Veterinary Research Communications (2026) 50:11
https://doi.org/10.1007/s11259-025-10940-4

BRIEF REPORT

The diagnostic and prognostic utility of complete blood count (CBC)-derived indices in dogs with sepsis caused by canine parvoviral infection

Tuğba Varlik[1] · Didem Algan[1] · Jose Ceron[2] · Zeki Yilmaz[1]

Received: 6 August 2025 / Accepted: 30 September 2025 / Published online: 29 October 2025
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Abstract

This study aimed to evaluate the diagnostic and prognostic value of complete blood count (CBC)-derived indices incorporating red blood cell (RBC) and platelet (PLT) parameters in dogs that met the criteria for sepsis due to canine parvovirosis (CP). Fifty-two client-owned dogs with CP and ten healthy controls were enrolled in this study. CBC-derived indices, along with serum CRP and albumin concentrations, were evaluated before (T0) and after treatment (T1 and T3). Dogs meeting the criteria for sepsis exhibited statistically significantly higher RDW/L ($P<0.001$), MCV/L ($P<0.001$), MPV/L ($P<0.001$), PLT/L ($P<0.001$), PCT/L ($P<0.001$), and PDW/L ratios ($P<0.001$) compared to the control group. Receiver operating characteristic curve analysis revealed high diagnostic and prognostic performance for MCV/L (AUC: >0.949) and MPV/L (AUC: >0.961). In conclusion, CBC-derived indices incorporating RBC and PLT parameters can provide useful information about the diagnosis and prognosis in dogs with sepsis produced by parvovirus. These findings, if corroborated in larger studies, would support their integration into clinical practice to enhance the early detection and risk stratification in canine sepsis.

Keywords Canine parvovirus · CBC-derived indices · CRP · Prognostic biomarkers · Sepsis · Dogs

Introduction

Canine parvovirosis (CP), caused by canine parvovirus (CPV), is a well-established naturally occurring model of sepsis in animals (Alves et al. 2020), which is characterized by key pathophysiological features, including leukopenia, endotoxemia, and systemic inflammation (Kocaturk et al. 2010, 2015; Alves et al. 2020). Early diagnosis and prognosis are essential in sepsis management (Yilmaz and Senturk 2007; Yilmaz et al. 2008).

Several CBC-derived inflammatory indices, particularly those normalized to white blood cell (WBC) counts, such as the neutrophil-to-lymphocyte (N/L) ratio, monocyte-to-lymphocyte (M/L) ratio, and platelet-to-lymphocyte (P/L) ratio, have been widely investigated to assess their diagnostic and prognostic value in dogs with CP (González-Domínguez et al. 2024). While some studies have reported associations between elevated N/L or P/L ratio and disease severity or outcome (Aydın 2024; González-Domínguez et al. 2024), others have found limited diagnostic or prognostic value (Pekmezci and Çolak 2021). Sevim et al. (2025) also demonstrated the prognostic utility of N/L, P/L, and P/N ratio but not to the M/L ratio in CPV-infected dogs. Moreover, N/L ratio may reflect treatment response rather than baseline prognosis (Muñoz et al. 2022).

These indices are usually focused on WBC analytes, with few exceptions, such as the P/L, and there is no information on how these indices change before and after treatment. Additionally, they are no reports about relationships of indices with serum inflammatory markers, including serum C-reactive protein (CRP), albumin, and CRP/albumin ratio.

✉ Zeki Yilmaz
zyilmaz@uludag.edu.tr

[1] Department of Internal Medicine, Faculty of Veterinary Medicine, Bursa Uludag University, Bursa 16059, Turkey

[2] Interdisciplinary Laboratory of Clinical Analysis, Interlab-UMU, Regional Campus of International Excellence 'Campus Mare Nostrum', University of Murcia, Murcia 30100, Spain

The lack of inclusion of other components of CBC, such as red blood cells (RBC) and platelets (PLT), may lead to an incomplete representation of the host's hematologic cellular responses in dynamic conditions, such as sepsis. Therefore, it could be suggested that composite indices combining WBC counts with the other components of CBC, such as RBC and PLT parameters, could provide a more comprehensive assessment of bone marrow function, reflecting not only leukopoietic but also erythroid and thrombopoietic activity (Kocaturk et al. 2024). Furthermore, assessing these indices not only at admission but also longitudinally, since dynamic changes in hematologic ratios may outperform single time-point values for risk stratification.

In human sepsis cohorts, indices that normalize RBC or PLT parameters to lymphocyte counts have been shown to improve interpretability and prognostic accuracy. For example, the red cell distribution width-to-lymphocyte ratio (RDW/L) and mean platelet volume-to-lymphocyte ratio (MPV/L) were independently associated with sepsis incidence and mortality in a large cohort of burn patients in the intensive care unit (Kim et al. 2024). Similarly, a newly derived CBC Sepsis Index (CBC-SI), which combines monocyte distribution width, N/L, and WBC, demonstrated excellent diagnostic accuracy for early sepsis detection in a cohort of over 50,000 patients presenting to the emergency department (Levin et al. 2025). These findings highlight that RBC- and PLT-normalized indices capture bone marrow stress and thrombopoietic alterations in conjunction with sepsis-associated lymphopenia, providing a more integrative view of disease pathophysiology. To our knowledge, such normalization strategies have not been systematically investigated in canine sepsis, which highlights the novelty of the present study.

The main objectives of this study were to investigate the diagnostic and prognostic value of CBC-derived indices normalized by RBC and PLT in dogs with CPV-induced sepsis. These indices were compared with serum positive (CRP) and negative (albumin) acute phase proteins, as well as their ratio (CRP/albumin), which are widely used inflammatory biomarkers in clinical practice (Kocaturk et al. 2010, 2015; Mazzaferro 2020; Muñoz et al. 2022).

Materials and methods

Study design

In this retrospective study, medical records of dogs diagnosed with CPV infection between January 1, 2020, and June 30, 2025, were reviewed from the archives of the Veterinary Teaching Hospital (Department of Internal Medicine, Faculty of Veterinary Medicine, Bursa Uludağ University, Türkiye) and two private small animal clinics (VetPlanet and Armilla Animal Hospital, Bursa, Türkiye). The initial study cohort comprised 135 CPV-positive cases. Following the application of predefined inclusion and exclusion criteria, 42 dogs met the eligibility requirements and were included in the final analysis — 29 of 74 cases from the Veterinary Teaching Hospital and 13 of 61 cases from the private clinics.

In this study, two groups were formed: a healthy control group ($n=10$) and a sepsis group ($n=42$), consisting of age-matched dogs ranging from 3 to 8 months, with mean ages of 5.2 and 5.7 months, respectively.

Inclusion and exclusion criteria

The inclusion criteria for the sepsis group were: (i) clinical signs consistent with CPV infection (such as diarrhea, vomiting, and lethargy), (ii) a positive fecal antigen test for CPV (Antigen Rapid CVP/CCV and CDV kit, Bionote, Korea, which has been reported to yield high specificity and positive predictive value, with 95% confidence intervals of 96.9–100% for both) (Walter-Weingärtner et al. 2021), (iii) fulfillment of systemic inflammatory response syndrome (SIRS) criteria based on specific clinical variables (body temperature, heart rate, and respiratory rate; cut off values were given in the sepsis definition) and hematological findings (total WBC count and differentials, as well as platelet count), and (iv) availability of complete hematology and biochemistry records. Exclusion criteria included (i) the presence of cachexia or malnutrition, concurrent systemic illness or parasitic infection, assessed by fecal flotation, blood smear, Giardia test, and metabolic diseases such as juvenile diabetes mellitus, hypothyroidism, and pancreatitis, assessed by serum biochemistry profile (blood glucose; thyroxine and cholesterol; and canine pancreatic lipase), (ii) incomplete medical records, and (iii) prior treatment with immunosuppressive drugs.

Additional examinations were performed to rule out common co-infections. In line with routine clinical protocol in the animal hospital, all dogs suspected of CPV infection were screened for co-infection with other viral pathogens, including canine coronavirus (CCV) and canine distemper virus (CDV). Screening was performed using either combined SNAP ELISA tests for CPV and CCV antigens or separate tests for CDV antigen (Antigen Rapid CVP/CCV and CDV kit, Bionote, Korea). Only animals that tested positive for CPV and negative for both CCV and CDV were included in the study. All dogs were also tested for coccidial oocysts using fecal flotation and for blood parasites (Babesia, Ehrlichia, and Hepatozoon species) on stained peripheral blood smears. Giardiasis was excluded using either fecal wet mounts at admission or a commercial SNAP

ELISA test (a combined test for Giardia, CCV, and CPV, Bionote, Korea) conducted within the first two days of hospitalization. All dogs included in the study tested negative for these pathogens. PCR testing for additional co-infections was not systematically performed due to resource and cost limitations.

Control dogs, brought to the hospital by their owners for routine check-ups, were age-matched, deemed clinically healthy based on normal physical examination findings, CBC, and serum biochemistry profiles. Since this study was conducted retrospectively using existing medical records from the hospital archives, it was exempt from ethical committee approval.

Sepsis definition

Systemic Inflammatory Response Syndrome (SIRS) can result from both septic causes (e.g., bacterial, fungal, protozoal, parasitic, or viral agents) and non-septic causes (e.g., burns, heatstroke, immune-mediated diseases, neoplasia, or trauma). Sepsis is specifically defined as SIRS occurring in the presence of a suspected or confirmed infection (Spillane et al. 2023). Accordingly, in this study, dogs were classified as septic if they met at least two of the SIRS criteria—namely: a body temperature < 38.1 °C or > 39.3 °C, heart rate > 120 beats per minute, respiratory rate > 20 breaths per minute, or WBC count < 6,000 or > 16,000 cells/µL—in combination with a positive CPV rapid antigen test result (Spillane et al. 2023). This classification is consistent with previous studies describing sepsis as a SIRS response to confirmed CPV infection (Yilmaz and Senturk, 2007; Sevim et al. 2025). In this study population, elevated serum CRP levels were used to support the presence of systemic inflammation, as described in our previous study (Kocaturk et al. 2015).

Hematobiochemistry analysis

The CBCs were measured using automated analyzers (HM5®, Abaxis; and BC-760, Mindray, China). The CBC-derived composite indices presented in this study were calculated manually, as described in our previous work (Kocaturk et al. 2024), as follows:

1. RBC-WBC composite Indices:
    i) MCV/L ratio: Mean corpuscular volume divided by the absolute lymphocyte count.
    ii) RDW/L ratio: Red cell distribution width divided by the absolute lymphocyte count.
2. PLT-WBC composite Indices:
    i) PLT/L ratio: Platelet count divided by absolute lymphocyte count.
    ii) PCT/L ratio: Plateletcrit divided by absolute lymphocyte count.
    iii) MPV/L ratio: Mean platelet volume divided by absolute lymphocyte count.
    iv) PDW/L ratio: Platelet distribution width divided by absolute lymphocyte count.
3. RBC-PLT composite Indices
    i) HCT/PCT ratio: Hematocrit divided by plateletcrit.
    ii) MCV/MPV ratio: Mean corpuscular volume divided by mean platelet volume.
    iii) RDW/PDW ratio: Red cell distribution width divided by platelet distribution width.
    iv) RDW/PLT ratio: Red cell distribution width divided by platelet count.
4. PLT-specific composite Indices
    i) MPV/PLT ratio: Mean platelet volume divided by platelet count.
    ii) MPV/PDW ratio: Mean platelet volume divided by platelet distribution width.
    iii) MPV/PCT ratio: Mean platelet volume divided by plateletcrit.

In this study, the primary focus was on four groups of novel CBC-derived composite indices, while the widely studied leukocyte-based indices (namely, the neutrophil-to-lymphocyte ratio [N/L] and monocyte-to-lymphocyte ratio [M/L]), were also included for comparative purposes. The N/L ratio was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. The M/L ratio was calculated by dividing the absolute monocyte count by the absolute lymphocyte count.

Serum CRP (mg/L) was measured using an automatic biochemistry analyzer (Vcheck Canine CRP 2.0, Bionote), while serum albumin (g/dL) was measured using an automated analyzer (VetScan®, Comprehensive diagnostic profile, Zoetis). The CRP/albumin ratio was calculated by dividing the CRP value by the albumin concentration (Park et al. 2018).

Monitoring and sampling

Monitoring and sample collection were carried out at three time points: at admission (T0), and at 24 (T1) and 72 (T3) hours following the initiation of treatment. The selection of these time points was influenced by previous findings indicating changes in WBC counts and differentials at T1 and

T3 following admission (T0) in CPV-infected dogs (Bastan et al. 2013). Therefore, this timeline was considered to provide a clinically meaningful framework for evaluating dynamic changes in CBC-derived indices.

Treatments

The treatment of CPV-infected dogs followed a standardized supportive protocol; while detailed procedures are available in the previously published studies (Yilmaz 2000; Rosati et al. 2007; Kocaturk et al. 2010; Mylonakis et al. 2016; Yalcin and Keser 2017; Mazzaferro 2020; Zhou et al. 2024), the essential steps are outlined below for completeness. All dogs were hospitalized in the infectious diseases isolation unit of the Veterinary Teaching Hospital and maintained in heated cages for at least three days. Although some dogs remained hospitalized beyond this period, depending on clinical progress, only data from the first 72 hours were included in the study. Discharge decisions were made on a case-by-case basis according to clinical improvement and stabilization."

Fluid therapy was initiated immediately upon admission and tailored to the patient's clinical status. Dogs in hypovolemic shock received rapid intravenous crystalloid boluses (up to 90–150 mL/kg/hour) until perfusion parameters normalized, while dehydrated but non-shock dogs were rehydrated over four hours. Maintenance fluid requirements (2–3 mL/kg/hour) were accounted for according to ongoing losses due to vomiting and diarrhea. Potassium chloride (20 mEq/L) was supplemented, and hydroxyethyl starch (10 mL/kg, IV bolus) was used if crystalloid therapy was insufficient. Dobutamine (1–10 µg/kg/min in 5% dextrose, IV continuous infusion; Mekard 250 mg/20 mL, Polifarma, Türkiye) was administered in cases where fluid therapy alone did not restore circulatory function. The infusion was titrated based on the patient's cardiovascular response. Continuous monitoring included assessment of mucous membrane color, capillary refill time, peripheral pulse quality, and heart sound intensity on auscultation. Vital parameters were re-evaluated every 5–10 min. When no improvement trend was observed in vital clinical parameters during the dobutamine infusion, the dose was increased in an attempt to enhance cardiovascular support. Dobutamine infusion was discontinued once clinical parameters were normalized.

Antibiotic therapy consisted of ampicillin (22 mg/kg, IV, q8h until vomiting ceased for 24 h, then 30 mg/kg, PO, q12h for 10 days), gentamicin (4 mg/kg, IV, q24h for 5 days, initiated only after euhydration in leukopenic dogs to minimize nephrotoxicity), and metronidazole (25 mg/kg, PO, q12h for 5 days). Metoclopramide (0.4 mg/kg, SC, q8–12 h) or maropitant (1 mg/kg, SC, q24h) was used as an antiemetic until vomiting resolved. This treatment protocol was based on standard CPV management guidelines (Tuteja et al. 2022; Zhou et al. 2024), but the essential steps are summarized here to ensure the manuscript is self-contained and comprehensible without referring to external sources.

Statistical analysis

Statistical analyses were performed using SigmaPlot 2000 (SPSS, Inc., Chicago, IL, USA). Normality of data distribution was assessed using the Shapiro–Wilk test, and homogeneity of variances was evaluated using Levene's test. At baseline (T0), statistical differences between the sepsis and control groups were evaluated using an unpaired t-test when data were normally distributed with equal variances; otherwise, the Mann–Whitney U test was applied. Within the sepsis group, measurements at three-time points (T0, T1, and T3) were analyzed using repeated measures ANOVA for normally distributed data. Holm–Sidak post hoc correction was applied for pairwise comparisons, when data were normally distributed and variances were equal. When assumptions for parametric testing were violated, the nonparametric Friedman test was used, followed by Dunn's post hoc test. Pearson's correlation coefficient was calculated for normally distributed variables to evaluate associations between CBC-derived composite indices and serum inflammatory markers. Of the dogs studied, 33 survived, but 9 died despite treatment. Receiver operating characteristic (ROC) curve analyses were conducted to evaluate the diagnostic and prognostic performance of each parameter (MedCalc software, Version 23.2.7). Data are presented as mean ± standard error of the mean (SEM), and a P-value less than 0.05 was considered statistically significant.

Results

The study results include a presentation of the diagnostic and prognostic value of the composite indices described in the Materials and Methods section for dogs with CPV.

Diagnostic value

Among the RBC-WBC composite indices, lymphocyte-normalized RBC indices, including the MCV/L and RDW/L, were significantly elevated in septic dogs compared to healthy controls ($P < 0.01$) (Fig. 1). In our analysis, these indices demonstrated higher AUCs (range: 0.950–0.972), sensitivity (range: 96–100%), and specificity (80%) compared to those of other CBC indices (Table 1).

The PLT-based indices included in this report (PLT/L, PCT/L, MPV/L, and PDW/L) were also significantly higher

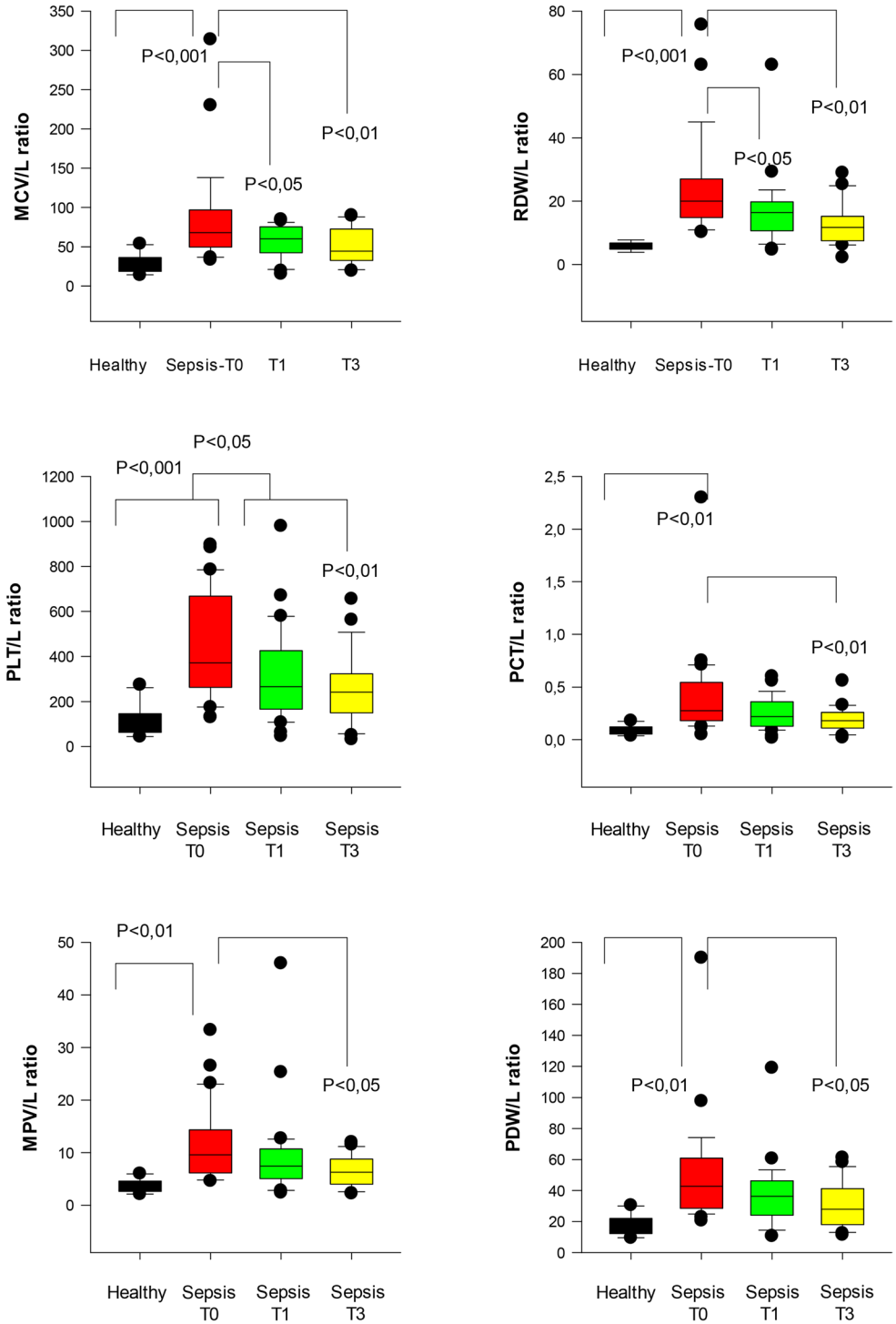

Fig. 1 CBC-derived indices combining lymphocyte counts with red blood cell (RBC) and platelet (PLT) parameters in dogs with sepsis secondary to canine parvovirus infection, measured at admission (T0), post-treatment day 1 (T1), and day 3 (T3), in comparison to healthy controls. ***MCV/L***: *Mean Corpuscular Volume-to-Lymphocyte Count Ratio;* ***RDW/L***: *Red Cell Distribution Width-to-Lymphocyte Count Ratio;* ***PCT/L***: *Plateletcrit-to-Lymphocyte Count Ratio;* ***PLT/L***: *Platelet Count-to-Lymphocyte Count Ratio;* ***MPV/L***: *Mean Platelet Volume-to-Lymphocyte Count Ratio;* ***PDW/L***: *Platelet Distribution Width-to-Lymphocyte Count Ratio*

in the sepsis group at T0 ($P<0.01$) (Fig. 1). ROC analysis revealed strong diagnostic performance for all four indices, with AUCs ranging from 0.942 to 0.962 (Table 1).

Of the ratios combining RBC and PLT parameters, only the RDW/PDW ratio was significantly higher in septic dogs at admission ($P<0.01$) (Fig. 2). Other indices in this group, including HCT/PCT, MCV/MPV, and RDW/PLT, did not show significant differences between groups.

The PLT-specific indices (MPV/PLT, MPV/PDW, and MPV/PCT) (Fig. 2) and WBC-specific indices (N/L and M/L ratio; Fig. 3) showed no statistically significant differences between groups at T0, although all exhibited a downward trend in the sepsis group.

Serum CRP and CRP/albumin ratio were significantly elevated in septic dogs ($P<0.001$), while serum albumin levels were reduced, albeit not significantly (Fig. 4). CRP

Table 1 Optimal cut-off values of CBC-derived indices for the diagnosis of sepsis in dogs with parvoviral infection, along with corresponding sensitivity, specificity, area under the curve (AUC), standard error (SE), and positive (+LR) and negative (–LR) likelihood ratios

Parameter	Cut-off	Sensitivity (%)	Specificity (%)	AUC	SE	+LR	-LR
WBC indices							
− N/L	≤1,47	42	100	0,645	0,08	N/A	0,5
− M/L	≤0,11	26	90	0,552	0,10	2,6	0,8
RBC-WBC indices							
− MCV/L	>34,0	96	80	0,950***	0,03	4,8	0,0
− RDW/L	>7,70	100	80	0,972***	0,02	5,0	0,0
Platelet-WBC indices							
− PLT/L	>156,0	93	90	0,953***	0,03	9,3	0,0
− PCT/L	>0,18	76	100	0,942***	0,03	N/A	0,2
− MPV/L	>4,25	100	80	0,962***	0,02	5,0	0,0
− PDW/L	>20,50	100	80	0,957***	0,03	5,0	0,0
RBC-Platelet indices							
− HCT/PCT	≤146,00	50	80	0,577	0,09	2,5	0,6
− MCV/MPV	>8,10	36	90	0,577	0,09	3,6	0,7
− RDW/PDW	>0,38	93	60	0,867***	0,06	2,3	0,1
− RDW/PLT	>0,079	40	90	0,597	0,09	4,0	0,6
Platelet indices							
− MPV/PLT	≤0,02	43	100	0,680**	0,08	N/A	0,5
− MPV/PDW	>0,18	83	0	0,557	0,10	0,8	N/A
− MPV/PCT	≤27,70	43	100	0,675*	0,08	N/A	0,5
Serum biomarkers							
− CRP mg/dl	>21,60	100	100	1,000***	0,00	N/A	0,0
− Albumin gr/dL	≤2,7	46	90	0,710*	0,08	4,7	0,5
− CRP/Albumin	>7	100	100	1,000***	0,00	N/A	0,0

*$P<0.05$; **$P<0.01$; and ***$P<0.001$

WBC: White Blood Cell Count; **N/L**: *Neutrophil-to-Lymphocyte Ratio;***M/L**: *Monocyte-to-Lymphocyte Ratio;***RBC**: Red Blood Cell Count; **MCV/L**: *Mean Corpuscular Volume-to-Lymphocyte Count Ratio;***RDW/L**: *Red Cell Distribution Width-to-Lymphocyte Count Ratio;***PCT/L**: *Plateletcrit-to-Lymphocyte Count Ratio;***PLT/L**: *Platelet Count-to-Lymphocyte Count Ratio;***MPV/L**: *Mean Platelet Volume-to-Lymphocyte Count Ratio;***PDW/L**: *Platelet Distribution Width-to-Lymphocyte Count Ratio;***HCT/PCT**: *Hematocrit-to-Plateletcrit Ratio;***MCV/MPV**: *Mean Corpuscular Volume-to-Mean Platelet Volume Ratio;***RDW/PDW**: *Red Cell Distribution Width-to-Platelet Distribution Width Ratio;***RDW/PLT**: *Red Cell Distribution Width-to-Platelet Count Ratio;***MPV/PLT**: *Mean Platelet Volume-to-Platelet Count Ratio;***MPV/PDW**: *Mean Platelet Volume-to-Platelet Distribution Width Ratio;***MPV/PCT**: *Mean Platelet Volume-to-Plateletcrit Ratio;***CRP (mg/dL)**: *C-reactive Protein*

and CRP/albumin ratio achieved perfect diagnostic accuracy (AUC: 1.000), whereas albumin alone showed only moderate performance (AUC: 0.710) (Table 1).

Prognostic value

Among the RBC-WBC composite indices, the MCV/L and RDW/L ratios progressively decreased from T0 to T3 ($P<0.05$) (Fig. 1). Both indices also demonstrated the highest prognostic accuracy among all the indices evaluated in this study, with AUCs of 0.979 (MCV/L) and 0.970 (RDW/L), and high sensitivity and specificity for mortality prediction (Table 2).

Among the PLT-based indices, significant reductions in all of them were observed over time, particularly between T0 and T3 ($P<0.05$–0.01) (Fig. 1). Among these, MPV/L and PDW/L showed AUCs of 0.970 and 0.808, respectively (Table 2).

The ratios combining RBC and PLT parameters (HCT/PCT, MCV/MPV, RDW/PLT, and RDW/PDW) as well as PLT-specific indices (MPV/PLT, MPV/PDW, and MPV/PCT) did not exhibit significant temporal changes throughout the monitoring period (Fig. 2). Their prognostic utility was limited, as reflected by AUC values below 0.700 in mortality prediction analyses (Table 2). Regarding the WBC-specific indices, the N/L ratio significantly decreased from T1 to T3 ($P<0.01$), whereas the M/L ratio remained statistically unchanged (Fig. 3).

Serum CRP levels were significantly elevated at T0 and declined steadily from T1 to T3 ($P<0.001$). Albumin levels showed a continuous decline from T0 to T3 ($P<0.05$), while the CRP/albumin ratio exhibited a parallel downward trend, with significantly lower values at T3 compared to both T0 and T1 ($P<0.001$) (Fig. 4). Despite these trends, serum CRP, albumin, and CRP/albumin ratio showed poor prognostic performance (AUC: 0.540–0.550), although albumin retained high specificity (Table 2).

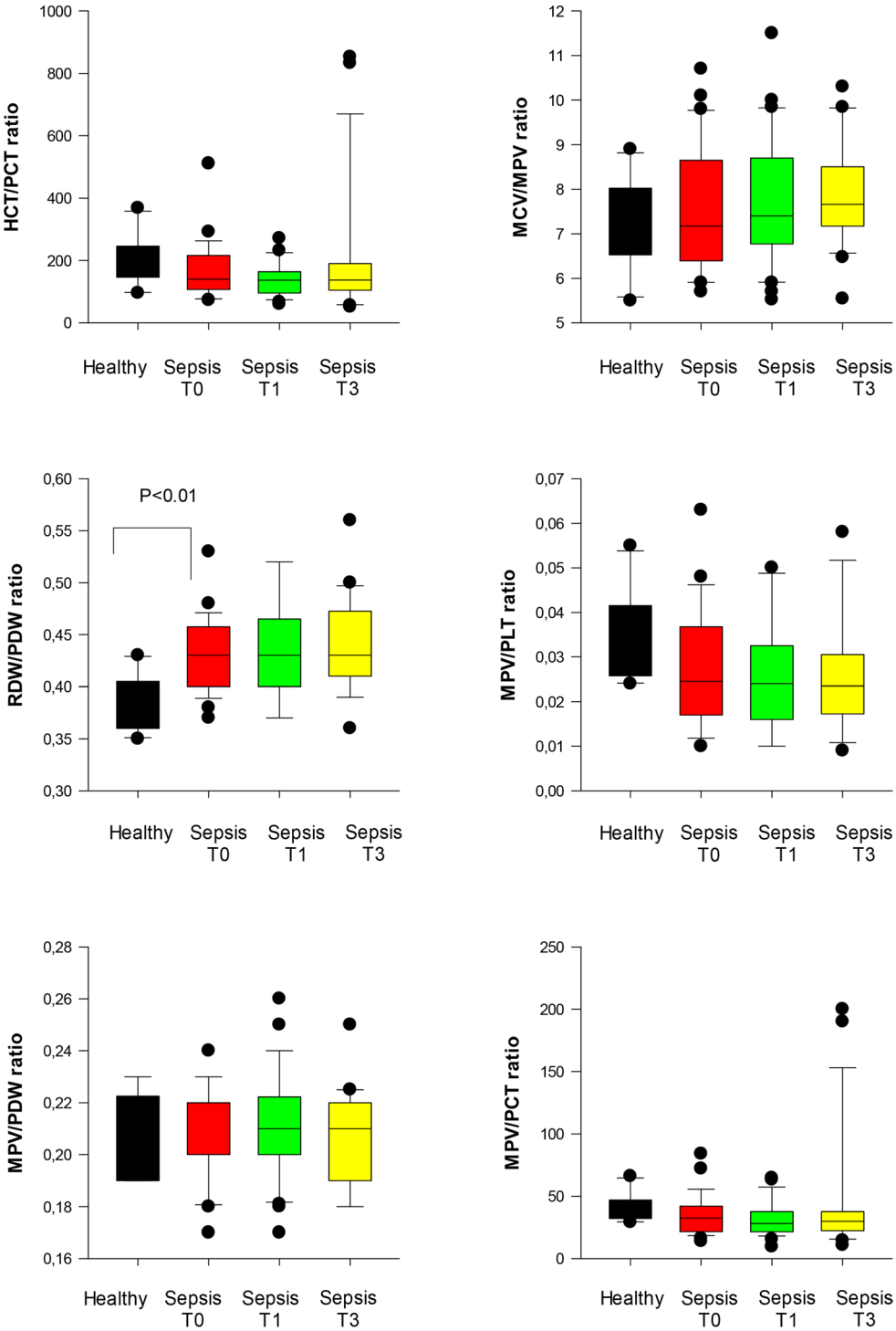

Fig. 2 CBC-derived indices combining platelet (PLT) parameters with red blood cell (RBC) metrics in dogs with sepsis secondary to canine parvovirus infection, measured at admission (T0), post-treatment day 1 (T1), and day 3 (T3), compared to healthy controls. ***HCT/PCT***: *Hematocrit-to-Plateletcrit Ratio;****MCV/MPV***: *Mean Corpuscular Volume-to-Mean Platelet Volume Ratio;****RDW/PDW***: *Red Cell Distribution Width-to-Platelet Distribution Width Ratio;****MPV/PLT***: *Mean Platelet Volume-to-Platelet Count Ratio;****MPV/PDW***: *Mean Platelet Volume-to-Platelet Distribution Width Ratio;****MPV/PCT***: *Mean Platelet Volume-to-Plateletcrit Ratio*

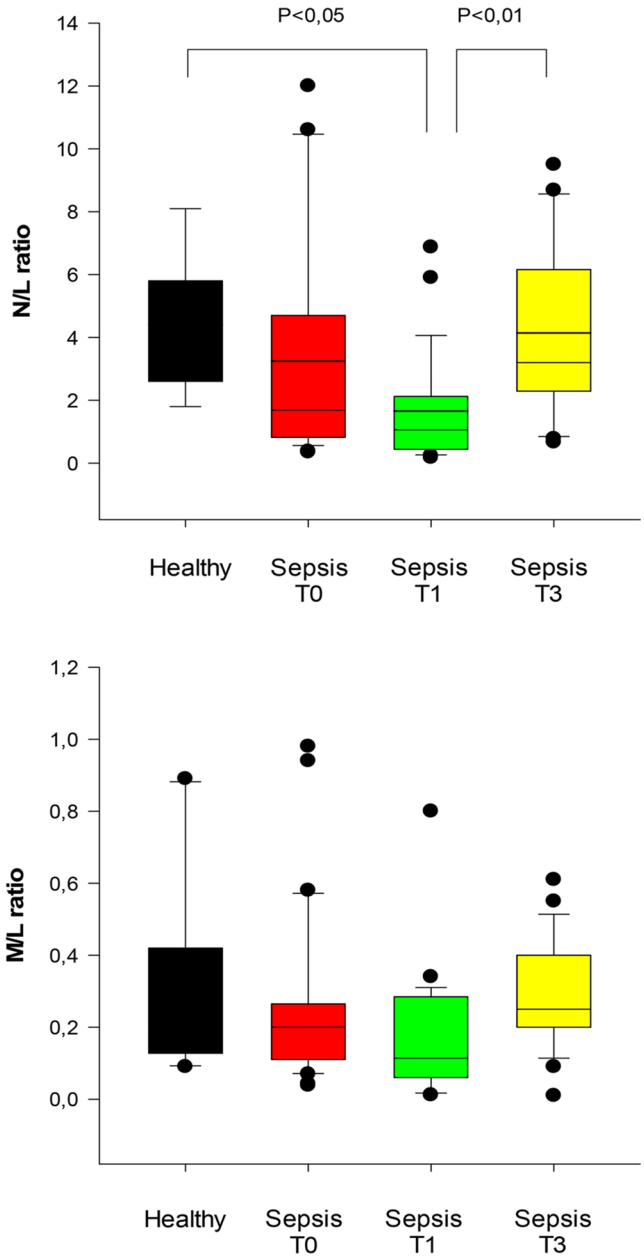

Fig. 3 Neutrophil-to-lymphocyte (N/L) and monocyte-to-lymphocyte (M/L) ratios in dogs with sepsis secondary to canine parvovirus infection, measured at admission (T0), post-treatment day 1 (T1), and day 3 (T3), in comparison to healthy controls

Correlations

Serum CRP showed strong positive correlations ($P<0.01$) with RDW/L; $r=0.445$, $P<0.01$ and PLT parameters such as MPV/L ($r=0.439$, $P<0.01$), PDW/L ($r=0.418$, $P<0.01$), PLT/L ($r=0.489$, $P<0.001$), and PCT/L ($r=0.503$, $P<0.001$). In contrast, the CRP/albumin ratio exhibited only a weak positive correlation with RDW/PLT ($r=0.316$, $P=0.057$).

Discussion

This study reveals dynamic changes in CBC-derived WBC, RBC, and PLT indices in dogs with CPV-related sepsis. Among these indices, RDW/L, MCV/L, MPV/L, PLT/L, PCT/L, and PDW/L demonstrated diagnostic relevance, while MCV/L and MPV/L showed stronger prognostic value. These simple and cost-effective markers may aid in early risk assessment and mortality prediction, but require further validation and integration into clinical practice.

Diagnostic value of CBC-Derived indices

Six of the newly evaluated indices in this report, encompassing RBC- and PLT-derived parameters (RDW/L, MCV/L, PLT/L, MPV/L, PCT/L, and PDW/L), demonstrated superior diagnostic performance. Their AUC values ranged from 0.942 to 0.962 ($P<0.001$), with sensitivity between 76 and 100% and specificity between 80 and 100%. These results substantially outperformed conventional WBC-derived ratios such as NLR and MLR, which yielded lower AUCs (0.552–0.645) and sensitivity (26–42%), although their specificity (90–100%) was comparable. This enhanced performance indicates that sepsis involves systemic alterations extending well beyond WBC activation. Excessive pro-inflammatory cytokine release, bone marrow suppression, and endothelial injury disrupt leukopoiesis, erythropoiesis, and thrombopoiesis (Yilmaz and Senturk 2007; Guclu et al. 2013; Agnello et al. 2021; Mylonakis et al. 2016; Mazzaferro 2020).

Lymphopenia is a key indicator of sepsis-induced immunosuppression and is markedly accentuated in CPV infection due to the virus's tropism for lymphoid tissues. In our study, PLT/L showed high diagnostic performance, with a sensitivity of 93%, a specificity of 90%, and an AUC of 0.953 ($P<0.001$). This would reflects the enhanced diagnostic contrast achieved when platelet indices are combined with lymphocyte counts. These findings are consistent with reports from human sepsis cohorts (Nayak et al. 2025) and canine studies (González-Domínguez et al. 2024; Sevim et al. 2025). Nevertheless, interpretation of this index requires caution, as sepsis can lead to thrombocytopenia due to consumption coagulopathy, splenic sequestration, or bone marrow suppression, while platelet clumping may further compromise measurement accuracy (Yilmaz and Senturk 2007).

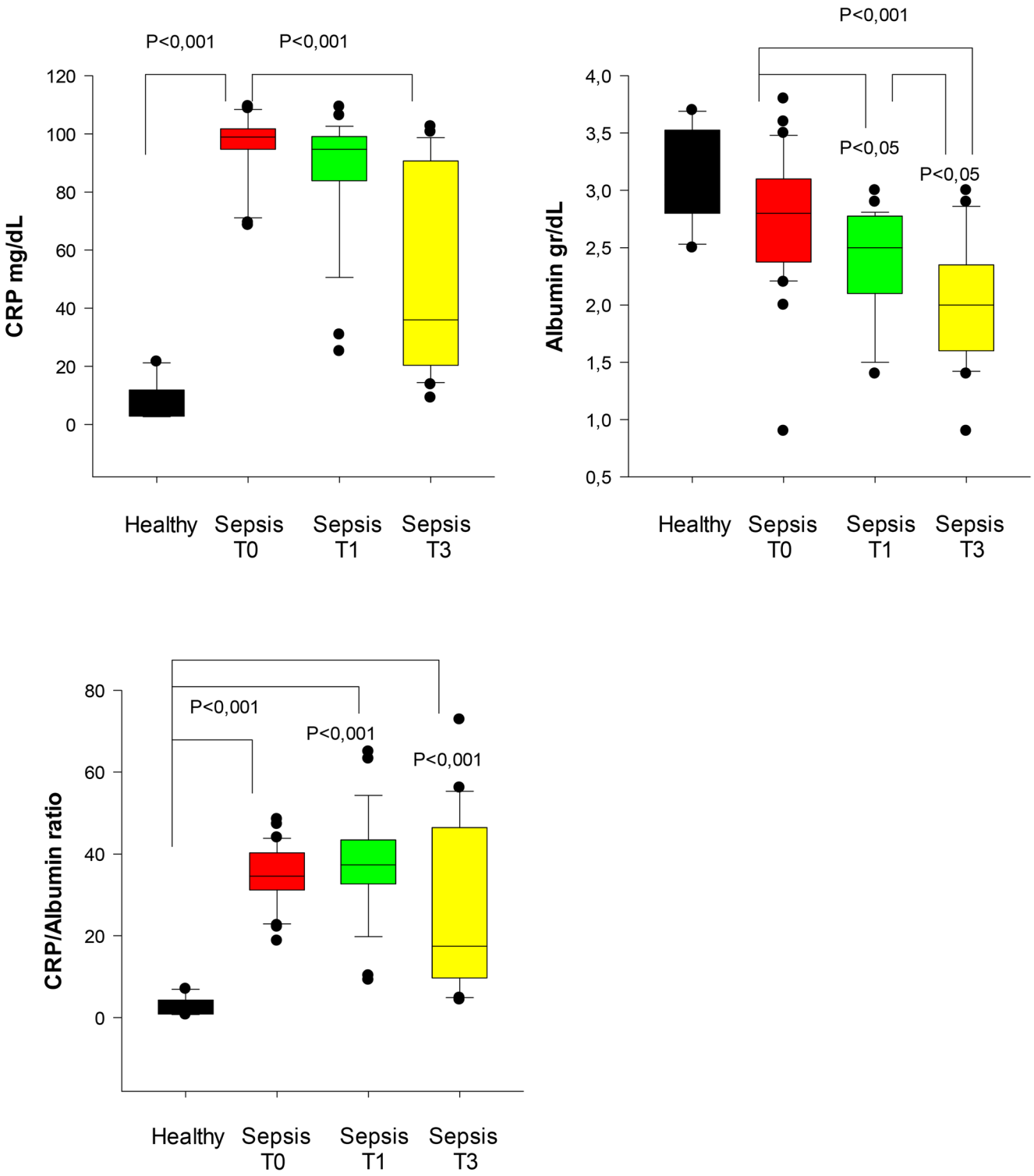

Fig. 4 Serum inflammatory markers C-reactive protein (CRP), albumin, and the CRP/albumin ratio in dogs with sepsis secondary to canine parvovirus infection, measured at admission (T0), post-treatment day 1 (T1), and day 3 (T3), compared to healthy controls

Table 2 Optimal cut-off values of CBC-derived indices for mortality prediction in dogs with sepsis due to parvoviral enteritis, including corresponding sensitivity, specificity, area under the curve (AUC), standard error (SE), and positive (+LR) and negative (–LR) likelihood ratios

Parameter	Cut-off	Sensitivity (%)	Specificity (%)	AUC	SE	+LR	-LR
WBC indices							
− N/L	≤1,14	80	78	0,713	0,17	3,6	0,2
− M/L	>0,18	80	52	0,520	0,11	1,6	0,3
RBC-WBC indices							
− MCV/L	>97,0	100	91	0,979***	0,02	12,0	0,0
− RDW/L	>24,5	80	80	0,800*	0,14	4,0	0,2
Platelet-WBC indices							
− PCT/L	>0,52	60	88	0,728	0,14	5,0	0,4
− PLT/L	>705,0	60	92	0,728	0,16	7,5	0,4
− MPV/L	>14,2	100	88	0,970***	0,03	8,3	0,0
− PDW/L	>62,8	80	84	0,808*	0,12	5,0	0,2
RBC-Platelet indices							
− HCT/PCT	>292,0	40	92	0,584	0,19	5,0	0,6
− MCV/MPV	>7,1	80	52	0,600	0,14	1,6	0,3
− RDW/PDW	≤0,39	60	88	0,700	0,14	5,0	0,4
− RDW/PLT	>0,08	60	72	0,556	0,19	2,1	0,5
− RDW/MPV	≤1,91	60	68	0,592	0,14	1,88	0,5
Platelet indices							
− MPV/PLT	>0,017	100	32	0,596	0,13	1,4	0,0
− MPV/PDW	≤0,17	20	100	0,520	0,16	N/A	0,8
− MPV/PCT	>20,4	100	20	0,536	0,14	1,2	0,0
Serum biomarkers							
− CRP mg/dl	>92,4	100	25	0,542	0,14	1,3	0,0
− Albumin gr/dL	≤2,2	40	97	0,540	0,18	14,0	0,6
− CRP/Albumin	>42	40	92	0,550	0,17	5,2	0,6

*$P<0.05$; and ***$P<0.001$

Abbreviations are given in the Table 1 legend

Prognostic value of CBC-Derived indices

During the course of treatment, significant reductions in RBC and PLT indices were observed, suggesting the normalization of erythropoietic and thrombopoietic responses during clinical recovery (Mahmood et al. 2014). Notably, MCV/L and MPV/L (AUC: 0.970 and 0.979; sensitivity: 100% for both; specificity: 88–91%, respectively) emerged as the most reliable prognostic markers of mortality in this study. These findings support recent reports in critically ill human patients with sepsis, demonstrating that composite hematologic indices provide superior prognostic accuracy compared with single parameters (Nayak et al. 2025). Consistently, a human study by Koçak and Urfalı (2025) reported that a CBC-derived composite index, MPV/PLT, offered diagnostic utility but lacked prognostic significance, a pattern closely aligned with our observations.

Among WBC-derived indices, only the N/L ratio showed a significant increase over time, while the M/L ratio remained unchanged. The absence of elevated N/L values in septic dogs may indicate delayed neutrophil mobilization or a transient redistribution of leukocyte subsets. Although some studies have reported increases in N/L and M/L ratios in CPV-infected dogs (Sevim et al. 2025; Muñoz et al. 2022), our findings more closely resemble those of other reports (González-Domínguez et al. 2024; Pekmezci and Çolak 2021), supporting the view that the prognostic utility of these WBC ratios is limited. The clinical course of sepsis is characterized by fluctuations in total and differential leukocyte counts; neutrophilic leukocytosis is commonly observed in sepsis cases (Pierini et al. 2020), whereas neutropenic leukopenia is more frequently associated with cases complicated by endotoxemia (Batmaz et al. 2003). These observations suggest that the conflicting results among studies regarding these indices may be related to differences in disease stage or sampling time, thereby reflecting the inherently dynamic nature of sepsis (Agnello et al. 2021).

Serum inflammatory biomarkers

Consistent with Montgomery et al. (2025), our analysis showed that neither CRP (AUC 0.542) nor the CRP/albumin ratio (AUC 0.550) provided strong prognostic value. While CRP demonstrated high sensitivity (100%) but poor

specificity (25%), the CRP/albumin ratio exhibited the opposite pattern, with low sensitivity (40%) and high specificity (92%). These contrasting performance metrics underscore the limitations of relying solely on isolated inflammatory markers to capture the complexity of sepsis progression.

Correlation analysis

The observed positive correlations between serum CRP and certain complete blood count (CBC) indices, such as RDW/L ($r=0.445$, $P<0.01$), MPV/L ($r=0.439$, $P<0.01$), and PDW/L ($r=0.418$, $P<0.01$), suggest that systemic inflammation may be associated with anisocytosis of PLTs and RBCs (Yilmaz et al. 2008; Stokes and Granger 2012; Katsaros et al. 2020). By contrast, the weak correlation between the CRP/albumin ratio and RDW/PLT ($r=0.316$, $P=0.057$) might reflect the influence of multiple confounding factors on serum albumin levels. In this study, the decrease in serum albumin levels was attributed to CPV-induced inflammation, considering its role as a negative acute phase protein. Although not directly investigated within the scope of this study, other potential mechanisms may be related to sepsis-associated endothelial injury and vascular leakage (Kocaturk et al. 2010, 2015).

Study limitations

The small sample size limits statistical power, particularly in subgroup analyses based on disease severity categories (mild, moderate, and severe) related to mortality. Regarding diagnostics, all dogs screened and tested negative for common parasitic and viral infections were included, although PCR confirmation was not performed for these pathogens, including CPV. Nonetheless, the high specificity and positive predictive value of SNAP CPV tests were considered sufficient to ensure diagnostic reliability and to support the validity of our findings (Walter-Weingärtner et al. 2021; Kocaturk et al. 2010). Another diagnostic limitation concerns the exclusion of Giardia infection, where the use of varying diagnostic methods across cases may have affected consistency in ruling out this concurrent pathogen. These diagnostic constraints reflect the resource and cost limitations of clinical settings, and should be considered when interpreting results. While supportive care protocols were standardized, individual therapeutic variability could have influenced changes in biomarker levels. Moreover, advanced inflammatory markers such as interleukin-6 and procalcitonin were not measured, limiting mechanistic interpretation and cross-study comparisons. Finally, the lack of long-term follow-up precluded the evaluation of persistent inflammation or delayed organ dysfunction. External validation of these indices across broader patient populations and disease contexts is necessary before widespread clinical application.

Conclusion

This study highlights the diagnostic and prognostic potential of novel CBC-derived composite indices, particularly those normalized to lymphocyte counts, for canine parvoviral sepsis. By integrating erythroid (RDW, MCV) and thrombopoietic (PLT, MPV) parameters into ratios indexed to lymphocyte counts, these markers offer a more nuanced reflection of the dynamic interplay between bone marrow stress, systemic inflammation, and lymphopenia. This lymphocyte-based normalization appears to enhance sensitivity and provides an advantage over traditional WBC-derived ratios. Their incorporation into routine diagnostics could serve as a rapid, cost-effective adjunct to established biomarkers, particularly in settings where advanced testing may not be readily available.

Beyond veterinary applications, these indices may hold translational value. Given the pathophysiologic similarities between canine and human sepsis, such markers could contribute to comparative research and inform future strategies in human critical care, especially in the context of early sepsis detection and monitoring.

However, cautious interpretation is warranted. Limitations such as variability in platelet measurements across analyzers, the impact of underlying hematologic disorders, and the lack of breed- and age-specific reference ranges may affect generalizability. Furthermore, as this was a retrospective, single-center study with a relatively small sample size, larger, multicenter prospective studies are needed to validate these findings, establish robust diagnostic thresholds, and explore their utility across other inflammatory conditions.

Author contributions ZY. conceived the study design; DA, and TV. contributed to sample collection, investigation, and evaluation; ZY. analyzed the data; JC. performed the serum CRP analysis; DA, and TV. prepared the first draft manuscript; ZY and JC. critically revised the manuscript. All authors read and approved the final version of the manuscript.

Funding None.

Data availability No datasets were generated or analysed during the current study.

Declarations

Ethics The study was conducted in accordance with animal welfare guidelines. As this was a retrospective study, approval from the institutional ethics committee was not required.

Consent for publication All the authors consent to publish the manu-

script.

Consent to participate All the authors consent to participate in publication.

Competing interests The authors declare no competing interests.

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