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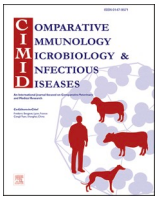

Clinical findings and prognostic factors for mortality in hospitalized dogs with leishmaniosis: aretrospective study

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ABSTRACT

This retrospective study evaluated factors responsible for mortality of dogs hospitalized for Canine Leishmaniosis. Medical records of 31 dogs with leishmaniosis from a Portuguese Veterinary Teaching Hospital were examined between August 2018 and January 2022. Females (n = 18) and pure breed dogs (n = 27) were overrepresented, with higher frequency of Labrador Retriever (n = 4). Median age was 7 years (interquartile range=7). Most had historical findings of lethargy (n = 26) and the commonest clinicopathological abnormality was hypoalbuminemia (n = 26). Eleven dogs were classified as LeishVet stage II, 10 stage III and 10 stage IV. Fourteen dogs (45.2%) died or were euthanized, with azotemia, leukocytosis, stage IV, absence of diagnosis before hospitalization and lack of leishmaniosis specific treatment during hospitalization contributing to mortality. Absence of hypoalbuminemia and stages II/III increased survival. Mean hospitalization length prior to discharge was 5.41days (± 1.84) and diarrhea prolonged hospital stay.

1. Introduction

Canine leishmaniosis (CanL) is a vector-borne disease caused by the parasite *Leishmania infantum*, which is transmitted to mammal hosts when infected female sand flies have a blood meal. The parasite expresses endemicity in the Mediterranean basin, South America, and Central and Southweast Asia [1]. There is an estimated 700,000–1.2 million new cases per year of cutaneous leishmaniosis in people worldwide with an additional estimated 100,000 cases of the visceral form. Both forms of disease are particularly frequent in southern Europe [2] with an estimated 700 autochthonous human cases reported annually. For every clinical case of human visceral leishmaniosis, there are an estimated 30–100 subclinical infections [3].

Seroprevalence ranges from 5% to 7–25% in domestic dogs throughout Southern Europe [3–5], being one the many factors contributing for dogs to remain an important reservoir of disease. Even apparently healthy infected dogs can result in sand fly infection, thereby promoting possible transmission to others.

Even in areas where the parasite is endemic, most of the infected dogs do not develop clinical signs or clinicopathological abnormalities. When clinical signs arise, they are often variable based upon the affected dog's immune response as well as parasitic load [6–8]. Dogs that launch a predominant T helper-1 (Th1) cell-mediated response to infection with *L. infantum* are more likely to override illness and/or remain apparently healthy. By contrast, those that experience a more significant Th2 humoral antibody-mediated response often develop moderate to severe manifestations of disease [6].

Ill dogs with CanL often present for evaluation of non-specific signs, including but not limited to lethargy, hyporexia, weight loss, vomiting, diarrhea, polyuria, and/or polydipsia. Physical examination of affected patients may disclose that they are febrile with generalized lymphadenomegaly, splenomegaly, and pale mucous membranes. Cutaneous lesions such as various types of dermatitis and onychogryphosis are also very frequently observed. Blepharitis and conjunctivitis, keratoconjunctivitis and uveitis are the predominant ocular findings associated with CanL [6]. Complete blood count (CBC) of patients with CanL can

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show abnormalities such as mild to moderate non-regenerative anemia, leukocytosis or leukopenia, along with others, whereas biochemistry profile with protein electrophoresis can express presence of, for example, hyperproteinemia, hyperglobulinemia, hypoalbuminemia, renal azotemia and elevation in liver enzymes activity [8]. Patients with CanL may also exhibit mild to severe proteinuria on urinalysis [6].

Anemia has been described as a negative prognostic factor for CanL [9]. The same can be said of azotemia [9,10], hypoalbuminemia, and lymphopenia [10]. Renal disease is the most common cause of death among dogs with CanL [11]. Absence of clinicopathological evidence of renal disease at time of diagnosis or evidence of renal disease without concurrent uremic signs are both favorable in terms of prognosis [12]. Approximately 75% of dogs without renal involvement will survive after being diagnosed with CanL for more than four years, if appropriately treated. Dogs with early stages of chronic kidney disease secondary to CanL that do not experience reduction of proteinuria after initiating treatment may present a poorer prognosis compared to those that demonstrate a decrease in this parameter. [13].

Several studies have shown that treatment with meglumine antimoniate and allopurinol, the most frequently prescribed protocol, can prolong survival times [9,14]. Nevertheless, the alternative combination of miltefosine and allopurinol is equally effective in the reduction or resolution of clinical disease [15]. An adequate follow-up of a meticulous physical exam, complete blood count, serum biochemistry, urinalysis with urinary protein-creatinine ratio and *Leishmania* serology is indicated to ensure that patients retain quality of life [8,13,14,16].

Currently, reports about CanL focus on outpatient care and monitoring as outlined above therefore, to the best of our knowledge, there are no reports concerning prognostic factors for mortality among hospitalized patients with CanL. The purpose of this study was to provide additional insight about prognostic factors for CanL specific to a hospitalized population of ill dogs and to quantify their impact on patient outcomes.

2. Material and methods

2.1. Data collection and analysis

The medical records of a Portuguese Veterinary Teaching Hospital were searched for dogs that had been admitted for hospitalization due to clinical leishmaniosis between August 2018 and January 2022. Patients that met inclusion criteria were identified by searching the computer database on-site for case-specific keywords (e.g. miltefosine, meglumine antimoniate, *Leishmania*) using hospital management software (GuruVet®).

The following information was collected for each patient: date of diagnosis; date of admission for hospitalization and date of discharge, death or euthanasia; patient signalment (age, sex, weight, reproductive status, breed); clinical signs and physical examination findings at presentation and/or during hospitalization; complete blood count, biochemical profile (urea, creatinine, alanine aminotransferease [ALT], alkaline phosphatase [ALP], 1,2-o-dilauryl-rac-glycero-3-glutaric-acid-(6′-methylresorufin) ester [DGGR] lipase), serum protein electrophoresis and urinary protein-to-creatinine ratio values; results of testing for concomitant vector-borne infection namely *Anaplasma* spp., *Dirofilaria immitis*, *Ehrlichia canis/Ehrlichia ewingii*, *Rickettsia conorii*, and *Babesia canis* (if available); anti-*Leishmania* serology results; medications administered during hospitalization; clinical outcome (discharge or death); and period of hospitalization.

Anaplasma spp., *D. immitis*, *E. canis/E. ewingii* were screened with the use of an IDEXX SNAP® 4Dx Plus Test performed in in-house laboratory, while *R. conorii* and *B. canis* were screened by an ELISA method performed in an outside laboratory.

Staging of disease was performed in accordance with the 2022 LeishVet guidelines [8].

2.2. Inclusion and exclusion criteria

Dogs were selected for this retrospective study if there was a documented history of hospitalization to either address clinical signs attributed to confirmed leishmaniosis or to initiate treatment.

Infection was considered present for each included patient based on antibody positivity for *Leishmania* detected by an ELISA method of quantitative serology (Leiscan ® *Leishmania* ELISA Test). Cases with a positive serology and compatible clinical and/or laboratorial signs attributed to leishmaniosis were selected. Being a retrospective study, data was obtained directly from medical data and decision on hospitalization and length individually assessed according to clinician's judgements. Timing of diagnosis was noted with respect to whether the patient had undergone confirmatory testing for leishmaniosis prior to hospitalization, or if the diagnosis was obtained at the time of hospitalization.

Dogs that had been diagnosed concurrently with other vector-borne infections or those that had developed CanL-associated sequelae (e.g. pancreatitis) were also included in the study.

Dogs were excluded if medical documentation was incomplete, if there were gaps in history taking or if physical examinations were not comprehensive, if there were concurrent non-infectious diseases not directly related to CanL (e.g. neoplasia), or if medical records demonstrated incomplete or ambiguous staging.

2.3. Statistical analysis

Data for each patient was individually entered into a standard Microsoft Excel database (Version 16.60 released in 2022). Descriptive and statistical analysis were performed using IBM® SPSS® Statistics software (Version 28.0 released in 2021).

Continuous data was tested for normality using a Shapiro-Wilk's W test, to choose whether to present mean and standard deviation or median and interquartile range according if data was normal or non-normal, respectively.

Comparative analysis of binominal variables was performed using the Pearson's chi-squared test or the Fisher's exact test, with a confidence interval of 95% ($P = 0.05$) for both, with P-value under 0.05 being considered statistically significant.

3. Results

Thirty-one dogs met inclusion criteria. Eighteen (58.1%) were females, six of which were intact (6/18; 33.3%). Of the thirteen males (41.9%), ten of which were intact (10/13; 76.9%). Median age of patients at initial presentation was 7 years old (IQR =7), ranging from 1 to 15 years old, and mean body weight was 22.3 kg (± 10.0).

Twenty-seven dogs (27/31; 87.1%) were purebred. Seventeen different breeds were present, with Labradors (n = 4), Boxers (n = 3), and Border Collies (n = 3) being overrepresented.

3.1. Clinical signs and physical examination findings

The primary complaints reported by the owners were lethargy (26/31; 83.9%) and weight loss (15/31; 48.4%). On physical examination, the most common manifestation of disease was pale mucous membranes (20/31; 64.5%). Less frequent findings were dermatological signs (e.g. cutaneous lesions at the nose and/or body and hyperkeratosis at the nose) (14/31; 45.2%), hyporexia/anorexia (14/31; 45.2%), diarrhea (13/31; 41.9%), vomiting or regurgitation (11/31; 35.5%), lameness or muscle atrophy (9/31; 29.0%), fever (8/31; 25.8%), respiratory signs associated with the upper and/or lower respiratory tract (7/31; 22.6%), neurological signs (altered mentation) (7/31; 22.6%), ocular signs (keratoconjunctivitis) (5/31; 16.1%) and epistaxis (4/31; 12.9%).

3.2. Laboratory findings

Main laboratory findings in the present study were as follows: hypoalbuminemia (26/31; 83.9%), thrombocytopenia (22/31; 71.0%), anemia (21/31; 67.7%), proteinuria (21/24; 87.5%), hypergammaglobulinemia (16/22; 72.7%), azotemia (14/31; 45.2%), increased ALT and/or ALP (11/26; 42.3%), leukocytosis (7/30; 23.3%), increased DGGR-lipase (7/10; 70.0%), and leukopenia (6/30; 20.0%).

Twenty-five patients in this study were screened for concomitant exposure to other vector-borne diseases (VBD) and seven (7/25; 28%) of these tested positive for at least one VBD - positivity for *R. conorii* in 3/25 (12.0%) of dogs, *E. canis/E. ewingii* in 2/25 (8.0%) of dogs, *A.*spp. in 2/25 (8.0%) of dogs, *B. canis* in 1/25 (4.0%) of dogs and *D. immitis* in 1/25 (4.0%) of dogs. One dog tested positive for both *D. immitis* and *A.* spp., and another tested positive for both *E. canis/E. ewingii* and *R. conorii*.

Of the seven dogs for which DGGR-Lipase was elevated , suggesting pancreatitis, three (3/7; 42.9%) were already under treatment for leishmaniosis with allopurinol and meglumine antimoniate, whilst the remaining four (4/7; 57.1%) did not have *Leishmania*-specific treatment ongoing.

3.3. Characterization of the disease

According with LeishVet guidelines [8], eleven (11/31; 35.5%) dogs were classified as stage II, ten (10/31; 32.3%) were stage III and 10 (10/31; 32.3%) were stage IV.

Eighteen dogs (18/31; 58.1%) had been previously diagnosed with leishmaniosis; 13 (13/31; 41.9%) were diagnosed upon intake.

3.4. Medical treatment during hospitalization

Hospitalized patients received a variety of treatment protocols. Leishmaniostatic (i.e. allopurinol) and/or leishmanicidal (i.e. meglumine antimoniate or miltefosine) drugs were administered to 26 dogs (26/31; 83.9%). Antibiotics were prescribed in 25 cases (25/31; 80.6%), with the combination of amoxicillin with clavulanic acid predominating (13/25; 52.0%), followed by enrofloxacin (12/25; 48.0%) and metronidazole (8/25; 32.0%). Fourteen (14/31; 45.2%) dogs were given glucocorticoids. Some dogs received combination therapy as outlined in Table 1.

Regarding leishmaniosis specific treatment, 16 (16/26; 61.5%) of the animals received a combination of meglumine antimoniate with allopurinol, whereas four (4/26; 15.4%) received miltefosine and allopurinol; five (5/26; 19.2%) were treated with only allopurinol and one (1/26; 3.8%) was only treated with meglumine antimoniate.

3.5. Clinical outcome

Clinical outcome was defined as one of two possibilities: death/euthanasia, or discharge. Fourteen patients (14/31; 45.2%) expired; 17 (17/31; 54.8%) survived to discharge. Of those that died in hospital, nine (9/14; 64.3%) had been euthanized.

All dogs that survived to discharge received at least one anti-*Leishmania* specific treatment. Twelve (12/17; 70.6%) had been treated with both meglumine antimoniate and allopurinol, three (3/17; 17.6%) had received only allopurinol and one (1/17; 5.9%) had been prescribed both miltefosine and allopurinol.

Concerning dogs that died or were submitted to euthanasia, nine (9/14; 64%) received at least one anti-*Leishmania* specific treatment. Three (3/9; 33%) received the combination of meglumine antimoniate and allopurinol; three (3/9; 33%) had miltefosine and allopurinol while two (2/9, 22%) received only allopurinol and one (1/9; 11%) only meglumine-antimoniate.

Prognostic factors that affected the outcome of these patients were evaluated and results are detailed in Table 2. Stage IV disease ($P = 0.027$), absence of diagnosis of the disease prior to hospitalization ($P = 0.033$), failure to prescribe leishmaniosis treatment during hospitalization ($P = 0.012$), leukocytosis ($P = 0.002$) and azotemia ($P = 0.012$) were associated with mortality. Absence of hypoalbuminemia ($p = 0.048$) and Stage II or III of disease ($p = 0.027$) increased the likelihood of survival to discharge.

3.6. Duration of hospitalization

Mean duration of hospitalization for the whole group was 5.26 (± 2.26) days. In detail, the mean time of hospitalization for dogs that died or were submitted to euthanasia were 5.07 (± 3.58) days. Concerning dogs that survived to discharge, the mean period of hospitalization was 5.41(± 1.84) days. Upon further inspection, the group that survived to discharge could be divided into two. One group averaged between one

Table 1
Description of the different combinations of therapies that animals received in this study.

Therapy received	Number of animals
	($n = 31$)
Leishmania specific medication + Antibiotics + Glucocorticoids	11/31 (35.5%)
Leishmania specific medication + Antibiotics	10/31 (32.3%)
Leishmania specific medication	5/10 (16.1%)
Antibiotics + Glucocorticoids	2/31 (6.5%)
Antibiotics	2/31 (6.5%)
Glucocorticoids	1/31 (3.2%)

Table 2
Assessment of the relation between clinical outcome and various parameters through comparative analysis of binominal variables.

Parameters	Clinical Outcome (death versus discharge)
	P-value
Treatment received during hospitalization	
Leishmaniosis treatment	0.012 *
Antibiotic treatment	0.664
Glucocorticoid treatment	0.076
Clinical signs and physical examination findings	
Fever	0.698
Diarrhea	0.481
Vomit/regurgitation	1.000
Lethargy	0.344
Dermatological signs	0.149
Pale mucous membranes	1.000
Anorexia	0.289
Weight loss	0.722
Epistaxis	0.107
Ocular signs	1.000
Musculoskeletal signs	0.233
Neurological signs	0.671
Respiratory signs	0.198
Laboratory findings	
Anemia	1.000
Leukocytosis	0.002 *
Leukopenia	0.657
Thrombocytopenia	1.000
Azotemia	0.012 *
Increased hepatic enzymes	0.701
Hypoalbuminemia	0.048 *
Hypergammaglobulinemia	1.000
Proteinuria	0.266
Concurrent infectious diseases	1.000
Increased DGGR-lipase	1.000
Timing of diagnosis	
Diagnosis of leishmaniosis prior to hospitalization	0.033 *
Staging of leishmaniosis	
II	0.027 *
III	
IV	

*Statistically significant.

and five days of hospitalization, whereas the other group was hospitalized for six or more days. Ten (10/17; 58.8%) dogs fit the former description, while 7 (7/17; 41.2%) fit the latter.

Factors that influenced hospitalization stay were identified and can be found on display in Table 3. Only diarrhea ($P = 0.035$) seemed to impact duration of hospitalization, lengthening hospital stay.

4. Discussion

Prior to this study, reports about CanL have focused on outpatient care and monitoring. This report is the first of its kind to reconsider data pertaining to signalment and clinical signs of dogs with CanL requiring hospitalization as well as to identify prognostic factors among hospitalized patients with CanL.

Historically, CanL was found to be more prevalent in male dogs [17–19] less than 3 years old or between 7 and 8 years of age [20]. By contrast, females were overrepresented in this study and, with some similarities to what was previously described, the number of adult dogs was disproportionately high. This variation in sex and age predisposition towards CanL is likely reflective of small sample size and in differences in local epidemiology.

While males were mostly intact, females had a bigger prevalence of neutering which may be associated to a perceived higher risk by owners of reproductive disease in non-castrated females.

The mean body weight of dogs in this study may be explained if one considers that large breed dogs might spend more time outdoors, thereby increasing their exposure to sand flies.

Purebred dogs were also overrepresented in this study as compared to mixes. While some studies do not show any breed predisposition [21], others have disclosed apparent increased prevalence among Boxers [19, 22], which aligned with our findings. It is possible that purebred dogs are at increased risk for developing CanL due to lack of hybrid vigor. Alternatively, it is possible that those who have the financial means to acquire purebred dogs are more likely to or more financially able to pursue hospitalization and cover cost of care.

In many cases, CanL was only diagnosed when clinical signs were already evident. The most frequent complaint presented by owners in the present study was lethargy. This is an inconsistent finding since some studies report that lethargy is uncommon [17], while others disclose that it is prevalent [23]. The fact that in the current study only hospitalized dogs were evaluated can prompt an overestimation of the real prevalence of this clinical sign, as these animals tend to present with a greater severity of the disease and a decrease of activity levels, easily identified by owners.

Consistent with previous studies, hypoalbuminemia was the most frequent clinicopathological abnormality [6,24]. This deficit in blood albumin can result from hepatic injury [25], renal damage [26], low protein intake [27] or any combination thereof. Moreover, albumin is a negative acute phase protein, which means that it can be decreased in response to tissue damage of multiple origins [10]. DGGR-Lipase, commonly measured to evaluated patients for pancreatitis, was measured in 10 dogs and was elevated in nearly 75% of them. This prompts the question of whether parasitic infection sets the stage for pancreatitis [28] as opposed to pancreatitis being a consequence of treatment. Pancreatitis has been previously described as an adverse outcome following treatment with meglumine antimoniate [29]. However, it is possible that pancreatitis could be triggered by the infection itself as opposed to the treatment regime.

About a quarter of the dogs in this retrospective study seemed to have been exposed or infected with additional vector-borne pathogens, stressing the potential role of co-infections in dogs with clinical leishmaniosis. Even though positivity to additional vector-borne pathogens did not seem to affect prognosis, complementary treatment against these concurrent pathogens should be considered since they can affect a patient's therapeutic response to specific treatment for CanL [30].

The number of animals presenting with higher stages of disease (Leishvet stage III and IV) were equal which may be an indication that in any of these stages hospitalization may be warranted. In daily practice, not every case is adequately classified according to this staging system, reinforcing the urgency to implement it as a standard procedure. To do so will require educating clinicians and pet owners alike with respect to an informed approach to treating CanL and its associated prognosis.

Stage IV of disease was associated with a poor clinical outcome, likely related to the severity of clinical signs and systemic repercussions of the disease. This is in alignment with that which has previously been reported for the disease [8]. Clinicians need to disclose that these patients exhibit higher mortality despite being hospitalization and that therefore prognosis remains guarded.

In the present study, a greater percentage of dogs had already been diagnosed with the disease by the time they were hospitalized. This highlights that leishmaniosis requires close and regular clinical monitoring since clinical relapse may occur and in some cases clinical signs may be severe enough to require hospitalization. It was also observed that lack of previous diagnosis contributed to a higher chance of death, possibly due to lack of awareness about the patients' health status.

With respect to in-hospital medical treatment, it varied a lot between patients, most likely due to the multiplicity of clinical signs exhibited by them. Therefore, even though a standardization of treatment protocols is a practical tool, most cases require an individual approach [6].

Regarding leishmaniosis specific treatment, most dogs were treated with a combination of meglumine antimoniate and allopurinol, a successful protocol for the medical management of CanL [31–34]. Although

Table 3
Comparison between Period of hospitalization and various parameters through comparative analysis of binominal variables.

Parameters	Time of hospitalization (1–5 days versus 6 or more days)
	P-value
Treatment received during hospitalization	
Leishmaniosis treatment	-[a]
Antibiotic treatment	0.603
Glucocorticoid treatment	1.000
Clinical signs and physical examination findings	
Fever	1.000
Diarrhea	0.035 *
Vomit/regurgitation	0.644
Lethargy	1.000
Dermatological signs	1.000
Pale mucous membranes	0.304
Anorexia	0.304
Weight loss	1.000
Epistaxis	0.593
Ocular signs	0.228
Musculoskeletal signs	0.228
Neurological signs	1.000
Respiratory signs	0.154
Laboratory findings	
Anemia	0.622
Leukocytosis	-[a]
Leukopenia	0.585
Thrombocytopenia	1.000
Azotemia	1.000
Increased hepatic enzymes	0.608
Hypoalbuminemia	0.593
Hypergammaglobulinemia	1.000
Proteinuria	0.525
Concurrent infectious diseases	0.266
Increased DGGR-lipase	1.000
Timing of diagnosis	
Diagnosis of leishmaniosis prior to hospitalization	1.000
Staging of leishmaniosis	
II	0.074
III	
IV	

*Statistically significant.
[a] No statistics were calculated due to absence of data in one of the categories.

data concerning its efficacy in hospitalized animals is scarce, this study supports its appropriate use in these cases.

Mortality for canine patients hospitalized due to CanL was elevated: about half of the patients in this study died or were euthanized during the hospitalization period. Euthanasia accounted for almost two-thirds of the total deaths and was most likely elected due to a perceived grave prognosis or poor estimated quality of life. To consider how to reduce mortality among patients requires us to revisit best practices surrounding initiation of treatment.

Whether to initiate CanL specific treatments as soon as possible during hospitalization is controversial. The onset of treatment may induce a transient clinical worsening due to potential side effects, such as nephrotoxicity and hepatotoxicity linked to meglumine antimoniate [16]. In this study, patients who did receive leishmaniosis specific treatment had an overall better outcome and all dogs that were discharged were treated with at least one anti-leishmanial drug. While data on the administration of leishmanicidal compounds during hospitalization is scarce, this study supports that it can be beneficial to rapidly start this type of treatment during hospitalization, especially because patients could be monitored closely for the occurrence of any potential life-threatening side effects. Furthermore, the most frequent treatment in cases where discharge was the outcome consisted of the combination of meglumine antimoniate and allopurinol. Although further studies are needed to clarify the most recommended anti-leishmanial treatment during hospitalization, these results may suggest that this specific protocol may improve patient outcomes.

The presence of leukocytosis in the CBC appeared to be associated with worse prognosis, a fact that could be related to a more significant inflammation/systemic reaction due to either leishmaniosis or a secondary bacterial infection. To author's knowledge, this is the first time reporting leukocytosis as a prognostic factor in CanL cases.

Albumin is a negative acute-phase protein and hypoalbuminemia is frequently present in several critical illness possibly leading to various complications given its many important functions such as maintaining colloid osmotic pressure [35]. In this study it seemed to have an impact on prognosis since dogs without hypoalbuminemia had a better outcome, similarly to what was previously reported where hypoalbuminemia was associated with worse prognosis [10]. The presence of hypoalbuminemia could be linked to substantial damage of the kidneys or liver in these patients contributing to poor prognosis.

Outcome of hospitalized patients did not seem to be affected by the presence of proteinuria, even though it has already been described as a factor associated with worse prognosis in previous reports [10]. Nevertheless, urinary protein-to-creatinine ratio was not available in all the cases, meaning that proteinuric dogs could have been underestimated. The present study also failed to find a statistically significant association between prognosis and lymphopenia, a parameter associated with worse prognosis, according to the same author [10], possibly due to decreased CD4 T helper cells mediated protective immune response or stress leukogram caused by clinical worsening.

The presence of azotemia, already known as a negative prognostic factor for CanL [9,10], was associated with a worse prognosis in this study. It is understandable that azotemia results in a worse prognosis because of the increased severity of clinical signs associated with kidney disease/potential glomerulonephritis, and also the longer period required for clinical improvement, which can influence the decision of euthanasia.

This study also highlights that the presence of diarrhea can significantly prolong hospitalization period. Such patients are at greater risk for dehydration, requiring intravenous fluid therapy and additional supportive care. Diarrhea in the context of hospitalization was not clarified in most dogs and may have a multifactorial etiology such as diet-induced diarrhea among other differentials. In fact, during hospitalization and particularly if dogs are hyporexic, several diets are often tried and may induce transient acute diarrhea. Curiously, chronic enterocolitis causing diarrhea has been described in animals infected with leishmaniosis [36–38], although it is still underreported. Future studies should be performed to further understand how CanL could contribute to diarrhea and take this in account when treating these patients as this could help decrease the duration of hospital stay.

Based upon our findings, it is reasonable to expect patients with CanL to be hospitalized for an average of 5 days duration. This information seems to be helpful as it allows clinicians to inform the client that the treatment will be extensive and provide more accurate patient cost of care estimates to the client, helping to plan ahead and be financially aware of the potential expenses.

Due to its retrospective nature, this study presented some limitations detailing a lack of consistent information for each animal and the inability to standardize the comprehensive nature of the physical exams performed at the admission or during hospitalization. Moreover, clinical staging was only possible in a limited sample size, impairing a robust interpretation of these results. Also concerning therapeutic decisions, data was based on medical records which often reflected the individual clinical judgement of the case, without justification of the clinical reason behind it. Lastly, considering that some of the laboratory tests were performed in different laboratories, it was not possible to create a mean value for each clinicopathological finding, since reference ranges differed.

In order to broaden the scope of our medical records review it would be useful to partner with neighboring facilities, as it would be a great way to obtain larger demographics. Additionally, a prospective study with the intent to establish a consensus concerning treatment for canine patients hospitalized due to clinical leishmaniosis should be performed.

5. Conclusions

This study confirms that mortality among dogs that require in-hospital support and treatment is high as almost half of them die in hospital or are euthanized. The presence of azotemia, leukocytosis, stage IV of disease, absence of diagnosis of the disease before hospitalization and lack of specific treatment for leishmaniosis during hospitalization were associated with worse prognosis, contributing to patient mortality. Contrastingly, absence of hypoalbuminemia and stages II and III of disease seemed more likely to result in discharge of the patient and therefore improve patient outcomes. Our data also shows that hospitalization period seems to increase with the presence of diarrhea as a clinical sign, enhancing the importance of instituting supportive care. Although larger studies are needed to evaluate additional prognostic factors and provide a better understanding of what parameters should be monitored more carefully in CanL this study opens new insights about prognostic factors in hospitalized dogs due to CanL infection.

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Credit authorship contribution statement

Carlota Carvalho Molina: participated in the design of the study, performed collection and analysis of data and drafted the manuscript. **Rodolfo Oliveira Leal:** conceived and coordinated the study and participated in its design and helped with data analysis and with the drafting of the manuscript. **Maria Joana Dias:** helped with data analysis and revised the manuscript. **Tiago Dias Domingues:** revised the manuscript for statistics. **Ryane E. Englar:** revised the manuscript for conceptualization. All authors read and approved the final manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial

interests or personal relationships that could have appeared to influence the work reported in this paper. The authors declare that they have no competing interests. Over the last two years, ROL and MJD were involved in two research trials on Canine Leishmaniosis (Nestle Purina and Bioiberica), both unrelated with this study.

Data Availability

The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request.

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Ethical approval and consent to participate

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