

# PERIPHERAL BLOOD CELL RATIOS AS PROGNOSTIC FACTORS IN FELINE ALIMENTARY LYMPHOMA

## A PRELIMINARY STUDY

Joana Fonseca

Faculty of Veterinary Medicine,  
Lusófona University, Lisbon, Portugal  
Superior School of Animal Health,  
Protection and Welfare, Polytechnic  
Institute of Lusofonia, Lisbon, Portugal

Joana Peixoto

Faculty of Veterinary Medicine,  
Lusófona University, Lisbon, Portugal  
Superior School of Animal Health,  
Protection and Welfare, Polytechnic  
Institute of Lusofonia, Lisbon, Portugal

João Martins

Faculty of Veterinary Medicine,  
Lusófona University, Lisbon, Portugal  
Superior School of Animal Health,  
Protection and Welfare, Polytechnic  
Institute of Lusofonia, Lisbon, Portugal

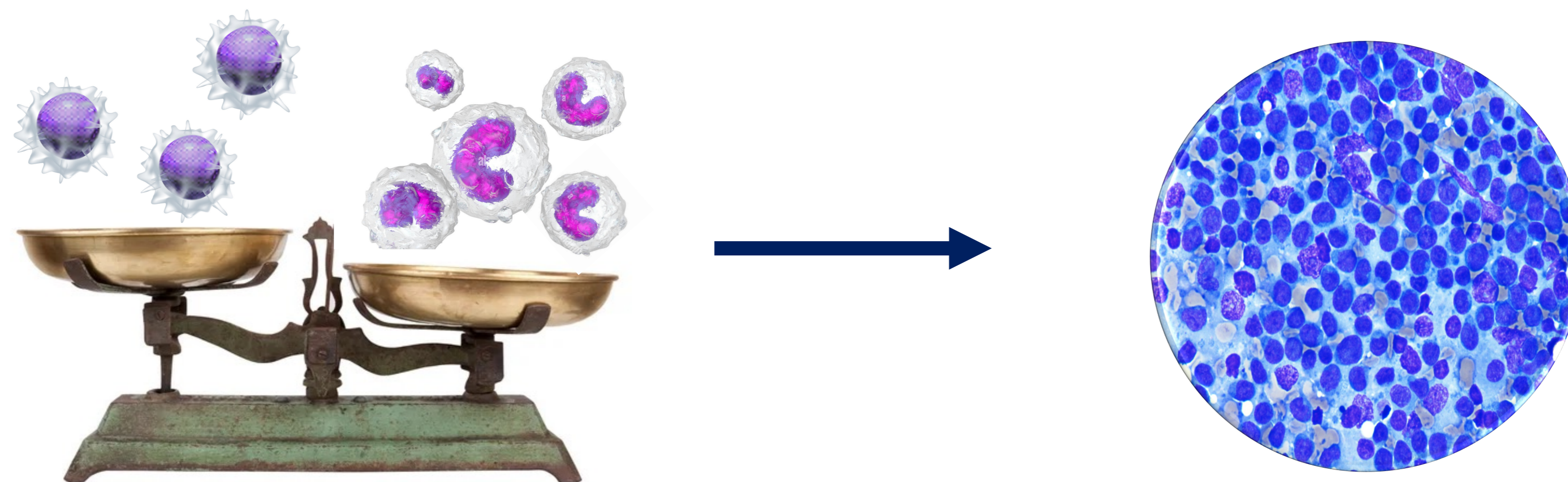
Joaquim Henriques

Faculty of Veterinary Medicine,  
Lusófona University, Lisbon, Portugal  
Anicura Atlântico, Oncology Referral  
Centre, Mafra, Portugal

Nazaré Pinto da Cunha

Faculty of Veterinary Medicine,  
Lusófona University, Lisbon, Portugal  
Vedis – Veterinary Expertise in  
Diagnosis, Porto, Portugal

THE IMPORTANCE OF PROGNOSTIC FACTORS IN ONCOLOGY INCLUDE SURVIVAL PREDICTION, THERAPEUTIC STRATEGIES SELECTION AND MANAGEMENT OF CAREGIVER'S EXPECTATIONS. PROGNOSTIC FACTORS REPORTED FOR ALIMENTARY LYMPHOMA (AL) IN CAT INCLUDE COMPLETE REMISSION (CR) TO TREATMENT, TRANSMURAL EXTENSION, FELV ANTIGENEMIA, WEIGHT LOSS, ELEVATED LDH, HYPOALBUMINEMIA, HYPOCOBALIMINEMIA, BICAVITARY INVOLVEMENT, DISEASE STAGE AND LYMPHOMA SUBTYPES ACCORDING TO THE WHO CLASSIFICATION<sup>(1,2)</sup>. PERIPHERAL BLOOD CELL RATIOS HAVE BEEN DESCRIBED AS EARLY PROGNOSTIC MARKERS IN HUMAN MEDICINE, INCLUDING HUMAN HODGKIN AND NON-HODGKIN LYMPHOMA, SUCH AS DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL)<sup>(3,4)</sup>. THERE ARE ONLY FEW STUDIES ON CANINE<sup>(5-7)</sup> AND FELINE<sup>(8)</sup> SPECIES. THIS STUDY AIMS TO DETERMINE THE PROGNOSTIC VALUE OF NEUTROPHIL-LYMPHOCYTE RATIO (NLR) AND LYMPHOCYTE-MONOCYTE RATIO (LMR) ON THE 60 DAYS SURVIVAL TIME ON FELINE AL.



### Material & Methods

- Thirty cats diagnosed with AL, between 2017 and 2023;
- Complete blood cell count (Procyte DX, IDEXX Laboratories, West-brook, ME, USA or BC-5300Vet, Mindray Bio-Medical Electronics, Shenzhen, China), blood smear examination, cytology and/or histopathologic diagnosis, complete staging and follow-up;
- NLR and LMR calculated based on absolute counts of peripheral blood samples obtained on the day of diagnosis;
- Blood ratios and its association with the 60 days survival time were studied with the Chi-square test. Receiver operating characteristic (ROC) curve analysis was used to determine the LMR cut-off value for predicting survival at 60 days. A minimum area under the curve (AUC) of 0.7 was required for consideration in the ROC model. A  $P < 0.05$  was considered significant.

### Results

Chi-square test showed that a low LMR is predictive of dead at 60 days ( $P=0,026$ ). There was no association between the NLR ratio and the survival time ( $P=0,457$ ). On ROC curve analysis, a cut-off point of 3,7 for LMR was achieved using the Youden index (Sensitivity + Specificity - 1) and had a sensitivity and specificity for predicting 60-days survival of 88,9% and 75%, respectively. The AUC for LMR was 0,806 (95% CI, 0,621-0,926) ( $P=0,001$ ). If aimed to be used as a screening teste, a LMR cut-off value of <8,54, would provide the maximum sensitivity (100%) and specificity (33%) for predicting 60 days survival time.

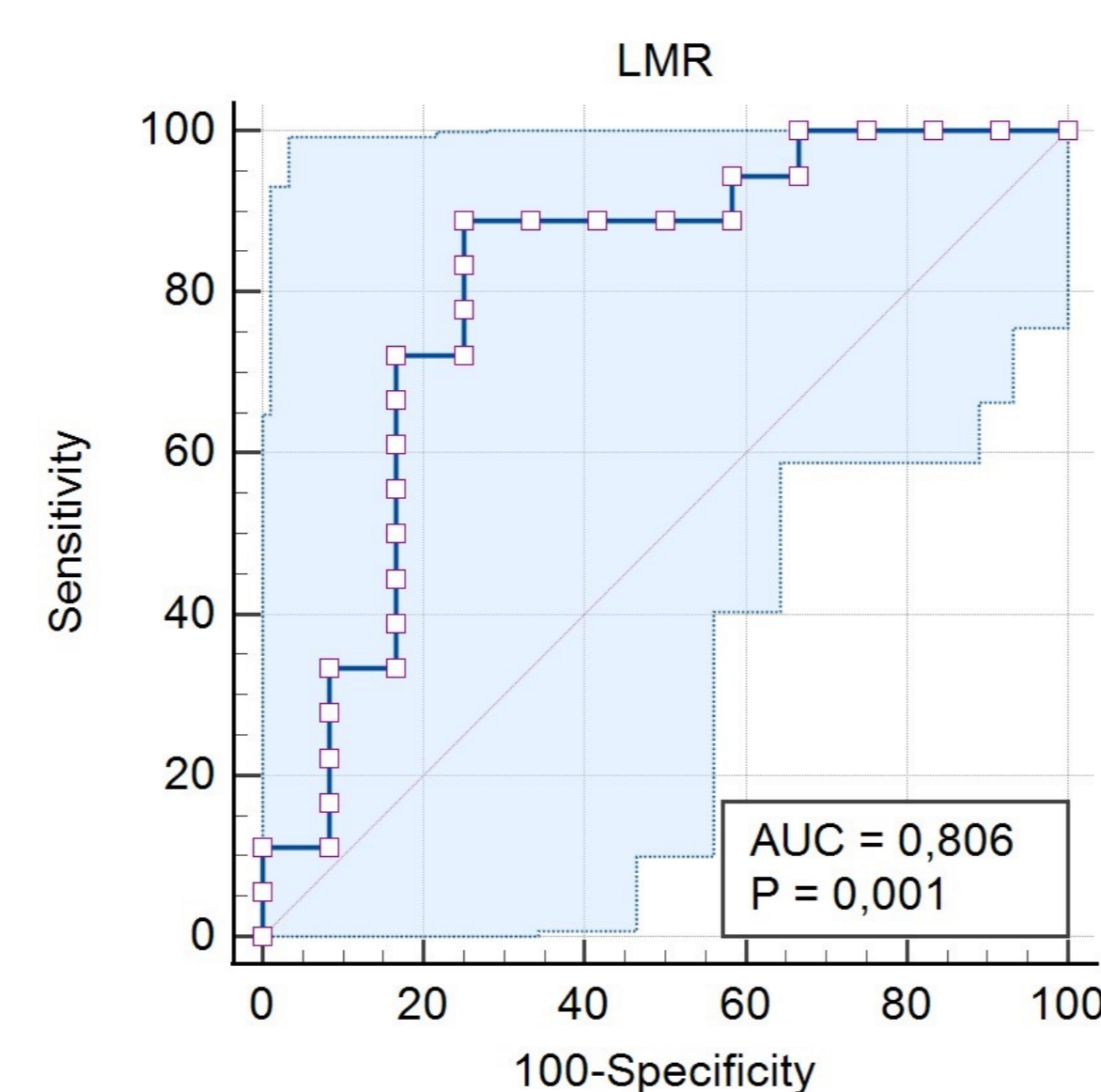


Figure 1 – ROC curve for the LMR cut-off determination at the time of diagnosis for predicting survival at 60 days in cats with AL. The AUC is 0.806 (95% confidence interval: 0,621-0,926;  $P = 0.001$ ).

### Discussion

The relationship between a low LMR and poor patient outcome in lymphoma is consistent with previous studies in canine, feline and human species. This association could have various explanations: tumor-associated macrophages (TAMs) in the tumor microenvironment promotes tumor progression, and peripheral monocyte levels are thought to correlate with TAMs. In contrast, peripheral lymphocytes are reduced in malignant tumors, most likely because lymphocytes enter the tumor area to suppress tumor cells, resulting in a decrease in the peripheral lymphocyte count<sup>(3-8)</sup>.

Our optimal LMR cut-off value of 3,7 is slightly higher than the one reported by Tagawa et al. in a study of 33 cats with high-grade lymphomas, with an optimal LMR cut-off value of 3.4 (sensitivity 100%; specificity 61%; AUC=0.809)<sup>8</sup>. Shimbo et al. reported a LMR cut-off value of 0,7 (sensitivity 73%; specificity 76%; AUC=0.794), in a study that included 43 dogs with high-grade lymphoma<sup>6</sup>. Finally, Davies et al. referred a cut-off of 1.43 (sensitivity 83%; specificity 63%; AUC 0.72) in 42 canine cases of multicentric centroblastic diffuse large B-cell lymphoma<sup>7</sup>. Our study was limited by its small population size and variable lymphoma subtypes within de AL group, but our results support the findings that a low LMR may serve as a prognostic factor in feline AL.

### Conclusion

These preliminary results suggest that LMR, but not NLR, may be a non-invasive predictive marker of a shorter survival time in feline AL. Further studies on a larger cohort of cases, divided according to specific lymphoma classification and with homogeneous inclusion criteria related to treatment, are needed to validate its clinical use.

### References

- Vail D, Pinkerton M, Young K. Withrow and MacEwen's Small Animal Clinical Oncology. Elsevier; 2020.
- Wolfesberger, B., Skor, O., Hammer, S. E., Flickinger, I., Kleiter, M., Rütgen, B. C., Schwendenwein, I., Tichy, A., Hittmair, K. M., Degasper, B., & Fuchs-Baumgartner, A. (2017). Does categorisation of lymphoma subtypes according to the World Health Organization classification predict clinical outcome in cats? *Journal of Feline Medicine and Surgery*, 19(8), 897–906.
- Gao, F., Hu, J., Zhang, J., & Xu, Y. (2021). Prognostic value of peripheral blood lymphocyte/monocyte ratio in lymphoma. *Journal of Cancer*, 12(12), 3407–3417.
- Kamiya, N., Ishikawa, Y., Kotani, K., Hatakeyama, S., & Matsumura, M. (2022). Monocyte-to-Lymphocyte Ratio in the Diagnosis of Lymphoma in Adult Patients. *International Journal of General Medicine*, 15, 4221–4226.
- Henriques, J., Felisberto, R., Constantino-Casas, F., Cabeçadas, J., & Dobson, J. (2021). Peripheral blood cell ratios as prognostic factors in canine diffuse large B-cell lymphoma treated with CHOP protocol. *Veterinary and Comparative Oncology*, 19(2), 242–252.
- Shimbo, G., Matsumoto, K., Miyahara, K., & Tagawa, M. (2019). Prognostic Value of Lymphocyte-to-Monocyte Ratio in Canine High-Grade Lymphoma Cases. *Journal of World's Poultry Research*, 9(3), 218–229.
- Davies O, Szladovits B, Polton G, Garden OA, Leo C, Lara-Garcia A. Prognostic significance of clinical presentation, induction and rescue treatment in 42 cases of canine centroblastic diffuse large B-cell multicentric lymphoma in the United Kingdom. *Vet Comp Oncol*. 2018 Jun;16(2):276–87.
- Tagawa M, Shimbo G, Miyahara K. Prognostic role of lymphocyte to monocyte ratio in feline high-grade lymphomas. *Can Vet J*. 2021 Oct;62(10):1095–1103.