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A systematic review of hematological prognostic indicators in canine malignant diseases and their application in human oncology

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Abstract

Malignant diseases are the leading causes of death in dogs and have many similarities to human cancers. Blood markers have great potential as noninvasive and readily available prognostic tools, but a systematic review in this area is lacking. This study aims to systematically review hematological prognostic markers in canine malignancies and investigate their application in human oncology. This PRISMA-based systematic review was conducted by searching PubMed, Google Scholar, and Web of Science. In canine lymphoma, NLR (cutoff 3.764), hypoalbuminemia, monocytosis, and leukocytosis were associated with reduced survival. In splenic angiosarcoma, NRR was an independent prognostic factor for disease-free survival (HR=1.837), and PLR was inversely associated with recurrence and death. In canine acute leukemia, normal neutrophil counts were associated with improved survival, and RTK-RAS mutations were found in 71% of cases, similar to humans, but DNMT3A and NPM1 mutations were not seen in dogs. In osteosarcoma and mammary carcinoma, significant molecular similarities were also identified between the two species. These findings have been confirmed in human oncology, and similar blood ratios have been proposed as prognostic markers in corresponding human malignancies. Simple hematological indices, especially the NLR, NRR, and PLR ratios, have high potential as prognostic factors, and the significant molecular similarities with humans make the dog a valuable model for comparative oncology. However, species differences necessitate prospective studies with large sample sizes for validation. A “one health” approach in this area could lead to significant advances in the diagnosis, prognosis, and treatment of cancer in dogs and humans.

Keywords: Hematologic Tests, Biomarkers, Tumor, Lymphoma, Leukemia, Osteosarcoma.

Introduction

Malignant diseases are among the leading causes of mortality in dogs (1). Their increasing prevalence in this species has attracted the attention of many researchers in comparative oncology (2). Canine lymphoma, one of the most common hematopoietic malignancies, has an incidence of approximately 20 to 100 cases per 100,000 dogs (3)and shows striking similarities to human non-Hodgkin lymphoma (4). These similarities, evident in clinical features, histology, and response to common treatments such as CHOP-based protocols, make the dog a valuable model for studying this type of cancer in humans (5, 6). Similarly, acute myeloid leukemia in dogs, despite its high heterogeneity (7, 8), shares clinical and biological features with its human counterpart and can serve as a model for investigating molecular mechanisms and developing targeted therapies (6, 9). Hemangiosarcoma (angiosarcoma), a rapidly growing malignant vascular tumor with early metastasis (10), also occurs in dogs and, due to its striking similarities to human angiosarcoma, is considered a model for comparative oncology research (11). Splenic hemangiosarcoma is a highly aggressive malignancy in dogs, characterized by rapid growth, local invasion, and early metastasis via the hematogenous route or by intraperitoneal infiltration of neoplastic cells after splenic rupture. Clinically, splenic hemangiosarcoma is often asymptomatic until the acute presentation of splenic rupture and hemoperitoneum, which severely limits opportunities for early diagnosis and timely therapeutic intervention, emphasizing the importance of identifying reliable blood biomarkers for early diagnosis and prognosis of this aggressive disease (12).

Early diagnosis, accurate prognosis, and monitoring of response to treatment are key components of successful management of malignant diseases (13). Surgical splenectomy is the cornerstone of initial treatment in dogs with splenic hemangiosarcoma. It is performed primarily to control life-threatening hemorrhage from splenic rupture and hemoperitoneum and to remove macroscopic masses (Figure 1). However, surgery alone is palliative and has a limited impact on long-term survival because micrometastatic disease is present in most cases at the time of diagnosis. Given that micrometastatic disease is usually present at the time of diagnosis, the clinical management of this tumor faces significant challenges, and despite therapeutic advances, including advances in diagnostic imaging, surgical techniques, and the use of adjuvant chemotherapy, the overall prognosis remains poor. This highlights the importance of finding reliable blood biomarkers for early diagnosis, more accurate prognosis, and monitoring response to treatment in this aggressive disease (12). In this regard, blood-derived biomarkers have a special place due to their noninvasive nature, relatively low cost, and high reproducibility (14). Despite significant advances in human oncology (15-17), finding an ideal biomarker that can be used simultaneously for diagnosis, prognosis, and prediction of treatment response in dogs remains a major challenge in veterinary medicine (18). Problems such as the lack of sufficient specificity in many protein biomarkers and the high variability of responses among individuals are major obstacles in this direction. However, new hope is emerging in the field of “liquid biopsy,” which, by examining various blood components, including circulating tumor cells, free nucleic acids, and exosomes, could revolutionize diagnostic and prognostic approaches in the near future (19).

One of the most important areas of study in blood markers is the evaluation of blood cell disorders and hematological findings (20). For example, inflammatory markers such as the acute-phase protein CRP in dogs with lymphoma are not only associated with disease stage and treatment response. Still, they can also serve as an indicator of disease recurrence (21). The lymphocyte-monocyte ratio (LMR) and the assessment of malignant cell infiltration into the bone marrow and peripheral blood have also been proposed as important prognostic factors in these patients (22).

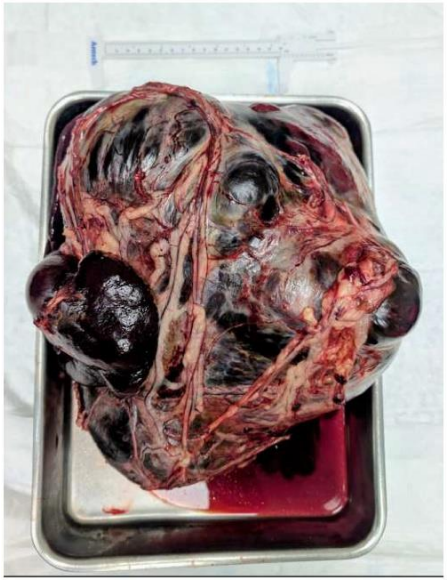

Figure 1. Postoperative general view of a canine splenic hemangiosarcoma with extensive hematoma. The spleen is markedly enlarged and deformed by a very large, multilobular splenic mass with extensive hemorrhage. The lesion shows mixed staining, with dark red areas corresponding to blood-filled cavities/hematoma and multifocal areas of hemorrhage and congestion beneath the splenic capsule, reflecting the tumor's fragile, highly vascular nature (Copyright MDPI) (12).

In addition, changes in platelet count (thrombocytosis) and coagulation markers, such as D-dimer, are also associated with an increased risk of thromboembolism. Still, they can also indicate metastasis and disease progression across various malignancies and are associated with reduced survival time in dogs (23). These findings suggest that a comprehensive panel of blood markers can provide a more accurate picture of the patient's clinical status and prognosis (24). As knowledge in molecular oncology expands, newer markers such as circulating microRNAs (miRNAs) and myeloid-derived suppressor cells (MDSCs) have also been proposed as potential biomarkers (25). In dogs with angiosarcoma, increased expression of miRNA-126 and miRNA-214 in the blood has been observed, which is associated with tumorigenesis and angiogenesis and can be used as an indicator for the diagnosis and monitoring of the disease (18, 26). In dogs with lymphoma, increased plasma levels of several miRNAs, including miR-21 (27), miR-155 (27, 28), and miR-222, have been associated with reduced progression-free survival (29). In addition, an increase in the percentage of myeloid-derived suppressor cells (MDSCs) has been observed in the blood of dogs with various advanced tumor types, and these cells play a key role in disease progression by weakening the immune system and facilitating tumor escape from the immune response (30). These findings suggest that the investigation of these novel biomarkers opens new horizons in the clinical management of canine malignancies (31).

The profound molecular and genetic similarities between canine and human malignancies provide a unique opportunity to use dogs as a model in translational studies (32-34). Studies of acute leukemia in dogs have shown that the disease shares genetic mutations with its human counterpart (9, 35)and affects key signaling pathways, such as the tyrosine kinase-RAS (RTK-RAS), reinforcing the dog’s suitability as a model for developing targeted drugs (9). However, there are also differences in mutation profiles between the two species that are important to understand for the appropriate use of

the animal model (36, 37). Similarly, canine lymphoma closely resembles human non-Hodgkin lymphoma (4, 38, 39), and its study could help identify new prognostic biomarkers and evaluate novel therapeutic approaches, such as immunotherapy (4, 40). Therefore, the use of a "One Health" approach in oncology will not only improve the diagnosis and treatment of cancer in dogs but could also lead to significant advances in treating similar cancers in humans (18, 41).
This study aimed to review hematological prognostic markers in canine malignancies systematically and to investigate their application in human oncology.

Methods

This study was conducted as a systematic review in accordance with the PRISMA 2020 statement guidelines. The target population included dogs with hematological malignancies and solid tumors (including lymphoma, angiosarcoma, acute leukemia, osteosarcoma, and mammary carcinoma) as well as human patients with similar malignancies to allow for cross-species comparisons. Exposure variables included hematological prognostic indicators, inflammatory and nutritional markers, and molecular markers. The comparison group included healthy dogs, dogs with non-neoplastic splenic lesions, and human normal data with similar genetic profiles. The outcomes of interest included the association of these indices with overall survival, progression-free survival, disease-free period, response rate, disease recurrence, and tumor progression. A systematic search was conducted in four reliable databases, including PubMed, Scopus, Web of Science, and Google Scholar, with a time frame from January 2019 to December 2025 to capture the most recent findings in this field. The search strategy was designed using a combination of MeSH terms and keywords with the Boolean operators AND and OR; keywords included "blood biomarkers," "prognostic indicators," "canine malignancies," "acute leukemia," "lymphoma," and "comparative oncology." All articles found were imported into EndNote 21, and duplicate articles were first removed automatically and then manually by two independent researchers. The screening process was performed in two stages. In the first stage, the titles and abstracts of all articles were reviewed by two independent researchers, and irrelevant articles, non-English articles, case reports with fewer than 5 patients, and non-systematic reviews were excluded. In the second stage, the full text of the remaining articles was carefully evaluated, and the inclusion and exclusion criteria were applied. Inclusion criteria included original articles with retrospective or prospective designs, systematic reviews, and relevant meta-analyses. These studies associated at least one blood marker with clinical outcome in canine malignancies; compared dogs and humans across species; were published in English; and were published between 2019 and 2025. Exclusion criteria included case reports with fewer than 5 patients, studies lacking extractable quantitative or qualitative data, studies unrelated to blood markers or malignancies, duplicate articles, and preprints. Two independent researchers performed the quality assessment. Data extraction was performed using a standard form in Excel software, and key information, including article characteristics, demographic characteristics, malignancy type, blood markers, clinical outcomes, and interspecies similarities, was extracted from each article. Due to the high heterogeneity of studies in terms of malignancy type, study population, measurement methods, and thresholds, it was not possible to perform a quantitative meta-analysis; therefore, the findings were categorized and reported as a narrative review based on malignancy type, and for markers that were replicated in at least two independent studies, a narrative summary of the direction and strength of association was provided. Due to the impossibility of conducting a meta-analysis, a statistical assessment of publication bias was not performed; however, to reduce publication bias, a search was conducted across four databases. In this study, all ethical principles in citing and reporting data were observed.

Results

Of the 480 articles identified across the four databases, 120 duplicates were removed, leaving 360 for title and abstract screening. At this stage, 270 articles were excluded. Of the remaining 90 articles after full-text review, 10 were excluded for the reasons mentioned. Finally, 80 articles were identified as eligible for inclusion in the systematic review (Figure 2).

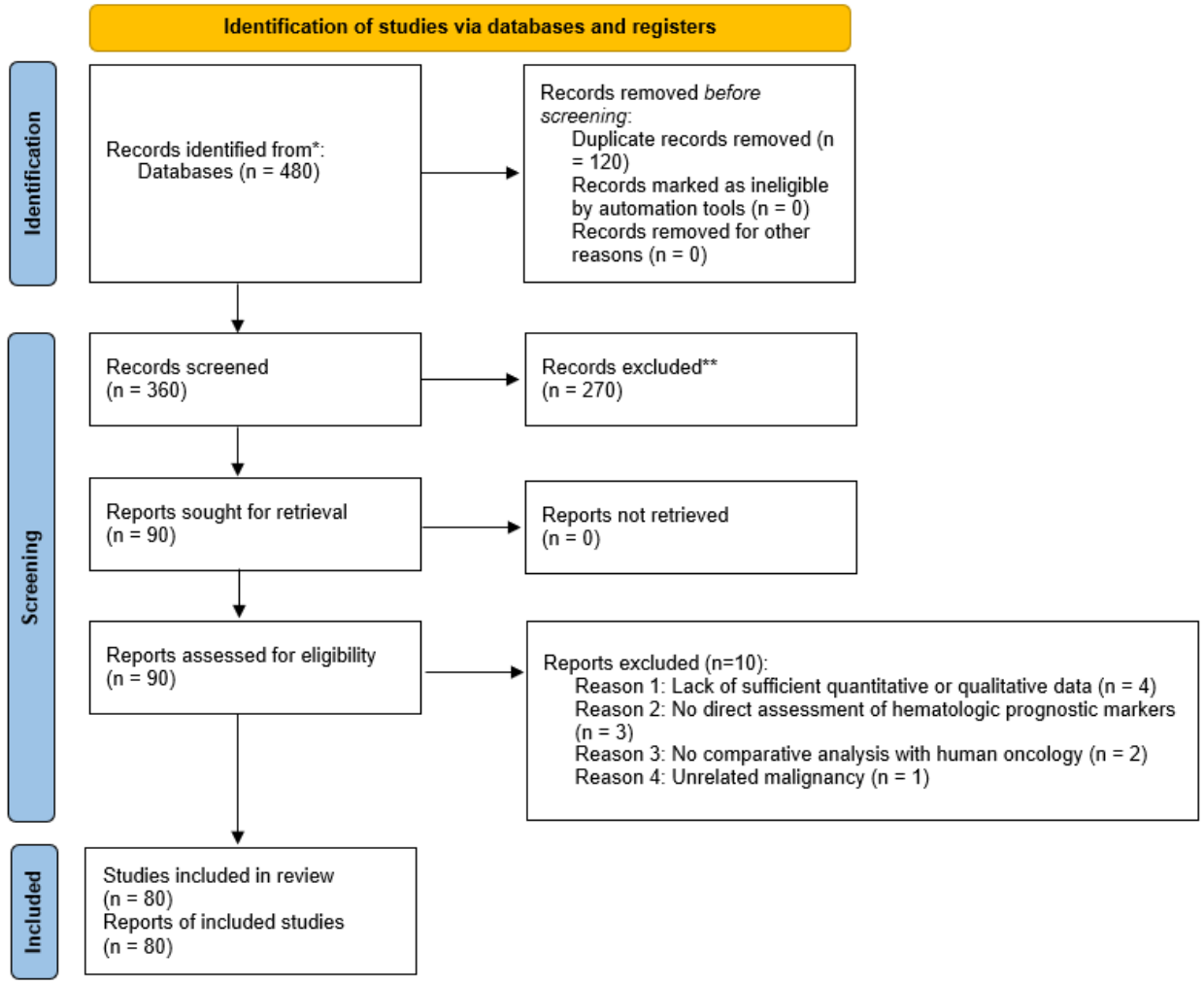

Figure 2. PRISMA 2020 flowchart: steps for screening and selecting articles for a systematic review.

Findings on hematological markers in canine lymphoma and their similarities to human lymphoma

Lymphoma, one of the most common hematopoietic malignancies in dogs, has an incidence of approximately 20 to 100 cases per 100,000 dogs (3) and shares significant clinical, histological, and therapeutic response similarities with human non-Hodgkin lymphoma (4, 5, 42). Several studies have investigated the prognostic value of hematological markers in this disease, and their results are important not only for veterinary oncology but also for a better understanding of the pathogenic mechanisms and prognosis in human lymphoma (43).

In a retrospective study of 41 dogs with high-grade multicentric lymphoma treated with COP or L-COP protocols, pre-treatment monocytosis

was significantly associated with a shorter median survival time in the COP group (44). This finding aligns with studies in human lymphoma patients, in which increased peripheral blood monocytes have been suggested as a negative prognostic factor and as indicative of myeloid activation in response to the tumor (45, 46). Hypoalbuminemia (serum albumin level <2.5 mg/dL) was identified as a negative prognostic marker in dogs treated with L-COP, both before treatment and 4 weeks after treatment (47). This finding has also been confirmed in human oncology, where hypoalbuminemia, an indicator of poor nutritional status, systemic acute phase response, and reduced body reserve capacity, is associated with a worse prognosis in various types of malignancies, including lymphoma (48-50). Leukocytosis at 4 weeks after treatment was also associated with a significant reduction in survival time, suggesting a role for the systemic inflammatory response in determining the fate of the disease (51).

The neutrophil-to-lymphocyte ratio (NLR), one of the most important systemic inflammatory markers in malignancies, has been studied in both species (52). In a study of 35 dogs weighing less than 10 kg with multicentric lymphoma, an increased NLR was associated with a worse prognosis. A cutoff value of 3.764 was established for the NLR, above which the risk of early disease progression and reduced survival was significantly increased (53). These findings are remarkably consistent with the human medical literature, where the NLR has been reported as an independent prognostic biomarker in non-Hodgkin lymphoma and other hematologic malignancies (54). In patients with diffuse large cell lymphoma (DLBCL), an increased pretreatment NLR is associated with reduced overall and progression-free survival (55), and this ratio is used as a simple, inexpensive, and readily available indicator for prognostic assessment. Dogs with clinical stage (substage b) also showed a higher rate of early progression than dogs with stage a, which is consistent with staging systems in human oncology (53).

Other flow cytometry-derived markers have also been proposed as prognostic factors in canine lymphoma. The lymphocyte-to-monocyte ratio (LMR) (56), bone marrow and peripheral blood infiltration by malignant cells, the CD4+/CD8+ ratio, the percentages of small CD5+ and CD8+ cells, CD25+ cells, and FOXP3+ cells have all been associated with prognosis in dogs with B-cell lymphoma. In human oncology, similar markers, including the CD4+/CD8+ ratio and the percentage of regulatory T cells (Treg), have been proposed as prognostic factors in lymphoma and other malignancies. However, higher-quality evidence is needed to definitively validate these markers and their clinical use in either species (22).

Hematologic findings in Canine hemangiosarcoma (Angiosarcoma) and comparison with human sarcomas

Canine splenic hemangiosarcoma is a highly malignant vascular neoplasm and among the most common and clinically important splenic tumors in dogs (12). This tumor, which accounts for approximately two-thirds of all malignant splenic tumors in dogs (57), bears striking similarities to human angiosarcoma, a rare but highly aggressive vascular neoplasm with a very poor prognosis. A recent study of 154 dogs that had undergone splenectomy examined the diagnostic and prognostic value of a complete blood count and its derived ratios, including the neutrophil-to-lymphocyte ratio (NLR), neutrophil-to-erythrocyte ratio (NRR), and platelet-to-lymphocyte ratio (PLR) (58). Results showed that dogs with splenic hemangiosarcoma (63 cases) had significantly higher neutrophil counts, increased NRR, lower platelet counts, and decreased PLR compared with dogs with nonneoplastic splenic lesions. The neutrophil-to-erythrocyte ratio was identified as an independent prognostic factor for disease-free interval (DFI), with a hazard ratio (HR) of 1.837; an increased NRR was associated with a higher risk of relapse and death. In contrast, the neutrophil-to-lymphocyte ratio did not show a significant association with prognosis in this study (58).

These findings are consistent with studies in patients with human angiosarcoma, in which an elevated neutrophil-to-lymphocyte ratio and thrombocytopenia are associated with a worse prognosis and reduced survival (59). However, the relative importance of the neutrophil-to-erythrocyte ratio versus the neutrophil-to-lymphocyte ratio in dogs suggests subtle differences in the systemic inflammatory response between the two species that may contribute to a better understanding of the mechanisms underlying angiosarcoma pathogenesis in both species (11, 58, 60). There are also significant molecular similarities between canine hemangiosarcoma and human angiosarcoma, particularly in the VEGF, PI3K/AKT, and RAS signaling pathways, making the dog a valuable model for studying this rare and aggressive cancer in humans (59).

The results of this study showed that dogs with splenic angiosarcoma (n=63) had significantly higher neutrophil counts (9.7 ± 14 vs. 9.6 ± 12; $p < 0.001$), increased neutrophil-to-erythrocyte ratios (3.7 ± 2.6 vs. 2.7 ± 3.7; $p < 0.001$), lower platelet counts (111 ± 145 vs. 213 ± 270; $p < 0.001$), and decreased PLR (4.160 ± 139 vs. 9.259 ± 278; $p < 0.001$) compared with dogs with non-neoplastic splenic lesions (n=63). These findings are consistent with studies in patients with soft tissue sarcomas and human angiosarcomas, where similar changes in blood cell counts and derived ratios have been reported. In human angiosarcoma, thrombocytopenia and an increased neutrophil-to-lymphocyte ratio are associated with worse prognosis and reduced survival (75-78) (59, 61-63). The neutrophil-to-erythrocyte ratio was identified as an independent prognostic factor for disease-free interval (DFI) with a hazard ratio (HR) of 1.837 (95% CI: 1.147 to 2.942; $p = 0.011$). However, for overall survival (OS), this association was not statistically significant ($p = 0.059$). An increased NRR was associated with a higher risk of relapse ($p < 0.001$) and death ($p = 0.012$), and an inverse relationship between PLR and relapse ($p = 0.015$) and death ($p = 0.033$) was observed. In contrast, NLR did not show a significant association with prognosis in this study, which may be due to differences in the pathogenic mechanisms of angiosarcoma compared with other malignancies (58). In human oncology, NLR has also been proposed as a prognostic biomarker in some sarcomas (64). Still, studies have shown that its importance varies by tumor type and disease stage, and in some malignancies, such as angiosarcoma, other blood ratios, such as PLR and NRR, may have greater prognostic value (65, 66).

Findings on hematological and molecular markers in acute canine leukemia and genetic similarities to human leukemia

Acute leukemias in dogs, despite their high heterogeneity, carry a very poor prognosis, with reported survival measured in weeks or months (35). These malignancies, including myeloid (AML), lymphoid (ALL), acute lineage-ambiguous leukemia (ALAL), and acute lineage-negative leukemia (ALNL) subtypes (67), share significant clinical, biological, and therapeutic similarities with human acute leukemias, making the dog a valuable model for comparative studies (2, 33, 68, 69). In a retrospective study of dogs with acute leukemia, a normal neutrophil count at presentation was found to significantly prolong survival ($p=0.027$) (70). There was also a trend toward decreased survival in dogs with anemia, and the use of cytosine in the chemotherapy regimen resulted in a modest but nonsignificant increase in median survival (71). These findings are consistent with studies in patients with human acute leukemia, where a normal neutrophil count at diagnosis indicates relatively preserved bone marrow function and myelopoietic capacity and is associated with a better prognosis (72).

Despite striking similarities, genetic studies have also shown important differences in the mutation profile of acute leukemia between dogs and humans. For example, while mutations in the DNMT3A and NPM1 genes are common and classic drivers of acute leukemia in humans, these mutations are either rare or absent in dogs. Instead, novel and more specific mutations in genes such as MED12, TPR, and CLIP1 have

been identified in dogs. Additionally, alterations in other signaling pathways, such as Hippo and NOTCH, as well as mutations in genes involved in epigenetic changes (such as KDM5C and EZH2), appear to be more common in canine leukemia. These differences indicate that although the dog is a valuable model for studying leukemia, a detailed understanding of these species differences is essential for the correct interpretation of results and their application to human therapy. Nevertheless, the frequent presence of mutations in the core RTK-RAS pathway and the similarity of mutation hotspots in the NRAS gene between the two species maintain the high potential of the canine model for studying pathogenic mechanisms and developing novel targeted therapies (9, 35).

Findings in Other Canine Malignancies and Their Application to Human Oncology

Beyond hematologic malignancies, there are significant molecular similarities between canine and human solid tumors, making the dog a valuable model for studying various types of human cancer. In osteosarcoma, the most common malignant bone tumor in both species, a study of differentially expressed genes (DEGs) in canine and human tumor samples identified 86 genes in common: 36 highly expressed, and 50 lowly expressed. Immunohistochemical examination of proteins corresponding to three of the identified genes (ASPN, STK3, BAMBI) in canine osteosarcoma tissues revealed distinct expression patterns across sex and anatomical location, which could deepen our understanding of the mechanisms of progression and metastasis of this cancer in both species (73).

In breast cancer, a leading cause of cancer-related mortality in women, canine mammary carcinoma (CMC) has emerged as a powerful adaptive model. Comprehensive transcriptomic analyses of CMC tissues, normal mammary tissues, and canine mammary carcinoma cell lines have revealed distinct gene expression signatures and enriched oncogenic pathways, highlighting networks associated with chemotherapy resistance, cell adhesion, and tumor progression. MicroRNA sequencing has also identified conserved oncogenic and tumor-suppressor signatures, including miR-206, miR-224, and miR-31, which regulate critical pathways in carcinogenesis. These findings suggest conserved molecular mechanisms between canine and human mammary tumors and expand the range of potential biomarkers with diagnostic and therapeutic value (74).

The proliferation marker thymidine kinase 1 (TK1), studied in human and canine hematological malignancies, has also shown strong comparative value for future research due to the high sequence similarity of the TK1 protein between the two species. TK1, a cell cycle S-phase-specific protein (75, 76), can be used in immunohistochemistry to detect RNA/protein expression in tissue samples and to measure protein/peptide activity or levels in patient serum. This marker, used primarily in human hematological malignancies, has also proven useful in canine malignancies, and findings from the canine model may have high comparative value for human research (77). This highlights the importance of a “One Health” approach in oncology, which will not only improve the diagnosis and treatment of cancer in dogs but could also lead to significant advances in treating similar cancers in humans.

Discussion

The findings of this systematic review provide a comprehensive overview of the potential of hematological markers as prognostic factors in canine malignancies and their application in human oncology. Simple hematological markers derived from complete blood counts, particularly systemic inflammatory ratios such as NLR, NRR, and PLR, obtained from routine, inexpensive hematology data, provide valuable information about the patient's immune status and systemic inflammation, as well as their relationship to tumor progression (58, 59). These findings are consistent with existing knowledge in human oncology, where blood cell-derived ratios have been proposed as prognostic biomarkers across various malignancies, and they indicate the

evolutionary conservation of these responses in mammals.

Neutrophil-to-lymphocyte ratio (NLR): While a study of splenic angiosarcoma did not find a significant association between NLR and prognosis (58), a study of lymphoma in underweight dogs identified this ratio as a strong, independent prognostic marker (53). This discrepancy may reflect differences in tumor type, study population, or study design. In lymphoma, a systemic malignancy with widespread immune involvement, systemic inflammation, and the host immune response play a more prominent role in determining disease outcome. In contrast, splenic angiosarcoma, despite being aggressive, may elicit a less pronounced systemic inflammatory response until advanced stages, or other mechanisms may dominate its prognosis. In human oncology, the prognostic importance of NLR also varies by tumor type and disease stage. In non-Hodgkin lymphoma and certain solid tumors, such as lung and colorectal cancers, NLR is considered an independent prognostic factor, whereas in other malignancies, such as sarcomas, its association with prognosis is less certain (78).

Neutrophil-to-erythrocyte ratio (NRR) and platelet-to-lymphocyte ratio (PLR): A multicenter study of splenic angiosarcoma identified NRR as an independent prognostic factor for disease-free survival. This finding is important because NRR is a composite measure of two major lines of defense, the inflammatory-myeloid response (neutrophils) and oxygen-carrying capacity (erythrocytes). Anemia, a common manifestation of advanced malignancies, is associated with an increased NRR and may indicate advanced disease and increased tumor invasion of the bone marrow (58). Conversely, decreased PLR in dogs with angiosarcoma and its association with a worse prognosis indicate a role for platelets beyond hemostasis. Platelets contribute to tumor angiogenesis by secreting growth factors such as VEGF and PDGF and protect tumor cells from immune responses by forming platelet-tumor aggregates (79). Therefore, thrombocytopenia observed in angiosarcoma and the resulting decrease in PLR may reflect increased platelet consumption in the tumor microenvironment or impaired platelet production due to bone marrow involvement. In human oncology, PLR has been proposed as a prognostic biomarker in various malignancies, including breast, lung, and gastrointestinal cancers, and its decrease is associated with worse prognosis (80).

Molecular markers and genetic similarities: Genetic studies of canine acute leukemia have revealed profound molecular similarities to human leukemia, particularly the high frequency of mutations in the RTK-RAS pathway and the presence of common mutagenic junctions in the NRAS gene. This finding reinforces the importance of the dog as a valuable model for studying human leukemia and for developing drugs targeting the RAS pathway. It suggests that dogs can serve as a spontaneous model with a healthy immune system to evaluate new therapies before entering human trials. However, notable differences remain, including the absence of mutations in DNMT3A and NPM1, which are common in human acute leukemia, and the presence of novel mutations, such as MED12 and TPR, in dogs (9). These differences indicate that although the dog is a suitable model for studying many aspects of leukemia, a thorough understanding of species differences is essential for the correct translation of findings to the human clinic. In addition, genetic and molecular similarities in osteosarcoma and breast cancer between the two species indicate broader evolutionary conservation of carcinogenesis pathways and make the dog a valuable model for studying these solid malignancies.

Novel biomarkers and prospects: Beyond traditional markers, novel biomarkers such as thymidine kinase 1 (TK1) and circulating microRNAs have opened new horizons for the diagnosis and prognosis of malignancies. TK1, a specific marker of the S phase of the cell cycle, has been studied in both human and canine hematological malignancies. The high sequence similarity between the two species makes TK1 a valuable comparative marker for future research.

Circulating microRNAs have also emerged as novel noninvasive biomarkers in both species, and their study in canine mammary carcinoma has revealed conserved signatures that could be used for the early diagnosis and prognosis of human breast cancer (75).

Study limitations and future challenges

Despite the promising findings, this systematic review has several limitations. Most available studies were retrospective, and many had small sample sizes. There is considerable heterogeneity across studies in malignancy type, treatment regimens, and measured parameters, making meta-analysis challenging. The lack of a standardized system for measuring and reporting blood parameters in veterinary studies is a major obstacle to the development of clinically valid biomarkers. Despite these limitations, recent research has shown that a "One Health" approach to oncology, which emphasizes the connections among human, animal, and environmental health, can accelerate scientific advances and lead to more effective treatments for both humans and animals.

Conclusion

This systematic review demonstrates that simple, inexpensive hematological indices, especially blood ratios such as NLR, NRR, and PLR, as well as inflammatory-nutritional markers such as serum albumin, have strong prognostic value in common canine malignancies, including lymphoma, angiosarcoma, and acute leukemia. These indices, which reflect the complex interplay among the host immune response, systemic inflammation, and tumor progression, can serve as valuable adjuncts in the clinical management of veterinary patients and as a model to better understand prognostic mechanisms in human malignancies. The remarkable molecular similarities between canine and human malignancies, particularly in key signaling pathways such as RTK-RAS in acute leukemia and in the gene expression profiles of osteosarcoma and mammary carcinoma, reinforce the role of the dog as a valuable model for translational and adaptive oncology.

However, species-specific differences in mutation profiles, such as the absence of DNMT3A and NPM1 mutations in canine acute leukemia, underscore the need for careful comparative studies and caution in directly generalizing findings. To definitively confirm these biomarkers and their entry into clinical practice in both species, prospective studies with large sample sizes, standardized designs, and advanced molecular methods, including next-generation sequencing, multiplex flow cytometry, and the examination of circulating microRNAs, are essential. In addition, developing combined panels of hematological and molecular markers can significantly improve prognostic accuracy and move both veterinary and human oncology toward precision medicine. A "One Health" approach in this area will not only help improve the diagnosis and treatment of cancer in dogs, but by providing natural and spontaneous models of the disease, it could also lead to significant advances in the treatment of similar types of cancer in humans, ultimately benefiting the health of both species.

Declarations and statements

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No funding was received to conduct this study.

Conflict of interest

The authors declare no conflicts of interest.

Data availability

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

Ethical approval

All applicable international, national, and/or institutional guidelines for writing a review paper were followed.

Author contribution

Conceptualization: [Sirous Rafiei Asl]; Methodology: [All Authors]; Formal analysis and investigation: [All Authors]; Writing - original draft preparation: [Seyed Mohsen Mousavi Fard]; Writing - review and editing: [All Authors]; Funding acquisition: [Self-funding]; Supervision: [Sirous Rafiei Asl]. All authors have checked and approved the final version of the manuscript for publication in this journal.

Consent to participate

Not applicable

Consent for publication

Not applicable

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Declaration of the use of generative AI

After the content was fully written, an AI-powered tool was used exclusively to review and refine the article's grammar, punctuation, and overall linguistic flow. The AI tool was used strictly as a proofreading and language-refinement assistant and was not employed at any stage to generate content, ideas, or article sections.

Abbreviations

The following abbreviations are used in this manuscript:

Lymphocyte to Monocyte Ratio (LMR)
Neutrophil to Lymphocyte Ratio (NLR)
Neutrophil to Red Blood Cell Ratio (NRR)
Platelet to Lymphocyte Ratio (PLR)

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