Survival estimates and outcome predictors in dogs with newly diagnosed diabetes mellitus treated in a veterinary teaching hospital

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Abstract

Background  Diabetes mellitus (DM) is one of the most common endocrine disorders in dogs, but prognostic factors are still largely unknown. The aim of this retrospective, single-centre, case series study was to determine overall survival time and identify the prognostic value of several clinical and clinicopathological variables in dogs with newly diagnosed DM.

Methods  Cases of DM were identified within the electronic medical records of one referral centre. Sixty-eight dogs with DM were included. Cox proportional hazards models were used to analyse variables associated with survival.

Results  The median survival time was 964 days (range 22–3140). In multivariable model analysis, length of survival was significantly shorter for dogs with higher haematocrit value (hazard ratio (HR) 1.06, 95 per cent confidence interval (CI) 1.00 to 1.13) and higher serum phosphate concentrations (HR 1.83, 95 per cent CI 1.13 to 2.97). Serum phosphate concentrations were above the reference interval in 24 of 65 (37 per cent) dogs.

Conclusion  Diabetic dogs have a good life expectancy. Hyperphosphataemia is a relatively common finding in dogs with newly diagnosed DM and represents a negative prognostic factor. The presence of pancreatitis might not be associated with an unfavourable outcome.

Introduction

The term diabetes mellitus (DM) describes a group of metabolic diseases characterised by chronic hyperglycaemia resulting from defects in insulin production, action or both. DM is one of the most frequent endocrinopathies in dogs. The prevalence of canine DM has been estimated, from first-opinion practices and insurance database populations, at about 0.3 per cent.

The most common form of DM in dogs resembles the human type 1 condition, characterised by permanent hypoinsulininaemia that requires exogenous insulin to maintain control of glycaemia, avoid ketoacidosis and survive. Transient or reversible DM is a rare event in dogs. The aetiology of type 1 DM has not been completely elucidated in dogs but is undoubtedly multifactorial, involving both genetic and environmental factors. DM generally occurs in middle-aged and older dogs; some studies indicate that females are at greater risk and breed predispositions have been suggested. Moreover, different risk factors, related to lifestyle and the presence of concurrent diseases, are believed to play a potential role in the development of DM in dogs.

Although the pathophysiological mechanisms, clinical aspects, diagnostic methods, treatment and monitoring options for dogs with DM have been investigated in a number of studies, only a few have mentioned life expectancy and prognostic factors of the disease. Furthermore, the predictive value of clinicopathological variables at the time of diagnosis has never been analysed in any study. This might be explained by the fact that the diagnosis of DM is often carried out in first-opinion veterinary practices, whereas referral centres see the case when insulin
treatment has already started; therefore, it is difficult to obtain laboratory data at the time of diagnosis, before treatment, for a large number of dogs from a single referral institution that uses a single internal laboratory. Detailed data about the outcome and prognostic factors of DM in dogs would help to characterise the disease better and, conceivably, make the owners more inclined to accept lifetime treatment for their dogs and maintain excellent compliance. Hence, the purpose of the present study was to assess the survival time and the prognostic significance of different clinical and clinicopathological variables evaluated in dogs newly diagnosed with DM.

Materials and methods
Inclusion criteria
The medical records of all diabetic dogs admitted to the Department of Veterinary Medical Sciences, University of Bologna, Italy, between January 2005 and December 2017 were reviewed. Dogs were included in the study if they had newly diagnosed DM, had not been treated for diabetes, and had follow-up examinations at the same institution until death or until the last re-evaluation for which records were available. Dogs were excluded if, at diagnosis, a thorough diagnostic evaluation (ie, complete blood count (CBC), chemistry profile and urinalysis) was not available or if the dogs had previously been treated by referring veterinarians.

Diagnostic procedures
DM was diagnosed on the basis of appropriate clinical signs (ie, polyuria, polydipsia, polyphagia, weight loss), persistent fasting hyperglycaemia and concomitant glycosuria. The concurrent presence of ketonuria established the diagnosis of diabetic ketoacidosis (DK), while ketonuria with an increased anion gap metabolic acidosis (venous blood pH <7.35 and bicarbonate concentrations <17.5 mmol/l) established the diagnosis of diabetic ketoacidosis (DKA). CBC, chemistry profile (which included measurement of serum fructosamine and/or blood glycated haemoglobin (Gly Hb) concentrations) and complete urinalysis were performed to identify clinicopathological abnormalities consistent with DM or concurrent disorders. Additional diagnostic procedures were carried out when clinically indicated.

CBC (CELL-DYN 3500R, Abbott Laboratories, Abbott Park, Illinois, USA (from year 2005 to year 2009, 15 dogs); Advia 2120 Hematology System, Siemens Healthcare Diagnostics, Erlangen, Germany (from year 2010 until the end of the study, 53 dogs)), chemistry profiles (AU400 and AU480, Beckman Coulter/Olympus, Brea, California, USA) and urinalyses were performed by standard laboratory methods at the medical laboratory of the referral institution. Serum fructosamine analysis was performed using a colorimetric nitroblue tetrazolium reduction method (17350H, Sentinel Diagnostics, Milano, Italy). Gly Hb was assessed by an immunoturbidimetric method, while total haemoglobin was measured using a colorimetric method (HbA1c, B00389, Beckman Coulter); the Gly Hb/total haemoglobin ratio was expressed as a percentage. The methods for measuring glycated proteins were subjected to internal validation.

Treatment protocol and monitoring
Dogs were managed using the therapeutic and monitoring protocol implemented at the authors’ institution. Insulin therapy was started at an initial dose of approximately 0.1–0.25 U/kg bodyweight twice daily, according to the insulin preparation administered. Dietary therapy was initiated simultaneously. As a standard procedure at the authors’ clinic, all diabetic dogs were reassessed at one, two to three, six to eight, and 10–12 weeks after diagnosis, and every four months thereafter, or as needed. Each re-evaluation included an assessment of history, physical examination and bodyweight. Furthermore, glycated proteins (ie, serum fructosamine and/or Gly Hb) were measured and a blood glucose curve (BGC) was performed. The decision on additional diagnostics (ie, routine laboratory evaluation, tests for concurrent diseases) was the responsibility of the clinician managing the case. Adjustments of insulin dosage, in the range of 10–25 per cent, were made on the basis of the owner’s perception of clinical signs in response to treatment, BGC and glycated protein concentrations.

Medical records review
Data obtained at the time of diagnosis from medical records included signalment, history (including administration of glucocorticoids and progestogens in the previous six months), physical examination findings, and laboratory test results that comprised CBC, serum chemistry profile and urinalysis. DK, DKA and any concurrent disease diagnosed at initial evaluation were recorded. Information concerning insulin therapy, including type of insulin, starting dosage and regimen of administration, was retrieved. The occurrence of diabetic remission (ie, insulin treatment was no longer required to maintain normal blood glucose level) was recorded. Date of death or survival of all cases was recorded and entered into the database, which was closed on December 31, 2017 before analysis. When necessary, owners were contacted.

Data analysis
Descriptive statistics were generated to characterise the study population. Continuous variables were presented as mean±sd or median and range (minimum and maximum value), depending on whether the data were normally or not normally distributed, respectively. Categorical variables were described with frequencies, proportions or percentages.
The median survival time was estimated using the Kaplan-Meier product limit method. The survival time was defined as the time between the diagnosis and the date on which the dog was last known to be alive or the date of its death due to any cause. Dogs had censored survival time if alive at the end of the study or lost to follow-up.

The following variables were investigated to determine their association with overall survival time: age, sex (male or female), reproductive status (entire or neutered), breed (crossbred or purebred), bodyweight, diet (petfood, home-made food or mixed), previous administration of corticosteroids and progestogens, clinical signs (polyuria, polydipsia, polyphagia, weight loss, cataracts, weakness, anorexia, vomiting), haematocrit (Hct) value, red blood cell count (RBC), mean corpuscular volume, mean corpuscular haemoglobin concentration, red blood cell distribution width and white blood cell count; neutrophils, lymphocytes, monocytes, eosinophils and platelet count; concentrations of glucose, fructosamine, Gly Hb, total bilirubin, total protein, albumin, cholesterol, triglycerides, creatinine, urea, total calcium, phosphate, sodium, potassium and chloride; serum activity of alkaline phosphatase (ALP), alanine transaminase (ALT), aspartate transaminase (AST) and gamma glutamyl transferase (GGT); and urinary specific gravity, urinary protein to creatinine ratio (UPC), urinary glucose and urinary ketone concentrations. The presence of ketosis/ketoacidosis, pancreatitis, Cushing’s syndrome, mitral and/or tricuspid valve disease, and any other concurrent disorders was considered. The type and the starting dose of insulin were also included in the analysis.

Univariate Cox proportional hazards regression analysis was used to screen potential predictors for subsequent inclusion in a multivariate model. Variables with a value less than 0.05 via univariate analysis were included in the final model-building process. Variables were then gradually removed until the model with the best fit was identified. In the model-building process, the selection of variables that were strongly collinear (ie, creatinine and urea concentrations) was also considered. Hazard ratios (HRs) and 95 per cent confidence intervals (CIs) were calculated.

Continuous variables associated with survival in the multivariate analysis were assessed by the receiver operating characteristic (ROC) curve analysis to select the optimum cut-off value, with the highest sensitivity and specificity, for prediction of the outcome. Survival of diagnostic groups was estimated by Kaplan-Meier analyses and compared by log-rank test. All statistical analyses were performed using a commercially available software program (MedCalc). The significance level was set at P<0.05.

**Results**

**Study population**

Of the 202 cases of canine DM that were retrieved from the records, 68 dogs met the inclusion criteria and were used in the analysis. One hundred and two dogs were excluded because the diagnosis had been made previously and they had been treated by private practitioners, 25 dogs were excluded because they had no follow-up examinations after the diagnosis, and seven dogs were excluded because the owners denied permission for a comprehensive diagnostic evaluation.

The characteristics of the study population are summarised in table 1. The median age at diagnosis was 10 years (range 5–14 years). There were 21 (31 per cent) entire females, 21 (31 per cent) spayed females, 11 (16 per cent) entire males and 15 (22 per cent) neutered males. All entire females (21 dogs) were spayed within four weeks after the diagnosis of DM. The median bodyweight was 11.5 kg (range 2.8–50.0 kg). Twenty different breeds were counted. The most commonly represented breeds were mixed breed (22), English setter (16) and Yorkshire terrier (6). At the time of diagnosis, 38.5 per cent of the dogs were fed with petfood, 23 per cent with home-made diet and 38.5 per cent with a mixed diet. Seven (10 per cent) dogs had been treated with corticosteroids or progestogens up to six months before admission.

The clinical signs reported at diagnosis by the owners or observed at the physical examination were—in order of frequency—polydipsia (93 per cent), polyuria (91 per cent), weakness (73 per cent), weight loss (48 per cent), vomiting (41 per cent), anorexia (35 per cent), polyphagia (28 per cent) and cataracts (25 per cent).

At the time of admission to the clinic, the median glucose concentration was 24.5 mmol/l (range 11.5–65.5), the mean fructosamine concentration was 537 μmol/l (sd ±149) and the mean blood Gly Hb concentration was 6.9 per cent (sd ±1.2). In comparison with the laboratory reference interval, other common alterations (present in more than 60 per cent of cases) in the chemistry profile were increased concentrations of serum ALP, ALT, AST, GGT and triglycerides, and decreased concentrations of sodium and chloride. Frequent abnormalities in urinalysis included increased UPC in 29 of 35 (83 per cent) dogs, and the presence of glucose and ketones in urine. Ketosis and ketoacidosis were diagnosed in two (3 per cent) and 26 (38 per cent) dogs, respectively. One or more concurrent diseases were documented in 34 (50 per cent) dogs, including 13 (19 per cent) with pancreatitis; eight (12 per cent) with mitral and/or tricuspid valve disease; seven (10 per cent) with Cushing’s syndrome; four with mammary neoplasia; three with hepatic disease; two each with hypothyroidism, urolithiasis or disseminated intravascular coagulation; and one each with inflammatory bowel disease, acute kidney injury or cutaneous mastocytoma.
Table 2

| Reason for euthanasia/death | Number recorded |
|----------------------------|-----------------|
| Diabetes mellitus deterioration | 7               |
| Neoplasia                   | 4               |
| Severe hypoglycaemia        | 3               |
| Respiratory diseases (Dyspnoea) | 3          |
| Anorexia/asthenia           | 3               |
| Neurological signs           | 2               |
| Aortic thromboembolus       | 2               |
| Intussusception              | 1               |
| Heart diseases               | 1               |
| Car accident injuries        | 1               |
| Drowning                     | 1               |
| Old age/physical deterioration | 1       |
| No cause recorded            | 8               |

With regard to treatment, 36 (53 per cent) dogs received lente insulin (Caninsulin, MSD, Boxmeer, The Netherlands), 12 (17.5 per cent) received neutral protamine hagedorn (NPH) insulin (Humulin I, Eli Lilly Italia SpA, Sesto Fiorentino - Firenze, Italy), 12 (17.5 per cent) received insulin glargine (Lantus, Sanofi SpA, Anagni - Frosinone, Italy), and insulin detemir (Levemir, Novo Nordisk A/S, Bagsværd, Denmark) was administered to eight (12 per cent) dogs. The median starting dose of insulin was 0.3 U/kg (range 0.02–1 U/kg) twice daily.

Survival analysis

Of the 68 diabetic dogs, at the time of censorship, 39 were dead, 24 alive and five had been lost to follow-up. In the former group, 15 dogs had undergone euthanasia and 24 had died spontaneously. Of the 39 dogs that had died by the end of the study, the cause of death or reason for euthanasia was recorded when possible (table 2). However, the cause of death was not supported by postmortem examination in any of the cases.

The median survival time of the 68 dogs was 964 days (range 22–3140 days). Fifty-four of the 68 (79 per cent) dogs lived more than six months, 43 of 68 (63 per cent) more than one year, 26 of 68 (38 per cent) more than two years, and 15 of 68 (22 per cent) more than three years (figure 1). Eleven of the 26 (42 per cent) dogs with DKA survived more than two years, and 12 (46 per cent) dogs with DKA were still alive by the end of the study.
Different variables were potentially associated with a poor outcome in the univariate analysis, including age, breed, RBC, Hct, glucose, ALP, urea, creatinine, phosphate and sodium concentrations, concurrent diseases, and Cushing’s syndrome (table 3). In the multivariate analysis, only two variables were retained in the model; in particular, higher Hct (HR 1.06, 95 per centCI 1.00 to 1.13) and higher serum phosphate concentrations (HR 1.83, 95 per centCI 1.13 to 2.97) at diagnosis were significantly associated with decreased survival time. Of the 65 dogs with available laboratory data concerning serum phosphate at diagnosis, concentrations of serum phosphate were above the reference interval in 24 of 65 (37 per cent) cases. Moreover, four of the seven (57 per cent) dogs with concurrent Cushing’s syndrome had hyperphosphataemia at the time of diagnosis. The ROC curve analysis showed that a serum phosphate concentration of 1.35 mmol/l and an Hct of 46 per cent were the optimal cut-offs to discriminate dogs with short-term survival from dogs with long-term survival. The median survival time was 1748 days (range 22–3140 days) in dogs with serum phosphate concentrations less than 1.35 mmol/l and 770 days (range 24–2905 days) in dogs with serum phosphate concentrations of at least 1.35 mmol/l (figure 2); however, the difference was not significant (P=0.10, log-rank test). A significant difference was reached in the Kaplan-Meier analysis of the Hct (P=0.04, log-rank test); the median survival time was 1089 days (range 96–3140 days) in dogs with Hct less than 46 per cent and 708 days (range 22–2242 days) in dogs with Hct of at least 46 per cent. The categorical variables that yielded a significant value in the Kaplan-Meier analysis (P<0.05, log-rank test) are reported in table 3. Factors such as serum fructosamine, blood Gly Hb, ketoacidosis and pancreatitis were not associated with survival time.

![Figure 1](image1.png)  Kaplan-Meier survival curve for 68 dogs with newly diagnosed diabetes mellitus. The solid line represents median survival time and the dashed lines 95 per cent confidence interval.

![Figure 2](image2.png)  Overall survival in Kaplan-Meier survival curves differentiating two groups of dogs with newly diagnosed diabetes mellitus according to initial serum phosphate (P) concentrations (mmol/l). Survival time has been truncated at four years.

**Table 3** Results of univariate and multivariate analyses: factors potentially associated with survival time (P<0.05) in dogs with newly diagnosed diabetes mellitus

| Variable | Median survival time, days (P value, log-rank test) | Hazard ratio (95% confidence interval) | P value, Cox regression |
|----------|--------------------------------------------------|--------------------------------------|------------------------|
| **Univariate Cox regression analysis** | | | |
| Age | – | 1.01 (1.00 to 1.02) | 0.042 |
| Breed (purebred v crossbred) | 1089 v 916 (0.025) | 2.17 (1.08 to 4.37) | 0.028 |
| Red blood cell count | – | 1.00 (1.00 to 1.00) | 0.007 |
| Haematocrit value | – | 1.08 (1.02 to 1.15) | 0.008 |
| Glucose | – | 1.04 (1.01 to 1.07) | 0.008 |
| Alkaline phosphatase | – | 1.00 (1.00 to 1.00) | 0.012 |
| Urea | – | 1.01 (1.00 to 1.02) | 0.008 |
| Creatinine | – | 1.00 (1.00 to 1.00) | 0.012 |
| Phosphate | – | 1.81 (1.13 to 2.94) | 0.015 |
| Sodium | – | 0.94 (0.90 to 0.99) | 0.037 |
| Concurrent diseases (0=absence v 1=presence)* | 1089 v 781 (0.045) | 1.94 (1.01 to 3.78) | 0.049 |
| Cushing’s syndrome (0=absence v 1=presence) | 993 v 645 (0.038) | 2.46 (1.01 to 5.97) | 0.045 |
| **Multivariate Cox regression analysis** | | | |
| Haematocrit value | – | 1.06 (1.00 to 1.13) | 0.032 |
| Phosphate | – | 1.83 (1.13 to 2.97) | 0.013 |

Survival time of diagnostic groups was estimated by Kaplan-Meier analysis and compared by log-rank test. *Concurrent diseases also include Cushing’s syndrome.
**Discussion**

The dogs in the current study had a median survival time of 964 days (32 months). This is longer than the median survival time of two months and 17.3 months reported for a population of insured diabetic dogs in Sweden and for a population of diabetic dogs attending first-opinion practice in England, respectively. This discrepancy may be attributable to the fact that survival times vary between countries and between socioeconomic regions within a country. Furthermore, dogs in the present study were handled in a referral clinic, which implies optimal case management and, possibly, attracts owners with greater motivation than first-opinion practices. In the two studies mentioned above, the fact that most of the deaths occurred shortly after DM diagnosis probably reflects a greater rate of elective euthanasia than in the current study. Mattin et al showed that insured diabetic dogs had an increased survival time. This may indicate that DM is a low-cost disease to diagnose, but its long-term management requires an important emotional and financial commitment, and therefore not all owners are willing to accept the lifetime treatment option. The results of the present study indicate that diabetic dogs, if well controlled, have a median survival time that can be over two years. The cause of death in diabetic dogs can often be related to diseases other than DM. Nevertheless, in the current study, considering the 31 dogs for which the cause of death/euthanasia was recorded, in at least 10 dogs the cause was diabetes-related.

The Hct value and serum phosphate concentrations were significantly associated with survival; therefore, at the time of diagnosis, dogs with higher Hct or serum phosphate concentrations had an increased risk of death. High Hct in diabetic dogs may be caused by dehydration/haemocconcentration resulting from osmotic diuresis; the latter is caused by the presence of glucose and ketone bodies in the urine that results in polyuria. Likewise, the presence of concomitant disorders that induce vomiting (e.g., pancreatitis) or that exacerbate polyuria (e.g., hypercortisolism) may result in a further deficiency of body fluids. Therefore, the finding of severe dehydration and secondary relative erythrocytosis, at the time of diagnosis, may indicate a severe and prolonged diabetic condition, or may suggest the presence of concomitant disorders. Unfortunately, the hydration status of the dogs included in the study was not precisely documented in the medical records, and thus it was not included in the analysis. Furthermore, it is possible that the effect of Hct on survival is minimal, as indicated by the results of the statistical analysis; for this reason, future investigations can be useful to confirm the prognostic potential of this variable.

An interesting finding of the current study was that a higher serum phosphate concentration at diagnosis was significantly associated with reduced survival time. The prognostic value of inorganic phosphorus has already been highlighted in other diseases. Fracassi et al found that increased serum phosphate concentrations were associated with a shorter life expectancy in a population of dogs with newly diagnosed pituitary-dependent hypercortisolism. Although it was not possible to figure out the cause of hyperphosphataemia in dogs of the aforementioned study, the authors argued that it might be a consequence of reduced renal excretion of phosphate, increased intestinal absorption of phosphate and mobilisation of phosphate from bone tissue. In the present study, Cushing’s syndrome was detected in seven dogs (10 per cent), among which four (57 per cent) had serum phosphate values above the reference range. In addition, hypercortisolism was found to be associated with a shorter survival time; therefore, it may represent a plausible explanation of the prognostic value of serum phosphate.

King et al reported that higher serum phosphate concentrations were associated with a poor outcome in cats with chronic kidney disease (CKD). Hyperphosphataemia during CKD is caused by a progressive reduction in renal function and the development of secondary renal hyperparathyroidism. In the current study some findings led to the supposition that the occurrence of CKD may be related to increased phosphate concentrations and reduced life expectancy; in fact, the majority of the study population consists of middle-aged and older dogs (median age 10 years), and UPC showed values above the reference interval in 83 per cent of cases with available laboratory data. These results suggest the need for more investigations on diabetic nephropathy, which is a common chronic complication in diabetic human beings and has occasionally been reported in diabetic dogs. Indeed, diabetic nephropathy is initially manifested as proteinuria, primarily albuminuria, and only when the changes in the glomerulus progress does it result in the development of azotaemia and clinical signs. However, in the present study, CKD was not reported as a cause of death. This may have been partly due to the fact that in many cases it was not possible to ascertain the cause of death, and in none of the cases was a postmortem examination performed.

Finally, an intriguing clue to the possible cause of hyperphosphataemia comes from research in human medicine, in which DM has been associated with a condition of ‘functional hypoparathyroidism’, which seems to be one of the factors leading to decreased bone mineral density in diabetic patients. Some studies have shown altered secretion of parathormone (PTH) in diabetic subjects; however, in none of these has it been possible to determine the specific cause. It has been assumed that hyperglycaemia may directly suppress PTH secretion and/or that insulin may be required for the maintenance of parathyroid secreting cells. Some authors also suggested that magnesium depletion, caused by osmotic diuresis, may be an explanation...
for the reduced secretion and action of PTH. Several studies observed increased renal calcium excretion, according to a lower PTH level, in diabetic subjects; moreover, one study reported a higher serum phosphate concentration and reduced renal phosphate excretion in diabetic human beings with decreased PTH levels. In the present study, the median serum phosphate concentration (1.4 mmol/l) and the mean total serum calcium concentration (2.4 mmol/l) were within the reference ranges; however, there was a tendency of the two values towards the upper and lower limits of the reference intervals, respectively. In addition, hyperphosphataemia and hypocalcaemia were detected in 37 per cent and 25 per cent of dogs, respectively. Similarly, in a large study involving 221 diabetic dogs, 20 per cent of subjects showed hyperphosphataemia and 47 per cent had hypocalcaemia at the time of initial examination. These interesting results show that there is an apparent basis for a connection between impaired calcium/phosphate homeostasis and DM in dogs. The data of the current study support the proposal that serum phosphate, at the time of diagnosis, may be a good indicator of long-term outcome. However, further prospective investigations are necessary to determine the exact aetiology/pathogenesis of the detected clinical-pathological abnormalities, to determine the clinical importance of these findings and to confirm the prognostic value of serum phosphate.

In the current study, the cut-off values of serum phosphate concentrations and Hct, which were used in the Kaplan-Meier analysis, were selected to have the highest sensitivity and specificity in order to discriminate the length of survival between diagnostic groups. However, their clinical usefulness appears limited. This is due to the fact that the cut-off values used are within the reference interval of the respective variables.

The presence of concomitant diseases and Cushing’s syndrome was associated with decreased survival time in univariate and Kaplan-Meier analyses, but not in multivariate analysis. This correlation might be explained by the insulin resistance induced by the presence of concomitant disorders, including hypercortisolism as one of the most common causes, which leads to the difficult management of DM; in turn, this results in a diminished propensity of the owners to pursue treatment and an unfavourable outcome. With regard to Cushing’s syndrome, this result supports a recent study showing that the occurrence of DM in dogs with hypercortisolism shortens life expectancy. However, univariate analysis does not take into account confounders; for this reason the association between the presence of Cushing’s syndrome, or concurrent diseases, and survival should be interpreted cautiously. Diagnosis of pancreatitis was not associated with survival, a finding that contrasts with a study performed in the UK, in which diabetic dogs with pancreatitis had an increased risk of death. These discrepancies may have resulted from differences in the veterinary facilities (first-opinion v referral clinic) and geographical locations between the studies.

DKA was diagnosed in 38 per cent of dogs, although it was not associated with length of survival. Hume et al reported that, in a population of dogs with naturally occurring DKA, 30 per cent of cases died or were euthanased during hospitalisation. However, because these studies had different study populations, methodologies and geographical locations, they are not directly comparable. In the current study, it is also worth mentioning that 42 per cent of dogs with DKA at diagnosis survived more than two years, and 46 per cent of DKA cases were still alive at the time of censorship. These results indicate that ketoacidosis, considered by practitioners as a life-threatening condition, is not necessarily associated with a negative prognosis. Therefore, treatment of DKA should always be pursued, consistent with the severity of underlying medical disorders.

Serum glucose was associated with survival in the univariate analysis, but there was no association between glycated proteins and life expectancy. In human medicine, Gly Hb has a strong predictive value for the complications of DM. In addition, higher Gly Hb values have been associated with an increased mortality risk. In the current study, the lack of association between glycated proteins and survival could be accounted for by the fact that laboratory data on serum fructosamine and Gly Hb concentrations were available in 47 per cent and 16 per cent of dogs, respectively. This deficiency of data is partially due to the fact that many dogs were admitted by the emergency service and endocrinologists saw the case at a later time, when the diagnostic tests had already been performed. The results might have been significant if more laboratory data had been included. Hence, in light of the prognostic importance of Gly Hb in human medicine, additional studies aimed at investigating the prognostic potential of glycated proteins are recommended.

The main limitation of the present study is the small number of cases included, which influenced the power of statistics. This derives from the very restrictive inclusion criteria. It is likely that some associations with survival were not detected because of this bias. Other limitations are largely related to the retrospective nature of the study and the incompleteness of some of the records. For instance, in some cases it was not possible to ascertain the cause of death, and the latter was not supported by postmortem examination in any of the cases. Furthermore, important data such as the body condition score were not recorded. Thus, the absence of some data may have partially biased the analysis. One limitation is that the laboratory reference intervals were not gathered from an age-matched control population but were those provided by the laboratory
for routine use. This could have influenced the number of dogs with abnormal laboratory findings reported in this study. However, the fact that clinicopathological data were obtained from a single medical laboratory represents a strength of the present study. Further strengths of the study are related to the management of the cases; indeed, all dogs were diagnosed, treated and monitored using standard protocols implemented at a single referral institution.

In conclusion, dogs with newly diagnosed DM had a good prognosis. The survival time was shorter in dogs with higher Hct value and higher serum phosphate concentrations. At diagnosis, the presence of pancreatitis might not represent a negative prognostic factor.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**Data availability statement** All data relevant to the study are included in the article.

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