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Diagnostic value of cell cycle arrest biomarkers, tissue inhibitor of metalloproteinase-2 (TIMP-2) and insulin-like growth factor binding protein 7 (IGFBP7), to identify dogs with acute kidney injury

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The cell cycle arrest biomarkers tissue inhibitor of metalloproteinase-2 (TIMP-2) and insulin like growth factor binding protein 7 (IGFBP7) have shown to be valuable biomarkers for early detection of acute kidney injury (AKI) in people. This prospective observational study aimed to validate and measure TIMP-2 and IGFBP7 in urine of dogs and to compare these values between healthy dogs, dogs with AKI, dogs with chronic kidney disease (CKD) and critically ill (CI) dogs. Forty-two client-owned dogs (healthy $n = 10$, AKI $n = 11$, CKD $n = 11$, CI $n = 10$) were included. Urine was sampled and stored at -80°C within 12 h. TIMP-2 and IGFBP7 were measured using respectively a Canine TIMP2 enzyme-linked immunoassay (ELISA) Kit and a Canine IGFBP7 ELISA Kit. Validation for serum was performed by the companies but for urine, the intra-assay coefficient of variation, sensitivity and matrix interference were assessed. Kruskal-Wallis tests with Bonferroni corrections for multiple comparisons were used to compare values between groups. Urinary TIMP-2 was significantly higher in the AKI group, when compared to healthy dogs ($P < 0.001$), dogs with CKD ($P = 0.029$) and CI dogs ($P = 0.022$). Urinary IGFBP7 could separate healthy dogs from dogs with AKI ($P < 0.001$) and CKD ($P = 0.022$), but could not differentiate the diseased groups. The product of TIMP-2 and IGFBP7 was significantly higher in the AKI group, compared to healthy dogs ($P < 0.001$), dogs with CKD ($P = 0.044$) and CI dogs ($P = 0.014$). The product of TIMP-2 and IGFBP7 and TIMP-2 could differentiate dogs with AKI from other patient groups and may be valuable biomarkers for AKI in dogs.

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Diagnostic value of urinary to serum neutrophil gelatinase-associated lipocalin (NGAL) ratio and fractional excretion of NGAL to differentiate dogs with acute kidney injury from healthy dogs, dogs with chronic kidney disease and critically ill dogs

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Urinary neutrophil gelatinase-associated lipocalin (uNGAL) is a promising biomarker of acute kidney injury (AKI), but does not differentiate between acute and chronic kidney disease (CKD) in dogs. In people, the urinary to serum NGAL ratio (u/sNGAL) and fractional excretion of NGAL (FeNGAL) have proven to be able to differentiate AKI from CKD. This prospective observational study aimed to compare the u/sNGAL and FeNGAL between healthy dogs, critically ill (CI) dogs and dogs with AKI and CKD. Forty-two client-owned dogs (healthy $n = 10$, AKI $n = 11$, CKD $n = 11$, CI $n = 10$) were included. Blood and urine were sampled and stored at -80°C within 12 hours of collection. Urinary and serum NGAL were measured with a previously validated Canine NGAL enzyme-linked immunoassays Kit. Subsequently u/sNGAL and FeNGAL were calculated. Kruskal-Wallis tests with Bonferroni corrections for multiple comparisons were used to compare values between groups. uNGAL and u/sNGAL could differentiate the healthy group from the other groups, but could not distinguish the diseased groups. Serum NGAL was higher in the AKI group than in the healthy ($P < 0.001$) and CI group ($P = 0.021$), but did not differ from the CKD group ($P = 1.000$). The FeNGAL was higher in the AKI group, compared to the healthy ($P < 0.001$) and CI dogs ($P = 0.018$), but failed to reach significance compared to the CKD group ($P = 0.112$). In conclusion, the u/sNGAL ratio and FeNGAL were not helpful to distinguish AKI from CKD. Serum NGAL and FeNGAL could differentiate AKI from CI dogs and may have value to predict AKI in hospitalized or CI dogs.

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Urinary neutrophil gelatinase-associated lipocalin (NGAL): A rapid lateral flow test in canine practice

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Urinary Neutrophil Gelatinase-Associated Lipocalin (uNGAL) has been identified as an early marker of acute kidney injury (AKI) in dogs, although its assessment, in clinical practice, is hardly feasible given the need to use ELISA assays. Furthermore, although higher levels of uNGAL are reported in AKI, similar findings are detected in other diseases. The aim of this study was to evaluate the usefulness of a canine specific point-of-care (POC) lateral flow immunoassay for semiquantitative uNGAL measurement in clinical practice. Measurement of uNGAL was performed on 147 canine urinary supernatants using “Dog NGAL ELISA Kit” (Bioporto) and “PRIMA Veterinary—AKI Rapid Test canine NGAL detection” (PRIMA Lab). The analyses were performed on left-over samples previously collected for diagnostic purposes. Based on history, clinical and laboratory data, dogs were grouped as follows: controls; urinary tract infections (UTI); urolithiasis; chronic kidney disease (CKD); acute kidney injury (AKI); AKI on CKD; extrarenal inflammatory diseases. Data were analyzed by MedCalc 20.218. Kruskal Wallis and post hoc tests showed significantly higher uNGAL levels in AKI, AKI on CKD, and extrarenal inflammatory groups when compared to CKD and UTI ($P < 0.05$). In the control group, the level of uNGAL was significantly lower than all others. A further grouping, based on the presence ($n = 30$) or absence ($n = 117$) of AKI, was applied on the canine population to perform a ROC curve using ELISA results, which are generated on a continuous scale. The cut-off of 29.7 ng/mL on the ROC curve determined a sensitivity of 96.7% and a specificity of 74.3%. Considering the POC device, the results were classified as negative (0 ng/mL), low (4 ng/mL), moderate (20 ng/mL) and high risk of AKI (90 ng/mL), based on the color chart provided by the manufacturer. A sensitivity of 97.6% and specificity of 55.6% were obtained using the cut-off of 20 ng/mL to discriminate between AKI or non-AKI dogs. Finally, Cohen's Kappa coefficient (K) of 0.72 showed good agreement between POC and ELISA results. In conclusion, good agreement was found between the POC test and the reference method in classifying patients with AKI. The relatively low specificity of both methods is due to the inherent characteristics of uNGAL, whose increase can be found in different disorders. However, based on its good sensitivity, the POC device may be a clinically relevant diagnostic tool in monitoring all those patients and/or clinical settings in which AKI may occur.

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Validation of a three-dimensional ultrasound device for non-invasive bladder volume measurement in dogs and cats

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Evaluation of urinary bladder volume (UBV) in veterinary medicine is largely under-used while it could be of great clinical importance for diagnosis of micturition disorders. The current reference method for measuring UBV in dogs and cats is based on invasive urethral catheterization. The evolution of medical technologies has allowed the emergence of 3D bladder ultrasound scanners of which one model has been validated in dogs only (BladderScan Prime Plus, Verathon). The aim of this study was to validate a new non-invasive three-dimensional bladder ultrasound device for the measurement of UBV (Portascan 3D (Laborie)) in dogs and cats.

Between December 2021 and March 2023, dogs and cats experiencing urinary catheterization for diagnostic or therapeutic issues were prospectively enrolled. The study was approved by local ethical committee. For each animal, signalment, urinalysis, and bladder content abnormalities visualized on conventional 2D ultrasound were collected. Animals were excluded if bladder presented major wall structure alterations (cystitis, intraluminal mass). Agreement between measurement of UBV estimated using the 3D ultrasound device and measurement of UBV obtained by catheterization (UBV reference) was quantified by using Bland-Altman analysis.

Eighteen dogs and 13 cats were enrolled, including 10 male dogs, 8 female dogs, 11 male cats and 2 female cats. One male dog and one female cat were excluded because of severe bladder damage (following cystostomy and encrusted cystitis respectively). Bland-Altman analysis revealed that 3D ultrasound device underestimated the real bladder volume by 4.9% [−14.7%; +4.8%]_{95%} in dogs and overestimated the real bladder volume by 11.1% [−0.8%; +22.9%]_{95%} in cats. The error of the device (in 90% of the cases) was between −36% and +26% in dogs and between −20% and +42% in cats compared to the real bladder volume (90% limits of agreement). Analysis also revealed an excellent concordance and reproducibility between both methods with a Lin's concordant correlation coefficient of 0.99 [0.96–1]_{95%} for dogs and 0.91 [0.59–0.97]_{95%} for cats.

This new 3-dimensional ultrasound device is non-invasive, fast, and easy-to-use procedure and seems to provide accurate values of UBV in dogs and cats according to present results. This is the first study to assess the use of non-invasive measurement of UBV in cats.

Disclosures

No disclosures to report

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Genitourinary dysplasia in dogs and cats: A case series

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Genitourinary dysplasia is a very rare condition only described in cats. This term represents several anatomical defects of both the urinary