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Multivariable analysis of the association between electrolyte disturbances and mortality in cats

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Abstract

Objectives Electrolyte disorders have been individually associated with mortality in small populations of cats with specific conditions, but the associations and interactions between electrolyte disturbances and outcome have not been evaluated in a large, heterogeneous population. It was hypothesized that abnormalities of sodium, chloride, potassium and calcium concentrations would be independently and proportionately associated with death from natural causes and with all-cause mortality in cats.

Methods An electronic database containing 7064 electrolyte profiles was constructed to assess the association between disorders of sodium, potassium, corrected-chloride and ionized calcium concentrations with non-survival by multivariable modelling. A second database containing 2388 records was used to validate the models constructed from the first database.

Results All four electrolytes assessed had non-linear U-shaped associations with case fatality rates, wherein concentrations clustered around the reference interval had the lowest case fatality rates, while progressively abnormal concentrations were associated with proportionately increased risk of non-survival (area under the receiver operator characteristic curve [AUROC] 0.689) or death (AUROC 0.750).

Conclusions and relevance Multivariable modelling suggested that these electrolyte disturbances were associated with non-survival and with death from natural causes independent of each other. The present study suggests that measurement of electrolyte concentrations is an important component of the assessment of cats in emergency rooms or intensive care units. Future studies should focus on confirming these associations in a prospective manner accounting for disease severity.

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Introduction

Maintenance of physiologic electrolyte concentrations is important for normal cellular function. Cats therefore possess multiple homeostatic mechanisms to prevent electrolyte disturbances and return abnormal concentrations to their setpoints.[1] Despite this, electrolyte disorders are commonly encountered in cats treated in emergency rooms and intensive care units.[2–4] Most electrolyte abnormalities are mild, pose minimal threat to life and result from conditions that alter fluid balance or cause electrolyte loss in excretions or effusions. In extremes, however, electrolyte disturbances are potentially fatal,[5] due to interference with acid–base status,[6,7] enzyme systems,[8] and the function of excitable tissues including nerves and muscles.[9–11]

Disorders of individual electrolytes have been associated with outcome in humans and in cats. Abnormal plasma sodium concentrations are associated with death in critically ill people, independent of disease severity,[12] and even small alterations can increase mortality risk.[13] Frequently, alterations in sodium concentration reflect abnormalities in water balance,[14] and the association between sodium disorders and outcome may partially

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reflect an association of fluid balance with mortality, since it is recognized that fluid overload adversely affects outcome.[15–17]

Chloride concentrations have a marked impact on osmolality and acid–base balance.[18] Increased plasma chloride decreases the strong ion difference (SID), causing acidosis, while decreased plasma chloride increases the SID, causing alkalosis.[18] Identification of chloride disorders aids the assessment of acid–base disturbances in cats, and may enhance recognition of the presence of unmeasured anions.[19] Iatrogenic hyperchloremia is a current focus of attention in human medicine, where extensive use of 0.9% saline for fluid resuscitation may increase mortality, potentially by increasing the risk of acute kidney injury.[20–23]

Hyperkalemia is a well-recognized risk factor for death in cats with kidney injury[24] and urinary tract obstruction.[25] Hypokalemia is also commonly encountered, although an association between hypokalemia and mortality has not been established.

Both hyper- and hypocalcemia are commonly encountered in cats.[26] Hypercalcemia has been associated with mortality, particularly in cats with kidney injury and cancer.[27] Ionized hypocalcemia is frequently seen in cats with pancreatitis,[28] and is associated with increased mortality in feline sepsis.[29]

Individual electrolyte disorders have been studied in small groups of cats with specific conditions, but associations between electrolyte disturbances and mortality have not been evaluated in a large, heterogeneous population. In addition, the potential for interactions between electrolyte disturbances to impact outcome has not been assessed. The present study sought to fill these knowledge gaps by analyzing the association between electrolyte abnormalities and outcome in cats. It was hypothesized that abnormalities of sodium, chloride, potassium and calcium concentrations would be independently and proportionately associated with death from natural causes and with all-cause mortality (including euthanasia) in cats.

Materials and methods

Electrolyte analyses

Electrolyte analyses were conducted using a point-of-care blood-gas analyzer on heparinized blood samples (RapidPoint 405; Siemens). Sodium concentrations were not corrected for glucose concentration. Raw chloride values were used to generate chloride concentrations corrected for changes in measured sodium concentration using equation 1.[30] The midpoint of the reference interval (153 mmol/l) was used as the normal sodium concentration. Local reference intervals for the blood gas analyzer were previously generated from 20 normal cats that were not part of the present study population and were considered healthy based on history, physical examination and results of complete blood count and serum chemistry profiles.

$$[Cl^-]_{Corrected} = [Na^+]_{Normal} / [Na^+]_{Measured} \times [Cl^-]_{Measured} \quad \text{Equation 1}$$

Case selection and database compilation

An electronic database of electrolyte analyses conducted between 31 May 2007 and 3 January 2015 in the institution emergency room or intensive care unit was searched. The database was curated to remove samples from species other than cats, samples with invalid case numbers or missing data and sample types other than blood (eg, effusion). Provided each entry was complete, then multiple samples from a single animal were kept in the database. Institution medical record systems were searched for data on patient signalment, outcome and hospitalization dates to create separate databases containing these distinct datasets. These were combined using a custom application (Visual Basic; Microsoft Visual Studio for Windows) that searched the databases via the unique patient identifier to create a final composite database containing the relevant data for each patient entry, corresponding to the date-time stamp from the electrolyte analyses. The final database was manually checked for accuracy by cross-referencing the database entries with the parent data sources for a randomized selection of cases, spanning the range of case numbers and representing 0.1% of cases.

Test database compilation

A second database of analyses conducted between 4 January 2015 and 3 January 2017 was generated as above. This second database was used to assess the predictive ability of the multivariable model developed using the first database, by calculating the predicted mortality probability for each profile in the second (test) database using the multivariable model generated from the first. These data were then compared against the actual outcomes from the test database using a receiver operating characteristic (ROC) curve.

Statistical analyses

Variables were tested for normality using the D'Agostino Pearson test, and appropriate descriptive statistics calculated. Parametric variables are presented as mean ±SD, while non-parametric variables are presented as median (minimum–maximum). Non-parametric continuous variables were compared using the Mann–Whitney U test and with box and whisker plots. For each electrolyte in every profile, the deviation of the measured electrolyte concentration from normal was calculated. These delta electrolyte values were computed by determining the absolute value (ie, numeric values without positive/negative signs) of the difference between measured values and reference interval midpoints (Na^+ 153 mmol/l, corrected Cl^- 122 mmol/l, K^+ 3.9 mmol/l and iCa^{2+} 1.27 mmol/l). To evaluate mortality in cats with abnormal electrolyte concentrations, data were banded into bins spanning the whole population. For sodium and chloride concentrations, these bins were 2 mmol/l wide, for potassium concentrations bins were 0.35 mmol/l wide and for calcium 0.1 mmol/l wide. The case fatality rates for each electrolyte concentration band were calculated and the percent case fatality plotted against electrolyte concentration. For multivariable logistic regression modeling, candidate predictor variables were identified if they were significantly associated with outcome by Mann-Whitney U test at $P < 0.1$ and had no evidence of collinearity (correlation coefficient <0.9). Candidate variables were entered using a forward stepwise method, using $P < 0.05$ for the likelihood ratio to add variables to the model. Model accuracy was determined using 2×2 classification tables, calibration was assessed using the Hosmer–Lemeshow goodness-of-fit test, utility was assessed using Nagelkerke's R^2, and discrimination was determined by calculating area under the ROC curve (AUROC). Values for AUROC between models were compared per Hanley and McNeil.[31,32] Alpha was set at 0.05. Statistical analyses were conducted using commercial software (Prism 7 for Mac OS X, GraphPad Software; SPSS Statistics 24, IBM).

Results

Demographics

Electrolyte data for the whole population are summarized in Table 1. Sex was recorded for 7520 profiles (98.9% of the database). The population consisted of 60.9% castrated males (n = 4583), 33.3% spayed females (n = 2500), 3.5% intact males (n = 266) and 2.3% intact females (n = 171). The overall case fatality rate was 19.8%, while the death rate (excluding euthanasia) was 3.1%. Breed was recorded for 4076 profiles (53.6% of the database) and included 25 breeds of cat. The 10 most common breeds were: domestic shorthair (n = 2970, 72.9%), domestic longhair (n = 488, 12.0%), Maine Coon (n = 180, 4.4%), Siamese (n = 86, 2.1%), mixed breed (n = 84, 2.1%), Persian (n = 53, 1.3%), Himalayan (n = 43, 1.1%), Manx (n = 27, 0.7%), Ragdoll (n = 27, 0.7%) and Exotic Shorthair (n = 22, 0.5%).

Individual electrolytes

There were prominent non-linear 'U' shaped relationships between electrolyte concentrations and case fatality rates for all four electrolytes assessed. Patients with electrolyte concentrations close to the median value (within reference intervals) had low case fatality rates, while patients with abnormal concentrations had increased case fatality rates proportionate to the degree of abnormality. These relationships were visible in the whole dataset and after cats that were euthanized were excluded, albeit less distinct. In general, there was substantial overlap between institution electrolyte reference intervals and the lowest case fatality rates.

Most cats with sodium concentrations within the reference interval had case fatality rates below the background fatality rate. In addition, cats with values up to 162 mmol/l had fatality rates below that of the whole population (Figure 1a). Cats with sodium concentrations below 150 mmol/l and above 162 mmol/l had consistently increased fatality rates compared with the whole population. After excluding euthanized cats, the U-shaped relationship was still apparent and the protective effect of a normal value became more prominent (Figure 1b). After excluding euthanized patients, cats with sodium values outside of the reference interval had death rates consistently above that of the whole population.

Table 1 Summary electrolyte data

Parameter	All cats (n = 7604)	Survivors (n = 6098)	Non-survivors (n = 1506)	Died (n = 195)
Age (years)	9 (4–12) [0–24]	8 (4–12) [0–24]	9 (5–12.8) [0–21]	11 (6–13) [0–20]
Na^+(mmol/l)	152.6 (148.9–155.6) [118.6–190.0]	152.8 (149.4–155.6) [119.9–184.4]	151.1 (146.2–155.3) [118.6–190.0]	150.0 (144.2–155.5) [126.2–171.3]
K^+(mmol/l)	3.89 (3.51–4.30) [1.14–11.04]	3.89 (3.52–4.26) [1.71–10.31]	3.95 (3.47–4.59) [1.14–11.04]	4.17 (3.61–4.86) [1.80–10.29]
Cl^- (mmol/l)	117 (113–121) [77–140]	118 (114–121) [77–140]	116 (110–120) [84–140]	116 (110–122) [90–137]
Corrected Cl^- (mmol/l)	117.6 (114.7–120.6) [81.5–147.4]	117.6 (115.0–120.5) [81.5–132.4]	117.1 (113.1–120.9) [88.4–147.4]	118.2 (114.8–121.3) [93.4–130.4]
iCa^{2+}(mmol/l)	1.21 (1.14–1.27) [0.32–3.01]	1.22 (1.16–1.28) [0.32–2.71]	1.17 (1.07–1.24) [0.61–3.01]	1.14 (1.02–1.23) [0.62–3.01]

Descriptive statistics for age and the electrolytes for all cats, survivors only, non-survivors (euthanized and died) and cats that died only. All parameters were non-parametric and thus are summarized as median (interquartile range) [minimum–maximum]

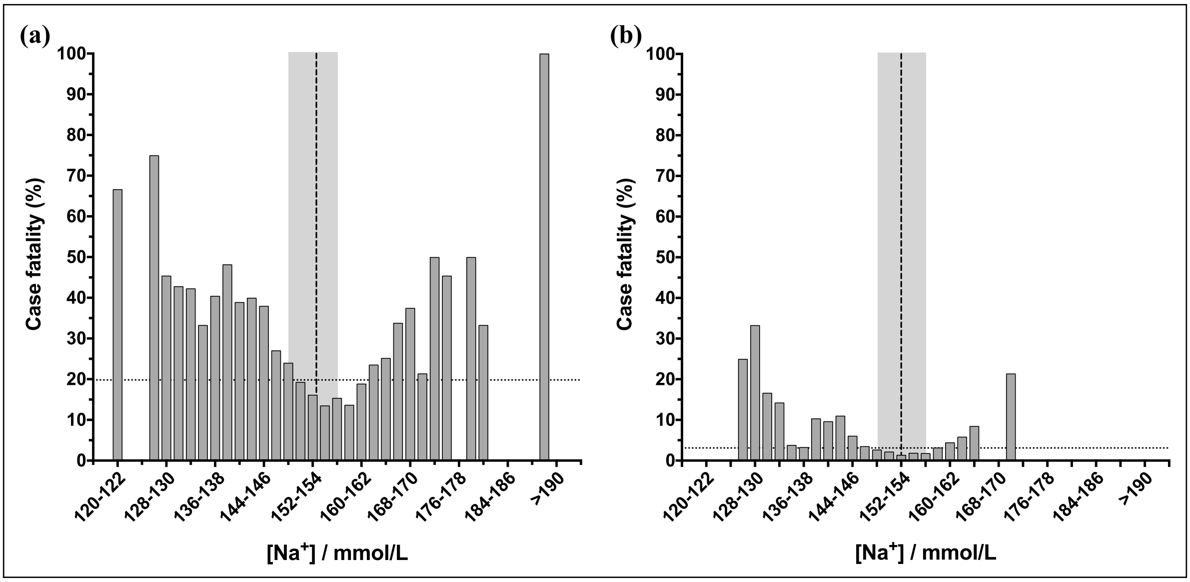

Figure 1 Feline blood sodium concentrations have a U-shaped relationship with case fatality rates. Low or high sodium concentrations are associated with increased case fatality rates compared with values within the reference interval (gray shaded box). Sodium concentrations were banded into 2 mmol/l bins and the percentage case fatality for the patients in each of these subgroups calculated. The horizontal dotted line denotes the case fatality rates across the dataset. The vertical dashed line represents the median value. Panel A represents data from all samples (n = 7604), including those from patients that were euthanized, while panel B represents data from patients that survived or died only (ie, euthanized patients were excluded) (n = 6293)

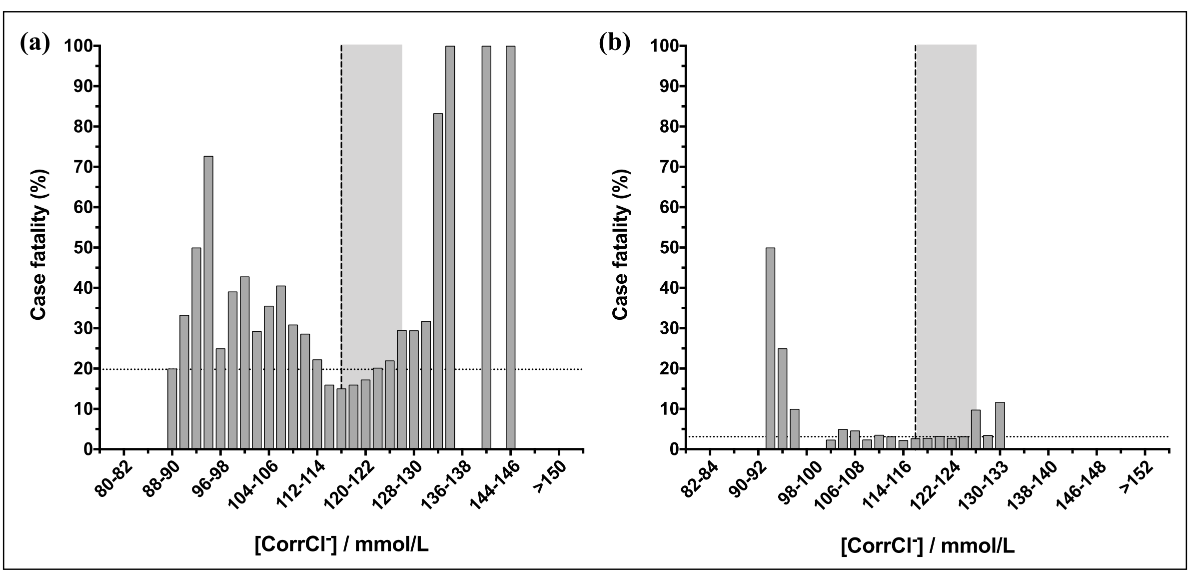

Figure 2 Feline corrected blood chloride concentrations have a U-shaped relationship with case fatality rates. Chloride values were corrected for sodium concentrations as follows: $[Cl^-]_{Corrected} = [Na^+]_{Normal} / [Na^+]_{Measured} \times [Cl^-]_{Measured}$. Low or high corrected-chloride concentrations are associated with increased case fatality rates for the whole population, but not once cats that were euthanized were excluded. Corrected-chloride values were banded into 2 mmol/l bins and the percentage case fatality for the patients in each of these subgroups calculated. The horizontal dotted lines denote the case fatality rates across the dataset. The vertical dashed line represents the median value. The gray shaded box represents the institution reference interval. Panel A represents data from all samples (n = 7604), including those from patients that were euthanized, while panel B represents data from patients that survived or died only (ie, euthanized patients were excluded) (n = 6293)

In contrast to sodium concentration, the U-shaped relationship between outcome and corrected-chloride values was only apparent in the whole population (Figure 2a). Once euthanized animals were excluded, no relationship between fatality rate and corrected chloride concentration was apparent (Figure 2b). Cats with

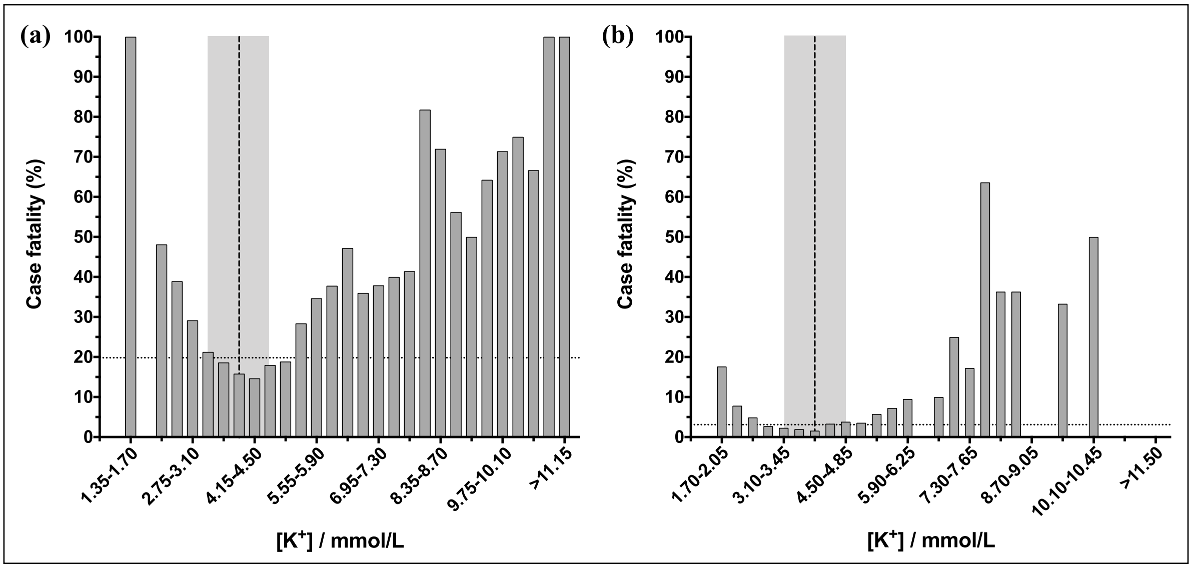

Figure 3 Feline blood potassium concentrations have a U-shaped relationship with case fatality rates. Low or high potassium concentrations are associated with increased case fatality rates. Blood potassium values were banded into 0.35 mmol/l bins and the percentage case fatality for the patients in each of these subgroups calculated. The horizontal dotted lines denote the case fatality rates across the dataset. The vertical dashed line represents the median value. The gray shaded box represents the institution reference interval. Panel A represents data from all samples (n = 7604), including those from patients that were euthanized, while panel B represents data from patients that survived or died only (ie, euthanized patients were excluded) (n = 6293)

corrected-chloride values close to the lower bound of the reference interval had lower than background case fatality rates, but this was not the case for cats with corrected-chloride concentrations at the upper end of the reference interval. The numbers of cats in the categories with markedly abnormal chloride concentrations were limited, but the data suggest that cats with corrected hyperchloremia may have higher fatality rates than those with equivalent magnitudes of corrected hypochloremia.

For both potassium and calcium concentrations, relationships between electrolyte concentrations and case fatality rates were displayed over narrower concentration ranges than for sodium or chloride. As was the case for sodium, cats with potassium concentrations in the reference interval tended to have lower case fatality rates in the whole population (Figure 3a) and after exclusion of euthanized cats (Figure 3b). In contrast to sodium and chloride, cats with potassium concentrations at either extreme had very high case fatality rates. There were more cats in groups with high potassium concentrations vs low, skewing the distribution. The relationship between ionized calcium and case fatality was also U-shaped, but this pattern was more difficult to discern due to the smaller concentration range for calcium values compared with the other electrolytes. As for potassium, case fatality rates were high for both severe hyper- and hypocalcemia. The reference interval for calcium concentration had limited overlap with groups with the lowest case fatality rates in the whole population (Figure 4a), but once euthanized cats were excluded, the reference interval mapped accurately to groups with the lowest death rates (Figure 4b).

Due to the non-linear relationships between electrolyte concentrations and case fatality rates, comparing the median values of survivors and non-survivors was not meaningful. Calculation of the absolute value of the deviation of the measured value from the reference interval midpoint (delta value) enabled comparison of the divergence from 'normal' in survivors and non-survivors. These delta electrolyte values were non-parametric (Table 2). Compared with survivors, non-survivors (including cats euthanized) had significantly larger delta electrolyte values (all P <0.001) (Figure 5a). Once cats that were euthanized were excluded, the delta electrolyte values were also significantly larger in cats that died compared with survivors for sodium, potassium and calcium concentration (all P <0.001), but not for corrected-chloride concentration (P = 0.772) (Figure 5b).

Multivariable logistic regression

All four delta electrolyte variables were associated with outcome in the whole population. No collinearity was identified, and hence all four were taken forward into multivariable logistic regression analyses. These variables were entered into a survival multivariable analysis in a forward stepwise fashion and retained in the final model if significantly (P <0.05) associated with outcome. The final model contained all four delta electrolyte variables, as independent predictors of survival (Table 3).

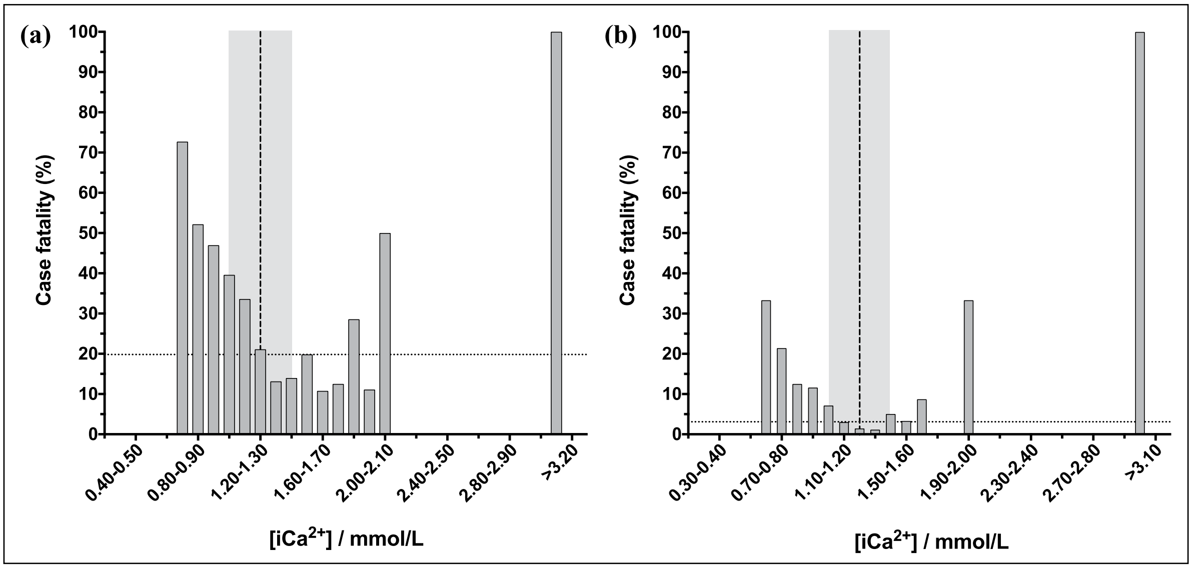

Figure 4 Feline ionized calcium concentrations have a U-shaped relationship with case fatality rates. Low or high ionized calcium concentrations are associated with increased case fatality rates. Ionized calcium values were banded into 0.10 mmol/l bins and the percentage case fatality for the patients in each of these subgroups calculated. The horizontal dotted lines denote the case fatality rates across the dataset. The vertical dashed line represents the median value. The gray shaded box represents the institution reference interval. Panel A represents data from all samples (n = 7604), including those from patients that were euthanized, while panel B represents data from patients that survived or died only (ie, euthanized patients were excluded) (n = 6293)

Table 2 Summary delta electrolyte data

Parameter	Survivors (n = 6098)	Non-survivors (n = 1506)	Died (n = 195)
Delta_Na^+ (mmol/l)	3.1 (1.4–5.5) [0.0–33.1]	4.6 (2.2–8.6) [0.0–37.0]	5.9 (2.7–9.7) [0.1–26.8]
Delta_K^+ (mmol/l)	0.37 (0.17–0.67) [0.0–6.41]	0.53 (0.24–1.09) [0.0–7.14]	0.59 (0.27–1.35) [0.0–6.39]
Delta_CorrectedCl^- (mmol/l)	4.6 (2.4–7.1) [0.0–40.5]	5.3 (2.7–9.2) [0.0–33.6]	4.7 (2.4–7.4) [0.0–28.6]
Delta_iCa^{2+} (mmol/l)	0.07 (0.03–0.12) [0.00–1.44]	0.12 (0.05–0.20) [0.00–1.74]	0.15 (0.08–0.25) [0.00–1.74]

Descriptive statistics for the delta electrolyte parameters, which represent the absolute difference (increase or decrease) between the measured electrolyte concentrations and the midpoint of the respective reference intervals for all survivors, non-survivors (euthanized and died) and cats that died only. All parameters were non-parametric and thus are summarized as median (interquartile range) [minimum–maximum]

The equation of the model was: ln(odds ratio) = 0.056 (Delta_Na^+) + 0.367(Delta_K^+) + 0.032(Delta_CorrCl^-) + 2.477(Delta_iCa^{2+}) − 2.395, where all delta electrolytes are measured in mmol/l. The Nagelkerke R^2 value was 0.103, indicating the model explained 10.3% of the variability in the data. The Hosmer-Lemeshow χ^2 value was 53.8 (P <0.001), indicating the model was not well fitted. ROC curve analysis of the probabilities predicted by the model suggested it was predictive of outcome; however (AUROC 0.689, P <0.001) (Figure 6a).

To assess whether the association between outcome and electrolyte disturbances was biased by including euthanized cats, the multivariable analysis was repeated using a dataset including only survivors (n = 6098) and cats that died (n = 195). Here, only three candidate predictors were considered for entry into the model, because delta corrected-chloride concentrations were not significantly different between survivors and cats that died. The final model predicting death included three delta electrolyte concentrations as independent predictors. The equation of the model was: ln(odds ratio) = 0.066(Delta_Na^+) + 0.483(Delta_K^+) + 3.138(Delta_Ca^{2+}) – 4.556, where all delta electrolytes are measured in mmol/l. The Hosmer-Lemeshow χ^2 value was 14.9, which was not significant (P = 0.062), indicating good model fit. The Nagelkerke R^2 value was 0.111. ROC curve analysis suggested the model

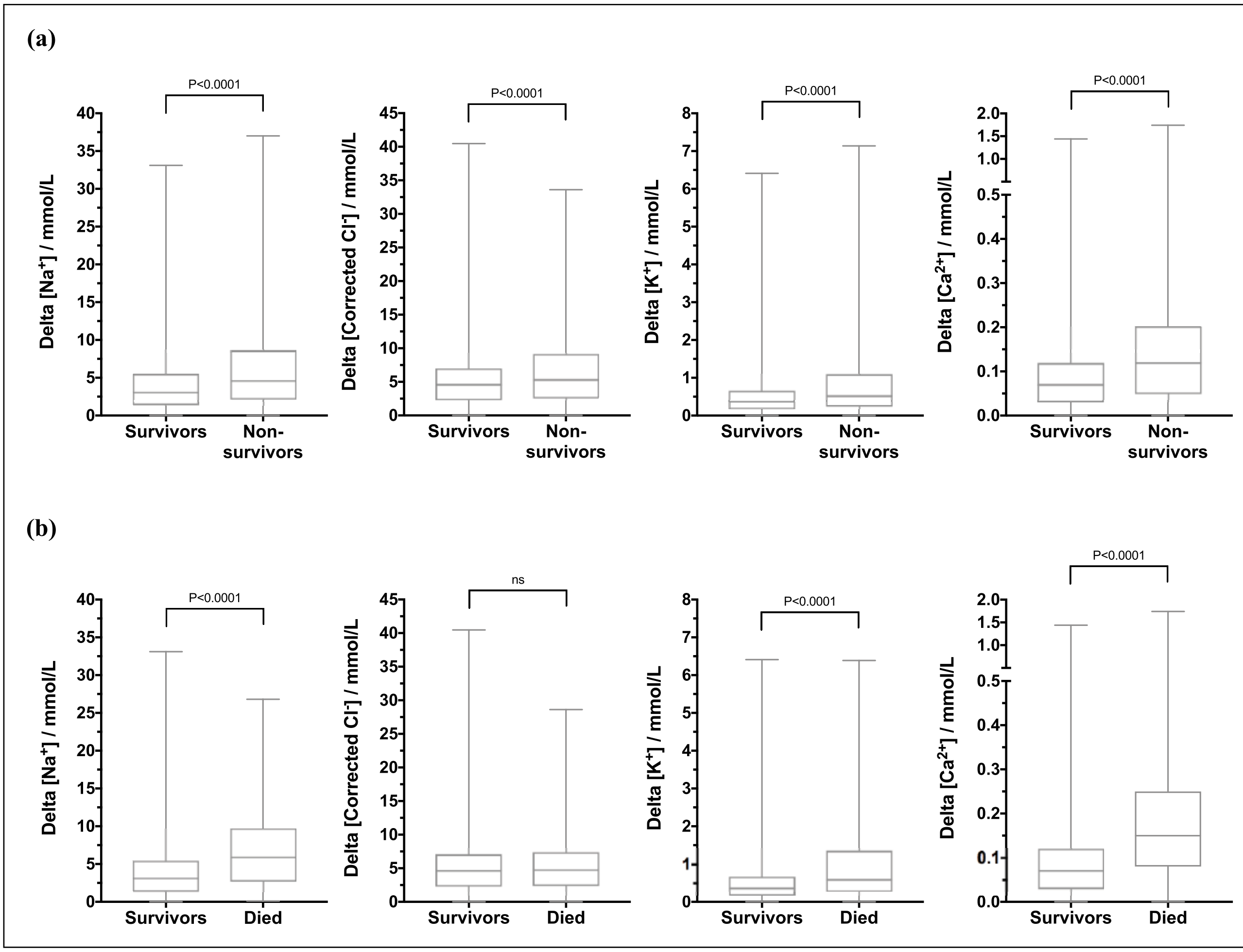

Figure 5 The degree of abnormality in measured electrolyte concentrations is significantly different between survivors and non-survivors. Box and whisker plots of the deviations between patient sodium, corrected-chloride, potassium and ionized calcium values from the midpoints of their reference intervals were constructed from a database of 7604 feline samples (panel A) and in 6293 cats after euthanized patients were excluded (panel B). The delta electrolyte concentrations were plotted according to outcome. The delta electrolyte values for all electrolytes were significantly larger for non-survivors compared with survivors (all P <0.001 by Mann–Whitney U-test), while only delta values for sodium, potassium and calcium were significantly different between cats that were discharged and those that died (all P <0.001 by Mann–Whitney U-test). ns = not significant

Table 3 Final multivariable model

Variable	Coefficient	SEM	Wald χ^2	df	P value	Odds ratio	95% CI lower	95% CI upper
Delta_Na+	0.056	0.006	78.584	1	<0.001	1.058	1.045	1.071
Delta_K+	0.367	0.038	94.192	1	<0.001	1.443	1.340	1.554
Delta_CorrCl–	0.032	0.006	25.215	1	<0.001	1.032	1.019	1.045
Delta_iCa2+	2.477	0.273	82.199	1	<0.001	11.908	6.970	20.343
Constant	–2.395	0.061	1536.139	1	<0.001	0.091		

The output from the multivariable modelling to predict outcome using deviations of electrolyte concentrations from the midpoints of their respective reference intervals as predictor variables. These predictor variables are labelled Delta_electrolyte to indicate that they represent deviations from normal in either direction (hyper- or hypo-)
df = degrees of freedom of the χ^2 test; CI = confidence interval

was discriminating for death (AUROC 0.750, P <0.001) (Figure 6b). Comparison of the AUROC values from the two outcome prediction models suggested that the model constructed for predicting death was significantly better than that for predicting outcome in non-survivors (including euthanasia) P = 0.006.

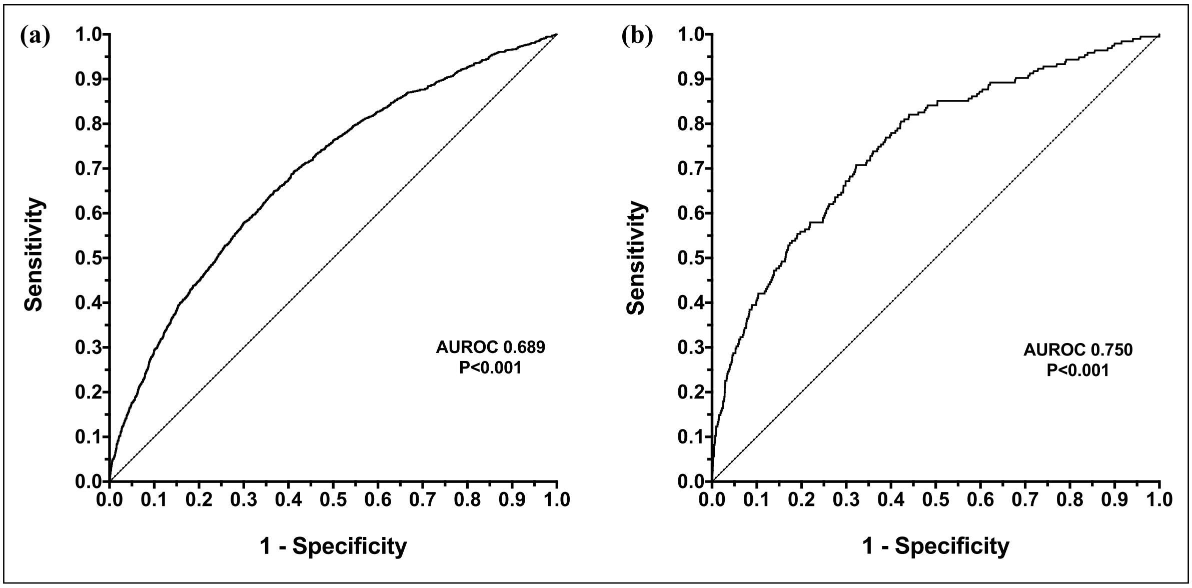

Figure 6 Receiver operating characteristic (ROC) curves for the survival probabilities as calculated by the final four-parameter multivariable model. Panel A displays the ROC curve for the initial population (n = 7604). The area under the ROC curve (AUROC) is 0.689, significantly different from 0.5 (P <0.001). Multivariable modelling was then used to identify independent predictors of outcome in cats that either survived or died. Panel B displays the ROC curve for this population (n = 6293) where the AUROC was 0.750, P <0.001

The predictive ability of the multivariable model of non-survival (including death and euthanasia) was then tested by calculating the predicted mortality probability for each profile in the second (test) database containing 2388 profiles. In the second population, where the overall case fatality rate was 15.7%, AUROC was 0.640, P <0.001. This AUROC value was significantly different from the value AUROC 0.689 calculated from the first database P = 0.008, suggesting the model was less discriminating for the second population.

Discussion

The present study suggests that in cats, disturbances of electrolyte concentrations are associated with survival to discharge. Specifically, the present study demonstrates that both increases and decreases in electrolyte concentrations proportionately increase the risk of non-survival (including euthanasia) and of death (excluding euthanasia). For three of four electrolytes evaluated, this association was present irrespective of whether euthanized cats were included in the analyses. The present study also suggests that distinct and separate electrolyte disturbances have a cumulative effect on mortality risk. The multivariable model contains four predictive variables indicating that each electrolyte disturbance independently and additively affects the likelihood of survival. In other words, patients with more than one disturbance in either direction are at greater risk of a poor outcome irrespective of the combination of electrolyte disturbances present, consistent with a recent study of human ICU patients.[33]

Previous studies have indicated that individual electrolyte abnormalities are associated with mortality.[34,35] The present study corroborates these findings and extends our understanding by identifying independent associations between electrolyte disturbances and outcome in two very large and heterogeneous groups of cats. The findings of the present study closely resemble findings of a similar study of electrolyte disturbances in dogs.[36]

The causes of the associations identified in the present study cannot be definitively discerned, owing to the retrospective methods employed. The limitations of the medical record systems also precluded easy analysis of the underlying diagnoses and hence identification of the root causes of the electrolyte abnormalities identified. Many patients had multiple diagnoses that obscure the true origins of the electrolyte disturbances present. It can be speculated, however, that marked variations in electrolyte concentrations negatively impact cellular processes that underpin tissue and organ function. At extreme concentrations, these effects may be sufficient to cause death irrespective of any other condition. The present study also suggests that less extreme abnormalities influence outcome in a cumulative manner.

Although the study design precludes causal association between electrolyte disturbances and outcome, the results of the present study can inform clinical practice. The strength of the association between death and electrolyte abnormalities suggests such disturbances should be taken seriously and that clinicians should take steps to identify and manage the underlying diseases. The magnitude of risk increases in a non-linear fashion as degree of abnormality increases, but even small disturbances in electrolyte concentrations within the reference interval may have consequences, consistent with data on electrolytes in people.[34]

Retrospective studies can be confounded by unknown and unmeasured variables such as the impact of therapy or disease progression and by selection or classification biases. The cats in the present study had diverse conditions and disease stages and were managed individually. The population likely included large numbers of cats with mild illness severity and most patients that died likely had multiple risk factors for mortality. The multivariable analyses indicated that the predictive values of the electrolyte disturbances were independent of each other, but they might be epiphenomena associated with illness severity. In similar studies of human patients, the availability of illness-severity scores such as APACHE II enables researchers to account of the degree of injury or disease.[13,20] This was not possible here, because the necessary data for calculation of established feline illness-severity scores were not available. Future studies gathering data prospectively might overcome this issue and confirm that electrolyte disturbances are independently associated with outcome.

The datasets evaluated here included more than one profile from some patients, which could have biased the results by increasing the signal strength (towards survival or non-survival) from individual patients. These effects, however, will have been substantially diluted by the very large dataset evaluated. Most patients in the databases had a low risk of death, as reflects the overall population seen at our institution. This may have detrimentally affected the multivariable modeling, by reducing the correlation between predicted and actual mortality at the extremes.[37]

With the exception of corrected-chloride, the relationships between outcome and electrolyte disturbances remained even after exclusion of euthanized cats, suggesting that electrolyte abnormalities are associated with mortality from natural causes. Comparisons of AUROC values indicated that electrolyte abnormalities are more discriminant for predicting death than for predicting all-cause mortality. The cause of the lack of association between death and corrected-chloride concentration is not clear. It seems unlikely to be related to case numbers given the persistence of the relationships identified between death and disorders of sodium, potassium and calcium after exclusion of euthanized cats. It is doubtful that clinicians would euthanize cats with corrected-chloride disorders at a disproportionate rate, but we cannot exclude that the knock-on effect on acid–base status associated with hyper-or hypo-chloremia might influence clinicians' interpretations of disease severity or prognosis. It is also possible that corrected-chloride disorders simply have a smaller influence on outcome in cats than they do in dogs.[36]

Conclusions

The present study suggests that disturbances in sodium, potassium, corrected-chloride or ionized calcium concentrations above or below the midpoint of the reference interval are associated with death in cats evaluated in an emergency room or intensive care unit. Future studies should focus on confirming these associations in a prospective manner accounting for disease severity.

Author note RG conceived the study, analyzed data and wrote the manuscript; SDR and DJF collected and analyzed data and edited the manuscript.

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