

# Retrospective study of the survival of cats with acquired chronic renal insufficiency offered different commercial diets

E. A. PLANTINGA, H. EVERTS, A. M. C. KASTELEIN, A. C. BEYENEN

**A retrospective study was carried out on the efficacy of seven commercial diets designed to be fed to cats with chronic renal failure. The median survival time of 175 cats that received conventional diets was seven months, whereas the median survival time of 146 cats given one of the seven diets was 16 months. The cats on the most effective of the diets had a median survival time of 23 months and those on the least effective diet had a median survival time of 12 months. The composition of the seven diets was comparable, except that the most effective diet had a particularly high content of eicosapentaenoic acid.**

CHRONIC renal failure is a common clinical condition in cats, and the prevalence of impaired kidney function increases with age (Burkholder 2000), reaching 30 per cent in cats over 15 years old (Krawiec and Gelberg 1989). The condition is characterised by an irreversible and progressive loss of kidney function, leading to azotaemia, uraemia and clinical signs associated with the kidneys' decreasing ability to perform their normal functions. Affected cats have a poor prognosis because the renal dysfunction generally progresses to its end stage (Polzin and Osborne 1995).

Nutritional management is essential in the treatment of chronic renal failure. In cats with induced renal failure, a restriction of phosphorus intake, as the only dietary variable, has been shown to reduce the extent of lesions observed in the kidneys postmortem (Ross and others 1982). It has been suggested that further dietary changes, such as reductions in the intakes of protein and sodium, increases in potassium, and a moderate base excess may contribute to reducing the progression of the condition (Plantinga and Beynen 2004). In dogs with experimental renal disease, the feeding of fish oil instead of either safflower oil or beef tallow diminished the rate of decrease in renal function (Brown and others 2000). It has also been suggested that the eicosapentaenoic acid (EPA) in fish oil alters eicosanoid metabolism and results in an increase in the production of vasodilatory mediators and a reduction in the production of proinflammatory eicosanoids, these changes being beneficial for renal function (Barcelli and Pollak 1985). Arachidonic acid is a competitive inhibitor of the conversion of EPA into eicosanoids (Siess and others 1980, Fischer and Weber 1983). It can be hypothesised that diets for the management of chronic renal failure in cats should be rich in EPA and satisfy their minimum requirement for arachidonic acid (Plantinga and Beynen 2004). Both of these fatty acids are essential for cats because cats lack the enzymatic activity to produce adequate amounts of them (Rivers and others 1975).

The use of specially designed diets to manage cats with chronic renal failure is now standard in veterinary practice. Elliott and others (2000) have shown that affected cats fed a special diet instead of a normal cat food survived longer, the median survival times being 20.8 and 8.7 months, respectively. On the market there is a wide variety of kidney diets for cats, produced by different manufacturers, which differ in their composition (Plantinga and Beynen 2004); they may therefore differ in their efficacy. The aim of this retrospective study was to compare the survival times of cats newly diagnosed with chronic renal failure that had been fed either a normal diet or different brands of kidney diets.

## MATERIALS AND METHODS

### Data

The database used in this study contained information on 88,037 cats, derived from 31 veterinary clinics in the Netherlands. The clinics used a computer-based practice management system (DAISY; Micpoint) and their consultation reports were collected electronically. Table 1 shows the compositions of the kidney diets that were prescribed.

### Data processing

Reports from deceased cats that had been at least eight years old were selected. The data were further selected with the help of search arguments ('cre\*', 'krea\*', 'BUN', 'urea' and 'ureum'), the asterisk indicating that all words beginning with 'cre' or 'krea' were eligible. The reports obtained were subjected to the inclusion criteria listed in Table 2. Thus, cats diagnosed with diseases other than chronic renal failure were excluded, these diseases being principally hyperthyroidism, diabetes mellitus and urolithiasis. For inclusion, the cause of death had to be chronic renal failure, diagnosed on the basis of the cat's history, clinical chemical data, clinical signs and the absence of other disease. Survival after diagnosis was in the period from 1999 to 2003.

From the reports selected, the following variables were extracted and classified: clinic code, breed, age, sex, plasma urea and creatinine concentrations at diagnosis, the use of a kidney diet (0 No, 1 Yes), the type of kidney diet (1 to 7), the use of an angiotensin-converting enzyme (ACE) inhibitor (0 No, 1 Yes) and the survival time after diagnosis (months). The kidney diets were as follows: 1 Hill's KD wet, 2 Hill's KD dry, 3 Leo FKW, 4 Leo FKD, 5 Royal Canin renal programme dry, 6 Waltham low phosphorus/protein wet, 7 Waltham low phosphorus/protein dry. The cats were classified according to the type of diet they were offered on the basis of the reports, that is, the diet prescribed by the veterinarians and/or the owner's choice not to feed a kidney diet. The diet had to be consumed for at least 75 per cent of the cat's survival time. No record was kept of the cats' daily food intake. The use of an ACE inhibitor was considered as a possible confounding factor.

### Statistical analysis

The data were analysed by using the statistical package GENSTAT 5 (Payne and others 1993). The initial model contained all the variables and the survival time as the dependent variable; each variable was removed successively and then added again to the model, to identify variables that significantly affected the variance in survival time. The procedure

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was carried out either with all the kidney diets pooled (kidney diet 0 or 1) or with specified brands (kidney diet 0 or 1 to 7), and single and multiple regression analyses were carried out with the selected variables. Kaplan-Meier survival curves were constructed and the mean and median survival times were calculated.

## RESULTS

After data processing, 321 reports were considered suitable. Table 3 shows the characteristics of the cats. Table 4 shows the types of diet offered in relation to the age and initial plasma urea and creatinine concentrations of the cats.

In the statistical model with the normal diet and all the kidney diets pooled, the variables clinic code, breed, age, sex, and the use of an ACE inhibitor did not significantly affect survival time, but diet, plasma creatinine and plasma urea did have a significant effect. The regression models were: survival time (months) =  $(22.00 - 0.454) \times \text{plasma urea (mmol/l)}$  ( $R^2_{\text{adj}}=0.064$ ,  $P<0.001$ ); survival time (months) =  $(22.86 - 0.027) \times \text{plasma creatinine } (\mu\text{mol/l})$  ( $R^2_{\text{adj}}=0.102$ ,  $P<0.001$ ); and survival time (months) =  $(8.483 + 10.50) \times (\text{kidney diet} = 1)$  ( $R^2_{\text{adj}}=0.229$ ,  $P<0.001$ ). The Kaplan-Meier survival curves for the last model are given in Fig 1. After combining the three significant predictors, the regression model with the highest predictive value was: survival time (months) =  $(15.47 + 9.51) \times (\text{kidney diet} = 1 - 0.339) \times \text{urea}$  ( $R^2_{\text{adj}}=0.283$ ,  $P<0.001$ ).

In further analyses, the brand of kidney diet was specified. Again, the variables clinic code, breed, age, sex and the use of an ACE inhibitor had no significant effect on survival time, but the variables plasma creatinine, plasma urea and the type of kidney diet did have a significant effect. Table 5 shows the estimated prolongation of the mean and median survival times by each kidney diet when compared with no dietary intervention. The incorporation of the variables plasma urea and creatinine into the model increased the percentage of variance accounted for, but did not affect the prolongation of survival time. The Kaplan-Meier survival curves for each type of kidney diet are shown in Fig 2.

## DISCUSSION

For the interpretation of this retrospective study it is important to understand its limitations. First, its validity depends on the accuracy of the reports received from the practitioners. Different veterinarians may diagnose and treat chronic renal failure in cats differently, and it could be suggested that the observed effect of the diets was biased by the attitude and expertise of the practitioners. However, it is reassuring that in the statistical analysis the clinic code had no effect on the cats' survival time. Other limitations are the assumption that the kidney diet bought by the cat's owner was indeed offered to the cat and the fact that various characteristics of the cats in the study were not taken into account. Such characteristics could be confounding factors.

The median survival time of the cats that did not receive one of the seven special diets was seven months, and the median survival time of the cats that received any of the seven diets was on average nine months longer. These data agree with those of Elliott and others (2000); the validity of the study may thus be acceptable.

Table 5 and Fig 2 show that the type of kidney diet influenced the survival time. Diet 3 was the most effective and diet 6 was the least effective when compared with normal cat food. The restriction of phosphorus intake is the mainstay of the treatment of cats with chronic renal failure, and a phosphorus level of 0.1 to 0.2 g/MJ in wet diets and 0.13 to 0.27 g/MJ in dry diets may be considered ideal (Plantinga and Beynen

TABLE 1: Composition of the seven brands of kidney diet

Diet	Type	Protein (g/MJ)	Phosphorus (g/MJ)	Sodium (g/MJ)	Potassium (g/MJ)	AA (g/MJ)	EPA (g/MJ)	Base excess* (mmol/kg DM)
1	Wet	12.6	0.20	0.13	0.48	0.25	0.05	168
2	Dry	13.1	0.24	0.12	0.42	0.03	ND	61
3	Wet	12.6	0.19	0.08	0.60	0.18	0.47	46
4	Dry	12.7	0.22	0.09	0.67	0.03	0.02	32
5	Dry	14.9	0.34	0.21	0.57	0.06	0.11	154
6	Wet	11.8	0.17	0.10	0.40	0.14	ND	35
7	Dry	12.8	0.21	0.11	0.49	0.02	ND	48

\* Base excess was calculated according to Kienzle and others (1991). Data derived from Plantinga and Beynen (2004)

AA Arachidonic acid, EPA Eicosapentaenoic acid, DM Dry matter, ND Not detected

TABLE 2: Criteria for the inclusion of the cats with chronic renal failure (CRF) in the study

Criterion	
Age at diagnosis	>8 years
Survival time after diagnosis	>2 months
Plasma urea	>14 mmol/l
Plasma creatinine	>175 $\mu\text{mol/l}$
Diet	Normal cat food or one type of kidney diet for at least 75 per cent of survival time
Health status	No diseases other than CRF
Cause of death	Related to CRF

TABLE 3: Characteristics of the 321 cats used in the study

Characteristic	
Age (mean [sd])	15.08 (2.91) years
Breed (%)	European shorthair 82.9, Persian 8.4, Siamese 3.1, other 5.6
Sex (%)	Male 2.2, male neutered 51.1, female 6.8, female neutered 39.9
Plasma urea (mean [sd])	19.3 (5.8) mmol/l
Plasma creatinine (mean [sd])	269.8 (90.0) $\mu\text{mol/l}$
Kidney diet (%)*	0 = 54.5, 1 = 45.5
ACE inhibitor (%)*	0 = 89.4, 1 = 10.6

\* 0 No, 1 Yes

ACE Angiotensin-converting enzyme

2004). Thus, diet 5 may be too rich in phosphorus (Table 1). It has been suggested that the ideal concentrations of sodium, potassium and arachidonic acid may be 0.04 to 0.06, 0.4 to 0.6 and 0.01 to 0.02 g/MJ, respectively (Plantinga and Beynen 2004). On this basis, all the diets contain too much sodium and too much arachidonic acid, but are optimal in potassium. On

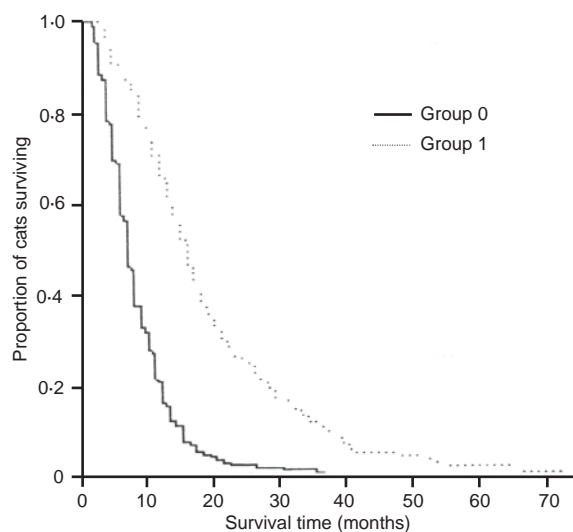


FIG 1: Kaplan-Meier survival curves for the model: survival time =  $(8.483 + 10.50) \times (\text{kidney diet} = 1)$  ( $R^2=0.229$ ). The difference in median survival between groups 0 and 1 is nine months. Group 0 No kidney diet used, Group 1 Kidney diet used

**TABLE 4: Mean ages and plasma urea and creatinine concentrations of the cats offered a normal diet and the seven kidney diets**

Diet	Number of cats	Age (years)	Plasma	
			Urea (mmol/l)	Creatinine ( $\mu\text{mol/l}$ )
Normal	175	15.5 <sup>a</sup>	20.6 <sup>a</sup>	277.1 <sup>a</sup>
1	5	16.6 <sup>ab</sup>	19.2 <sup>ab</sup>	313.2 <sup>ab</sup>
2	56	14.2 <sup>b</sup>	16.5 <sup>b</sup>	242.1 <sup>b</sup>
3	24	14.7 <sup>ab</sup>	17.3 <sup>b</sup>	269.5 <sup>ab</sup>
4	9	15.4 <sup>ab</sup>	18.5 <sup>ab</sup>	257.7 <sup>ab</sup>
5	10	14.5 <sup>ab</sup>	16.7 <sup>ab</sup>	209.2 <sup>b</sup>
6	35	14.7 <sup>ab</sup>	20.2 <sup>ab</sup>	278.6 <sup>ab</sup>
7	7	14.0 <sup>ab</sup>	15.4 <sup>ab</sup>	276.3 <sup>ab</sup>

<sup>a, b</sup> Different superscripts within the column indicate significant differences between the diets ( $P < 0.05$ )

**TABLE 5: Mean (sd) and median survival times of the cats offered a normal diet and the seven kidney diets**

Diet	Survival time (months)		Number of cats	P*
	Mean (sd)	Median		
Normal	8.47 (5.49)	7.0	175	
1	18.8 (9.61)	13.5	5	<0.10
2	18.1 (10.6)	16.0	56	<0.001
3	29.7 (10.6)	23.0	24	<0.001
4	16.8 (6.22)	16.0	9	<0.05
5	17.4 (8.98)	17.0	10	<0.05
6	14.0 (10.0)	12.0	35	<0.005
7	21.9 (8.49)	19.0	7	<0.01

\* Difference versus normal diet

the assumption that the optimal value for the base excess is 150 to 350 mmol/kg dry matter (Plantinga and Beynen 2004), the base excess of diets 1 and 5 may be considered appropriate. The ideal content of EPA may be 0.2 to 1.0 g/MJ (Plantinga and Beynen 2004), which would imply that only diet 3 has the ideal level. A major difference between diet 3, which gave the longest increase in survival time, and diet 6, which gave the shortest, appears to be their EPA content. The authors suggest that the efficacy of diet 3 may be explained by its high concentration of EPA. Controlled research is necessary to investigate the role of EPA in the survival of cats with chronic renal failure.

The use of an ACE inhibitor had no significant effect on the survival time of the cats, whereas there is evidence that ACE inhibitors may be beneficial in dogs with renal disease. A study by Brown and others (2003) showed that enalapril was effective

in modulating progressive renal injury, which was associated with a reduction of glomerular and systemic hypertension and proteinuria, but not glomerular hypertrophy. The efficacy of ACE inhibitors in cats has not been reported, but these drugs are frequently prescribed for cats with chronic renal failure.

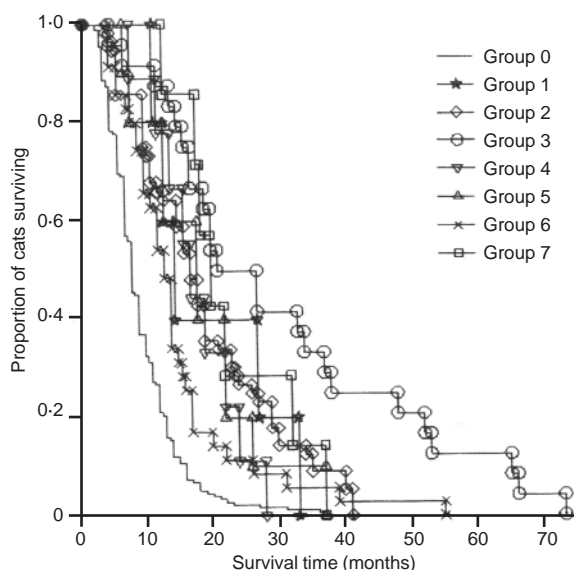
The results of this study provide further evidence that commercial kidney diets can prolong the survival time of cats with chronic renal failure. The data indicate that diet 3 prolonged the survival time most; it is relatively low in phosphorus and sodium, but high in potassium, arachidonic acid and EPA. The superior performance of diet 3 may be due to the complex combined effects of its constituent parts, but interpreting the results together with earlier findings, it appears that the low level of phosphorus and the high levels of potassium and EPA, particularly the latter, may be its most important characteristics. This result is clearly important for assisting manufacturers in the formulation, and veterinarians in the selection, of suitable diets for treating cats with chronic renal failure.

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**FIG 2: Kaplan-Meier survival curves for the seven types of kidney diet (groups 1 to 7 refer to the diet codes)**

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