Association of laboratory data and death within one month in cats with chronic renal failure

OBJECTIVES: To retrospectively compare the data taken at the first visit of 34 cats with chronic renal failure surviving more than one month (surviving group) and 16 cats dying within one month (non-surviving group).

METHODS: Records were collected on cats with chronic renal failure presented to a private veterinary practice in Nagoya, Japan, from March 1996 to March 2005. All cats with chronic renal failure diagnosed on the basis of case histories, clinical signs (such as, lethargy, anorexia, loss of bodyweight and vomiting) and a high plasma creatinine (>180 μmol/l) were included in the study.

RESULTS: Plasma creatinine, urea nitrogen, inorganic phosphate, packed cell volume and urine protein/creatinine ratio were significantly different between cats of the surviving and non-surviving groups. In the surviving group, survival statuses were recorded, and laboratory data was obtained within one month before death in 13 cats. In the 13 cats, plasma creatinine, packed cell volume and urine protein/creatinine ratio showed significant differences between the data taken within one month before death and that taken at first visit, and only urine protein/creatinine ratio exhibited a consistent alteration (increase) in relation to first visit data.

CLINICAL SIGNIFICANCE: These results indicated that plasma creatinine, urea nitrogen, inorganic phosphate, packed cell volume and urine protein/creatinine ratio were associated with death within one month and urine protein/creatinine ratio was most likely to be associated with mortality in cats with chronic renal failure.

INTRODUCTION

It is well known that the kidney is able to continue functioning using compensatory responses, even when it is partially damaged. However, when the damage reaches a critical level, renal function deteriorates according to the hyperfiltration theory even when no further injury is sustained (Brown and Brown 1995, Brenner and others 1995, Brenner and others 1999). Some cats with chronic renal failure (CRF) maintain a relatively stable condition for a long time, while others die with rapid deterioration of renal function (Elliott and Barber 1998, Elliott and others 2003).

In feline CRF, the variation of survival time may depend on the fact that the underlying causes of renal injury are often unidentified (Polzin and Osborne 1995). Another reason may be that there is no adequate examination to correctly determine the condition of each cat with CRF. CRF generally progresses from diminished renal reserve, to renal insufficiency, to renal failure and then to the uraemia stage (Chew and DiBartola 1986). In cats at the diminished renal reserve or renal insufficiency stages, determinations of glomerular filtration rate (GFR) or plasma creatinine concentration (P-Cr) may help to make a diagnosis of CRF (Polzin and others 2000). However, GFR and P-Cr do not always reflect the stage of CRF correctly as they are often modified by prerenal factors such as hypovolaemia, low cardiac output and peripheral vasodilatation.

Proteinuria has not been regarded as a prognostic factor in cats with CRF (Elliott and Barber 1998, Polzin and others 2000). Some cats with glomerulonephritis have a relatively good prognosis with slight azotaemia, even with severe proteinuria (Nash and others 1979, Arthur and others 1986). However, proteinuria is one of the important prognostic factors in human CRF (Remuzzi and Bertani 1998, Ruggenenti and others 1998).

To reconfirm the importance of laboratory examinations, including proteinuria, as indicators associated with mortality in cats with CRF, haematology, biochemistry, blood pressure and urinalysis data, including urine protein:creatinine ratio (UP:Cr) were retrospectively compared between cats with CRF that survived more than one month and those that died within one month of the first visit. Additionally, the survival status of cats that
survived more than one month after the first visit was recorded, and laboratory data was obtained within one month of death from the cats in the surviving group that died and compared with data taken at the first visit.

**MATERIALS AND METHODS**

**Animals**

Records were collected on cats with CRF presented to a private veterinary practice in Nagoya, Japan, from March 1996 to March 2005. All cats with CRF diagnosed on the basis of case histories, clinical signs (such as, lethargy, anorexia, loss of body-weight and vomiting) and a high P-Cr (>180 μmol/l) (Elliott and Barber 1998) were included in the study. Cats with specific renal diseases, such as polycystic kidney, hydronephrosis, renal tumour or urolithiasis, were excluded from the study based on laboratory examinations and diagnostic imaging. Cats with feline infectious peritonitis, feline leukaemia virus, cardiac failure, neoplasia, hyperthyroidism, nephrotic syndrome, nephritic syndrome and systemic lupus erythematosus were also excluded.

Cats were divided into two groups: the surviving and non-surviving groups. The surviving group consisted of cats living longer than one month after first examination, while the non-surviving group included cats dying within one month after first examination. The data obtained at the first visit were compared between cats in the surviving and non-surviving groups. In the surviving group, the survival status was followed whenever possible until the end of the study. For the cats in the surviving group, laboratory data taken closest to time of death was compared with the data taken at the first visit.

**Sample collection, laboratory examination and blood pressure measurement**

Peripheral venous blood had been collected into a lithium heparin tube for plasma biochemical measurements, into a microhaematocrit tube to determine the packed cell volume (PCV) and into a sample inlet of a blood gas analyser. Urine specimens had been collected by cystocentesis for urinalysis.

Among the variables, P-Cr was essential in the current study to comply with the CRF diagnostic criteria. Other variables were determined as much as possible in terms of the volume of samples collected and the financial means of the owner. The tests were conducted in the order of priority as follows: PCV, UPr:Cr, plasma concentrations of urea nitrogen, inorganic phosphate and potassium concentration, urine culture, systolic blood pressure and venous blood bicarbonate ion (HCO₃⁻) concentration. However, in cats with clinical signs suggestive of hypertension and urinary sediment results suggestive of urinary tract infection, the blood pressure and urine culture were always determined. UPr:Cr values determined from samples with positive urine culture were excluded from the analysis.

P-Cr, urea nitrogen, inorganic phosphate and potassium were determined using a dry chemistry system (Spotchem; Arkray). PCV was measured with a microhaematocrit centrifuge and HCO₃⁻ was determined using a portable blood gas analyser (GASTAT-mini; Techno Medica). Urine protein concentration was determined using the pyrogallol red-molybdate complex method (Watanabe and others 1986) and urine creatinine concentration was determined by the 3,5-dinitrobenzoic acid method (Doi and others 1997) using a dry chemistry system. UPr:Cr was calculated by dividing the urine protein concentration by the urine creatinine concentration (White and others 1984, Monroe and others 1989). Urine culture was carried out using a blood agar medium (Poremedia; Eiken Chemical) and a portable incubator (SD incubator; All Japan Veterinary Co-operative) by a standard technique. A growth of more than 100 colony-forming units (CFU)/ml within 24 hours was judged as positive.

Blood pressure was measured by an oscillometric method (BP100D; Fukuda-ME) in sternal recumbency or sitting with the owner present. The measurement site was the forelimb and the cuff was approximately 40 per cent of the size of the circumference of the measuring site. Measurements of blood pressure were performed five times and the mean was calculated. Data obtained during physical movement were not used.

**Statistical analysis**

Differences in P-Cr, urea nitrogen, inorganic phosphate, PCV, UPr:Cr, potassium, HCO₃⁻ and blood pressure were compared between the surviving and non-surviving groups and were analysed using Mann-Whitney U tests (Statistical Add-Ins for Excel 1.11; NAG). Urine cultures were analysed using Fisher’s exact tests (JMP 5.1.1; SAS). Differences in P-Cr, urea nitrogen, inorganic phosphate, PCV and UPr:Cr were compared between the data within one month before death and those at first visit in the surviving group and were analysed using Mann-Whitney U tests. With all statistical analyses, a P value less than 0.05 was taken to indicate significance.

**RESULTS**

**Case materials and clinical course**

Fifty cats were included in the study. Thirty-four were assigned to the surviving group and 16 to the non-surviving group. The age of the cats was from five to 22 (median 12.5) years in the surviving group and six to 19 (median 13) years in the non-surviving group. There were 16 males (10 neutered and six entire) and 18 females (11 neutered and seven entire) in the surviving group and six males (four neutered and two entire) and 10 females (five neutered and five entire) in the non-surviving group.

The surviving group consisted of 28 domestic shorthair, four Persian and two Siamese cats, weighing from 1.7 to 6.6 kg. The non-surviving group consisted of 15 domestic shorthair cats and a Persian cat, weighing from 1.7 to 4.0 kg.

The cats with CRF had been managed individually according to the owners’ wishes. Specifically, the cats received a commercial diet food for CRF (Prescription Diet Feline k/d; Hill’s Colgate); intravenous infusions of 60 to 140 ml/kg a glucose-electrolyte solution (Solden 1; Terumo) daily; subcutaneous injections
of 50 to 150 ml lactated Ringer’s solution (Solulact; Terumo) twice or three times a day; and/or 100 U/kg human recombinant, erythropoietin, (ESPO; Sankyo) once to three times a week; 15 to 50 mg/kg aluminium hydroxide (Alumigel; Chugai) twice a day; 0.25 to 1.00 mmol potassium citrate (Polycitra-K; Alza) twice a day; 10 to 50 mg/kg calcium carbonate (Precipitated calcium carbonate; Ken-ei) twice a day; 50 mg/kg calcium carbonate; and/or blood transfusions. Cats with severe dehydration received fluid therapy for at least two or three days.

No cats were euthanased during the study period. Cats of the non-surviving group died within one month of the first examination and their survival times were from 32 to 1433 (median 288) days. In 13 of these 18 cats, laboratory data was obtained within one month before death. At the end of the study, eight cats were still alive and their survival time was from 31 to 2721 (median 184) days. The remaining eight cats were lost to follow up, but they were confirmed to have lived for at least 31 and up to 1386 (median 576.5) days.

Comparison of data between surviving and non-surviving groups
Table 1 shows a comparison of the data between the surviving and non-surviving groups. P-Cr, urea nitrogen, inorganic phosphate, UPr:Cr, potassium, blood pressure and positive rate of urine culture in the non-surviving group tended to be higher than those of the surviving group. PCV and HCO₃⁻ tended to be lower in the non-surviving group. P-Cr, urea nitrogen, inorganic phosphate, PCV and UPr:Cr were significantly different between the two groups.

Comparison of data at first visit and within one month before death in the surviving group
Table 2 shows a comparison of the data at first visit and that taken within one month before death in the surviving group. P-Cr and UPr:Cr increased and PCV decreased significantly in the data taken within one month before death compared with that taken at first visit, but urea nitrogen and inorganic phosphate did not change significantly. Also, unusual changes were found in P-Cr, urea nitrogen, inorganic phosphate and PCV (decrease in P-Cr, urea nitrogen and inorganic phosphate and increase in PCV in the data taken within one month before death) in three, four, three and two cats, respectively, but UPr:Cr increased without exception in all 13 cats (Fig 1).

**DISCUSSION**

Statistically significant differences were seen in P-Cr, urea nitrogen, inorganic phosphate and PCV between the surviving and non-surviving groups and in P-Cr and PCV between the data taken within one month before death and that taken at first visit in the surviving group. These four

### Table 1. Comparison between the surviving and non-surviving groups of cats with chronic renal failure

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number of data</th>
<th>Range</th>
<th>Median</th>
<th>95% CI</th>
<th>Number of data</th>
<th>Range</th>
<th>Median</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma creatinine (µmol/l)</td>
<td>34</td>
<td>185.6 to 636.5</td>
<td>238.7</td>
<td>238.7 to 318.2</td>
<td>16</td>
<td>265.2 to 990.1</td>
<td>481.8</td>
<td>424.3 to 663.0</td>
<td>9.6 x 10⁻⁶*</td>
</tr>
<tr>
<td>Urea nitrogen (mmol/l)</td>
<td>30</td>
<td>10.4 to 56.8</td>
<td>22.8</td>
<td>22.5 to 34.6</td>
<td>16</td>
<td>18.9 to 71.4</td>
<td>54.3</td>
<td>40.3 to 59.3</td>
<td>4.3 x 10⁻⁴*</td>
</tr>
<tr>
<td>Inorganic phosphate (mmol/l)</td>
<td>27</td>
<td>0.8 to 6.0</td>
<td>1.7</td>
<td>1.7 to 2.7</td>
<td>11</td>
<td>2.3 to 6.5</td>
<td>5.2</td>
<td>3.8 to 6.9</td>
<td>3.6 x 10⁻⁶*</td>
</tr>
<tr>
<td>Packed cell volume (1/l)</td>
<td>32</td>
<td>0.18 to 0.49</td>
<td>0.35</td>
<td>0.31 to 0.36</td>
<td>16</td>
<td>0.16 to 0.42</td>
<td>0.29</td>
<td>0.23 to 0.31</td>
<td>2.2 x 10⁻³*</td>
</tr>
<tr>
<td>Urine protein/creatinine ratio</td>
<td>28</td>
<td>0.01 to 1.44</td>
<td>0.22</td>
<td>0.22 to 0.47</td>
<td>13</td>
<td>0.5 to 0.64</td>
<td>1.33</td>
<td>1.06 to 3.60</td>
<td>4.6 x 10⁻³*</td>
</tr>
<tr>
<td>Potassium (mmol/l)</td>
<td>22</td>
<td>2.5 to 4.7</td>
<td>4.1</td>
<td>3.1 to 4.2</td>
<td>13</td>
<td>3.1 to 6.0</td>
<td>4.3</td>
<td>3.8 to 4.9</td>
<td>0.365</td>
</tr>
<tr>
<td>HCO₃⁻ (mmol/l)</td>
<td>5</td>
<td>8.5 to 20.6</td>
<td>16.2</td>
<td>9.1 to 21.0</td>
<td>3</td>
<td>14.3 to 14.4</td>
<td>14.4</td>
<td>11.1 to 19.6</td>
<td>0.882</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>10</td>
<td>110 to 224</td>
<td>143.5</td>
<td>126 to 178</td>
<td>8</td>
<td>110 to 205</td>
<td>148.5</td>
<td>125 to 177</td>
<td>0.949</td>
</tr>
<tr>
<td>Urine culture</td>
<td>13</td>
<td>Positive 3</td>
<td>Negative 10</td>
<td>7</td>
<td>Positive 3</td>
<td>Negative 4</td>
<td>0.6126</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CI: Confidence interval
*With significant difference (P<0.05)

### Table 2. Comparison between the data at first visit and that taken within one month before the death of the cats in the surviving group

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number of data</th>
<th>At first visit</th>
<th>Median</th>
<th>95% CI</th>
<th>Within one month before death</th>
<th>Median</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma creatinine (µmol/l)</td>
<td>13</td>
<td>309.4</td>
<td>185.6 to 636.5</td>
<td>279.5 to 465.8</td>
<td>13</td>
<td>548.1</td>
<td>238.7 to 1105.0</td>
<td>454.8 to 763.7</td>
</tr>
<tr>
<td>Urea nitrogen (mmol/l)</td>
<td>13</td>
<td>22.8</td>
<td>14.6 to 56.8</td>
<td>22.5 to 34.6</td>
<td>13</td>
<td>54.3</td>
<td>18.9 to 71.4</td>
<td>40.3 to 59.3</td>
</tr>
<tr>
<td>Inorganic phosphate (mmol/l)</td>
<td>11</td>
<td>32</td>
<td>1.1 to 6.0</td>
<td>1.8 to 4.0</td>
<td>11</td>
<td>5.6</td>
<td>1.7 to 6.5</td>
<td>3.3 to 5.9</td>
</tr>
<tr>
<td>Packed cell volume (1/l)</td>
<td>13</td>
<td>0.35</td>
<td>0.23 to 0.49</td>
<td>0.31 to 0.36</td>
<td>13</td>
<td>0.29</td>
<td>0.16 to 0.42</td>
<td>0.23 to 0.31</td>
</tr>
<tr>
<td>Urine protein/creatinine ratio</td>
<td>13</td>
<td>0.34</td>
<td>0.01 to 0.95</td>
<td>0.21 to 0.53</td>
<td>13</td>
<td>1.35</td>
<td>0.55 to 2.95</td>
<td>1.01 to 1.77</td>
</tr>
</tbody>
</table>

*With significant difference (P<0.05)
Variables have been previously considered as important prognostic factors for mortality in feline CRF (Barber and Elliott 1998, Elliott and Barber 1998, Polzin and others 2000). It was further suggested that a decrease in HCO₃⁻ (Elliott and others 2003) and an increase in blood pressure (Elliott and others 2001) might also relate to death in feline CRF. By contrast, significant differences in HCO₃⁻ and blood pressure were not seen between the surviving and non-surviving groups, presumably because of the insufficient number of samples. Further investigation into these details is required to predict values of HCO₃⁻ and blood pressure in cats with CRF.

Although proteinuria has previously been regarded as a marker of the severity of underlying renal disease, the results of many studies (Mort and others 1986, Remuzzi and Bertani 1990, Eddy and others 1991, Magil 1995) indicated that proteins filtered through the glomerular capillary have an intrinsic renal toxicity that could possibly contribute to the progression of renal lesions in rats and human beings. Recently, it has been reported that in dogs with CRF initial determination of proteinuria is of value in refining prognoses (Jacob and others 2005). However, in cats with CRF importance of proteinuria remains unclear.

In cats, the magnitude of proteinuria is usually represented as UPr:Cr that correlates with 24-hour urinary protein loss (Monroe and others 1989, Adams and others 1992). In the present study, UPr:Cr of the non-surviving group was significantly higher than that of the surviving group. Additionally, UPr:Cr of the data taken within one month before death in the surviving group was significantly and consistently higher than the data taken at the first visit. These results documented that cats surviving less than one month had higher UPr:Cr and cats surviving more than one month after first examination had lower UPr:Cr, but it became high before death. Of course, these results do not prove that proteinuria is a factor driving progression of feline CRF because this study is a retrospective analysis and investigated only the relationship between each variable and death within one month. A prospective longitudinal study would be required to examine the predictive value of UPr:Cr.

The results of the present study suggested that P-Cr, urea nitrogen, inorganic phosphate, PCV and UPr:Cr were associated with death within one month and that UPr:Cr might be most likely to be associated with impending death in cats with CRF. Therefore, the judgement of a short-term prognosis for cats with CRF should be made comprehensively using these five variables including UPr:Cr.

The following conclusions are drawn:

**Conclusions**

P-Cr, urea nitrogen, inorganic phosphate, PCV and UPr:Cr were confirmed to be associated with death within one month in cats with CRF. Additionally, these five analyses, UPr:Cr appeared to be most likely to be associated with impending death. Therefore, the medical judgement as to whether a cat with CRF is close to the end of life should be based on the comprehensive use of these five variables including UPr:Cr.


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