

Can cortisol measurements predict prognosis in dogs requiring hospitalization?

From two papers reported in recent years to clinical applications

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I Introduction.

Many years ago, a patient who had been diagnosed with adrenocortical hyperplasia (HAC) and had been receiving no treatment for it, developed renal failure and died suddenly just before being discharged from the hospital, despite having made good progress with inpatient treatment. Although the cause of death is unknown because an autopsy was not performed, it is clear that the patient had HAC. This case made us think about such issues as whether the death was sudden due to blood clots and how stressful hospitalization could be. The key words "hospitalization," "stress," and "cortisol" came to mind, and serum cortisol concentration (SCC) was measured in addition to general blood test items under various conditions during hospitalization (number of hospital days, location of kennel [upper and lower], etc.). In the process of doing so, I happened to notice that patients with elevated SCC at 24 hours after admission tend to have a poorer prognosis. This led me to investigate the relationship between SCC and prognosis in patients with various diseases, until I came up of the paper presented here. Coincidentally, a research group at a university in the UK also reported almost the same results at the same time, so we will introduce the use of SCC measurement as a biomarker to predict prognosis based on these two papers.

Scientific Paper 1

Yuki M, et al. Investigation of serum cortisol concentration as a potential prognostic marker in hospitalized dogs: a prospective observational study in a primary care animal hospital. BMC Vet Res. 2019 May 24;15(1):170. doi:10.1186/s12917-019-1919-4.

In a primary care hospital (the author's hospital) population, 67 dogs with various diseases were examined for biomarkers (neutrophil count, lymphocyte count, blood glucose, SCC, etc.) that may be useful in predicting prognosis at 0 and 24 hours post-hospitalization, and their usefulness were compared.

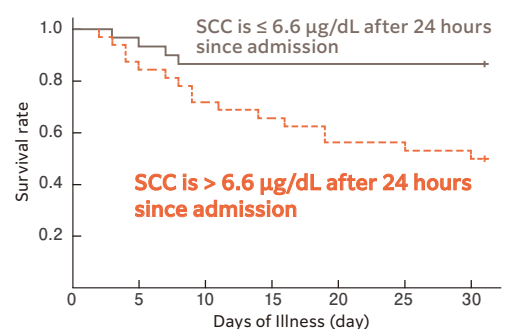
RESULTS

When predicting survival at 30 days, SCC had the highest area under the curve (AUC)* (0.72) at 24 hours after admission, with a sensitivity of 89.5% and specificity of 61.9% at the optimal cutoff value of 6.6 µg/dL. Multivariate analysis showed that SCC was an independent prognostic factor (Figure 1).

Conclusion

SCC, a stress marker, is a useful prognostic biomarker for dogs with a variety of diseases requiring hospitalization.

Figure 1: Kaplan-Meier survival curves for SCC at 24 hours post-hospitalization



Scientific Paper 2

Swales H, et al. Evaluation of serum cortisol concentration as a prognostic indicator for nonsurvival to hospital discharge in critically ill dogs. J Am Vet Med Assoc. 2020 May 1;256(9):1034-1040. doi:10.2460/javma.256.9.1034.

The medical records of 229 dogs that required hospitalization and had SCC measured within 3 days of admission were retrospectively reviewed in a secondary care hospital (a small animal teaching hospital at a university in the UK).

RESULTS

The SCC of dogs that failed to be discharged and died was significantly higher (8.5 µg/dL) than the SCC of dogs that were discharged (4.5 µg/dL). The AUC* of SCC for predicting death during hospitalization was 0.72, with a sensitivity of 58% and specificity of 80% at the optimal cutoff value of 7.6 µg/dL. The sensitivity and specificity of SCC at the upper cutoff value (5.8 µg/dL) were 67% and 64%, respectively.

Conclusion

SCC can predict prognosis as part of a comprehensive evaluation of a severe disease.

* Area under the curve (AUC) : The higher the value, the higher the predictive and diagnostic ability of the outcome (up to 1.0)
AUC 0.9 -1.0 : High accuracy, AUC 0.7-0.9 : Moderate accuracy, AUC 0.5-0.7 : Low accuracy

Clinical Application

Although the two reports presented here are based on very different populations, primary care hospitals (hospitals where patients are first seen when they first become ill) and secondary care hospitals (hospitals where patients with diseases that cannot be treated by primary care hospitals are concentrated), the results are almost identical (note that both reports exclude patients who have received drugs that may affect the hypothalamic-pituitary-adrenal (HAC) axis [e.g., glucocorticoids and ketoconazole], as well as patients with HAC and hypoadrenocorticism).

How should we clinicians make use of the results of these studies? Is it to predict death after 30 days or during hospitalization? Perhaps most importantly, we should reevaluate the diagnosis according to the results of the SCC and change a "bad prognosis" to a "good prognosis". As a specific example of the use of SCC in our hospital, we have experienced cases of severe bacterial prostatitis, bacterial cystitis, and liver abscess with high SCC at 24 hours after admission, which were successfully treated and discharged from the hospital by reviewing the choice of antibiotics before the results of drug sensitivity testing. We also have seen a case where despite good control of infection by antibiotics, the patient's SCC was high and the CRP concentration remained high, so the diagnosis was reviewed, and a complicating disease was found. This led to improvement of the patient's condition. The following is a summary of this case.

Clinical Case

Miniature Dachshund, 11 years old, unneutered male, came to the hospital with a main complaint of not urinating or being restless and vomiting after eating.

General Physical Examination Findings

The patient weighed 8.3 kg, had a body temperature of 39.2 °C, and a heart rate of 140 beats/min.

Blood Test Findings

Increased platelet counts (927,000 / μ L) and elevations in ALT (311 U/L), AST (55 U/L), ALP (598 U/L), and GGT (33 U/L) were observed.

X-ray Examination Findings

Prostate enlargement was observed.

Ultrasound Examination Findings

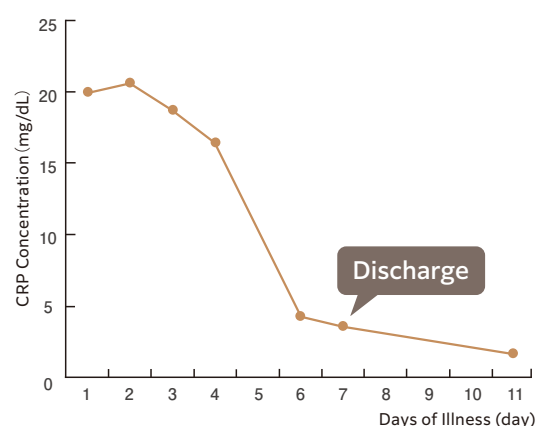
There was enlargement of the prostate gland (diffusely hypoechoic) and thickening of the bladder mucosa (5 mm).

Urine Testing Findings

Urine test paper showed pH 7.5, protein (2+), occult blood (3+), leukocytes (2+), and leukocytes (+) and bacteria (2+) in urine sedimentation.

Based on the above, we diagnosed bacterial cystitis and associated cholangitis, and prescribed ampicillin (20 mg/kg, BID, PO), famotidine (0.5 mg/kg, BID, PO), and metoclopramide (0.2 mg/kg, BID, PO). However, by the next day, the patient was inactive and unable to stand, and her BUN (49.3 mg/dL), Cre (2.5 mg/dL), K (5.9 mEq/L), and CRP (19.9 mg/dL) levels were elevated, so she was switched to inpatient treatment. Additional examination of the prostatic gland fluid showed neutrophil phagocytosis of bacteria, and the diagnosis of bacterial prostatitis was made, and intravenous enrofloxacin (10 mg/kg, SID, SC) and saline

Figure 2: CRP concentrations in relation to the drugs administered to the patients.



Enrofloxacin
10 mg/kg, SID, SC

Ampicillin
20 mg/kg, BID, SC

Prednisolone
1 mg/kg, BID, SC

solution were administered. The SCC at 24 hours after admission was 11.6 μ g/dL. On the fourth day, despite the decrease in liver enzyme activity and azotemia, and the absence of bacteria in the prostrate fluid and urine, there was no improvement in clinical signs and CRP concentration is still high (16.4 mg/dL). Since the SCC was elevated, arthrocentesis was performed to review the diagnosis (fever of unknown origin), and numerous neutrophils were found. Prednisolone (1 mg/kg, BID, SC) was subsequently started, and the clinical signs improved and the CRP concentration rapidly decreased, leading to complete recovery (Figure 2).

**Extracted from Kainuma D, et al, Clinical application of serum cortisol concentration as a prognostic marker : Three clinical case reports on dogs, Chubu Small Animal Clinical Research Presentation (2019)

Therefore, since the measurement of SCC has the potential to predict the outcome of dogs requiring hospitalization, it may be a good idea to add the measurement of SCC to the blood tests that are generally performed. We hope that the use of SCC measurement will change "bad prognosis" to "good prognosis" in as many cases as possible.

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