contribute to soft tissue calcium phosphate deposits. Humans with end-stage renal disease and a high sCaPP have significantly more calcified coronary plaques than do controls. High sCaPP may result in increased calcium deposition in coronary artery plaques and promote plaque rupture. In humans, myocardial calcification has been reported to be positively correlated with left ventricular function. In particular, deaths resulting from coronary artery disease and sudden deaths were significantly related to high sCaPP as a linear function. For every increase in sCaPP of 10 mg²/dL², the relative risk of sudden death increases by 7%. In dogs with naturally occurring CKD, sCaPP appears to increase with progression of the disease. In a study of dogs with CKD, sCaPP was found to be correlated to serum parathyroid hormone concentration, and in dogs with CKD at IRIS stage 3 (serum creatinine concentration, 2.1 to 3 mg/dL) or worse, sCaPP was significantly different from that in healthy control dogs. No data regarding high sCaPP and risk of death in dogs affected by CKD are available, to our knowledge.

The purpose of the study reported here was to retrospectively assess the usefulness of sCaPP as a predic-

**ABBREVIATIONS**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>CKD</td>
<td>Chronic kidney disease</td>
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<tr>
<td>GFR</td>
<td>Glomerular filtration rate</td>
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<tr>
<td>IRIS</td>
<td>International Renal Interest Society</td>
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<tr>
<td>sCaPP</td>
<td>Serum calcium-phosphorus concentration product</td>
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tor of mortality rate in a group of dogs with naturally occurring CKD at different stages of severity. An sCaPP > 70 mg²/dL² was hypothesized to be associated with increased mortality rate in dogs with CKD.

Materials and Methods

Case selection and medical records review—Records of client-owned dogs of different breeds, sex, age, and weight referred to the Mario Modenato Veterinary Teaching Hospital for nephrological consultation between December 2008 and December 2010 were reviewed. Apparently healthy dogs had been referred to the nephrology service because of previous episodes of polyuria and polydipsia or evaluation of overall renal function before minor surgery. For each dog, data regarding history, results of biochemical analyses and urinalysis, and ultrasonographic findings were collected from the medical record to confirm the diagnosis of primary renal disease and its chronic nature or to determine that the dog was healthy. At the time of the initial examination, the dog's history was recorded and a complete clinical evaluation was performed; findings of that evaluation were included in the medical record. All dog owners were asked for informed consent so that serum and plasma samples could be stored for research purposes.

Results of a renal panel together with those of a CBC (volume of blood used, 5 mL) and urinalysis performed at the time of the initial examination were obtained from the medical record of each dog: variables of interest included plasma concentrations of creatinine and urea and serum concentrations of albumin, total protein, total and ionized calcium, and phosphorus. Inclusion criteria for dogs with CKD included a documented history of CKD and ultrasonographic findings and laboratory test results indicating stable CKD of at least 3 months’ duration. Exclusion criteria for dogs with CKD included a documented history of acute kidney injury, ultrasonographic findings or laboratory signs of acute kidney injury, and serum azotemia secondary to urinary obstruction or volume-responsive acute kidney injury. For dogs with CKD, the stage of disease was classified according to the 2011 IRIS guidelines on the basis of plasma creatinine concentration as follows: stage 1, < 1.4 mg/dL (< 123.7 μmol/L); stage 2, 1.4 to 2.0 mg/dL (123.7 to 176.8 μmol/L); stage 3, 2.1 to 5.0 mg/dL (185.6 to 442 μmol/L); stage 4, > 5.0 mg/dL (> 442 μmol/L).

Glomerular filtration rate was tested in each dog by means of an iohexol plasma clearance assay, and results were obtained from the medical record. In the present study, plasma iohexol clearance < 60 ml/min/m² was considered to represent a decreased GFR. Additional data obtained for dogs with CKD included clinical signs at the initial evaluation and prescribed treatments and diets. For dogs with CKD, follow-up information was available for a 455-day period or until time of death; for healthy dogs, information was obtained from owners at 6-month intervals.

Plasma iohexol clearance assay—Prior to the assay procedure, food was withheld from each dog for 12 hours. Each dog was accurately weighed, and an IV catheter was placed in each cephalic vein. One of those catheters was used to collect the blood samples and the other to administer the contrast medium. Before injection of the contrast medium (iohexol), an initial blood sample (0.5 mL) was collected and put into a tube containing heparin. The syringe used for contrast medium administration was weighed before addition of the contrast medium (empty weight), when full of iohexol (preadministration weight), and after the injection of contrast medium into the dog (postadministration weight) to determine the exact injected dose. The contrast medium was slowly administered through the IV catheter (64.7 mg/kg [29.41 mg/lb] dose administered in a 60-second period). The completion of the injection represented the 0-minute time point. A blood sample (0.5 mL) was obtained from each dog on 5 occasions: at 5, 15, 60, 90, and 180 minutes. Blood samples were collected in tubes containing heparin and centrifuged to obtain plasma. Each plasma sample underwent high-performance liquid chromatography analysis. Plasma iohexol concentration-time curves were analyzed through a bicompartimental kinetic model.

Biochemical analyses—Plasma creatinine and urea concentrations and serum total calcium, phosphorus, and albumin concentrations were measured by use of a laboratory analyzer. Serum ionized calcium concentration was determined through a selective ion hemosat analysis machine, which measures potential difference of the sample. The sCaPP was calculated by multiplying serum total calcium concentration by serum phosphorus concentration. An sCaPP > 70 mg²/dL² was considered abnormal, and an sCaPP ≤ 70 mg²/dL² was considered normal.

Statistical analysis—Statistical analysis was performed with standard software programs. All data were tested for normality by means of the Kolmogorov-Smirnov test. The data are reported as median and range. A value of P < 0.05 was considered significant. Variance analysis among mean values of sCaPP in healthy dogs and in dogs with IRIS stage 1, 2, 3, or 4 disease was performed by means of a Kruskal-Wallis test followed by a Dunn multiple comparison test. Linear regression analysis and Spearman correlation coefficient analysis were used to assess the correlation of plasma creatinine concentration and sCaPP, plasma creatinine and serum phosphorus concentrations, and plasma creatinine and serum calcium concentrations for dogs at each stage of the IRIS classification. Kaplan-Meier survival curves were determined for dogs that had an sCaPP ≤ and > 70 mg²/dL² within the study population and for dogs at each IRIS disease stage. Cox proportional hazards regression models were used to examine the association of survival rate and initial serum ionized calcium concentration, serum phosphorus concentration, sCaPP, plasma creatinine concentration, feeding of a diet formulated for dogs with CKD (renal diet), and administration of phosphate binders.

Results

Of 102 dogs referred for nephrological consultation between December 2008 and December 2010, 66 were eligible for inclusion in the study. For 31 of these 66 dogs, a definitive diagnosis of CKD had been made on the basis of azotemia, reduced urine specific gravity, renal proteinuria (urinary protein-creatinine concentration ratio, > 0.5), and abnormal renal morphology detected during ultrasonographic examina-
The stages of disease (according to IRIS guidelines) among these 31 dogs were as follows: stage 2, 7 dogs; stage 3, 13 dogs; and stage 4, 11 dogs. Owing to the retrospective nature of the study, it was not possible to enroll the same number of dogs for each stage of IRIS disease classification. As a consequence, there was a significantly lower number of dogs with stage 2 CKD, compared with the number of dogs at each of the other stages of disease and the number of healthy dogs.

In the remaining 35 dogs, no abnormalities were detected by CBC, biochemical analyses, urinalysis, or ultrasonography, although some dogs had had previous episodes of polyuria and polydipsia. However, for purposes of the present study, plasma iohexol clearance < 60 L/min/m² was considered to represent a decreased GFR. On the basis of GFR assessments, 13 of these 35 apparently healthy dogs were considered to have early CKD and were classified as having IRIS stage 1 disease (plasma creatinine concentration < 1.4 mg/dL [123.7 µmol/L]).

**Table 1**—Median (range) sCaPP and serum total calcium, phosphorus, and ionized calcium concentration in 22 healthy dogs and 44 dogs with IRIS stage 1, 2, 3, or 4 CKD.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Healthy dogs</th>
<th>1 (n = 13)</th>
<th>2 (n = 7)</th>
<th>3 (n = 13)</th>
<th>4 (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total calcium (mg/dL)</td>
<td>9.10 (8.20–11.00)*</td>
<td>9.10 (8.20–11.00)*</td>
<td>9.40 (8.10–14.00)*</td>
<td>10.10 (7.90–18.40)*</td>
<td>9.95 (6.30–10.70)*</td>
</tr>
<tr>
<td>Phosphorus (mg/dL)</td>
<td>3.00 (2.00–4.50)*</td>
<td>4.03 (3.00–6.00)*</td>
<td>4.20 (2.30–5.21)*</td>
<td>7.00 (3.30–14.90)*</td>
<td>22.62 (11.60–31.80)*</td>
</tr>
<tr>
<td>Ionized calcium (mmol/L)</td>
<td>1.50 (1.17–1.39)*</td>
<td>1.28 (1.12–1.40)*</td>
<td>1.34 (1.15–1.40)*</td>
<td>1.15 (0.98–1.30)*</td>
<td>1.01 (0.80–1.25)*</td>
</tr>
<tr>
<td>sCaPP (mg²/dL²)</td>
<td>29.11 (24.00–36.00)*</td>
<td>37.35 (25.20–70.20)*</td>
<td>43.26 (20.76–47.26)*</td>
<td>69.12 (51.92–150.5)*</td>
<td>221.50 (80.64–275.20)*</td>
</tr>
</tbody>
</table>

Within a variable, values with different letters superscript letters are significantly (P < 0.05) different.

**Figure 1**—Scatterplots of plasma creatinine concentration versus sCaPP (A) or serum phosphorus concentration (B) in 11 dogs with IRIS stage 4 CKD. Spearman correlation analysis revealed a significant correlation between plasma creatinine concentration and sCaPP (P = 0.03; R = 0.79) and between plasma creatinine and serum phosphorus concentration (P = 0.02; R = 0.78) in these dogs.

**Figure 2**—Kaplan-Meier survival curve for dogs with CKD that had an sCaPP ≤ 70 mg²/dL² (black curve) or > 70 mg²/dL² (red curve). Dogs with an sCaPP ≤ 70 mg²/dL² included all dogs with IRIS stage 1 and 2 disease and 9 dogs with IRIS stage 3 disease. Dogs with an sCaPP > 70 mg²/dL² included 4 dogs with IRIS stage 3 disease and 11 dogs with stage 4 disease. The median survival time of the dogs with an sCaPP > 70 mg²/dL² was 20 days, and the median survival time of the dogs with an sCaPP ≤ 70 mg²/dL² could not be computed because > 50% of dogs were still alive at the end of the study. Black rectangles and red triangles represent times at which 1 dog died.
concentrations were tested for normality (Kolmogorov-Smirnov test) and did not follow a Gaussian distribution. Those variables in healthy dogs and dogs with each stage of CKD were summarized as median and range (Table 1). The median sCaPP for healthy dogs and dogs with stage 1, 2, 3, and 4 disease differed significantly (Kruskal-Wallis test; \( P < 0.001 \)). Results of a Dunn posttest indicated that there was a significant (\( P < 0.001 \)) difference in sCaPP between healthy dogs and dogs with IRIS stage 3 disease, healthy dogs and dogs with stage 4 disease; dogs with stage 1 versus 4 disease, and dogs with stage 2 versus 4 disease, but not between dogs with stage 3 versus 4 disease (\( P > 0.05 \)).

Spearman tests revealed no significant correlation between plasma creatinine concentration and sCaPP in healthy dogs and dogs with stage 1, 2, or 3 disease; between plasma creatinine and serum phosphorus concentrations in healthy dogs and dogs with stage 1, 2, or 3 disease; and between plasma creatinine and serum total calcium concentrations in healthy dogs and dogs with stage 1, 2, 3, or 4 disease. In dogs with stage 4 disease, significant correlations were found between plasma creatinine concentration and sCaPP (\( P = 0.03 \); \( R = 0.79 \)) and between plasma creatinine and serum phosphorus concentrations (\( P = 0.02 \); \( R = 0.78 \), Figure 1).

All healthy dogs and dogs with stage 1 and 2 disease had sCaPP \(< 70 \text{ mg/dL}^2\). Among the 13 dogs with stage 3 disease, 9 had sCaPP \(< 70 \text{ mg/dL}^2\) and 4 had sCaPP \(> 70 \text{ mg/dL}^2\). All 11 dogs with stage 4 disease had sCaPP \(> 70 \text{ mg/dL}^2\). Among the 51 dogs with an sCaPP \(≤ 70 \text{ mg/dL}^2\), 17 survived and 10 died during the 455-day follow-up period. Among the 15 dogs with an sCaPP \(> 70 \text{ mg/dL}^2\), 2 survived and 13 died.

Kaplan-Meier survival analysis for dogs with CKD revealed that dogs with an sCaPP \(> 70 \text{ mg/dL}^2\) had a significantly (\( P = 0.002 \)) higher mortality rate than dogs with an sCaPP \(≤ 70 \text{ mg/dL}^2\) (hazard ratio, 4.2). The median survival time of the dogs with an sCaPP \(> 70 \text{ mg/dL}^2\) was 30 days, and the median survival time of the dogs with an sCaPP \(≤ 70 \text{ mg/dL}^2\) could not be computed because > 50% of dogs were still alive at the end of the study (Figure 2).

Results of Cox proportional hazards regression analysis indicated that survival time was not affected by initial serum ionized calcium concentration, serum phosphorus concentration, plasma creatinine concentration, feeding of a renal diet, or administration of phosphate binders. Only sCaPP was significantly (\( P = 0.04 \)) associated with a reduction in the survival time (Table 2). Furthermore, the Cox regression coefficient was positive for sCaPP indicating that the increase in sCaPP was related to a higher probability of death.

### Discussion

Results of the present retrospective study in dogs with CKD indicated that high sCaPP seemed to develop more in the late than early stages of the disease. Median sCaPP increased significantly with the progression of the stage of disease. No dogs in the early stages of the disease (IRIS stages 1 and 2) were receiving phosphate binders or other medications to alter calcium-phosphorus metabolism, so the discrepancy in serum phosphorus concentration and sCaPP between dogs in the early and late stages of CKD may suggest an increased urinary excretion of phosphorus in dogs with stage 1 or 2 disease, compared with dogs with stage 3 or 4 disease. Regardless, although high sCaPP and hyperphosphatemia were more prevalent in dogs with late-stage CKD, no significant correlation between sCaPP and plasma creatinine concentration and between serum phosphorus and plasma creatinine concentrations was found in dogs with stage 1, 2, or 3 disease. In dogs with stage 4 disease, both the sCaPP (\( P = 0.03 \); \( R = 0.79 \)) and serum phosphorus concentration (\( P = 0.02 \); \( R = 0.78 \)) had a positive linear correlation with plasma creatinine concentration. This finding may be related to the different effect of progressive modifications of GFR on urinary phosphorus excretion. Most dogs with stage 4 disease with high sCaPP had both hyperparathyroidism and hypocalcemia. In this group of dogs, the increase in serum phosphorus concentration was sufficiently high to balance out the reduction in serum ionized calcium concentration and to result in an sCaPP > 70 mg/dL^2.

The highest sCaPP was associated with dogs that had stage 4 disease, in which it reached > 3 times the cutoff of 70 mg/dL. Although there are no published reports of studies in veterinary patients, to our knowledge, a strict relationship between renal dysfunction and adverse cardiovascular events in humans has been documented.

The survival curves for dogs with CKD that had an sCaPP > 70 mg/dL^2 and for dogs that had an sCaPP ≤ 70 mg/dL^2 were markedly different. Dogs that had an sCaPP > 70 mg/dL^2 had a significantly (\( P = 0.002 \)) higher mortality rate, compared with dogs that had an sCaPP ≤ 70 mg/dL^2 (hazard ratio, 4.2). Moreover, dogs with an sCaPP > 70 mg/dL^2 had a median survival time of 30 days, whereas for the dogs that had sCaPP ≤ 70 mg/dL^2, median survival time could not be calculated because > 50% of dogs were still alive at the end of the study. With the exception of dogs with stage 1 disease, other dogs with CKD had moderate to severe clinical signs. For this reason, most dogs with stage 3 or 4 disease had already been receiving treatment from the referring veterinarian. Most dogs with stage 2 CKD were already receiving a renal diet, and dogs with stage 1 CKD were generally subclinically affected and had no important serum biochemical abnormalities. For this reason, none of the dogs with stage 1 disease were receiving low-phosphate diet or treatment. No dog with CKD was provided with

### Table 2—Results of Cox proportional hazard regression analysis of the associations of factors at the time of initial examination with survival time for 44 dogs with CKD.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Regression coefficient</th>
<th>SD</th>
<th>( \chi^2 )</th>
<th>( P ) value</th>
<th>Hazard ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>sCaPP</td>
<td>0.04</td>
<td>0.02</td>
<td>4.22</td>
<td>0.04</td>
<td>1.04</td>
</tr>
<tr>
<td>Serum total calcium concentration</td>
<td>-0.10</td>
<td>0.22</td>
<td>0.21</td>
<td>0.65</td>
<td>0.91</td>
</tr>
<tr>
<td>Serum phosphorus concentration</td>
<td>-0.19</td>
<td>0.14</td>
<td>2.00</td>
<td>0.16</td>
<td>0.62</td>
</tr>
<tr>
<td>Plasma creatinine concentration</td>
<td>-0.14</td>
<td>0.11</td>
<td>1.53</td>
<td>0.22</td>
<td>0.72</td>
</tr>
<tr>
<td>Phosphate binders</td>
<td>0.44</td>
<td>0.88</td>
<td>0.43</td>
<td>0.51</td>
<td>1.56</td>
</tr>
<tr>
<td>Renal diet</td>
<td>-0.70</td>
<td>0.78</td>
<td>0.50</td>
<td>0.37</td>
<td>0.50</td>
</tr>
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</table>
an esophagostomy tube, and renal diets were generally mixed with other commercial or homemade food to make them more palatable. In the present study, the most common clinical signs were polyuria, polydipsia, weakness, dysorexia, and vomiting. Polyuria, polydipsia, and weakness were present in all dogs with stage 2 CKD, and only 1 dog had gastrointestinal tract problems. No dogs with stage 1 or 2 disease were receiving phosphate binders. Among dogs with stage 3 CKD, 3 of the 4 dogs with an sCaPP > 70 mg²/dL² were being treated with aluminum hydroxide, and all dogs with stage 4 CKD were being treated with phosphate binders.

In the present cohort of dogs with CKD, Cox proportional hazards regression analysis revealed that the role of increased sCaPP as a predictor of negative outcome was not influenced by concomitant administration of a renal diet or phosphate binders. Serum calcium-phosphorus concentration product seemed to be a more reliable index of negative outcome than serum total calcium or phosphorus concentration. This finding may be explained by the fact that serum calcium and phosphorus concentrations can be modified independently. High serum phosphorus concentrations may be associated with normal to high serum total calcium concentrations, resulting in high sCaPP. Moreover, serum phosphorus concentration may be so high as to overlap a condition of hypocalcemia, leading to high sCaPP. On the other hand, if hypocalcemia is very severe or hyperphosphatemia is not markedly high, the sCaPP may be apparently normal. The sCaPP appears to be a better indicator of calcium-phosphorus modifications than either serum calcium or phosphorus concentration alone.

The present study—a retrospective investigation designed to assess the role of sCaPP as a predictor of mortality rate in a group of dogs at different stages of naturally occurring CKD—had several limitations. Owing to the retrospective nature of the study, it was not possible to enroll the same number of dogs for each stage of IRIS disease classification. As a consequence, there was a significantly lower number of dogs with stage 2 CKD, compared with the number of dogs at each of the other stages of disease and the number of healthy dogs.

Follow-up of the study dogs was limited to evaluation of mortality rate over a 455-day period but did not consider changes over time in sCaPP and serum concentrations of phosphorus, total calcium, and ionized calcium and plasma concentrations of creatinine and urea. Only sCaPP measured at the first evaluation at the nephrology service of the Mario Modenato Veterinary Teaching Hospital was assessed, and measurements obtained at subsequent recheck examinations were not analyzed. Also, given the retrospective nature of the present study, we did not evaluate concentrations of either parathyroid hormone or fibroblast growth factor-23, so it was not possible to diagnose early stages of secondary renal hyperparathyroidism in the dogs.

In the present study, a cutoff of sCaPP at 70 mg²/dL² was chosen to classify values as normal or abnormal because, in humans with CKD, an sCaPP > 70 mg²/dL² is related to an increased relative risk of death and negative outcome. In cats and dogs, an sCaPP > 70 mg²/dL² is related to a higher prevalence of metastatic calcifications. In human medicine, recommendations from the Kidney Disease: Improving Global Outcomes guidelines suggest maintenance of sCaPP ≤ 55 mg²/dL². Chronic hemodialysis patients with an sCaPP > 72 mg²/dL² had a 34% higher risk of death, compared with those with sCaPP between 42 and 52 mg²/dL². The present study of dogs with CKD did not investigate the prognostic role of sCaPP between 55 and 70 mg²/dL².

Results of the present study indicated that an sCaPP > 70 mg²/dL² was an accurate predictor of negative outcome and short-term mortality rate, which seemed to be independent from plasma creatinine concentration, in dogs with CKD. Detection of hyperphosphatemia and high sCaPP should be considered possible predictors of negative outcome in dogs with CKD.

**References**

Effects of a dexmedetomidine constant rate infusion and atropine on changes in global perfusion variables induced by hemorrhage followed by volume replacement in isoflurane-anesthetized dogs

Thaísa D. Cândido et al

Objective—To evaluate the effects of a dexmedetomidine constant rate infusion (CRI) and atropine on changes in global perfusion variables induced by hemorrhage and volume replacement (VR) in isoflurane-anesthetized dogs.

Animals—8 adult dogs.

Procedures—Each dog was anesthetized twice, with a 2-week interval between anesthetic sessions. Anesthesia was maintained with 1.3 times the minimum alveolar concentration of isoflurane with and without dexmedetomidine (1.6 µg/kg, IV bolus, followed by 2 µg/kg/h, CRI). Dogs were mechanically ventilated and received an atracurium neuromuscular blockade during both sessions. During anesthesia with isoflurane and dexmedetomidine, atropine was administered 30 minutes before baseline measurements were obtained. After baseline data were recorded, 30% of the total blood volume was progressively withdrawn and VR was achieved with an equal proportion of autologous blood.

Results—Following hemorrhage, cardiac index, oxygen delivery index, and mixed-venous oxygen saturation were significantly decreased and the oxygen extraction ratio was significantly increased from baseline. The anaerobic threshold was not achieved during either anesthetic session. When dogs were anesthetized with isoflurane and dexmedetomidine, they had a significantly lower heart rate, cardiac index, and mixed-venous oxygen saturation during VR than they did when anesthetized with isoflurane alone. Plasma lactate concentration, mixed venous-to-arterial carbon dioxide difference, base excess, and anion gap were unaltered by hemorrhage and VR and did not differ between anesthetic sessions.

Conclusions and Clinical Relevance—Results indicated that the use of a dexmedetomidine CRI combined with atropine in isoflurane-anesthetized dogs that underwent volume-controlled hemorrhage followed by VR did not compromise global perfusion sufficiently to result in anaerobic metabolism. (Am J Vet Res 2014;75:964–973)