

# Application of the Sequential Organ Failure Assessment Score to predict outcome in critically ill dogs: Preliminary results

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## Summary

In human medicine the Sequential Organ Failure Assessment (SOFA) score is one of the most commonly organ dysfunction scoring systems used to assess critically ill patients and to predict the outcome in Intensive Care Units (ICUs). It is composed of scores from six organ systems (respiratory, cardiovascular, hepatic, coagulation, renal, and neurological) graded according to the degree of the dysfunction. The aim of the current study was to describe the applicability of the SOFA score in assessing the outcome of critically ill dogs. A total of 45 dogs admitted to the ICU was enrolled. Among these, 40 dogs completed the study: 50 % survived and left the veterinary clinic. The SOFA score was computed for each dog every 24 hours for the first 3 days of ICU stay, starting on the day of admission. A statistically significant correlation between SOFA score and death or survival was found. Most of the dogs showing an increase of the SOFA score in the first 3 days of hospitalization died, whereas the dogs with a decrease of the score survived. These results suggest that the SOFA score system could be considered a useful indicator of prognosis in ICUs hospitalized dogs.

Keywords: SOFA score, critically ill dogs, prognosis

## Anwendung des Sequential Organ Failure Assessment Score zur Beurteilung kritisch erkrankter Hunde: Erste Ergebnisse

In der Humanmedizin ist der Sequential Organ Failure Assessment (SOFA) Score ein häufig gebrauchter Parameter zur Beurteilung kritisch erkrankter Patienten und zur Prognosestellung bei Intensivbehandlung. Der Score setzt sich aufgrund der Funktionsfähigkeit von sechs organischen Systemen (Atmung, Kreislauf, Leber, Koagulation, Nieren, Neurologie) zusammen. Ziel dieser Studie war die Anwendung des SOFA und das Ergebnis bei kritisch erkrankten Hunden festzuhalten. Von insgesamt 45 Hunden unter Intensivpflege haben 40 Tiere die Studie beendet und von diesen haben 50 % überlebt. Der SOFA Score wurde für jeden einzelnen Hund während der ersten 3 Tage nach Aufnahme alle 24 Stunden berechnet. Es konnte eine statistisch signifikante Korrelation zwischen SOFA Score und Tod bzw. Überleben gefunden werden. Die meisten Hunde, die während der ersten 3 Tage eine Erhöhung des SOFA Scores aufwiesen sind gestorben, Hunde mit einer Abnahme des Scores haben den Versuch überlebt. Die Ergebnisse zeigen, dass der SOFA Score ein nützlicher Indikator für die Prognose von Hunden unter Intensivbehandlung sein kann.

Schlüsselwörter: System SOFA score, Hunde in kritischer Lage, Prognose

## Introduction

In human medicine several scoring systems have been developed and they are widely used in Intensive Care Unit (ICU) populations to evaluate the severity of illness and prognosis (Moreno et al., 1999; Jones et al., 2009; Chen

et al., 2011). There are two main categories of general prognostic models: first, those evaluating the severity of illness as Acute Physiology and Chronic Health Evaluation II (APACHE II) and Simplified Acute Physiology Score II (SAPS II) and Mortality Prediction Model II (MPM II), and secondly, models quantifying organ dis-

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function and failure, of which the most used is the Sequential Organ Failure Assessment (SOFA) (Freire et al., 2010). This score was created some years ago by the Working Group on Sepsis-related Problems of the European Society of Intensive Care Medicine to describe objectively and quantitatively the degree of organ dysfunction over time and to evaluate in ICU septic patients (Vincent et al., 1996; Vincent et al., 1998). Originally it was called Sepsis-related Organ Failure Assessment score but later, when it was realized that it could be applied equally well in non-septic patients, the acronym SOFA was taken to refer to Sequential Organ Failure Assessment (Minne et al., 2008). The SOFA scoring scheme assigns 1 to 4 points to each of the following six organ systems depending on the level of dysfunction: respiratory, circulatory, renal, haematology, hepatic and central nervous system. The total SOFA score is obtained by the sum of the six systems scores that results in a number varying from 0 to 24 (Minne et al., 2008; Lal et al., 2011). Although the score was not developed to predict outcome or risk of mortality, several studies showed the relationship between organ dysfunction and mortality (Freire et al., 2010; Wong et al., 2010). A greater SOFA score for each organ was associated with an increasing mortality rate and a higher total SOFA score predicts higher ICU mortality rate (Lee et al., 2008; Pedroso et al., 2010; Boeck et al., 2011). Actually during the first days of ICU admission the SOFA score is considered a good indicator of prognosis in medical and postsurgical ICU patients (Antonelli et al., 1999; Cornet et al., 2005; Zygun et al., 2006; Lee et al., 2008; Neumann et al., 2008; Namendys-Silva et al., 2009).

To our knowledge, with exception of Glasgow Coma Score that quantifies the degree of central nervous system failure, scoring systems have not yet been developed and used in ICU recovered dogs. The objective of the study was to assess the applicability of the SOFA scoring system in critically ill dogs and to evaluate its utility in predicting the outcome.

## Material and Methods

### Animals

For this study, a total of 45 privately owned dogs admitted to the ICU from December 2009 to May 2011 were enrolled. The dogs, 24 males and 21 females, were 1 to 16 years old and weighed 5 to 55 kg. They belonged to different breeds: 3 West Highland White Terrier, 6 German Shepherd Dog, 3 Siberian Husky, 4 American Staffordshire Terrier, 2 Giant Schnauzer, 2 Akita Inu, 1 American Cocker Spaniel, 2 Dogue de Bordeaux, 1 King Charles Spaniel, 5 Labrador Retriever, 3 Rottweiler, 4 Golden Retriever, 9 cross-breeds. At admission all dogs carried out complete blood count, serum biochemical analysis (total proteins, albumin, glucose, cholesterol, creatinine, urea, bilirubin, alanine aminotransferase and alkaline phos-

phatase activities, electrolytes), urinalysis, arterial blood gas analysis and pH. Then, clinical investigations were completed as necessary on an individual basis to reach a reliable diagnosis. Twenty dogs were diagnosed with systemic inflammatory response syndrome (SIRS) and 20 dogs were diagnosed with sepsis. The loss of local control or an overly activated response to an inflammatory process, independent of its cause, results in an exaggerated systemic response which is clinically identified as SIRS (Davis and Hagen, 1997). The dogs were considered to having SIRS if they had two or more of the following criteria: heart rate > 120 beats/min; respiratory rate > 20 breaths/min; temperature > 102.6 °F or < 100.6 °F; white blood cell count > 16000/ml or < 6000/ml or bands neutrophils > 3 % (De Laforcade, 2009). Sepsis is defined as the systemic inflammatory response syndrome to bacteria, viral, protozoal or fungal infection. Dogs were diagnosed with sepsis if they had SIRS and an infection (Brady and Otto, 2001; Boller and Otto, 2009). Informed consent was obtained from the dog's owners. The study was performed according to animal welfare consideration and regulation.

### SOFA score computation

The SOFA score was computed every 24 hours for the first 3 days of ICU stay, starting on the day of admission and according to the modalities described in literature (Tab. 1) (Ceriani et al., 2003; Cholongitas et al., 2006; Honarmand et al., 2009). Laboratory data necessary for the computation of the score were obtained once a day, while clinical parameters were checked every 6 hours. The metatarsal artery was cannulated and the catheter was connected to a blood pressure transducer for direct blood pressure measurement. For the calculation of the ratio between arterial partial pressure of oxygen and fraction of inspired oxygen ( $\text{PaO}_2/\text{FiO}_2$ ), the  $\text{FiO}_2$  was directly provided by the machine in mechanically ventilated dogs ( $n = 3$ ). In dogs with oxygen supplementation by nasal cannula ( $n = 4$ ), the administration of oxygen was interrupted for 1 hour before the measurement of the  $\text{PaO}_2/\text{FiO}_2$  ratio. The  $\text{FiO}_2$  was thus considered 0.21 as well as in dogs without oxygen supplementation ( $n = 33$ ). In the calculation of the score, the worst values for each parameter in a 24-hour period were used (Janssens et al., 2000; Doerr et al., 2011). The total and the mean SOFA score for each dog were also computed. The total SOFA score was calculated as the sum of all daily SOFA scores, while the mean score was defined as the ratio of total score to the length of stay (LOS) in the ICU (Lopes Ferreira et al., 2001). The LOS in the ICU was measured as number of days from admission to the ICU to discharge.

### Statistical analysis

Statistical analysis was performed by use of a freeware statistical software package (R, version 1.2.0, 2008). To assess

Table 1: The SOFA score system.

Variables	SOFA score				
	0	1	2	3	4
<b>Respiration</b> *PaO <sub>2</sub> /FiO <sub>2</sub> (mmHg)	> 400	≤ 400	≤ 300	≤ 200*	≤ 100*
<b>Coagulation</b> Platelets (× 10 <sup>3</sup> /μl)	> 150	≤ 150	≤ 100	≤ 50	≤ 20
<b>Liver</b> Bilirubin (mg/dl)	< 0.6	0.6–1.4	1.5–5.0	5.1–11.0	> 11.1
<b>Cardiovascular</b> Hypotension	no hypotension	*MAP < 60 mmHg	*dopa ≤ 5 or dobu	*dopa > 5 or epi ≤ 0.1 or norepi ≤ 0.1	*dopa > 15 or epi > 0.1 or norepi ≤ 0.1
<b>Central nervous system</b> Glasgow Coma Score	15	13–14	10–12	6–9	< 6
<b>Renal</b> Creatinina (mg/dl)	< 1.4	1.4–1.9	2.0–3.4	3.5–4.9	> 5.0

\*Adrenergic agents administered for at least one hour (doses given are in μg/kg × minute). Norepi = norepinephrine; dopa = dopamine; dobu = dobutamine; epi = epinephrine.

\*\*PaO<sub>2</sub>/FiO<sub>2</sub> = arterial partial pressure of oxygen/fraction of inspired oxygen

\*MAP = mean arterial pressure

#With respiratory support

normal distribution of data, the Shapiro-Wilk Normality test was performed. Metric data are presented as median, minimum and maximum values and tested for significance by use of the Wilcoxon rank sum test. Nominal data were expressed as a percentage and/or frequency and analyzed using  $\chi^2$  statistic. Correlations were evaluated using the non-parametric Spearman Rank Correlation Test (Rs). A *P* value < 0.05 was considered significant.

## Results

Among the 45 enrolled dogs, 40 dogs completed the study. Among these, 20 dogs survived and left the veterinary clinic, while 20 dogs died (7 dogs were euthanized at owners' request for the deterioration of their clinical condition and 13 dogs died spontaneously). Five dogs were lost during the study: 3 dogs were euthanized at owners' request for economic reasons and 2 died within the first 2 days of hospitalization. In total, 55% of the enrolled dogs died. Daily, total and medium SOFA score values of the survived and non-survived dogs are reported in Table 2. A significant correlation between SOFA score in the first 3 days of hospitalization and death or survival was found (*p* < 0.001). The total and the medium SOFA score were also significantly different between the non-survived and survived dogs (*p* < 0.001). A significant association between increase or decrease in SOFA score during the first 3 days of hospitalization and the outcome was found (*p* < 0.001). In fact, in the 20 dogs in which there was an increase in the SOFA score, 19 died and only 1 survived. Instead, the 19 dogs in which there was a decrease in SOFA score, 18 survived and one died. The dog in which the SOFA score remained stable survived. The median of LOS in

the ICU was 5.05 days (range 3–9 days) and 5.2 days (range 3–8 days), respectively, for the non-survived and

Table 2: Daily, total and medium SOFA score in survived and non-survived dogs.

	Survived dogs	Non-survived dogs	<i>P</i>
	Median (min-max)	Median (min-max)	
<b>Daily SOFA score</b>			
day 1	5 (2–7)	7 (5–9)	< 0.001
day 2	3.5 (1–7)	8 (6–10)	< 0.001
day 3	2 (1–6)	9 (7–11)	< 0.001
<b>Total SOFA score</b>	10 (4–20)	24.5 (19–30)	< 0.001
<b>Medium SOFA score</b>	3.30 (1.3–6.7)	8.15 (6.3–10)	< 0.001

Table 3: SOFA score in dogs with SIRS\* and in dogs with sepsis.\*\*

	Dogs with SIRS	Dogs with sepsi	<i>P</i>
	Median (min-max)	Median (min-max)	
<b>Daily SOFA score</b>			
day 1	6 (2–9)	6 (2–9)	> 0.05
day 2	4.5 (1–9)	6.5 (1–10)	> 0.05
day 3	3.5 (1–10)	8 (1–11)	> 0.05

\*SIRS = the dogs were considered to having SIRS if they had two or more of the following criteria: heart rate > 120 beats/min; respiratory rate > 20 breaths/min; temperature > 102.6 °F or < 100.6 °F; white blood cell count > 16000/ml or < 6000/ml or bands neutrophils > 3%. \*\*sepsis = the dogs were diagnosed with sepsis if they had SIRS and an infection.

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the survived dogs. There was no significant correlation between LOS in the ICU and the death or the survival of the dogs.

The SOFA score values of the dogs with SIRS and the dogs with sepsis in the first 3 days of hospitalization are shown in Table 3: significant differences were not found. The median of LOS in the ICU was 4.65 days (range 3–9 days) and 5.6 days (range 3–8 days), respectively, for the dogs with SIRS and for the dogs with sepsis: there was no significant difference. In addition, there was not a significant correlation between SOFA score in the 3 days of hospitalization and the length of hospitalization.

### Discussion

In accordance with human medicine (Zygun et al., 2006; Jones et al., 2009; Namendys-Silva et al., 2009; Freire et al., 2010; Chen et al., 2011; Doerr et al., 2011), the results of our study support strongly that the SOFA score has a good ability to discriminate between surviving and non-surviving dogs after the admission to ICU. In agreement with the literature (Janssens et al., 2000; Lopes Ferreira et al., 2001; Ceriani et al., 2003), daily SOFA score values are shown to be a good indicator of prognosis and both the total and the mean SOFA score are useful in predicting the outcome. In accordance with the literature (Alsous et al., 2000; Moine et al., 2002; De Campos et al., 2008), in our work the highest SOFA score values were related to a worse prognosis. During the first 3 days of hospitalization, an increase in the SOFA score value was associated with a higher risk of death, while a decrease in the SOFA score value was correlated to a favorable outcome. This could be explained by the fact that in dogs as well as in humans the SOFA score quantifies the degree of organ dysfunction already present on ICU admission or the degree of dysfunction that appears during hospitalization (Antonelli et al., 1999; Cholongitas et al., 2006; Lal et al., 2011). Thus, a higher score or its increase over time cor-

responds to a major organ dysfunction (Moreno et al., 1999; Alsous et al., 2000; Ceriani et al., 2003). For this reason, though a prognostic scoring system cannot replace the clinical evaluation of the patients, we think that the SOFA score could help the intensive care physician to accurately and reliably measure the severity of illness in the ICU dogs. This method is simple, easy to repeat and allows to perform serial SOFA score measurements to follow the dynamic of illness during hospitalization. In fact, as reported in human literature (De Campos et al., 2008; Honarmand et al., 2009), the SOFA score could be an important tool to detect an early development of the organ dysfunction in ICU dogs and could facilitate the decision of instituting an organ support. On the basis of our data, it could improve the physician's estimate of prognosis and, hence, be useful in making clinical decision. As shown in our study and in accordance with human medicine (Lopes Ferreira et al., 2001), a decreasing SOFA score is associated with an improved outcome, prompting an early aggressive therapy to reduce mortality. The SOFA score could also be used to reflect a patient response to therapeutic strategies and allow to monitor the daily progresses of the ICU dogs. In addition, as suggested in human literature (Lopes Ferreira et al., 2001; Jones et al., 2009), the SOFA score could be an useful tool to stratify and compare the patients in clinical trials. In our study there was no significant difference in SOFA score values between the dogs with SIRS and the dogs with sepsis. Therefore, it can be assumed that the SOFA score could be used in all critically ill dogs regardless of the disease that puts their lives at risk (Minne et al., 2008).

In conclusion, evaluation of the SOFA score in ICU hospitalized dogs appears to be a good prognostic indicator and it could be used to quantify the degree of organ dysfunction present on admission or that develops during hospitalization without any information about the reason for admission. However, these results are preliminary and further studies are needed to determine the applicability of the SOFA score in predicting the outcome of critically ill dogs.

#### Utilisation du «Sequential Organ Failure Assessment Score» pour évaluer des chiens critiquement malades: premiers résultats

En médecine humaine, le Sequential Organ Failure Assessment (SOFA) est un paramètre utilisé fréquemment pour juger l'état de patiente critique et pour poser un pronostic dans les soins intensifs. Le score est basé sur la capacité fonctionnelle de 6 systèmes organiques (respiration, circulation, foie, coagulation, reins, neurologie). Le but de cette étude était d'apprécier l'utilisation du SOFA et son résultat chez des chiens critiquement malades. Sur 45 chiens placés sous soins intensifs, 40 ont terminé l'étude et 50% d'entre eux

#### Applicazione del «Sequential Organ Failure Assessment Score» per valutare la prognosi in cani in condizioni critiche: risultati preliminari

In medicina umana il Sequential Organ Failure Assessment (SOFA) score è uno dei sistemi più comunemente utilizzati per valutare i pazienti critici e per predirne la prognosi nelle unità di terapia intensiva. Esso è composto dagli score provenienti da sei sistemi organici (respiratorio, cardiovascolare, epatico, coagulativo, renale e neurologico) classificati sulla base del livello di funzionalità. Lo scopo di questo studio è stato quello di valutare l'applicabilità del SOFA score per predire la prognosi di cani in condizioni critiche.

ont survécus. Le score SOFA a été calculé toutes les 24 heures pendant les 3 premiers jours après la prise en charge. On a pu trouver une corrélation statistiquement significative entre le score SOFA et la survie respectivement la mort des patients. La plupart des chiens qui ont présenté une élévation du score SOFA durant les 3 premiers jours sont décédés, ceux présentant une diminution ont survécus. Ces résultats montrent que le score SOFA peut être un indicateur utile pour le pronostic de chiens placés en soins intensifs.

Per tale scopo sono stati utilizzati 45 cani ricoverati in un'unità di terapia intensiva. Tra questi, 40 cani hanno completato lo studio: il 50% è sopravvissuto ed ha lasciato la clinica veterinaria. Il SOFA score è stato calcolato per ogni cane ogni 24 ore per i primi 3 giorni di ricovero a partire dal giorno di ammissione. È stata trovata una correlazione statisticamente significativa tra SOFA score e morte o sopravvivenza dei cani. La maggior parte dei cani in cui si è verificato un incremento del SOFA score nei primi 3 giorni di ricovero è morta, mentre i cani in cui c'è stata una diminuzione sono sopravvissuti. Questi risultati suggeriscono che il SOFA score potrebbe essere considerato un utile indicatore di prognosi nei cani ricoverati nelle unità di terapia intensiva.

Parole chiave: SOFA score, cani in condizioni critiche, prognosi

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