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High-Grade Gastrointestinal Lymphoma in Cats: Clinical Features, Treatment Patterns and Survival – a Retrospective Cohort Study

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Abstract

Feline gastrointestinal lymphoma is the most common digestive tract neoplasm in cats and represents an aggressive malignancy with poor outcome. This retrospective cohort study aimed to characterize the clinical features, treatment patterns, and survival outcomes of cats diagnosed with high-grade gastrointestinal lymphoma at two veterinary hospitals between 2018 and 2026. Eighteen cats met the inclusion criteria, with a mean age of 9.1 years and predominance of neutered males. Vomiting (66.7%), anorexia (50.0%) and weight loss (50.0%) were the most frequent presenting signs, while laboratory abnormalities included neutrophilia (38.9%), leukocytosis (27.8%) and anemia (22.2%). Treatment consisted of surgery alone (n = 3), chemotherapy alone (n = 8) or a combination of both (n = 7) with lomustine and prednisolone being the most employed chemotherapy protocol (n = 8). The median overall survival for the cohort was 394 days (95% CI 318–470 days) and median progression-free survival was 144 days (95% CI 45–243 days). Among the hematologic variables evaluated, leukocytosis emerged as a significant negative prognostic factor for overall survival (42 vs 415 days; p = 0.012), while neutrophilia was significantly associated with shorter progression-free survival (51 vs 554 days; p = 0.029). No significant differences in survival were detected based on treatment modality or chemotherapy protocol, although the small sample size limits the interpretation of subgroup analyses. These findings suggest that readily available hematologic parameters may serve as useful prognostic indicators in cats with high-grade gastrointestinal lymphoma and that lomustine based protocols represent a frequently used alternative to traditional multi-agent chemotherapy in clinical practice. Larger prospective studies are warranted to validate these observations.

Introduction

Cancer accounts for approximately 35% of deaths in cats, with gastrointestinal (GI) lymphoma being the most common neoplasm of the digestive tract (Kent et al., 2022; Szafron et al., 2026). Feline gastrointestinal lymphoma exhibits considerable heterogeneity in its biological behavior, clinical presentation and therapeutic response.

In general, feline lymphoma is classified according to anatomical location (gastrointestinal, mediastinal, multicentric and extranodal forms), histology grade (low, intermediate or high), cell size (small or large) and immunophenotype (T or B- cell) (Paulin et al., 2018; Lin et al., 2021). In veterinary medicine, the lymphoma classification model proposed by Moore et al. (2012) remains one of the most widely used. This model categorizes GI lymphomas as transmural (high-grade T-cell/EATL type I) or mucosal (low-grade/EATL type II) (P. F. Moore et al., 2012; Alaggio et al., 2022; Szafron et al., 2026). Large Granular Lymphocytic Lymphoma (LGLL) is the least common, but it is associated with the most aggressive and rapidly progressing form of the disease (Szafron et al., 2026).

Although low-grade intestinal lymphoma is the most common presentation, intermediate- to high-grade gastrointestinal lymphoma accounts for approximately 20% of cases and represents a clinically important subgroup because of its aggressive behavior, rapid progression and poorer prognosis (Vail et

al., 2020). Clinical signs are often non-specific and include vomiting, diarrhea, anorexia and weight loss. Compared with low-grade intestinal lymphoma, high-grade disease is more frequently associated with acute clinical deterioration, focal intestinal masses, transmural intestinal involvement and marked abdominal lymphadenopathy (A. S. Moore & Frimberger, 2024; Szafron et al., 2026).

Histopathology remains the reference standard for diagnosis and classification; however, in cases of high-grade lymphoma, cytology of intestinal masses or enlarged lymph nodes may provide a reliable diagnosis (Marsilio et al., 2023; Szafron et al., 2026). Common ultrasonographic findings in cats with GIL include gastrointestinal wall thickening, loss or alteration of normal wall layering and enlargement of mesenteric and jejunal lymph nodes (Freiche et al., 2021).

The recommended treatments for feline high-grade gastrointestinal lymphoma include CHOP (cyclophosphamide, doxorubicin, vincristine and prednisolone) and COP (cyclophosphamide, vincristine and prednisolone) chemotherapy protocols. Additional treatment options, such as abdominal radiotherapy, have also been described both as primary treatment and as rescue therapy for refractory cases (Williams et al., 2010; Parshley et al., 2011; Vail et al., 2020; Gieger et al., 2021). A multicentric retrospective study published in 2024, involving 57 cases with intermediate-to high-grade gastrointestinal lymphoma (I/HG) or LGLL reported an overall response rate of 42% to CHOP and COP based protocols with a median progression-free survival (PFS) of 148 days (Bernardo Marques et al., 2024).

Lomustine has been used both as rescue therapy, where its administration was associated with longer survival times (Bernardo Marques et al., 2024), and as first-line agent, with reported response rates of 35.8% and a median PFS of 51 days (Kim et al., 2026). Nevertheless, information regarding the treatment of feline intermediate- to high-grade gastrointestinal lymphoma remains limited, and an optimal therapeutic approach has yet to be established (Vail et al., 2020; A. S. Moore & Frimberger, 2024). Several treatment modalities have been described, including COP- and CHOP-based chemotherapy, VAPC protocols (vincristine, L-asparaginase, prednisolone, cyclophosphamide), lomustine-based chemotherapy, abdominal radiotherapy, and multimodal approaches combining surgical resection of discrete gastrointestinal masses with adjuvant chemotherapy (Gouldin et al., 2017; Gieger et al., 2021; Bernardo Marques et al., 2024; Larsen et al., 2024; A. S. Moore & Frimberger, 2024).

Reported outcomes remain variable, with median progression-free survival typically ranging from 2 to 6 months and median overall survival ranging from approximately 3 to 14 months for I/HG lymphoma (Mahony et al., 1995; Gouldin et al., 2017; Kwak et al., 2021; Bernardo Marques et al., 2024; Larsen et al., 2024; A. S. Moore & Frimberger, 2024). Despite recent studies, information on feline high-grade gastrointestinal lymphoma remains limited, particularly regarding real-world treatment choices and prognostic factors. Therefore, the aim of this retrospective study was to describe the clinical features, diagnostic findings, treatment patterns and potential prognostic factors in cats with high-grade gastrointestinal lymphoma treated at two veterinary hospitals between 2018 and 2026.

Material and Methods

Case Selection

Medical records of cats diagnosed with gastrointestinal lymphoma at two veterinary hospitals between 2018 and 2026 were retrospectively reviewed. To be included, cats had to have a confirmed diagnosis of high-grade gastrointestinal lymphoma of the gastrointestinal tract, with or without regional lymph node involvement, based on cytology and/or histopathology. For cases diagnosed by cytology alone, inclusion required a cytological description compatible with high-grade lymphoma by a pathologist, namely a monomorphic population of intermediate to large atypical lymphoid cells – an approach consistent with published criteria for the cytological diagnosis of feline gastrointestinal lymphoma (Finotello et al., 2018). Gastrointestinal involvement was confirmed by abdominal ultrasonography in all cases, based on the presence of intestinal wall thickening, loss of normal wall layering and/or mesenteric lymphadenopathy. Cats were excluded if they had low-grade gastrointestinal lymphoma, large granular lymphocytic lymphoma, if they had evidence of lymphoma in any location other than the gastrointestinal tract or incomplete medical records. Staging procedures included a complete blood count, serum biochemistry and abdominal ultrasound in all cats; thoracic radiographs were performed at the clinician's discretion.

Data collected included age and body weight at diagnosis, sex, breed, FIV/FeLV status, previous treatments, and vaccination and deworming history. Physical examination findings and laboratory data, including hematological and serum biochemical parameters (hepatic, renal, and protein profiles), were retrieved from the medical records. Physical examinations findings, hematology and biochemistry such as hepatic, renal and proteins parameters were retrieved from the data records.

The recorded diagnostic data consisted of the date of diagnosis, ultrasonography, cytology results, biopsies, PARR (PCR for Antigen Receptor Rearrangements) tests when available, immunohistochemistry and the definitive diagnosis. The cats were treated with surgery and/or chemotherapy. Whenever sufficient clinical and imaging information was available, treatment response was retrospectively categorized according to the criteria defined by the Veterinary Cooperative Oncology Group (VCOG) (Nguyen et al., 2015):

- Complete Remission (CR) : the disappearance of all detectable target lesions on clinical examination or diagnostic imaging and the resolution of clinical signs attributable to the tumor.
- Partial Remission (PR): at least 30% decrease in the sum of the diameters of target lesions, taking as reference the baseline sum, with no evidence of new lesions.
- Stable Disease (SD): a decrease of less than 30% or an increase of less than 20% in the sum of the diameters of target lesions, taking as reference the smallest sum of diameters recorded since the start of treatment, and with no new lesions
- Progressive Disease (PD): the appearance of one or more new lesions, or at least a 20% increase in the sum of diameters of target lesions (with an absolute increase of 5mm) compared with the

smallest sum recorded since treatment initiation.

Thus, progression-free survival (PFS) was defined as the interval from start of treatment to the date of progressive disease or death. Disease progression was assessed based on clinical records, diagnostic imaging findings, and both clinical and imaging follow-up evaluations. Overall survival (OS) was defined as the interval from start of treatment to death from any cause. Animals still alive at the end of the study were censored. Their survival time is calculated as the interval from start of treatment to the end date of the study (Nguyen et al., 2015; Bernardo Marques et al., 2024).

Statistical analysis

The following data were collected using the electronic medical record system of the two hospitals, formatted in Microsoft Excel and then analyzed using Statistical Package for the Social Sciences (SPSS) software, version 29.0. Categorical variables were presented as absolute and relative frequencies, while numerical variables were expressed as mean± standard deviation, median and range. Survival curves were generated using the Kaplan-Meier method, both survival rates and progression-free survival were compared using the log-rank test. A p-value < 0.05 was considered statistically significant. Cats that were alive at the end of the study or lost to follow-up were censored at the last recorded contact.

Results

Of the 39 cats initially screened in the study, 18 cats met all the inclusion criteria. Four cats were excluded because they had lymphoma affecting areas other than the gastrointestinal tract and lymph nodes, seven cats were excluded because of incomplete medical records and ten cats with low-grade and large granular gastrointestinal lymphoma were excluded. The study group had an age of 9.1 ± 2.8 years (with the youngest patient aged 4 and the oldest 14). Of the 18 cats, 8 were spayed females, 10 were neutered males and no intact males or females were recorded in this study. The average weight of the group was 4.8 kg ± 1.4 kg (ranging from 2.3 kg to 6.9 kg). The breeds included were European Domestic cat (17/18) and Siamese (1/18). 12 cats (66.7%) were tested for FIV and FeLV thus 1 cat was FIV-positive. No FeLV-positive cats were identified. Regarding vaccinations status, 11 cats (61.1%) were up to date with their vaccination schedule, 3 cats were not vaccinated (16.7%), and 4 cats (22.2%) did not provide any information on this category.

Vomiting was the most common clinical sign (12/18; 66.7%) in this cohort, followed by anorexia (9/18; 50.0%), weight loss (9/18; 50.0%), lethargy (5/18; 27.8%), diarrhea (4/18; 22.2%), palpable abdominal mass (2/18; 11.1%), jaundice (5.6%) and hematochezia (1/18; 5.6%).

Among cats with complete blood counts, abnormalities are summarized in Table 1. The most frequent alterations were neutrophilia (7/18; 38.9%), anemia (4/18; 22.2%) and leukocytosis (5/18; 27.8%). The most frequent alterations in biochemical analysis were azotemia (n = 6) and hypoalbuminemia (n = 4) (Table 1). Among the clinical variables evaluated, leukocytosis and neutrophilia were significantly associated with survival. Leukocytosis at diagnosis was significantly associated with shorter OS (log-

rank p = 0.012; Fig. 1A). Similarly, neutrophilia was significantly associated with shorter PFS (log-rank p = 0.029; Fig. 1B). Given the small group sizes, these results should be interpreted with caution.

Figure 1

A

Overall survival according to leukocyte counts at diagnosis in cats with high-grade gastrointestinal lymphoma. Cats with leukocytosis (n = 5) had a significantly shorter median overall survival (42 days, 95% CI 26–58 days) compared to those with normal or decreased leukocyte count (n = 12; 415 days, 95% CI 113–717 days), log-rank p = 0.012.

B

Overall survival according to neutrophil counts at diagnosis in cats with high-grade gastrointestinal lymphoma. No significant overall survival difference between neutrophilia group and normal or decreased neutrophil group (log-rank p = 0.153)

C

Progression-Free Survival according to leukocyte count at diagnosis in cats with high-grade GI lymphoma. No significant PFS difference between leukocytosis group and normal or decreased leukocyte group (log-rank p = 0.071)

D

Progression-Free Survival according to neutrophil count at diagnosis in cats with high-grade GI lymphoma. Cats with neutrophilia (n = 7; median PFS = 51 days, 95% CI 24–78 days, red line) had significantly shorter PFS than cats without neutrophilia (n = 10; median PFS 554 days, 95% CI 0–1412; log-rank p = 0.029, blue line). Tick marks indicate censored observations.

Table 1
Hematologic and serum biochemistry abnormalities in cats with I/HG alimentary lymphoma

	Reference Interval	Available (n)	Increased (n)	Decreased (n)	Normal (n)	Missing (n)
Hematology						
Hematocrit	(26–49) %	17	0	4	13	1
Leukocyte	(5.5–19.5) 10^9/l		5	1	11	
Neutrophils	(2.320–12.580) 10^9l		7	0	10	
Platelets	(100–518) 10^9/l		1	2	14	
Biochemistry						
Albumin	(2.3–3.5) g/dl	13	1	4	8	5
Total Protein	(5.7–7.8) g/dl	14	1	3	10	4
Globulin	(2.7–5.2) g/dl	10	0	0	10	8
ALT	(22–84) U/l	13	2	2	9	5
ALP	(9–53) U/L	13	2	0	11	5
BUN	(17.6–32.8) mg/dl	15	6	1	8	3
Creatinine	(0.80–1.80) mg/dl	13	1	0	12	5
T4	(0.9–3.7) µg/dl	2	0	0	2	16
Calcium	(8.8–11.9) mg/dl	5	1	2	2	13
Glucose	(71–148) mg/dl	14	2	0	12	4

Legend: n = number of cats; ALT = alanine aminotransferase; ALP = alkaline phosphatase; BUN = Blood Urea Nitrogen; T4 = total thyroxine

Abdominal ultrasonography was performed in all the cats. Diagnostic sampling included cytology alone (6/18; 33.3%), biopsy alone (8/18; 44.4%), or both cytology and biopsy (4/18; 22.2%). Immunohistochemistry was performed on biopsies from two cats and showed positive results for *CD3* (*Cluster of Differentiation 3*). No PARR analysis was performed in this study.

Among the 18 cats, 3 underwent surgery alone, 8 received chemotherapy alone and 7 underwent a combination of surgery and chemotherapy (Table 2). The overall response rate (CR + PR) was 66.7% for surgery alone, 62.5% for chemotherapy alone and 100% for combination therapy. A total of 15 cats received chemotherapy, distributed across four different treatment protocols (Table 2). The most frequently used protocol was the combination of lomustine and prednisolone (n = 8/15), followed by CHOP (n = 4/15), chlorambucil and prednisolone (n = 2/15) and COP (n = 1). Among the 8 cats treated with lomustine + prednisolone, 5 achieved CR, 1 achieved PR, 1 had progressive disease and 1 was lost to follow-up. Among the 2 cats treated with chlorambucil and prednisolone, 1 achieved CR and 1 achieved PR. With the CHOP protocol, 1 cat achieved CR, 2 achieved PR and one cat had progressive disease. One cat treated with COP achieved PR.

Table 2
Protocol treatments in cats with high-grade gastrointestinal lymphoma and their response.

	CR (n)	PR (n)	SD (n)	PD (n)	Lost follow-up (n)	Total (n)
Type of treatment						
Surgery	2				1	3
Chemotherapy	4	1		2	1	8
Surgery + Chemotherapy	3	4				7
Total cats received treatment (n)						18
Type of chemotherapy						
CHOP	1	2		1		4
COP		1				1
Chlorambucil + Prednisolone	1	1				2
Lomustine + Prednisolone	5	1		1	1	8
Total cats received chemotherapy (n)						15

Kaplan-Meier analysis was performed to estimate overall survival (OS) and PFS for the 18 cats with high-grade GI lymphoma. The median OS for the cohort was 394 days (95% CI 318–470 days) and the median PFS was 144 days (95% CI 45–243 days). No significant differences in OS were observed according to surgical treatment, administration of chemotherapy, or chemotherapy protocol (log-rank test, $p > 0.05$ for all comparisons; Table 3). Among cats receiving chemotherapy, the median OS was 347 days for CHOP/COP, 643 days for chlorambucil and prednisolone and 346 days for lomustine and prednisolone. Despite these numerical differences, no statistically significant differences in survival were detected among the chemotherapy protocols evaluated (log-rank test, $p = 0.133$; Table 3).

Table 3
Survival analysis for high-grade GI lymphoma in 18 cats who underwent surgery or chemotherapy

Variable	Group	n	Death	Median OS (days)	95% CI for median	Mean OS (days)	Log-rank p
Surgery	No	8	4	347	0-771	515	0.929
	Yes	10	7	394	276–512	423	
Chemotherapy	No	3	1	922	n/c	922	0.116
	Yes	15	10	347	275–419	399	
CHOP/COP		5	2	347	n/c	230	0.133
Lomustine/Prednisolone		8	3	346	41-1041	305	
Chlorambucil/Prednisolone		2	2	643	318–470	634	
n/c = not calculated							

Discussion

The clinicopathological profile of the cats included in the present study was broadly consistent with previous reports on feline high-grade GI lymphoma. The average age at diagnosis was 9.1 years, aligning with the previously reported age range of 9.5–10 years (Kwak et al., 2021; A. S. Moore & Frimberger, 2024). Neutered males comprised 55% of the cohort, similar to the 53–57% described in the literature (Bernardo Marques et al., 2024; A. S. Moore & Frimberger, 2024). European Domestic Shorthair cats were the predominant breed, reflecting the distribution reported in earlier studies and likely representing the breed demographics of the general feline population (Larsen et al., 2024). Mean body weight (4.8 kg) was slightly higher than the 3.9–4.5 kg reported elsewhere, which may reflect regional differences or small sample size (Kwak et al., 2021; A. S. Moore & Frimberger, 2024). In the present study, only 1 cat of 12 tested cats was FIV-positive, and none tested FeLV-positive. These findings are consistent with the literature, as feline GI lymphoma has the lowest association with FeLV antigen among lymphoma subtypes, detected in only 0–12% of the cases (Barrs & Beatty, 2012; Szafron et al., 2026). The low FeLV prevalence can be correlated to the widespread implementation of vaccination programs, which have significantly reduced retrovirus-associated lymphomas (Paulin et al., 2018). Regarding FIV, despite an increased risk of lymphoid neoplasia in affected cats, the low prevalence in our study is consistent with other European studies (Rolph & Cavanaugh, 2022).

The most common clinical signs in the retrospective study were vomiting (66.7%), anorexia (50.0%), followed by lethargy (27.8%) and diarrhea (22.2%). These findings are broadly consistent with previous reports of high-grade GI lymphoma, where vomiting, anorexia and weight loss are the most frequently reported clinical signs (Barrs & Beatty, 2012; Bernardo Marques et al., 2024; A. S. Moore & Frimberger, 2024). The proportion of cats presenting with diarrhea (22.2%) in our study was lower than the 50–65%

described in low-grade GI lymphoma (Paulin et al., 2018) but similar to the 22% reported in a study of 57 cats with high-grade and large granular lymphocyte GI lymphoma (Bernardo Marques et al., 2024). This may reflect the pronounced vomiting and obstructive clinical presentation in high-grade form, where diarrhea is a less dominant feature (Bernardo Marques et al., 2024). Palpable abdominal mass was detected in only 11.1% of cats in our study, which is lower than the majority of cats with high-grade disease described in the literature (Barrs & Beatty, 2012; A. S. Moore & Frimberger, 2024). The low frequency of palpable abdominal masses observed in this cohort indicates that the absence of this finding does not rule out high-grade gastrointestinal lymphoma, particularly in cats presenting with compatible gastrointestinal signs and ultrasonographic abnormalities. Laboratory abnormalities in this study included neutrophilia (38.9%), anemia (22.2%), and leukocytosis (27.8%). Anemia and leukocytosis are well-recognized findings in GI lymphoma (Barrs & Beatty, 2012; Vail et al., 2020), with frequencies of 48.8% and 51.2% reported in Japanese study of 41 cats with high-grade GI lymphoma (Inazumi et al., 2024). The lower prevalence in our study may reflect earlier diagnosis or a smaller proportion of cats with chronic GI blood loss. Notably, leukocytosis and neutrophilia emerged as a significant negative prognostic factor in our study. Cats with leukocytosis at diagnosis had a median OS of only 42 days compared to 415 days in cats with normal leukocyte counts (log-rank p = 0.012). Similarly, cats with neutrophilia had a significantly shorter median PFS of 51 days vs 554 days in cats without neutrophilia (log-rank p = 0.029). The neutrophil -to-lymphocyte ratio (NLR) has been established as an independent prognostic marker in feline neoplasia. Petrucci et al (2021) demonstrated that an elevated NLR was independently associated with shorter PFS in cats with mammary carcinomas, while Naito et al (2021) confirmed high NLR as an independent predictor of poor outcome in feline malignant mammary tumors (Naito et al., 2021; Petrucci et al., 2021). In human lymphoma, leukocytosis and elevated NLR are well-established negative prognostic factors (Cellini et al., 2024). In addition, Moore and Frimberger (2024) demonstrated that the lymphocyte:monocyte ratio was a significant independent predictor of PFS in 55 cats with alimentary lymphoma, further supporting the role of leukocyte ratios as prognostic tools in feline GI lymphoma (A. S. Moore & Frimberger, 2024). Our findings may suggest that neutrophilia and leukocytosis are associated with a more aggressive disease phenotype, although confirmation in larger cohort is required (Vail et al., 2020). These readily available hematologic parameters may therefore represent useful prognostic indicators in cats with high-grade GI lymphoma. However, given the small number of cats in both the leukocytosis (n = 5) and neutrophilia (n = 7) groups, these results should be interpreted with caution.

All 18 cats underwent abdominal ultrasonography which is consistent with the standard of care reported in larger study. Moore and Frimberger (2024) performed baseline abdominal ultrasonography in all 55 and Bernardo Marques et al (2024) used abdominal imaging in all 57 cats. Ultrasonographic findings in high-grade lymphoma typically include transmural intestinal thickening, loss of normal wall layering and mesenteric lymphadenopathy (Gieger et al.,2021). Regarding diagnostic sampling, biopsy alone was the most common method (44.4%), followed by cytology (33.3%) and both methods in 22.3% of cases. This distribution is similar to the 55 cats study where diagnosis was histopathology in 58% and cytologic in 42% of cases (A. S. Moore & Frimberger, 2024). It is important to note that for high-grade GI lymphoma, a

combination of abdominal ultrasonography and cytology of accessible mass lesions or enlarged lymph nodes is often considered sufficient for diagnosis (Paulin et al., 2018). In a study of 28 cats with high-grade lymphoma, cytology alone was performed in 27 cats, further illustrating that cytologic diagnosis is commonly used and may be considered sufficient in many cases when supported by compatible imaging findings and cytomorphology (Kim et al., 2026).

In the present study, 15 of 18 cats received chemotherapy and 10 underwent surgery. Among the 15 cats treated, the most used protocol as first-line therapy was lomustine and prednisolone (n = 8), followed by CHOP (n = 4), chlorambucil and prednisolone (n = 2), and COP (n = 1) (Table 3). This distribution is notable because the current standard of care for first-line therapy of high-grade GI lymphoma in cats is multi-agent chemotherapy based on CHOP or COP (Vail et al., 2020; Szafron et al., 2026). Lomustine, an oral agent, has traditionally been reserved for rescue therapy in cats with relapsed or refractory lymphoma, rather than as a first-line agent (Smallwood et al., 2021; Bernardo Marques et al., 2024). In the multicentric study by Marques et al (2024) involving 57 cats with high-grade lymphoma treated with CHOP or COP, lomustine was used as rescue therapy in 33% of cases and was associated with significantly longer survival in the group that received it. The median OS of 394 days observed in this cohort is notably longer than several prior reports of feline high-grade GI lymphoma. Bernardo Marques et al. reported a median OS of only 131 days in 57 cats treated with COP- or CHOP based protocols, while Inazumi et al. documented a median OS of 150 days in 43 cats receiving L-asparaginase as first-line therapy (Bernardo Marques et al., 2024; Inazumi et al., 2024). Gieger et al. described a median of 101 days with lomustine and abdominal radiation and Tidd et al. reported a median OS of 96 days for all cats undergoing surgical mass resection (Tidd et al., 2019; Gieger et al.,2021). Our result is more comparable to the 412-days median OS reported by Pui Yung Anna et al. in 41 cats treated with COVP protocol, although the GI subset in that study had a median OS of only 203 days (Pui Yung Anna et al., 2025). Several factors may have contributed to the relatively long OS observed in this cohort, although the study design does not allow their individual impact to be determined. Although surgery was not associated with a significantly longer overall survival in the present study, this result should be interpreted with caution. In cats with high-grade gastrointestinal lymphoma, surgery is usually not considered a curative treatment by itself, but it may have an important role in selected cases, particularly when disease is localized and associated with an intestinal mass, obstruction, perforation risk or the need for diagnostic confirmation (Crouse et al., 2018). Previous studies have reported meaningful survival times in cats treated with combined surgery and chemotherapy, with a median survival of 417 days after surgical resection followed by adjuvant CHOP-based chemotherapy in one study (Gouldin et al., 2017; Tidd et al., 2019), suggesting that multimodal treatment may be beneficial in carefully selected patients. This is further supported by a recent study of cats with colorectal intermediate or high-grade lymphoma, in which surgical resection alone or combined with medical management was associated with prolonged survival (Holenova et al., 2025). In the present cohort, cats treated with surgery and chemotherapy did not show a clear survival advantage over cats treated with chemotherapy alone. However, the small number of cats, the retrospective design and the lack of detailed stratification according to tumor distribution prevent firm conclusions regarding the impact of surgery on outcome. Previous studies have

reported median overall survival times ranging from 77 to 280 days with chemotherapy alone (Mahony et al., 1995; H. Zwahlen, 1998) and to up 417 days in cats receiving combined surgery and adjuvant chemotherapy (Gouldin et al., 2017). Two studies have specifically evaluated lomustine and prednisolone as a first-line treatment for high-grade GI lymphoma in cats, reporting a response rates of 50% (Rau & Burgess, 2017) and a median PFS of 51 days (Kim et al., 2026). In the present study, lomustine and prednisolone were the most frequently used first-line protocol, despite CHOP- and COP-based protocols being more commonly recommended in the literature for high-grade gastrointestinal lymphoma (Szafron et al., 2026; Vail et al., 2020). This treatment pattern differs from that reported in most published studies and likely reflect clinician and owner preferences for an oral, well-tolerated regimen that minimizes hospital visits, a consideration that has also been acknowledged in the literature (Kim et al., 2026).

This study has several limitations. Its retrospective design resulted in incomplete clinical information and non-standardized diagnostic, staging and treatment protocols. The sample size was small, which limited statistical power and prevented multivariable analysis. Treatment allocation was not randomized and was influenced by clinician recommendation, owner decision, patient condition and tumor presentation, introducing selection bias. Response assessment was based on medical records and was not standardized prospectively. In addition, the small number of cats within individual treatment groups limited meaningful comparisons between chemotherapy protocols and may have reduced the ability to detect clinically relevant differences in outcome. Diagnostic confirmation was obtained by either cytology, histopathology, or both, introducing some degree of heterogeneity in case classification. Finally, although data were collected from two institutions, the relatively small cohort may limit the generalizability of the findings.

Declarations

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Competing Interests

The authors have no relevant financial or non-financial interests to disclose

Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Jules Bourrelly, Monica Monteiro and Gonçalo Petrucci. The first draft of the manuscript was written by Jules Bourrelly and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request

Ethics approval

Ethical review and approval were not required for this study because it was a retrospective analysis of anonymized clinical data obtained from pre-existing medical records, with no direct animal procedures or client interactions.

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Figures

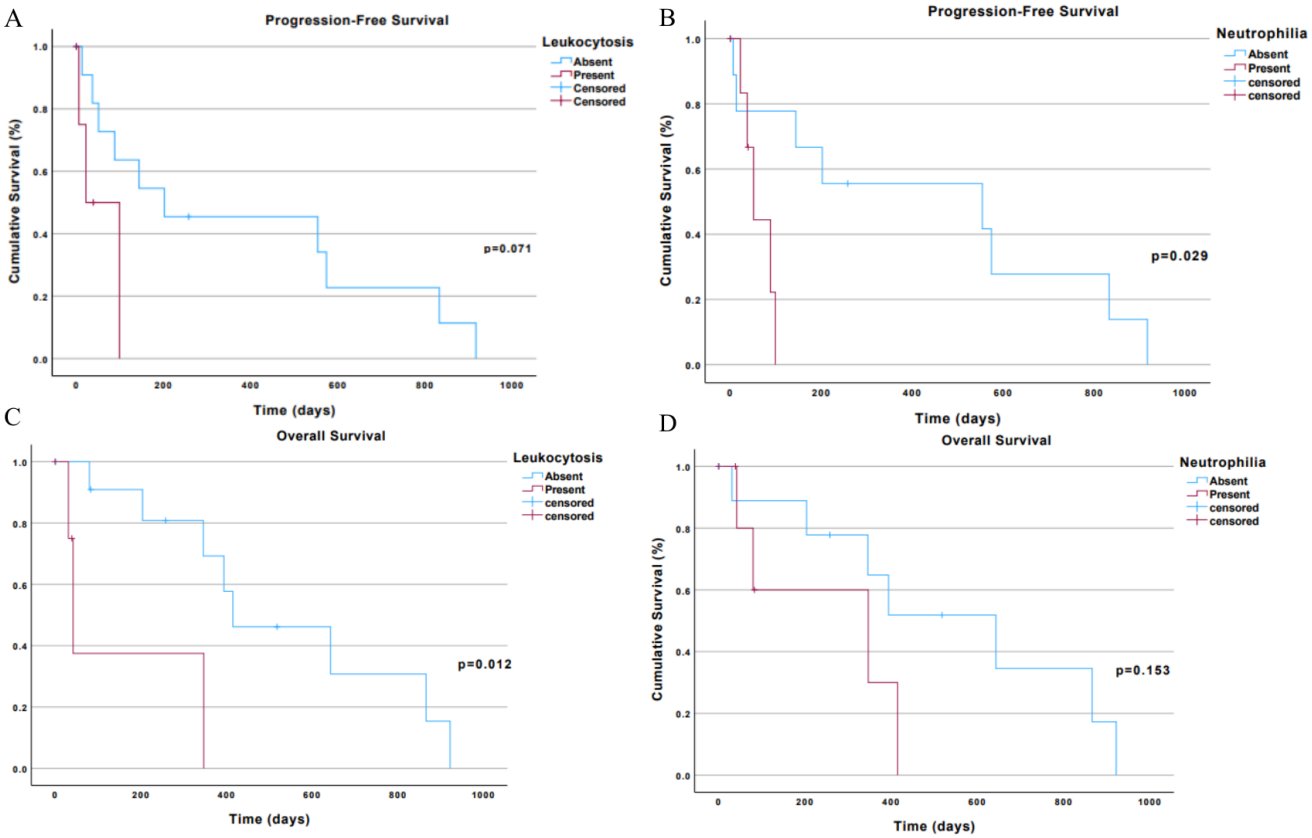


Figure 1

A: Overall survival according to leukocyte counts at diagnosis in cats with high-grade gastrointestinal lymphoma. Cats with leukocytosis (n = 5) had a significantly shorter median overall survival (42 days, 95% CI 26 – 58 days) compared to those with normal or decreased leukocyte count (n = 12; 415 days, 95% CI 113 – 717 days), log-rank p = 0.012.

B: Overall survival according to neutrophil counts at diagnosis in cats with high-grade gastrointestinal lymphoma. No significant overall survival difference between neutrophilia group and normal or decreased neutrophil group (log-rank p = 0.153)

C: Progression-Free Survival according to leukocyte count at diagnosis in cats with high-grade GI lymphoma. No significant PFS difference between leukocytosis group and normal or decreased leukocyte group (log-rank p = 0.071)

D: Progression-Free Survival according to neutrophil count at diagnosis in cats with high-grade GI lymphoma. Cats with neutrophilia (n = 7; median PFS = 51 days , 95% CI 24 – 78 days, red line) had significantly shorter PFS than cats without neutrophilia (n = 10; median PFS 554 days, 95% CI 0 – 1412; log-rank p = 0.029, blue line). Tick marks indicate censored observations.