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Section **Fields (of activity)**

Evaluation of plasma procalcitonin kinetics in dogs with bacterial infections for the development of an individualised procalcitonin-guided antimicrobial therapy

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Key words
Canine, antimicrobial stewardship, antimicrobial resistance

Aim of the study
The use of antimicrobials in small animal medicine contributes to the selection and dissemination of multi-drug resistant bacteria. The overall aim of this study was to assess whether plasma procalcitonin (pPCT) is a useful biomarker to guide antimicrobial therapy in dogs with bacterial infections. More specifically, we aimed to (i) evaluate day-to-day variability of pPCT in healthy dogs; (ii) determine pPCT kinetics in dogs with bacterial sepsis, acute diarrhoea or bacterial pneumonia and relevant control populations; (iii) evaluate the effect of general anesthesia, arthroscopy and tibial plateau leveling osteotomy (TPLO) on pPCT concentrations in dogs with uneventful surgical recovery.

Material and methods
A prospective, longitudinal, observational study was designed. Power analysis was performed using an epidemiological calculator (Sergeant, ESG, 2018. Epitools Epidemiological Calculators; Ausvet; available on: http://epitools.ausvet.com.au.) based on previously reported PCT concentrations in healthy and septic dogs. Power analysis indicated that at least 16 subjects per group were needed. Dogs were enrolled in the following disease groups (healthy, dogs meeting criteria for septic or non-infectious systemic inflammatory response syndrome (SIRS), dogs with acute diarrhea with or without sepsis criteria, dogs with bacterial pneumonia or non-infectious pneumonia and dogs undergoing TPLO. Blood was collected on 3-5 different time points to assess pPCT kinetics and correlations with C-reactive protein (CRP), white blood cell count, neutrophil count, albumin and bilirubin concentrations. Samples were analyzed using a previously validated canine PCT ELISA (Biovendor, Nashville, USA). Statistical analysis was performed using NCSS 2020.
Baseline characteristics of dogs were compared using the Kruskal-Wallis-ANOVA-Test or the Friedman-Rank-Test. Bonferoni test was used as a post-hoc test to correct for multiple comparisons. Inter- and intra-individual variability were calculated using the formula standard deviation/mean*100. Correlation analysis was performed with the Spearman Rank Correlation Test. In septic dogs, antimicrobial pre-treatment was correlated with pPCT concentrations using logistic regression analysis. Statistical significance was set at $p<0.05$.

Results and significance
Median pPCT in healthy dogs (n=16) was 110 pg/ml (range of 49 pg/ml – 195 pg/ml), with no significant variation between three consecutive sampling days. Inter-individual variability was higher (36%) than intra-individual vari-

ability (15%). There was no significant difference in median pPCT between healthy dogs and dogs with bacterial sepsis (n=17) or non-infectious SIRS (n=16), dogs with acute diarrhea with () or without sepsis criteria (n=) and dogs with bacterial pneumonia (n=14) or non-infectious pneumonia (n=9). However, in septic dogs pPCT concentrations were significantly higher in non-survivors than in survivors. Prior treatment with antimicrobials was not associated with pPCT concentrations in septic dogs.
In the TPLO group, pPCT concentrations temporarily decreased immediately after surgery, likely due to dilutional effects of perioperative fluid therapy. In contrast, median CRP was above the reference range (<10.5 mg/l) in dogs with SIRS (100.7 mg/l; IQR 67 – 141.9) or sepsis (131.9 mg/l; IQR 75.7 – 194.8) and significantly decreased within the first 4 days of successful treatment of sepsis.
Based on these results we conclude that because of a relatively high inter individual variability of pPCT, serial individual measurements might be more useful than a population based reference interval. General anesthesia, arthroscopy and TPLO surgery do not lead to an increase of pPCT. Unfortunately, pPCT has poor discriminatory power to identify dogs with bacterial infections and does not correlate with clinical resolution of infection. It therefore is not a useful biomarker to guide antimicrobial therapy in dogs with bacterial sepsis, acute diarrhea or pneumonia. At present, CRP therefore remains the most useful and widely available marker to potentially guide antimicrobial treatment decisions in dogs

Publications, posters and presentations

Rompf, J. (2021) Biological variation of plasma procalcitonin in clinically healthy dogs. ECVIM online congress 01.-04.09.2021.

Rompf, J. (2022) Plasma procalcitonin (pPCT) as a marker for bacterial infection in dogs. Doctoral dissertation, Veterinärmedizinische Fakultät, Universität Bern (August 2022).

Rompf, J., Lutz B, Marti, E.; Mirkovitch, J.; Peters, L.; Adamik, K.; Schüpbach-Regula, G.; Hettlich, B.; Willi, B.; Schuller, S. (2022) Serum procalcitonin kinetics in healthy dogs and dogs undergoing tibial plateau leveling osteotomy. Accepted in Journal of Veterinary Clinical Pathology (in press).

Rompf, J. (2022) Kinetics of procalcitonin plasma concentrations in dogs with bacterial sepsis. ECVIM congress 31.08.-03.09.2022, Göteborg, Sweden.

Rompf, J., Lutz B, Marti, E.; Mirkovitch, J.; Peters, L.; Adamik, K.; Eiermann, J.; Schüpbach-Regula, G.; Hettlich, B.; Willi, B.; Schuller, S. (2022) Plasma procalcitonin and c-reactive protein in dogs with bacterial sepsis and non-infectious systemic inflammatory response syndrome. Submitted to Journal of Veterinary Internal Medicine.

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