

RISK OF DEATH IN HOSPITALIZED DOGS WITH HEMOSTATIC PROFILE DISORDERS

ALMEIDA, Bruno Albuquerque de ¹;
BORENSTEIN, Ana Paula Soares ²;
OKANO, Felipe Yuji ²;
CASTILLO, Mônica Alejandra Camargo ³;
WISSMANN, Daiani ¹;
VALLE, Stella de Faria ⁴.

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¹Veterinary Clinics Hospital, Federal University of Rio Grande do Sul (UFRGS, Universidade Federal do Rio Grande do Sul); ²Veterinary School of UFRGS; ³Graduate Program in Veterinary Sciences of UFRGS; ⁴Adjunct Professor at the Veterinary School of UFRGS.

ABSTRACT

Identifying patients who have a higher risk of death is crucial to define appropriate risk classification, treatment and prognosis, which can result in a favorable outcome. The objective of this retrospective study was to evaluate whether the prolongation of prothrombin times, activated partial thromboplastin, and thrombocytopenia are indicators of death risk in hospitalized canine patients. A retrospective study using medical records (2014-2018) of the Laboratory of Veterinary Clinical Analysis at the Federal University of Rio Grande do Sul identified 218 patients. Dogs having a single disorder in laboratory tests did not differ from the control. Groups presenting patients with multiple changes showed three times more death risk than the control group and a cumulative incidence of death higher than 29%.

Keywords: Prothrombin time. Activated partial thromboplastin time. Platelets. Thrombocytopenia.

Identifying patients who have a higher risk of death is crucial to define appropriate risk classification, treatment and prognosis, which can result in a favorable outcome. The laboratory evaluation of blood coagulation aims to identify the causes and define intensity of injuries in the hemostatic system, commonly caused by hemorrhagic and thrombotic diseases. Animals need a balanced and controlled hemostatic system to prevent excessive blood loss, maintain adequate blood flow for the distribution of oxygen to tissues, allow repair and recovery of damaged vessels, and remove blood clots (BAKER, 2012).

Homeostatic profile changes have already been studied in dog populations in specific conditions like disseminated intravascular coagulation (BATEMAN et al., 1999), septic peritonitis (BENTLEY et al., 2013), immune-mediated hemolytic anemia (MORAES et al., 2016) and infectious diseases as leptospirosis (BARTHÉLEMY et al., 2017). However, this association was not performed in a heterogeneous population. The objective of this retrospective study was to evaluate if an increase in prothrombin times (PT), activated partial thromboplastin time (APTT), and thrombocytopenia are indicators for the risk of death in hospitalized canine patients.

A retrospective study using medical records from the Laboratory of Veterinary Clinical Analysis, at the Federal University of Rio Grande do Sul, from 2014 to 2018, was developed. Hospitalized patients' files were selected when they had laboratory tests of prothrombin time (PT), activated partial thromboplastin time (APTT), and platelet count included. PT and APTT were performed as described by Duda (2014), and platelet count using a hematological analyzer (ProCyte Dx, IDEXX Laboratories) and checked in blood smears stained by Diff-Quick Stain by platelet estimation of 100x. Patients with platelet count lower than 200,000 platelets/uL were considered thrombocytopenic (JAIN, 1995). The exclusion criteria for registries were (1) patients with samples containing platelet aggregation or fibrin (detected by hematological analyzer or in microscopic evaluation of blood smear), (2) patients with incomplete results, and (3) patients who had exams with an interval of more than two days. Death registries were obtained from medical records.

Included patients were initially classified into groups as they presented one or a combination of the following disorders: thrombocytopenia, prolongation of PT or APTT. Fisher's exact test

(IBM SPSS Statistics software v. 22, IBM Corp. Armonk) was used to verify the association of deaths with the presence of disorders in laboratory tests (risk factors). The level of significance was defined as $p < 0.05$ and the relative risk (RR) was calculated using the equation $RR = CI_{\text{exposed}} / CI_{\text{unexposed}}$, where CI represents cumulative incidence.

The database included 353 dogs, but the criteria above excluded 135: 66 had incomplete laboratory exams, 38 patients demonstrated platelet aggregation in the sample, and 31 had a platelet count with an interval exceeding two days. Thus, 218 dogs are further classified into groups that can be seen in Table 1 and population aged between 1 to 16 years. Groups 6, 7 and 8 showed a higher proportion of death than the control group (Table 2), and groups 3 and 5 were not statistically analyzed due to the low number of observations.

Table 1 - Classification of dogs according to laboratory tests disorder.

Groups	Total	Deaths	Cumulative incidence of deaths (%)
1 No laboratorial changes (control)	93	9	9.7
2 Thrombocytopenia	28	6	21.4
3 Prolonged PT	1	0	0
4 Prolonged APTT	35	8	22.9
5 Thrombocytopenia and prolonged PT	0	0	0
6 Thrombocytopenia and prolonged APTT	27	8	29.6
7 Prolonged PT and APTT	14	7	50.0
8 Thrombocytopenia, prolonged PT and APTT	20	8	40.0

PT: Prothrombin time, APTT: Activated partial thromboplastin time.

Table 2 - Fisher's Exact Test group comparison (p-value) of death frequency.

Groups	2	4	6	7	8
1	0.11	0.07	0.02	0.00	0.00
2	-	1	0.55	0.08	0.21
4	-	-	0.57	0.09	0.22
6	-	-	-	0.31	0.54
7	-	-	-	-	0.73

P-values lower than 0.05 show a different death rate among groups.

Group 2 showed a similar risk of death to the control group. Single hemostatic profile changes could express an individual variation or a mild disorder and could not be harmful to the hemostasis process. The study has not evaluated other hemostatic exams to confirm these statements and etiology or severity of hemostatic disorder was not a scope of this study.

Only one dog has demonstrated PT increase, and dogs with concomitant thrombocytopenia were not observed (group 5). In human patients, PT increase is considered a useful test to monitor the efficiency of treatment with procoagulants, but not to assess the risk of bleeding (LIPPI et al., 2007), which could worsen the clinical condition resulting in death. It was previously reported that PT would be a relatively insensitive parameter to individual reductions in coagulation factors, requiring a marked decrease in prothrombin concentration (<20%), factor V, VII, or X (<35%) for the PT prolongation (BURNS, 1993). Due to the reduced number of dogs, this parameter was not included in the statistical analysis.

Dogs with acute traumatic coagulopathy, manifesting changes in two or more coagulation tests, demonstrated a higher risk of death (HOLLOWAYCHUK et al., 2014), as we found using a heterogeneous dog population. The APTT increase has regarded a highly predictive indicator of non-survival correlated with the severity of the disease (HOLLOWAYCHUK et al., 2014). Among PT and APTT change factors, there are accelerated consumption or lack of factor production.

Groups presenting patients with multiple disorders showed three times more death risk than the control group and a cumulative incidence of death higher than 29%. However, these

results should be supplementary in the definition of the prognosis associated with a complete clinical and laboratory evaluation.

RISCO DE ÓBITO EM CÃES HOSPITALIZADOS COM DESORDENS DO PERFIL HEMOSTÁTICO

RESUMO

Identificar pacientes que possuem um risco maior de morte é crucial para definir a classificação de risco apropriada, tratamento e prognóstico, os quais podem resultar em um resultado favorável. O objetivo deste estudo foi avaliar se o prolongamento dos tempos de protrombina, tromboplastina parcialmente ativada e trombocitopenia são indicadores para o risco de óbito de pacientes caninos hospitalizados. O estudo retrospectivo utilizando os registros médicos (2014 a 2018) do Laboratório de Análises Clínicas Veterinárias na Universidade Federal do Rio Grande do Sul identificou 218 pacientes. Cães que apresentavam uma única alteração em exames laboratoriais não diferiram do controle. Grupos compostos de pacientes com múltiplas alterações mostraram um risco de óbito três vezes maior que o grupo controle e uma incidência cumulativa de óbito maior que 29%.

Palavras-chave: Tempo de protrombina. Tromboplastina ativada parcial. Plaquetas. Trombocitopenia.

RIESGO DE MUERTE EN PERROS HOSPITALIZADOS CON DESORDENES DEL PERFIL HEMOSTÁTICO

RESUMEN

Identificar a los pacientes con mayor riesgo de muerte es crucial para definir la clasificación de riesgo, el tratamiento y el pronóstico adecuados, lo que puede dar lugar a un resultado favorable. El objetivo de este estudio fue evaluar si la prolongación de los tiempos de protrombina, la tromboplastina parcialmente activada y la trombocitopenia son indicadores del riesgo de muerte en perros hospitalizados. El estudio retrospectivo con registros médicos (2014 a 2018) del Laboratorio de Análisis Clínico Veterinario de la

Universidade Federal de Rio Grande do Sul identificó a 218 pacientes. Los pacientes con un solo cambio en las pruebas de laboratorio no difirieron del control. Los grupos que presentaron pacientes con múltiples cambios mostraron un riesgo de muerte tres veces mayor que el grupo control y una incidencia acumulada de muerte mayor al 29%.

Palabras clave: Tiempo de protrombina. Tromboplastina parcial activada. Plaquetas. Trombocitopenia.

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Corresponding author:

Stella de Faria Valle.

Av. Bento Gonçalves, 9090, Porto Alegre, RS, Brasil.

stellavalle@gmail.com