

The immunomodulator **Transferon®** induces changes in cortisol and catecholamines to improve survival in puppies with sepsis

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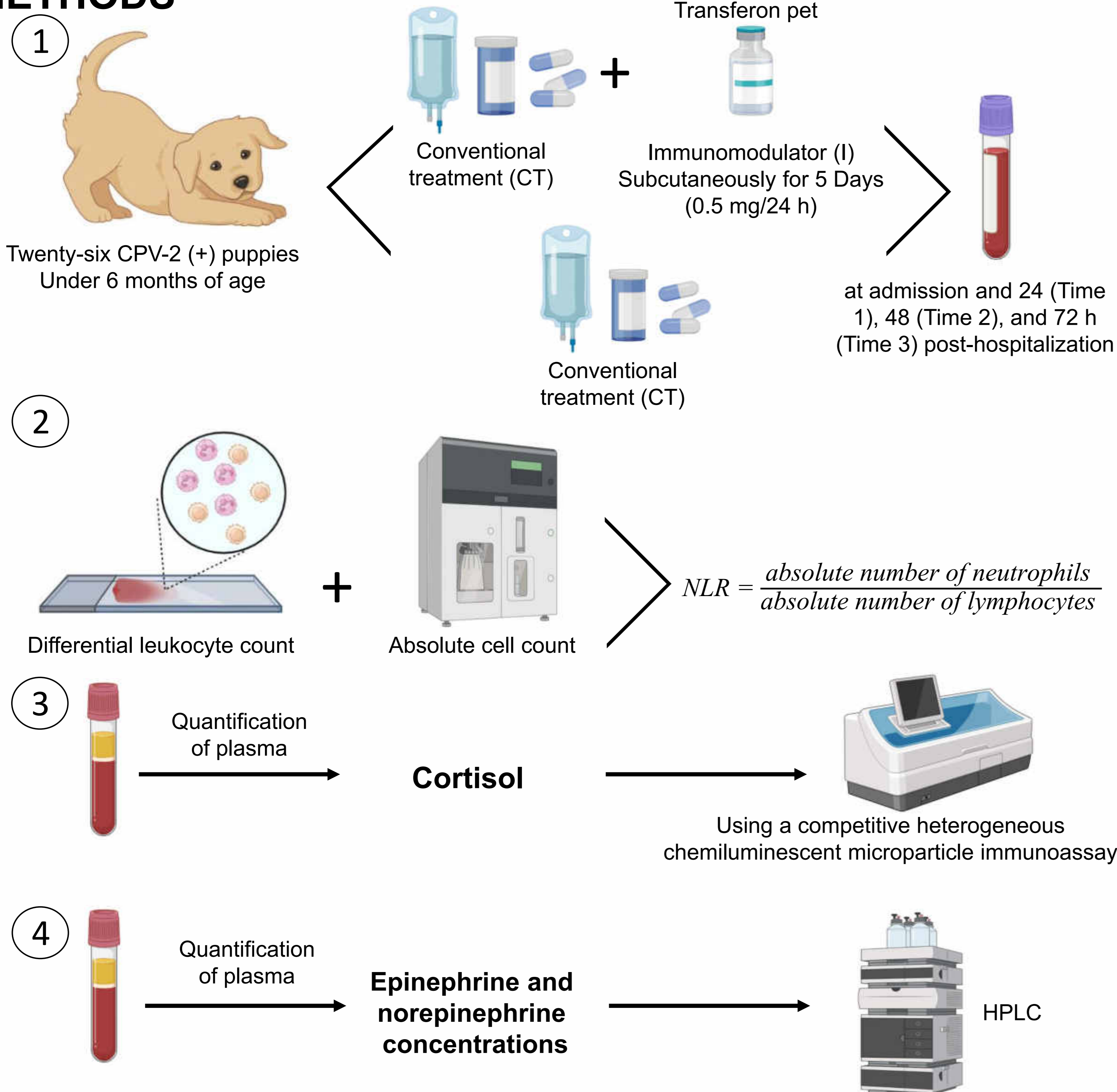
INTRODUCTION

The Neutrophil-to-lymphocyte ratio (NLR) is a cheap and easy-to-obtain biomarker that mirrors the balance between innate and adaptive immunity¹. High cortisol levels increase neutrophils while simultaneously decreasing lymphocyte counts^{1,2}. Likewise, endogenous catecholamines may cause leukocytosis and lymphopenia³. In this study, our group evaluated changes in NLR, cortisol, and catecholamine in puppies with sepsis secondary to CPE. We compare two groups of puppies, one treated conventionally vs. another that received an immunomodulatory (*Transferon pet*) as adjuvant treatment, this is composed of a complex mixture of low-molecular-weight peptides, the most abundant peptide is extracellular monomeric ubiquitin (meUb)⁴. The meUb have been immunoregulatory and anti-inflammatory functions mediated by CXCR4 observed in vitro and in vivo when administered orally or parenterally⁵.

OBJECTIVE

To evaluate NLR alteration in sepsis secondary to canine parvoviral enteritis treated with and without an immunomodulator in puppies.

METHODS



The values obtained were organized by time and treatment. The slope (m), generated by the changes in analyte levels, secondary to the treatments, was calculated with the values on days 1 and 3 using the formula below.

$$m = \frac{\text{value of analyte at day 3} - \text{value of analyte at day 1}}{\text{day 3} - \text{day 1}}$$

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ETHICAL APPROVAL

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RESULTS AND DISCUSSION

Puppies administered with the immunomodulator showed an increase in the survival rate (87.5%) in comparison with puppies that received CT (50%) at day 3 of clinical follow-up.

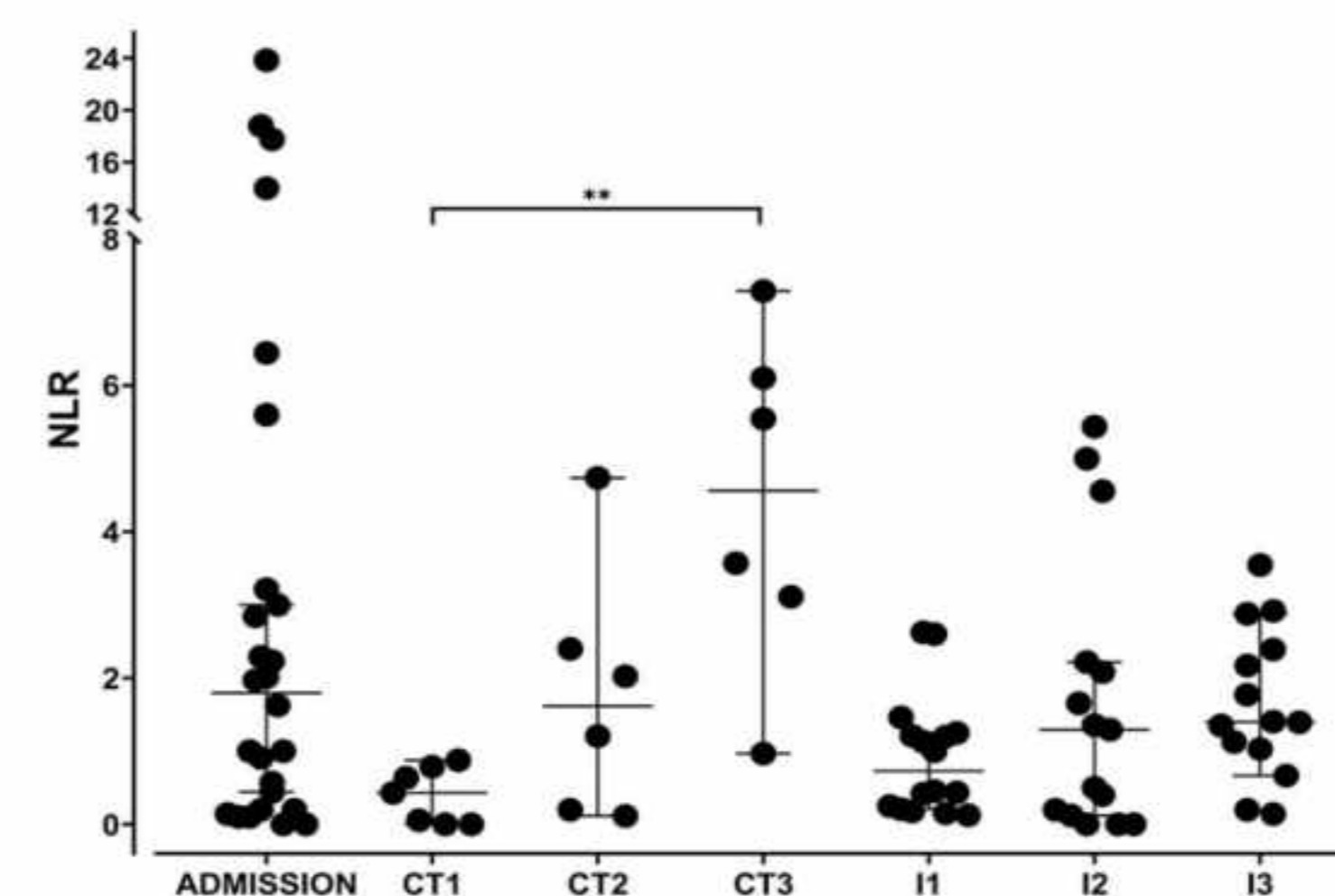


Figure 1. The graph shows NLR at admission and three subsequent days of treatment (critical time). Each dot represents a puppy. There are statistical differences between days 1 and 3 in the conventional treatment group. Kruskal-Wallis test, Dunn's post-hoc test. Median \bar{A} 95% interval confidence. ** = P \leq 0.01. CT = conventional treatment; I = immunomodulator.

The immunomodulator induced a slight and smooth decrease in cortisol and epinephrine levels during the first 72 h. Unlike the abrupt reduction in TC, it may be associated with the improvement of NLR

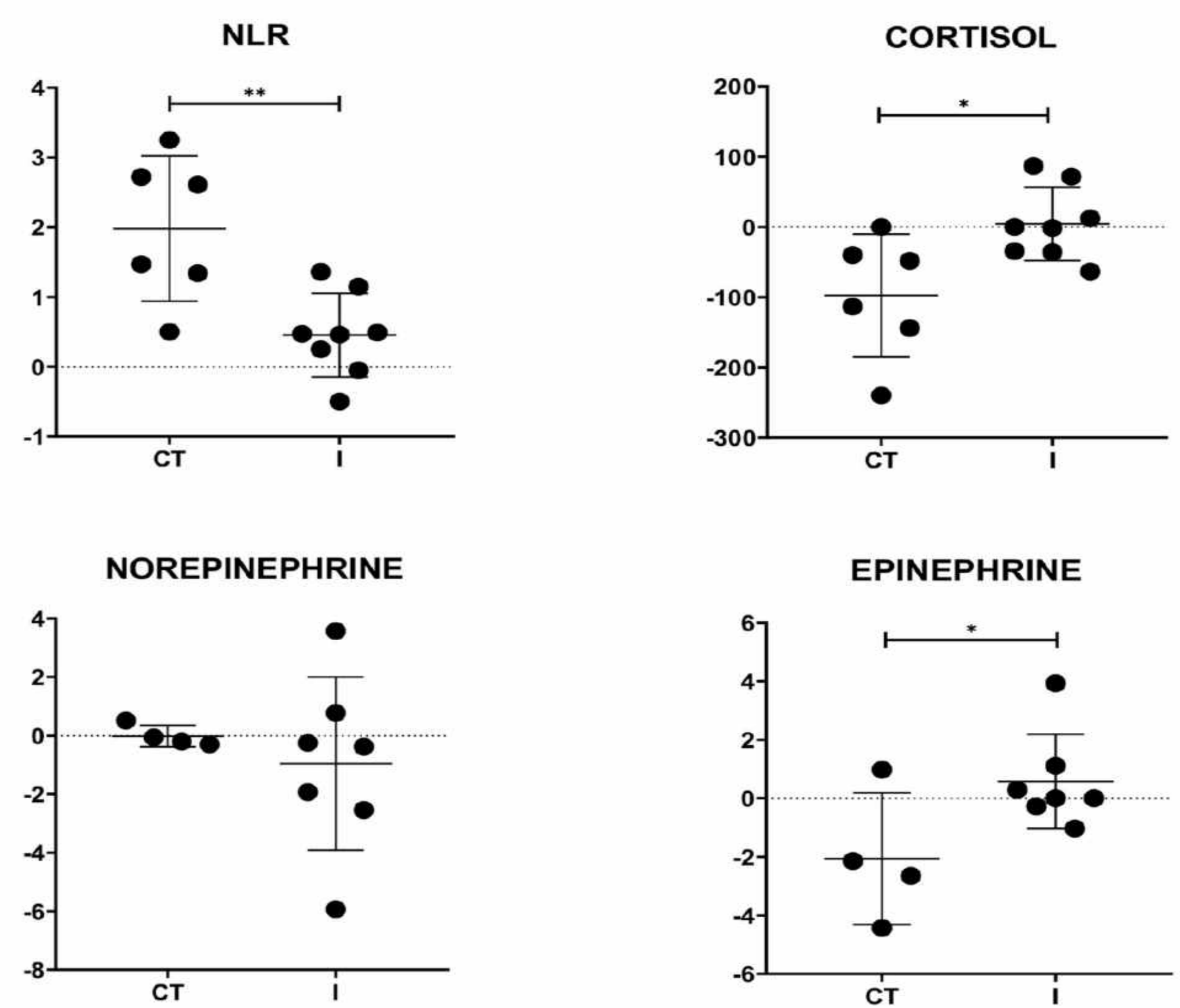


Figure 2. Statistical differences were observed in NLR, cortisol, and epinephrine slopes. A positive slope shows an increase in initial value while a negative one evidences a decrease. t-tests were carried out. Each dot represents a puppy. Mean \bar{A} SD. * = P \leq 0.05; ** = P \leq 0.01. CT = conventional treatment; I = immunomodulator.

CONCLUSION

Our hypothesis is that extracellular mUb may increase the vagal tone in puppies with CPE through the interaction between meUb-CXCR4, this last expressed in the vagus nerve and modulating the immune response. We propose that using a Ub-containing immunomodulator rich in extracellular mUb modulate levels of catecholamines and cortisol that allows the survival condition in puppies despite the sepsis.

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