



Research Article

Evaluation of hematologic indices in parvovirus infected dogs with systemic inflammatory response syndrome (SIRS)

K. Sevim^{a,*}, E.Ç. Çolakoğlu^a, U. Kaya^b^a Department of Internal Medicine, Cardiology Unit, Faculty of Veterinary Medicine, Ankara University, 06070, Ankara, Turkey^b Department of Biostatistics, Faculty of Veterinary Medicine, Hatay Mustafa Kemal University, 31060, Hatay, Turkey

ARTICLE INFO

Keywords:

Blood indices

Dog

Parvovirus

SIRS

ABSTRACT

Canine parvoviral enteritis (CPE) is a highly contagious, acute viral disease that mainly affects young dogs and can lead to systemic inflammatory response syndrome (SIRS), sepsis, endotoxemia and even death. The study aimed to evaluate the diagnostic and prognostic potential of hematological indices such as MLR, NLR, PLR, PNR and SII in CPV-infected dogs with SIRS at first admission. The retrospective study was performed on 51 CPV-infected and 20 healthy dogs. MLR, NLR, PLR, PNR, and SII indices were determined and compared between groups. A receiver operating characteristic (ROC) curve analysis was carried out to determine thresholds of sensitivity and specificity for hematologic indices.

NLR, PLR, and PNR were the best predictors for supporting a diagnosis of parvoviral enteritis, with AUC values of 0.685, 0.762, and 0.884, respectively. Moreover, PLR and PNR, with AUC values of 0.740 and 0.769, respectively, were the most suitable indices to determine the prognosis of dogs with parvoviral enteritis with SIRS. In conclusion, these indices can be used as potential indicators for predicting disease outcomes and supporting a diagnosis of CPV-infected dogs with SIRS at first admission.

Introduction

Canine parvoviral enteritis (CPE) is a highly contagious, life-threatening, viral disease that usually affects dogs under six months of age¹. The disease is caused by canine parvovirus type 2 (CPV-2), producing haemorrhagic enteritis in puppies². These pathogenic enteric viruses replicate in gastrointestinal and lymphoid tissue and cause damage to the intestinal mucosa. These pathological changes result in vomiting, hemorrhagic diarrhea, and dehydration. Destruction of the intestinal barrier facilitates the translocation of intestinal bacteria and endotoxins into the systemic circulation and may lead to systemic inflammatory response syndrome (SIRS), sepsis, endotoxemia, and even death³.

Systemic inflammatory response syndrome (SIRS) is an abnormal inflammatory response resulting from infectious or non-infectious causes. SIRS can be defined in dogs with two or more of the following criteria: abnormalities in body temperature, heart and respiratory rate, and leukocyte count⁴.

Biomarkers such as procalcitonin, interleukin 6-8-10, lactate, and C-reactive protein (CRP) have been used in the evaluation of SIRS and

sepsis in dogs.^{5,6} However, ability to assess some of the above listed biomarkers is limited in veterinary medicine due to cost and accessibility⁷. The unclear duration of hospitalization and prognosis in dogs with CPV can be emotionally and financially challenging for owners⁸. Therefore, simple, economical, and easily accessible parameters that can be obtained immediately and widely at the veterinary patient's first admission seem to be essential in determining the disease severity⁹.

The leukocyte count during CPV enteritis is generally significantly changed. The most numerous leukocytes in the blood of dogs are neutrophils. Neutrophils destroy microorganisms such as bacteria, viruses, and parasites. In parvoviral enteritis, severe neutropenia is caused by the destructive effect of the virus on precursor cells in the bone marrow, migration due to sepsis or endotoxemia, and severe neutrophil loss through the intestinal wall¹⁰. Lymphocytes interact with the innate and adaptive immune systems in infection and regulate the inflammatory response¹¹. Lymphocyte depletion is usually seen in parvoviral enteritis due to various mechanisms, including lymphoid tissue destruction, endogenous release of cortisol, and protein-losing enteropathy.^{10,12} Monocytes differentiate into macrophages and are responsible for phagocytosis of microorganisms, and dead or damaged cells, releasing

* Corresponding author.

E-mail address: ksevim@ankara.edu.tr (K. Sevim).<https://doi.org/10.1016/j.tcam.2025.100977>

cytokines and presenting antigens to lymphocytes. Monocytes are essential in parvoviral enteritis, such as removing necrotic debris and viral inactivation¹³ Platelets interact with different immune cells in inflammatory diseases. Platelets synthesize various factors that affect systemic inflammation and support the immune response¹⁴ Direct effects of the virus and/or immunological components may cause thrombocytopenia² On the other hand, an increase in platelet activation due to the inflammatory response is reported in dogs with SIRS¹² Blood leukocyte counts and morphology are relatively constant in health, but leukocyte numbers can change quickly during the disease process. This change can be used to evaluate the veterinary patient's response to treatment or predict prognosis¹⁰ The monocyte-to-lymphocyte ratio (MLR), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), platelet-to-neutrophil ratio (PNR), and systemic immune-inflammatory index (SII) are new indices easily obtained from complete blood count. These indices associated with prognosis have been studied in human and veterinary medicine and have been found to be associated with prognosis.^{7,8,15–19}

The aims of this retrospective study were to measure the MLR, NLR, PLR, PNR, and SII indices in CPV-infected dogs with SIRS at first admission and determine whether these ratios are associated with the disease and the prognosis. No study has defined all these indices in dogs with SIRS due to parvoviral enteritis. We hypothesized that dogs with CPE and SIRS would have inflammation-related hematologic alterations that could be used as potential diagnostic and prognostic biomarkers.

Materials and methods

Animals

This study retrospectively used data from dogs referred to Ankara University Veterinary Teaching Hospital. Written consent from the owners and the written permission of teaching hospital management were obtained. The present study was carried out in accordance with the principles of the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes and the requirements of European Union Directive 2010/63 on the protection of animals used for experimental and other scientific purposes.

Medical records were analyzed to identify dogs diagnosed with CPE. To be included in the study, dogs had to be diagnosed with CPE with a positive parvovirus faecal antigen test (Anigen, Hasvet®), display clinical signs such as vomiting, diarrhea/bloody diarrhea, anorexia and dehydration, and a complete blood count (CBC) was performed on the first day of admission to the hospital. Dogs with CPE were considered SIRS+ if they presented two or more of the following criteria: body temperature $< 38.1^{\circ}\text{C}$ or $> 39.2^{\circ}\text{C}$; heart rate $> 120/\text{min}$; respiratory rate $> 20/\text{min}$; WBC count $< 6000/\mu\text{L}$ or $> 16000/\mu\text{L}$ ⁴ The study did not include dogs that did not meet the SIRS criteria, that had previously used medications or been vaccinated, or that had incomplete medical records. Demographic information (age, sex, and breed) and white blood cells (WBC), neutrophils (NEUT), monocytes (MONO), lymphocytes (LYM), eosinophils (EOS), red blood cells (RBC), haemoglobin (HGB), haematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCHC), mean corpuscular haemoglobin concentration (MCHC), platelet (PLT) and mean platelet volume (MPV) values were recorded. MLR²⁰, NLR²⁰, PLR²¹, and PNR⁹ values were calculated as previously described. SII was calculated as follows: $\text{SII} = \text{P} \times \text{N}/\text{L}$, where P, N, and L are peripheral platelet, neutrophil, and lymphocyte counts, respectively²² Dogs were classified as survivors (SUR) if they survived to discharge or non-survivors (NSUR) if they died due to natural causes. No puppies included in this study were euthanized. Age-matched puppies with normal clinical examination findings and brought for routine vaccination or health checks were included in the study as the control group (Control). Demographic information, complete blood count values, and calculation of indices mentioned above were also performed on the healthy group.

Statistical methods

All statistical analyses were performed using Stata 12/MP4 and MedCalc Version 9.2. The variables were examined with the Kolmogorov-Smirnov test and Levene test as parametric test assumptions. The differences in CBC and hematologic indices among the three groups were analyzed using one-way ANOVA with the Duncan test (post-hoc test) when parametric test assumptions were met and the Kruskal-Wallis test with Dunn test (post-hoc test) otherwise. Receiver operating characteristic (ROC) analysis was used to determine a predicted threshold for identification of canine parvoviral enteritis and ex-status. ROC curves for the detection of canine parvoviral enteritis and ex-status were obtained for hematologic indices that were found to be statistically significant. Sensitivity, specificity, 95 % confidence interval, and area under the curve (AUC) were calculated for each indices. All data were presented as mean $\pm$ standard error of mean (SEM). Differences with $p < 0.05$ were considered statistically significant.

Results

A total of 63 dogs were found in the database with a diagnosis of CPE. Four dogs were excluded because a CBC was not performed at first admission, and eight were excluded for failing to meet SIRS criteria. Fifty-one dogs were enrolled in the study. Fifteen of the 51 dogs died on different days before discharge and constituted the non-survivors' group (NSUR, $n = 15$). Thirty-six dogs survived to discharge and were constituted the survivor's group (SUR, $n = 36$). The control group consisted of 20 dogs (Control, $n = 20$). The mean ages were 3.86, 4.40, and 3.20 months for SUR, NSUR and the Control group, respectively. The study comprised 29 females (40.8 %) and 42 males (59.2 %). There were 22 different breeds; the most common were mixed breeds ($n = 20$, 28.2 %), Turkish Kangal ($n = 13$, 18.3 %), and German shepherd ($n = 5.7$ %) dogs.

The variables obtained from complete blood counts in three groups are shown in Table 1. The ROC curve analysis was performed to identify sensitivity and specificity thresholds for hematological indices showing a statistically significant difference between groups. Two different ROC analyses were performed. The first was performed to determine the critical thresholds (i.e. highest specificity and sensitivity) of hematologic indices in predicting outcomes, and the second one was to determine an estimated threshold to discriminate between dogs with parvoviral enteritis and the control group. The ROC curves analysis results for determining critical thresholds, specificity, sensitivity, AUC, and P values are presented in Tables 2 and 3. PLR and PNR, with AUC values of 0.740 and 0.769, respectively, were the most suitable indices to determine the prognosis of dogs with parvoviral enteritis developing SIRS. In addition, NLR, PLR, and PNR are the best predictors for supporting a diagnosis of parvoviral enteritis, with AUC values of 0.685, 0.762, and 0.884, respectively.

Discussion

This retrospective study aimed to determine the diagnostic value of indices such as MLR, NLR, PLR, PNR, and SII and their association with prognosis in CPV-infected dogs with SIRS at first admission. In this study, statistically significant difference between NLR, PLR, and PNR values of infected and healthy dogs suggests that these parameters are useful tools for supporting a diagnosis of parvoviral enteritis in dogs. Moreover, NSUR group had higher PLR and PNR values compared to SUR and the Control group. Further investigation revealed that these values were the most appropriate indices for predicting the prognosis of parvoviral enteritis dogs with SIRS.

NLR is an easily accessible and cost-effective biomarker representing the balance between innate and adaptive immune responses and indicating the concomitant presence of inflammation and stress¹⁹ In human medicine, bacterial, fungal, and viral infections^{23–25}, stroke²⁶,

Table 1

The results obtained by comparing the complete blood counts and indices of the three groups.

Parameters	Groups			p
	NSUR	SUR	Control	
WBC	2.88 ± 0.46 ^c	6.08 ± 0.49 ^b	10.91 ± 0.62 ^a	<0.001 ^e
LYM	0.65 ± 0.06 ^c	1.18 ± 0.12 ^b	2.78 ± 0.22 ^a	<0.001 ^e
MONO	0.17 ± 0.03 ^c	0.37 ± 0.03 ^b	0.90 ± 0.06 ^a	<0.001 ^e
NEUT	2.34 ± 0.35 ^c	4.51 ± 0.41 ^b	6.96 ± 0.56 ^a	<0.001 ^e
EOS	0.06 ± 0.03	0.10 ± 0.03	0.14 ± 0.06	0.665 ^e
RBC	6.46 ± 0.21 ^a	6.19 ± 0.21 ^a	4.90 ± 0.26 ^b	<0.001 ^d
HGB	14.33 ± 0.53 ^a	13.92 ± 0.56 ^a	11.18 ± 0.66 ^b	0.002 ^d
HCT	40.19 ± 1.60 ^a	38.72 ± 1.63 ^a	31.74 ± 1.82 ^b	0.007 ^d
MCV	62.10 ± 1.05	62.11 ± 1.09	64.93 ± 1.27	0.197 ^d
MCH	22.17 ± 0.33	22.41 ± 0.37	22.80 ± 0.42	0.637 ^d
MCHC	35.77 ± 0.51	36.15 ± 0.31	35.25 ± 0.35	0.209 ^d
PLT	365.87 ± 29.92	354.17 ± 23.3	381.30 ± 34.01	0.703 ^e
MPV	9.38 ± 0.30 ^a	8.90 ± 0.18 ^a	7.85 ± 0.34 ^b	0.002 ^d
SII	1569.40 ± 316.06	1242.28 ± 109.48	1161.12 ± 271.42	0.354 ^e
NLR	4.00 ± 0.76 ^{ab}	4.61 ± 0.52 ^a	2.83 ± 0.34 ^b	0.041 ^e
PNR	634.97 ± 381.12 ^a	123.48 ± 22.43 ^b	56.9 ± 4.24 ^c	<0.001 ^e
MLR	0.25 ± 0.03	0.36 ± 0.04	0.33 ± 0.02	0.124 ^e
PLR	630.13 ± 66.81 ^a	414.67 ± 55.8 ^b	156.22 ± 20.45 ^c	<0.001 ^e

WBC, white blood cells; NEUT, neutrophils; MONO, monocytes; LYM, lymphocytes; EOS, eosinophils; RBC, red blood cells; HGB, haemoglobin; HCT, haematocrit; MCV, mean corpuscular volume; MHC, mean corpuscular haemoglobin; MCHC, mean corpuscular haemoglobin concentration; PLT, platelet; MPV, mean platelet volume; SII, systemic immune-inflammatory index; PNR, platelet-to-neutrophil ratio; PLR, platelet-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio.

^{a,b,c} Different lower cases indicate statistical differences (Wilcoxon test, Kaplan-Meier, Breslow test, $p < 0.001$).

^d ANOVA.

^e Kruskal-Wallis test.

myocardial infarction²⁷, severe trauma²⁸, cancer²⁹, post-surgical complications³⁰ and any condition that triggers SIRS¹⁵ have been reported to increase the number of circulating neutrophils, thus increasing the NLR. Furthermore, NLR has been associated with mortality in certain diseases such as heart diseases, chronic lower respiratory diseases, pneumonia, and kidney diseases³¹. In this study, NLR was higher in dogs with SIRS than in healthy dogs due to severe decrease in lymphocyte count. This is in accordance with previous studies reporting higher NLR in septic dogs.^{7,16,17} On the other hand, González-Domínguez et al. reported that NLR did not reach a statistically significant difference between dogs that died from parvovirus and those that survived⁸. The absence of a control group and not considering the dogs' age and vaccination status in the mentioned study could explain the difference between the two findings.

Table 2

Predicted thresholds for defining survival and death status in canine parvoviral enteritis. Obtained by comparing the data of the NSUR and SUR group.

Parameters	Threshold	Sensitivity	%95 CI for Se	Specificity	%95 CI for Sp	AUC	p
PNR	>70.5	100.0	78.0- 100.0	52.8	35.5- 69.6	0.740	0.003
PLR	>484	73.3	44.9- 92.0	77.8	60.8- 89.9	0.769	<0.001

95 % CI, 95 % confidence interval. Se, Sensitivity; Sp, Specificity; PNR, platelet-to-neutrophil ratio; PLR, platelet-to-lymphocyte ratio.

Table 3

Predicted thresholds for the identification of canine parvoviral enteritis. Obtained by comparing data from all dogs with parvoviral enteritis and the control group.

Parameters	Threshold	Sensitivity	%95 CI for Se	Specificity	%95 CI for Sp	AUC	p
NLR	>2.25	86.3	73.7- 94.3	50.0	27.2- 72.8	0.685	0.005
PNR	>92.16	56.9	42.2- 70.6	100.0	83.0- 100.0	0.762	<0.001
PLR	>175	90.2	78.6- 96.7	80.0	56.3- 94.1	0.884	<0.001

95 % CI, 95 % confidence interval. Se, Sensitivity; Sp, Specificity; PNR, platelet-to-neutrophil ratio; PLR, platelet-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio.

Authors of another study³² reported that the NLR was lower in the septic group compared to the non-septic group. The different aetiology and disease stages may explain our findings. In a study determining the prognostic importance of NLR in dogs with septic peritonitis³³, no significant difference was found between the septic and non-septic groups. This discrepancy could be due to disease development and progression that may affect the leukocyte pattern. Guglielmini et al. reported that NLR in dogs with acute pancreatitis (AP) did not differ between non-survivors and survivors and had no prognostic utility⁹. This discrepancy between studies is due to the difference in inclusion criteria and concurrent diseases causing pancreatitis, potentially affecting outcomes. According to the present study, NLR can provide a good indicator for predicting disease diagnosis, but it should be carefully combined with other findings (clinical symptoms, blood results, etc.) to make a correct decision.

PLR is a ratio between platelet and lymphocyte counts measured in peripheral blood. This index represents the balance between immunomodulatory and inflammatory processes (platelet count) and the immune response (lymphocyte count)⁸. The median total lymphocyte count was significantly lower in NSUR. However, there was no statistically significant difference in platelet count between groups. Lymphoid tissue destruction, endogenous cortisol release and protein-losing enteropathy may cause a decrease in lymphocyte count in dogs with CPV.^{10,12} The present study shows that dogs with CPV had higher PLR than those in the control group at admission. Moreover, PLR at a cut-off value of >484 with a good AUC (0.769) may serve as a good indicator to predict disease survival and prognosis, and the findings are in line with previous studies.^{8,34,35} At the same time, PLR can provide a good indicator to support disease diagnosis. The authors of another study⁹ reported that although the PLR value was higher in dogs with AP than in the healthy group, it did not indicate prognostic usefulness. The different roles of inflammatory cells and cytokines in acute pancreatitis and parvoviral enteritis may explain this discrepancy. Because in AP, neutrophils activate a nonspecific immune reaction, T helper lymphocytes decrease significantly in a short time from the onset of AP, and platelets can affect leukocyte functions through cytokines⁹. Yazlık et al. reported that the platelet counts and PLR values of the dogs with SIRS were lower than the others⁷. They explained the reason for this situation: cytokine release and thrombocytosis. A possible explanation for this discrepancy in the study above is that the effect of sepsis caused by intrauterine bacteria and the aetiology of pyometra took a long time. However, the present study only assessed parvoviral enteritis, which likely influenced blood results due to the impact of sepsis associated with intestinal bacteria and the acute disease process. The present study clearly showed that PLR is a useful tool to support the diagnosis of CPV dogs with SIRS at first admission and to predict disease survival and prognosis.

The present study indicated that monocyte count was lower in NSUR, and this difference was statistically significant between groups.

Migration to the inflamed tissue and lymphoid tissue damage may contribute to monocyte decline¹³ Although NSUR decreased MLR value in our study sample, no statistically significant difference existed between groups. These results are compatible with previous studies.^{8,36,37} Other studies^{10,13} reported that the increase in monocyte number also reduced the risk of death in CPE. As previously reported by Yazlık et al. MLR could be a diagnostic parameter for dogs with pyometra⁷ This discrepancy could be explained by the fact that pyometra is a chronic problem with a longer course than CPE. In this study, no significant association was observed between MLR and diagnosis or prognosis. However, the results of this present study suggest that further evaluation of MLR may be necessary in future larger-scale studies.

SII is a new index that reflects the degree of systemic inflammation and has demonstrated prognostic significance.^{14,22} SII in infected dogs was greater than in healthy ones in the present study. When comparing this biomarker between infected dogs (SUR and NSUR), NSUR had greater SII values. However, this difference between the two groups was not statistically significant. Similar to our results, Yazlık et al. indicated that SII indices were higher in dogs with pyometra compared to control group, but this difference was not statistically significant⁷ In human medicine, it was reported that SII is a prognostic indicator of poor outcomes in patients with hepatocellular carcinoma and small-cell lung cancer and is a promising tool for treatment strategy decisions.^{22,38} In veterinary medicine, there is a lack of knowledge about SII. Our study contributes and underlines that there is a greater need for more research regarding these ratios.

The present study observed that the NSUR had a lower neutrophil count than the SUR and Control group, and this difference was statistically significant ($p < 0.001$). The destructive effect of the virus on the bone marrow, migration due to severe infection and loss of neutrophils due to destruction of the intestinal wall can cause neutropenia¹⁰ However, there was no statistically significant difference in platelet count between groups. Accordingly, it was determined that the PNR value was higher in NSUR and SUR than in healthy dogs due to severe decrease in neutrophil count. Moreover, PNR at a cut-off value of >70.5 with a good AUC (0.740) can serve as a good indicator to predict disease survival and supporting a diagnosis, within the scope of prognosis. Similarly, Wu and Qin reported that PNR is an independent predictor of mortality in people with sepsis³⁹ Lui et al. indicated that the PNR value was lower in lupus nephritis (LN) patients with infection, and this was due to the presence of anti-platelet antibodies and the accumulation of neutrophil leukocytes. The authors reported that PNR may potentially distinguish between infection and flare in lupus nephritis²³ The level of damage to the bone marrow and/or tissues and the severity of the disease process that is too acute for a bone marrow response to occur affect the immune response, particularly neutrophil leukocytes, and lead to differences in values such as PNR¹⁰

The major limitation of our study is its retrospective nature. MLR, NLR, PLR, PNR, and SII were evaluated only at the time of hospital admission in the present study. However, evaluating these parameters on certain days may be more valuable.

Conclusions

Considered together, CPV-SIRS+ non-surviving dogs in the current study population had importantly higher PLR and PNR values at first admission. According to the sensitivity (%) and specificity (%) values obtained from ROC analysis, PLR and PNR were the most useful biomarkers for supporting a diagnosis of CPE and predicting disease outcomes. At the same time, NLR may provide a good indicator for predicting disease diagnosis. In conclusion, these indices can be used for supporting the diagnosis of CPV dogs with SIRS at first admission and also as potential indicators in predicting disease outcomes. However, the indices mentioned above should be carefully combined with other parameters to make an appropriate decision. It should be noted that these indices are used as markers that the disease is present, but do not replace

the classical diagnostic tools available to diagnose the disease. Further studies are necessary to evaluate the accuracy and usefulness of threshold values of the mentioned parameters in larger numbers of dogs.

CRediT authorship contribution statement

K. Sevim: Writing – review & editing, Writing – original draft, Resources, Data curation. **E.Ç. Çolakoğlu:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Investigation, Conceptualization. **U. Kaya:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation.

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.

Acknowledgments

We wish to thank our colleagues and staff for their technical assistance.

References

- Eregowda CG, De UK, Singh M, et al. Assessment of certain biomarkers for predicting survival in response to treatment in dogs naturally infected with canine parvovirus. *Microb Pathog.* 2020;149, 104485.
- Goddard A, Leisewitz AL. Canine parvovirus. *Vet Clin North Am Small Anim Pract.* 2010;40:1041–1053.
- Alves F, Prata S, Nunes T, et al. Canine parvovirus: a predicting canine model for sepsis. *BMC Vet Res.* 2020;16:1–11.
- Hauptman JG, Walshaw R, Olivier NB. Evaluation of the sensitivity and specificity of diagnostic criteria for sepsis in dogs. *Veterinary Surg.* 1997;26:393–397.
- Eckersall PD, Bell R. Acute phase proteins: biomarkers of infection and inflammation in veterinary medicine. *Veterinary J.* 2010;185:23–27.
- Troia R, Giunti M, Goggs R. Plasma procalcitonin concentrations predict organ dysfunction and outcome in dogs with sepsis. *BMC Vet Res.* 2018;14:111.
- Yazlık MO, Mutluer İ, Yıldırım M, Kaya U, Çolakoğlu HE, Vural MR. The evaluation of SIRS status with hemato-biochemical indices in bitches affected from pyometra and the usefulness of these indices as a potential diagnostic tool. *Theriogenology.* 2022;193:120–127.
- González-Domínguez A, Cristobal-Verdejo JI, López-Espinar C, et al. Retrospective evaluation of hematological ratios in canine parvovirus: 401 cases. *J Vet Intern Med.* 2024;38:161–166.
- Guglielmini C, Crisi PE, Tardo AM, et al. Prognostic role of red cell distribution width and other routine clinico-pathological parameters in dogs with acute pancreatitis. *Animals.* 2022;12:3483.
- Goddard A, Leisewitz AL, Christopher MM, Duncan NM, Becker PJ. Prognostic usefulness of blood leukocyte changes in canine parvoviral enteritis. *J Vet Intern Med.* 2008;22:309–316.
- Kalli I, Leontides LS, Mylonakis ME, Adamama-Moraitou K, Rallis T, Koutinas AF. Factors affecting the occurrence, duration of hospitalization and final outcome in canine parvovirus infection. *Res Vet Sci.* 2010;89:174–178.
- Paul BR, Kumar De U, Sarkar VK, et al. Prognostic potential of thrombocyte indices, acute phase proteins, electrolytes and acid-base markers in canine parvovirus infected dogs with systemic inflammatory Response Syndrome. *Top Companion Anim Med.* 2023;56–57, 100803.
- Alves FS, Barbosa BC, Coelho NDG, et al. Clinical and hematological prognostic factors in dogs with parvoviral enteritis and sepsis. *Semin: Ciências Agrárias.* 2019; 40:1477.
- Incir S. The role of immature granulocytes and inflammatory hemogram indices in the inflammation. *Int J Med Biochem.* 2020;3:125–130.
- Buonacera A, Stancanelli B, Colaci M, Malatino L. Neutrophil to lymphocyte ratio: an emerging marker of the relationships between the immune system and diseases. *Int J Mol Sci.* 2022;23:3636.
- Dinler Ay C. Neutrophil to lymphocyte ratio as a prognostic biomarker in puppies with acute diarrhea. *J Veterinary Emerg Critic Care.* 2022;32:83–89.
- Muñoz AI, Maldonado-García JL, Fragozo A, et al. Altered neutrophil-to-lymphocyte ratio in sepsis secondary to canine parvoviral enteritis treated with and without an immunomodulator in puppies. *Front Vet Sci.* 2022;9.
- Sevim K, Çolakoğlu EÇ, Kaya U. The impact of peripheral blood cell ratios in dogs with diffuse B-cell small lymphocytic lymphoma treated with CHOP protocol. *Ankara Üniversitesi Veteriner Fakültesi Dergisi.* 2024;71:51–56.
- Zahorec R. Neutrophil-to-lymphocyte ratio, past, present and future perspectives. *Bratislava Med J.* 2021;122:474–488.
- Tiainen S, Rilla K, Hämäläinen K, Oikari S, Auvinen P. The prognostic and predictive role of the neutrophil-to-lymphocyte ratio and the monocyte-to-lymphocyte ratio in

- early breast cancer, especially in the HER2+ subtype. *Breast Cancer Res Treat.* 2021; 185:63–72.
21. Xia L, Li W, Zhai J, Yan C, Chen J, Yang H. Significance of neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, lymphocyte-to-monocyte ratio and prognostic nutritional index for predicting clinical outcomes in T1–2 rectal cancer. *BMC Cancer.* 2020;20:208.
 22. Hu B, Yang XR, Xu Y, et al. Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. *Clin Cancer Res.* 2014;20:6212–6222.
 23. Liu P, Li P, Peng Z, et al. Predictive value of the neutrophil-to-lymphocyte ratio, monocyte-to-lymphocyte ratio, platelet-to-neutrophil ratio, and neutrophil-to-monocyte ratio in lupus nephritis. *Lupus.* 2020;29:1031–1039.
 24. Lowsby R, Gomes C, Jarman I, et al. Neutrophil to lymphocyte count ratio as an early indicator of blood stream infection in the emergency department. *Emerg Med J.* 2015;32:531–534.
 25. Niu D, Huang Q, Yang F, et al. Serum biomarkers to differentiate gram-negative, gram-positive and fungal infection in febrile patients. *J Med Microbiol.* 2021;70.
 26. Li W, Hou M, Ding Z, Liu X, Shao Y, Li X. Prognostic value of neutrophil-to-lymphocyte ratio in stroke: a systematic review and meta-analysis. *Front Neurol.* 2021;12.
 27. Lee MJ, Park SD, Kwon SW, et al. Relation between neutrophil-to-lymphocyte ratio and index of microcirculatory resistance in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Am J Cardiol.* 2016;118:1323–1328.
 28. Park JM. Neutrophil-to-lymphocyte ratio in trauma patients. *J Trauma Acute Care Surg.* 2017;82:225–226.
 29. Lee PY, Oen KQX, Lim GRS, et al. Neutrophil-to-lymphocyte ratio predicts development of immune-related adverse events and outcomes from immune checkpoint blockade: a case-control study. *Cancers.* 2021;13:1308.
 30. Fest J, Ruiter TR, Groot KB, et al. The neutrophil-to-lymphocyte ratio is associated with mortality in the general population: the Rotterdam Study. *Eur J Epidemiol.* 2019;34:463–470.
 31. Song M, Graubard BI, Rabkin CS, Engels EA. Neutrophil-to-lymphocyte ratio and mortality in the United States general population. *Sci Rep.* 2021;11:464.
 32. Pierini A, Gori E, Lippi I, Ceccherini G, Lubas G, Marchetti V. Neutrophil-to-lymphocyte ratio nucleated red blood cells and erythrocyte abnormalities in canine systemic inflammatory response syndrome. *Res Vet Sci.* 2019;126:150–154.
 33. Hodgson N, Llewellyn EA, Schaeffer DJ. Utility and prognostic significance of neutrophil-to-lymphocyte ratio in dogs with septic peritonitis. *J Am Anim Hosp Assoc.* 2018;54:351–359.
 34. Dourmashkin LH, Lyons B, Hess RS, Walsh K, Silverstein DC. Evaluation of the neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios in critically ill dogs. *J Veterinary Emerg Critic Care.* 2023;33:52–58.
 35. Pierini A, Gori E, Lippi I, Lubas G, Marchetti V. Are leukocyte and platelet abnormalities and complete blood count ratios potential prognostic markers in canine sepsis? *Front Vet Sci.* 2020;7.
 36. Gülersoy E, Naseri A. Hematological status in septic or non septic dogs due to parvoviral enteritis. *Dicle Üniversitesi Veteriner Fakültesi Dergisi.* 2022;15:45–52.
 37. Pekmezci D, Konaçoğlu GN, Çolak ZN. A preliminary study for determination of neutrophil to lymphocyte, monocyte to lymphocyte and platelet to lymphocyte ratios in dogs with Canine Distemper Virus infection. *J Anatolian Environ Animal Sci.* 2022;7:437–443.
 38. Hong X, Cui B, Wang M, Yang Z, Wang L, Xu Q. Systemic immune-inflammation index, based on platelet counts and neutrophil-lymphocyte ratio, is useful for predicting prognosis in small cell lung cancer. *Tohoku J Exp Med.* 2015;236: 297–304.
 39. Wu D, Qin H. Diagnostic and prognostic values of immunocyte ratios in patients with sepsis in the intensive care unit. *J Infect Dev Countr.* 2023;171:1362–1372.

Further reading

40. Liu Y, Du X, Chen J, et al. Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19. *J Infect.* 2020;81:6–12.