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Evaluation of quick sequential organ failure scores in dogs with severe sepsis and septic shock

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OBJECTIVES: To evaluate the prognostic utility of the quick sequential organ failure assessment score in dogs with severe sepsis and septic shock presenting to an emergency service, and evaluate the clinical value of the quick sequential organ failure assessment score to predict severe sepsis and septic shock.

MATERIALS AND METHODS: The quick sequential organ failure assessment score was calculated by evaluating respiratory rate (>22 breaths per minute), arterial systolic blood pressure (≤ 100 mmHg) and altered mentation. The quick sequential organ failure assessment scores with respiratory rate cut-offs of greater than 22, greater than 30 and greater than 40 were compared. Cases were defined as dogs presented to the emergency room and met at least 2 systemic inflammatory response syndrome criteria, had documented infection, and at least one organ dysfunction. A control population of dogs included animals with non-infectious systemic inflammatory response syndrome.

RESULTS: Forty-five dogs with severe sepsis and septic shock and 45 dogs with non-infectious systemic inflammatory response syndrome were included in the final analysis. The quick sequential organ failure assessment provided poor discrimination between survivors and non-survivors for severe sepsis and septic shock (area under receiving operating characteristic curve, 0.51; 95% confidence interval, 0.35 to 0.67). Discrimination remained poor when quick sequential organ failure assessment greater than 30 and quick sequential organ failure assessment greater than 40 scores were calculated (area under receiving operating characteristic curve, 0.56; 95% confidence interval, 0.39 to 0.72, and 0.54; 95% confidence interval, 0.36 to 0.71). The quick sequential organ failure assessment of at least 2, quick sequential organ failure assessment greater than 30 of at least 2 and quick sequential organ failure assessment greater than 40 of at least 2 produced sensitivity and specificity to detect severe sepsis and septic shock of 66.7% and 64.5%, 62.2% and 71.1%, 44.4% and 80%, respectively.

CONCLUSION AND CLINICAL SIGNIFICANCE: Scoring systems utilised in emergency rooms should have high sensitivity to reduce missed sepsis cases and treatment delays. The use of the quick sequential organ failure assessment for severe sepsis and septic shock demonstrated poor mortality prediction and low sensitivity to detect canine patients with severe sepsis and septic shock and should not be used alone when screening for sepsis.

INTRODUCTION

Despite multiple progressive definitions, sepsis has remained difficult to define and diagnose condition in human and animal patients alike (Singer *et al.* 2016, Haydar *et al.* 2017, Summers *et al.* 2021). Initial definitions included the systemic inflammatory response syndrome (SIRS) criteria plus infection, which is highly sensitive but not as specific when diagnosing sepsis in canines and humans (Hauptman *et al.* 1997, Seymour *et al.* 2016). In one human study, SIRS at least 2 excluded one in eight otherwise similar patients with infection, organ failure and substantial mortality (Kaukonen *et al.* 2015). In a feline veterinary study, SIRS at least 3 appeared to be fairly insensitive for many cats to diagnose sepsis, therefore authors adjusted their definition for SIRS to the presence of at least 2 of the SIRS criteria, which is the same guideline used to diagnose SIRS in dogs (Babyak & Sharp 2016). These human and veterinary studies may suggest that a single “threshold” SIRS score to diagnose sepsis may not be advisable.

In humans, severe sepsis (SS) was previously defined as the presence of infection and at least one organ dysfunction (Puskarich & Jones 2020). The most current definition, Sepsis 3.0, defines it as a life-threatening organ dysfunction due to a dysregulated host response to infection and has eliminated the term “severe sepsis” (Singer *et al.* 2016). However, in veterinary medicine, the definitions remain consistent with the initial 1991 definition, which defines sepsis as SIRS with an infectious nidus (Kenney *et al.* 2010, Boller & Otto 2014, Sharp 2019).

Sepsis is associated with high morbidity and mortality in both human and veterinary medicine (Purvis & Kirby 1994, Boller & Otto 2014). The rapid detection of sepsis in the emergency room (ER) may provide the benefit of early intervention, which may translate to an improved survival rate among septic patients. Unfortunately, the diagnosis of sepsis is very complex and there is no single test, examination finding, or scoring system that is a reliable indicator. As the human definitions have been evolving, numerous outcome and prediction systems have also evolved in hopes of identifying sepsis sooner to decrease the mortality rate. To improve recognition, it is recommended to use validated sepsis scoring systems (Seymour *et al.* 2016). The Sequential-related Organ Failure Assessment (SOFA) scoring system is meant to be a complement to other scoring systems and involves quantifying the severity and number of organ failures using six body systems graded on a scale of 0 to 4, with higher scores associated with increased severity (Vincent *et al.* 1996). The quick SOFA (qSOFA) score was developed to evaluate patients with suspected infection using alterations in the three major body organ systems (altered mental state, hypotension and tachypnea) on a sliding scale of 0 to 3 (Freund *et al.* 2017). A score of at least 2 qSOFA points is associated with a longer ICU stay and a greater risk of death (Singer *et al.* 2016). The qSOFA score was proposed as a risk stratification tool that is more specific than the SIRS criteria

to predict mortality and recognise organ dysfunction in human patients with sepsis (Du & Weng 2017, Finkelsztejn *et al.* 2017).

In a recent veterinary study (Stastny *et al.* 2022), authors retrospectively evaluated the prognostic utility of qSOFA scores in dogs with sepsis treated surgically. They demonstrated that qSOFA may help identify patients at risk for death or euthanasia, as patients with a qSOFA score of at least 2 were 7.1 times more likely to die or be euthanized compared with dogs with a qSOFA less than 2. In another veterinary paper (Ortolani & Bellis 2021), qSOFA scores were evaluated in a general population of critically ill dogs, and it was not associated with survival.

The presence of one or more organ dysfunctions in human and veterinary patients with sepsis is associated with worse outcomes (Moreno *et al.* 1999, Kenney *et al.* 2010, Ripanti *et al.* 2012). Timely detection of this population of patients and subsequent early treatment may be imperative. One observational cohort study by Askim *et al.* examined the clinical usefulness of qSOFA to predict SS in a population of people presented to an emergency department. The qSOFA at least 2 demonstrated a sensitivity of 32% and specificity of 98% to detect people with SS. To the best of the authors’ knowledge, no veterinary studies have evaluated the prognostic and diagnostic performance of qSOFA in dogs with severe sepsis and septic shock (SS/SH).

The objective of this study was to evaluate the clinical usefulness of the qSOFA score to predict in-hospital mortality in dogs with SS/SH presented to the ER by using different respiratory rate cut-offs. Another objective was to examine the clinical value of the qSOFA score to predict SS/SH in critically ill dogs presented to the ER. We hypothesized that dogs with greater qSOFA scores would be more likely to die or be euthanized, but the qSOFA score would have poor sensitivity for the detection of SS/SH.

METHODS

This was a retrospective cohort study. Computer-based medical records were reviewed from dogs that presented through the veterinary medical teaching hospital emergency service between January 1, 2010 and December 31, 2019 using the search terms “sepsis” or “septic”. Dogs were included if the following values were recorded at the time of admission to the hospital: temperature, heart rate, mentation, respiratory rate, systolic blood pressure (SBP), and available CBC and chemistry results. Cases were included when dogs were presented to the ER and transferred to the ICU, met two or more SIRS criteria, and had documented infection and at least one organ dysfunction.

Case exclusion criteria were determined by the absence of documented infection or organ dysfunction, if less than two SIRS criteria were met, there was inadequate bloodwork, absence of initial triage parameters, or if they were euthanized before admission to the ICU or performance of source control surgery.

A control group of dogs included animals that met two or more SIRS criteria secondary to a non-infectious aetiology (N-SIRS group). They were age-matched with dogs in SS/SH group by random selection during the same time period in a one-to-one ratio. Similar to the SS/SH group, control dogs were presented to the ER and transferred to the ICU. Control patients were required to have adequate triage records and minimal bloodwork to calculate qSOFA and SIRS scores. The inflammatory hepatobiliary disease was defined as conditions involving liver parenchyma and/or gall bladder secondary to inflammatory non-infectious causes diagnosed based on cytology and/or bacterial culture. Acute haemorrhagic diarrhoea syndrome (AHDS) was diagnosed based upon the presence of an acute onset of haemorrhagic diarrhoea without any other identifiable causes unrelated to AHDS (e.g. drug adverse effects, parasites, coagulopathy, etc) (Unterter *et al.* 2014). Anaphylaxis was diagnosed based upon the presence of type 1 hypersensitivity reaction (chemosis, urticaria) and acute-onset dysfunction of two or more body systems, or cardiovascular dysfunction alone secondary to a suspected or witnessed allergen exposure (e.g. owner-reported observed exposure to an insect bite or medication) (Sampson *et al.* 2006, Quantz *et al.* 2009, Turner *et al.* 2021).

The following SIRS criteria were used in the study: rectal temperature less than 38.1°C or greater than 39.2°C; heart rate greater than 120/minute; respiratory rate greater than 20/minute; WBC less than $6 \times 10^9/L$ or greater than $16 \times 10^9/L$ or greater than 3% band neutrophils (Hauptman *et al.* 1997). Documented infection was identified from the record as having one of the following diagnostics presents a positive bacterial culture, gross evidence of bacterial contamination of the abdominal or pleural cavities confirmed via exploratory surgery or intracellular bacteria on cytology. Organ dysfunction was defined as proposed by Kenney *et al.* with modifications of renal dysfunction (following the acute kidney injury definitions of the International Renal Interest Society), hepatic dysfunction (to comply with the local institutional reference range), and an addition of the central nervous system dysfunction (Ripanti *et al.* 2012). Renal dysfunction was defined as a baseline creatinine greater than 132.6 $\mu\text{mol/L}$ or an increase in creatinine of at least 26.5 $\mu\text{mol/L}$ within 48 hours. Cardiovascular dysfunction was defined as arterial hypotension (SBP less than 90 mmHg or MAP less than 65 mmHg) requiring vasopressors. Respiratory dysfunction was defined as a need for supplemental oxygen, mechanical ventilation, or a PaO₂ of less than 65 mmHg or SpO₂ less than 95% on room air. Hepatic dysfunction was defined by total bilirubin greater than 17 $\mu\text{mol/L}$. Coagulation dysfunction was defined as a platelet count less than $100 \times 10^9/L$. Central nervous system dysfunction was defined by a modified Glasgow Coma Score of less than 15 in the absence of traumatic brain injury or preexisting brain pathology. SS was defined as the presence of infection, at least two variables compatible with SIRS, and at least one organ dysfunction. SH was defined as having SS plus persistent hypotension (SBP less than 90 mmHg or MAP less than 65 mmHg) despite fluid resuscitation (Usman *et al.* 2019). The outcome was defined as survival to discharge or non-survival (death or euthanasia).

Each patient was assigned a qSOFA score using admission variables by evaluating respiratory rate, mentation, and SBP. A

respiratory rate of greater than 22 breaths per minute constituted a score of 1, and up to 22 scored zero. For assignment of the mentation for qSOFA, 1 point was assigned for any abnormal mentation, including those recorded as dull, obtunded or stuporous (Stastny *et al.* 2022). SBP, as measured with a Doppler or oscillometric device, up to 100 mmHg constituted a score of one, and greater than 100 mmHg scored zero. A minimum of zero points and a maximum of three points could be assigned to a patient.

To evaluate the predictive ability of qSOFA with different respiratory rate cut-offs, qSOFA30 and qSOFA40 were created. For qSOFA30 and qSOFA40, a respiratory rate of greater than 30 or 40 per minute, respectively, constituted a score of one, and up to 30 or 40, respectively, scored zero. The rest of the qSOFA was calculated as described above.

Additional information recorded included age, body weight, sex, APPLEfast score (Hayes *et al.* 2010) and mentation score as validated by Hayes *et al.* (2010) (0 – normal; 1 – able to stand unassisted, responsive but dull; 2 – can stand only when assisted, responsive but dull; 3 – unable to stand, responsive; 4 – unable to stand, unresponsive).

Statistical analysis

Statistical analysis was performed via commercially available software (SAS version 9.4). Normality was determined using Kolmogorov–Smirnov method and visual examination of histograms. Continuous variables are expressed as the mean \pm standard deviation (sd) when normally distributed and as the median with the minimum and maximum range (min to max) when non-normally distributed. Categorical data are presented as absolute numbers and percent frequencies. Student's *t*-test was used to compare the values of normally distributed continuous variables, and the Mann-Whitney U test was used to compare the values of non-normally distributed continuous variables. Categorical variables were compared using the chi-squared test or Fisher's exact test, as appropriate. The area under the receiving operating characteristic curve was used to compare the prognostic utility of the qSOFA score to predict mortality using different respiratory rate cut-offs. The ROC curves were compared with each other by using the DeLong and Clarke-Pearson method (the ROCCON-TRAST statement in SAS). A logistic regression model was built with non-survival as the dependent variable, and age, presence of SS/SH and qSOFA score with different abnormal respiratory rate cut-offs (qSOFA, qSOFA30 and qSOFA40) as independent variables. The adjustment for age was performed to reduce the potential bias resulting from age differences in the groups being compared. No additional variables were included in the multivariate logistic regression model to prevent overfitting. Values of $P < 0.05$ were considered significant.

RESULTS

There were 628 cases identified with a clinical suspicion of sepsis. There were 89 excluded due to an absence of bloodwork, 107 excluded due to an absence of documented infection, 79 excluded due to a lack of organ dysfunction, 15 excluded due to absence of at

Table 1. Comparison of population data between dogs with severe sepsis or septic shock and non-infectious SIRS

Variable	All dogs (n=90)	SS/SH group (n=45)	N-SIRS group (n=45)	P value
Age, years	7.2 (±3.9)	7.3 (±3.7)	7 (±4.1)	0.7
Sex, n (%)				0.15
Male neutered	31/90 (34.4)	14/45 (31.1)	17/45 (37.8)	
Male entire	10/90 (11.1)	7/45 (15.6)	3/45 (6.7)	
Female spayed	37/90 (41.1)	21/45 (46.7)	16/45 (35.6)	
Female entire	12/90 (13.3)	3/45 (6.7)	9/45 (20)	
Body weight, kg	19.4 (2.3 to 73.5)	26.8 (2.3 to 73.5)	10.6 (3.2 to 56)	0.03
Heart rate, bpm	150 (30 to 230)	150 (100 to 230)	150 (30 to 200)	0.7
Body temperature, °C	38.7 (35.3 to 41.6)	38.8 (37.4 to 41.6)	38.6 (35.3 to 40.3)	0.01
Respiratory rate, bpm	46 (20 to 100)	52 (28 to 100)	42 (20 to 100)	0.2
Number of panting dogs, n%	14/90 (15.6)	8/45 (17.8)	6/45 (13.3)	0.56
Blood pressure systolic, mmHg	122.7 (±32.8)	120.7 (±30)	124.7 (±35.8)	0.6
Mentation score (0 to 4)	0 (0 to 4)	1 (0 to 4)	0 (0 to 4)	<0.001
WBC, ×10 ⁹ /L	13.5 (0.7 to 86.4)	13.7 (0.7 to 86.4)	11.5 (3.5 to 29.1)	0.2
Died, n (%)	45/90 (50)	29/45 (64.4)	16/45 (35.6)	0.006
Euthanized, n (%)	22/45	17/29 (58.6)	5/16 (31.3)	0.08
Euthanized for financial reason, n (%)	2/22	2/17	0/5	1

Data are mean (±sd) or median (min to max range) if normally or non-normally distributed, respectively

Mentation score (Hayes et al. 2010): 0 – normal; 1 – able to stand unassisted, responsive but dull; 2 – can stand only when assisted, responsive but dull; 3 – unable to stand, responsive; 4 – unable to stand, unresponsive

N-SIRS Non-infectious systemic inflammatory response syndrome, SS/SH Severe sepsis or septic shock, WBC White blood cell count

Table 2. Patients categorised by source of sepsis and non-infectious SIRS

SS/SH group	n (%)	N-SIRS group	n (%)
Septic peritonitis	25/45 (55.5)	Inflammatory hepatobiliary disease	10/45 (22.2)
Hepatobiliary infection	8/45 (17.8)	Acute pancreatitis	10/45 (22.2)
Pyothorax	4/45 (8.9)	Anaphylaxis	9/45 (20)
Pyometra	2/45 (4.4)	Acute haemorrhagic diarrhoea syndrome	5/45 (11.1)
Bacterial prostatitis	2/45 (4.4)	Acute kidney injury	3/45 (6.6)
Septic joint	1/45 (2.2)	Acute gastroenteritis	3/45 (6.6)
Bite wounds	1/45 (2.2)	Chylothorax	2/45 (4.4)
Bacterial pneumonia	1/45 (2.2)	Addisonian crisis	1/45 (2.2)
Bacterial endocarditis	1/45 (2.2)	Spontaneous hemoperitoneum	1/45 (2.2)
		Immune-mediated polyarthritis	1/45 (2.2)

N-SIRS Non-infectious systemic inflammatory response syndrome, SS/SH Severe sepsis or septic shock

least two SIRS criteria, and 293 excluded due to fulfilling multiple exclusion criteria. The SS/SH group included a total of 45 dogs, with 38 cases (84.4%) in SS and seven cases (15.6%) in SH. The N-SIRS group included 45 age-matched dogs. The mean age of dogs in SS/SH and N-SIRS groups were 7.3 (±3.7) and 7 (±4.1) years, respectively. Dogs in the SS/SH group had greater body weight ($P=0.03$), higher body temperature ($P=0.01$) and greater mentation score ($P<0.001$) in comparison with the N-SIRS group (see Table 1 for details). A total of 14 of 90 dogs were panting at admission in both groups. Eleven of 14 panting dogs had qSOFA = 1, 2 of 14 dogs had qSOFA = 2 and 1 of 14 dogs had qSOFA = 3.

The most common breeds in the combined cohort of dogs were Labrador (9/90), mixed-breed dog (9/90), dachshund (8/90), German shepherd (5/90), schnauzer (4/90), Rottweiler (3/45), Yorkshire terrier (3/90), boxer (2/45), Collie (2/45), Doberman (2/45), Basset hound (2/90), Boston terrier (2/90), miniature pinscher (2/90) and Rat terrier (2/90).

The most common causes of sepsis in dogs with SS/SH included septic peritonitis ($n=25/45$, 55.5%), hepatobiliary infection ($n=8/45$, 17.8%) and pyothorax ($n=4/45$, 8.9%). In the N-SIRS group, inflammatory hepatobiliary disease ($n=10/45$, 22.2%), acute pancreatitis ($n=10/45$, 22.2%) and anaphylaxis ($n=9/45$, 20%) were the most prevalent disease processes (see Table 2).

Among patients with SS/SH, 30 of 45 (66.7%) dogs fulfilled the qSOFA at least two criteria, whereas only 16 of 45 (34.8%) dogs in the N-SIRS had qSOFA at least 2 ($P=0.003$). These differences remained statistically significant between the two groups for qSOFA30 greater than 2 ($P=0.002$) and qSOFA40 greater than 2 ($P=0.01$). There was no statistical difference between SS/SH and N-SIRS groups with respect to the number of dogs positive for qSOFA at least 1 and qSOFA at least 3 regardless of the respiratory rate cut-off used (see Table 3). The qSOFA at least 2, qSOFA30 at least 2 and qSOFA40 at least 2 produced sensitivity and specificity to detect SS/SH of 66.7% and 64.5%, 62.2% and 71.1%, 44.4% and 80%, respectively.

Two of seven dogs with SH had qSOFA = 3, four of seven dogs had qSOFA = 2 and one of seven dogs had qSOFA = 1. Two of seven dogs with SH had qSOFA30 = 3, four of seven dogs had qSOFA30 = 2 and one of seven had qSOFA = 0. Two of seven dogs with SH had qSOFA40 = 3, two of seven dogs had qSOFA40 = 2, two of seven dogs had qSOFA40 = 1 and one of seven dogs had qSOFA40 = 0. The qSOFA at least 2, qSOFA30 at least 2 and qSOFA40 at least 2 produced sensitivity and specificity to detect SH of 85.7% and 51.8%, 85.7% and 57.8%, 57.1% and 69.9%, respectively.

Overall, in-hospital mortality was 45 of 90 (50%) cases, with 29 of 45 (64.4%) dogs in the SS/SH group and 16 of 45 (35.6%)

in the N-SIRS group ($P=0.006$). Of the 29 dogs that did not survive in SS/SH group, 17 were euthanized and 12 died. Fifteen of 17 dogs were euthanized due to poor prognosis, and two of 17 dogs were euthanized for financial reasons. Of the 16 dogs that did not survive in the N-SIRS group, five were euthanized due to a poor outcome, and none of these patients had a financial reason for euthanasia mentioned in the medical records.

When dogs in the SS/SH group were categorised based on survival and non-survival status, there was no statistical difference in their baseline characteristics at admission except for the APPLEfast score being greater in non-survivors (Table 4).

The qSOFA score provided poor discrimination between survivors and non-survivors for cases with SS/SH, non-infectious SIRS and the combined population of dogs regardless of the abnormal respiratory rate cut-off used (Table 5).

Of the 29 dogs that did not survive in the SS/SH group, only 19 of them were identified by the qSOFA at least 2 in the ER when respiratory rate cut-offs greater than 22 or greater than 30 were used, whereas only 13 of 29 dogs were identified by the qSOFA40 at least 2 (Table 6). The sensitivity, specificity, and

accuracy to predict non-survival using different qSOFA scores and respiratory rate cut-offs are presented in Table 7.

In the multi-variable regression analyses, the age and the presence of SS/SH were predictive of non-survival *versus* survival. The presence of SS/SH increased the odds of non-survival by 3.4 times (95% confidence interval: 1.4 to 8.4, $P=0.01$). When qSOFA, qSOFA30 and qSOFA40 were added to the multi-variable regression analysis model, they were not predictive of non-survival (Table 8).

DISCUSSION

This is the first study in veterinary literature evaluating the prognostic utility and performance of a qSOFA score to diagnose SS/SH in dogs presented to an emergency service. This retrospective cohort study found that qSOFA score provided poor discrimination between survivors and non-survivors for dogs with SS/SH. In addition, the qSOFA score demonstrated a poor sensitivity and fair specificity to detect this population of canine patients. The change of respiratory cut-offs from greater than 22 to greater than 30 or 40 breaths per minute further decreased qSOFA sensitivity, increased its specificity and did not change its predictive ability to discriminate survivors from non-survivors.

Table 3. Patients categorised by number of qSOFA criteria met and respiratory rate cut-offs

	All dogs, n (%)	SS/SH group, n (%)	N-SIRS, n (%)	P value
RR>22				
qSOFA \geq 1	89/90 (98.9)	45/45 (100)	44/45 (97.8)	1
qSOFA \geq 2	46/90 (51.1)	30/45 (66.7)	16/45 (34.8)	0.003
qSOFA \geq 3	14/90 (15.6)	8/45 (17.8)	6/45 (13.3)	0.56
RR>30				
qSOFA \geq 1	86/90 (95.6)	44/45 (97.8)	42/45 (93.3)	0.62
qSOFA \geq 2	41/90 (45.6)	28/45 (62.2)	13/45 (28.9)	0.002
qSOFA \geq 3	12/90 (13.3)	8/45 (17.8)	4/45 (8.9)	0.35
RR>40				
qSOFA \geq 1	73/90 (81.1)	39/45 (86.7)	34/45 (75.6)	0.18
qSOFA \geq 2	29/90 (32.2)	20/45 (44.4)	9/45 (20)	0.01
qSOFA \geq 3	9/90 (10)	7/45 (15.6)	2/45 (4.4)	0.16

RR Respiratory rate, qSOFA Quick sequential organ failure assessment, N-SIRS Non-infectious systemic inflammatory response syndrome, SS/SH Severe sepsis or septic shock

Table 5. Area under receiver operating characteristic (AUROC) curve for qSOFA, qSOFA30 and qSOFA40 to distinguish survivors from non-survivors

	qSOFA	qSOFA30	qSOFA40
All dogs	0.52 (0.41 to 0.64)	0.50 (0.39 to 0.61)	0.52 (0.41 to 0.63)
SS/SH group	0.51 (0.35 to 0.67)	0.56 (0.39 to 0.72)	0.54 (0.36 to 0.71)
N-SIRS group	0.64 (0.5 to 0.77)	0.66 (0.53 to 0.79)	0.59 (0.44 to 0.73)

All values represent areas under receiver operating characteristic curve with 95% confidence intervals

N-SIRS Non-infectious systemic inflammatory response syndrome, qSOFA Quick sequential organ failure assessment

Table 4. Comparison of population data between survivors and non-survivors in dogs with severe sepsis or septic shock

Variable	All dogs with SS/SH (n=45)	Survivors (n=16)	Non-survivors (n=29)	P value
Age, years	7.3 (\pm 3.7)	6.2 (\pm 4)	8 (\pm 3.4)	0.12
Sex, n (%)				0.17
Male neutered	14/45 (31.1)	5/16 (31.3)	9/29 (31)	
Male entire	7/45 (15.6)	5/16 (31.3)	2/29 (6.9)	
Female spayed	21/45 (46.7)	5/16 (31.3)	16/29 (55.2)	
Female entire	3/45 (6.7)	1/16 (6.3)	2/29 (6.9)	
Body weight, kg	26.9 (2.3 to 73.5)	20 (3.7 to 36.2)	30.6 (2.3 to 73.5)	0.12
Heart rate, bpm	150 (100 to 230)	148 (100 to 196)	150 (100 to 230)	0.74
Body temperature, °C	38.9 (37.4 to 41.6)	38.8 (37.4 to 40.6)	38.9 (37.8 to 41.6)	0.9
Respiratory rate, bpm	52 (28 to 100)	42 (28 to 100)	54 (28 to 100)	0.19
Blood pressure systolic, mmHg	120.7 (\pm 29.9)	123 (\pm 30)	119 (\pm 30.6)	0.7
Mentation score (0 to 4)	1 (0 to 4)	1 (0 to 3)	1 (0 to 4)	0.4
WBC, $\times 10^9$ /L	13.7 (0.7 to 86.4)	13.7 (3.1 to 78.8)	14.2 (0.7 to 86.4)	0.7
APPLEfast score	25.5 (\pm 5)	23.4 (\pm 4.9)	26.8 (\pm 4.6)	0.04
Dogs in septic shock, n (%)	7/45 (15.6)	1/16 (6.3)	6/29 (20.7)	0.39

Data are mean (\pm sd) or median (min to max range) if normally or non-normally distributed, respectively

Mentation score (Hayes *et al.* 2010): 0 – normal; 1 – able to stand unassisted, responsive but dull; 2 – can stand only when assisted, responsive but dull; 3 – unable to stand, responsive; 4 – unable to stand, unresponsive

SS/SH Severe sepsis or septic shock, WBC White blood cell count, APPLE Acute patient physiologic and laboratory evaluation.

Table 6. Patients categorised by number of qSOFA criteria met and survival versus non-survival status in dogs with severe sepsis or septic shock

	All dogs, n(%)	Survivors, n%	Nonsurvivors, n%	P value
RR>22				
qSOFA≥1	45/45 (100)	16/16 (100)	29/29 (100)	1
qSOFA≥2	30/45 (66.7)	11/16 (68.7)	19/29 (65.5)	0.83
qSOFA≥3	8/45 (17.8)	2/16 (12.5)	6/29 (20.7)	0.7
RR>30				
qSOFA≥1	44/45 (97.8)	16/16 (100)	28/29 (96.5)	1
qSOFA≥2	28/45 (62.2)	9/16 (56.3)	19/29 (65.6)	0.54
qSOFA≥3	8/45 (17.8)	2/16 (12.5)	6/29 (20.7)	0.7
RR>40				
qSOFA≥1	39/45 (86.7)	13/16 (81.3)	26/29 (89.6)	0.65
qSOFA≥2	20/45 (44.4)	7/16 (43.8)	13/29 (44.8)	0.95
qSOFA≥3	7/45 (15.5)	2/16 (12.5)	5/29 (17.3)	1

qSOFA Quick sequential organ failure assessment, RR Respiratory rate

Table 7. Sensitivity and specificity of qSOFA score with various cut-offs to predict non-survival in dogs with severe sepsis or septic shock

	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Accuracy, % (95% CI)
RR>22			
qSOFA≥1	100 (92.1 to 100)	2.2 (0.06 to 11.8)	51.1 (40.4 to 61.8)
qSOFA≥2	48.9 (33.7 to 64.2)	46.7 (31.7 to 62.1)	47.8 (37.1 to 58.6)
qSOFA≥3	13.3 (5 to 26.8)	82.2 (68 to 92)	47.8 (37.1 to 58.6)
RR>30			
qSOFA≥1	93.3 (81.7 to 98.6)	2.2 (0.06 to 11.8)	47.8 (37.1 to 58.6)
qSOFA≥2	46.7 (31.7 to 62.1)	55.6 (40 to 70.4)	51.1 (40.4 to 61.8)
qSOFA≥3	13.3 (5 to 26.8)	86.7 (73.2 to 95)	50 (39.3 to 60.7)
RR>40			
qSOFA≥1	84.5 (70.5 to 93.5)	22.2 (11.2 to 37.1)	53.3 (42.5 to 63.9)
qSOFA≥2	31.1 (18.2 to 46.7)	66.7 (51 to 80)	48.9 (38.2 to 59.7)
qSOFA≥3	11.1 (3.7 to 24)	91.1 (78.8 to 97.5)	51.1 (40.4 to 61.8)

RR Respiratory rate, qSOFA Quick sequential organ failure assessment, CI Confidence interval

Table 8. Predictors of non-survival in critically ill dogs with severe sepsis or septic shock and non-infectious SIRS

Model	OR	OR 95% CI	P value
Basic model			
Age	1.17	1.04 to 1.32	0.01
SS/SH	3.4	1.4 to 8.4	0.01
qSOFA model			
Age	1.17	1.04 to 1.33	0.01
SS/SH	4.2	1.56 to 11	0.005
qSOFA	0.65	0.34 to 1.25	0.2
qSOFA30 model			
Age	1.17	1.04 to 1.3	0.01
SS/SH	4.15	1.5 to 11.2	0.005
qSOFA30	0.7	0.37 to 1.3	0.27
qSOFA40 model			
Age	1.17	1.04 to 1.3	0.01
SS/SH	3.6	1.4 to 9.4	0.01
qSOFA40	0.9	0.5 to 1.5	0.65

Each model used the independent variables below each model to predict non-survival as the dependent variable. For qSOFA, qSOFA30 and qSOFA40 models, the abnormal respiratory rate cut-offs were chosen greater than 22, 30 and 40 breaths per minute, respectively

OR Odds ratio, CI Confidence interval, qSOFA Quick sequential organ failure assessment score, SIRS Systemic inflammatory response syndrome, SS/SH Severe sepsis or septic shock

Scoring systems are tools that may increase the clinical suspicion for sepsis and encourage emergency veterinarians to perform time-sensitive interventions and educate pet owners. Ideally, scoring

systems utilised in ERs should have good sensitivity to minimise missed sepsis cases. Consistent with the human literature, our study showed that qSOFA is not a sensitive scoring system to predict mortality (Simpson 2016, Williams *et al.* 2017, Jiang *et al.* 2018, Usman *et al.* 2019). In addition, Askim *et al.* looked at qSOFA's ability to detect SS in people presented to the emergency department. In that study, qSOFA at least 2 demonstrated a sensitivity of 32% and specificity of 98%. In our study, qSOFA at least 2 was 66.7% sensitive and 64.5% specific to identify SS/SH in canine patients. Unfortunately, a scoring system with low sensitivity may lead to treatment delays, whereas a poorly specific diagnostic tool will favour overtreatment. This begs the question of whether or not more sensitive but less specific scoring systems are more advantageous in the emergency setting, particularly in the hands of less experienced clinicians to catch septic patients early on. The most recent Surviving Sepsis Campaign guidelines (Evans *et al.* 2021) recommend against using qSOFA as a single-screening tool for diagnosing SS/SH. The results of our study also support this recommendation demonstrating the poor diagnostic ability of qSOFA score in a population of canine patients. Since our study was primarily focused on the evaluation of the qSOFA score to identify canine patients with SS/SH at risk of death, further research is warranted to replicate our findings.

Our results are consistent with the previous veterinary study (Ortolani & Bellis 2021) that showed qSOFA score was not a useful predictor of mortality in a general population of critically ill dogs. On the other hand, another veterinary study (Stastny *et al.* 2022) demonstrated that dogs diagnosed with septic peritonitis and other causes of surgically treated sepsis with a qSOFA of at least 2 might have a higher risk of in-hospital mortality, which is consistent with some human studies (Ho & Lan 2017). The discrepancy in the results between different studies may be explained by the inherent heterogeneity of the sepsis population, and it may be impossible to identify a single scoring system that serves the purpose that qSOFA intends to achieve.

In the current study, the original qSOFA score was contrasted to a modified qSOFA score (qSOFA30 and qSOFA40) by changing the respiratory rate cut-off from greater than 22 to greater than 30 or 40 breaths per minute, respectively. Since the normal resting respiratory rate for a dog in the hospital setting may exceed 20 to 30 breaths per minute (Bragg *et al.* 2015, Reineke

et al. 2015, Stellato *et al.* 2020), we chose to test these cut-offs in our study. As with any other scoring system utilising respiratory rate in dogs, the presence of physiologic “panting” may lead to a falsely increased total score. Similar to the Ortolani & Bellis (2021) study, the authors of this study considered “panting” to correspond to a respiratory rate greater than 22 breaths per minute. In our study, the majority of panting dogs (11/14) had qSOFA = 1. Therefore, even if these dogs were panting due to physiologic reasons such as stress or anxiety, it would not have significantly changed the number of dogs that met qSOFA at least two criteria. In a prospective setting, it may be beneficial to obtain a respiratory rate after stress and anxiety are addressed.

Currently, there is no updated definition for sepsis in veterinary medicine that is comparable to the Sepsis-3 guidelines in human medicine. For this study, sepsis was considered to be an infection plus SIRS at least 2. SS was defined as the presence of sepsis and at least one organ dysfunction, which resembles the Sepsis-3 definition of sepsis (Seymour *et al.* 2016, Singer *et al.* 2016, Du & Weng 2017, Finkelsztain *et al.* 2017). The rationale to focus on the canine patients with SS/SH was that evaluation of the scoring systems to detect septic patients with organ dysfunction is more important for emergency clinicians because these animals represent the sickest population of septic patients and their timely recognition and resuscitation are imperative. Also, since the definition of SS is very similar to the definition of Sepsis 3.0, the results of this study could be extrapolated to patients meeting Sepsis 3.0 criteria.

As with most retrospective studies, our study had limitations. Our data was dependent on the availability and accuracy of medical records. Numerous cases were excluded due to inadequate documentation of triage parameters and other pertinent information. This could have introduced selection bias. It should be noted that the SIRS criteria and the qSOFA both use a respiratory rate as a method of enrolment, so by using SIRS as one of the criteria for sepsis identification, it will be more likely that individuals will meet the qSOFA criteria.

Another limitation is the availability of humane euthanasia in veterinary medicine, which may bias the outcome. In this study, the authors excluded dogs that were euthanized before admission to the ICU or performance of source control surgery to minimise this bias. Also, upon review of the medical records, we identified only two patients that were euthanized due to financial reasons with the rest being euthanized due to a perceived poor prognosis.

An additional limitation was the fact that the qSOFA score has not been validated in veterinary medicine. Previously published veterinary studies investigating the utility of qSOFA score in dogs with surgically treated sepsis (Ortolani & Bellis 2021, Stasny *et al.* 2022) and a general population of critically ill dogs (Ortolani & Bellis 2021) did not include healthy control dogs either. In this study, the authors used an APPLE_{fast} score, which was previously validated in veterinary medicine. As opposed to the qSOFA score, the APPLE_{fast} score was associated with mortality in this population of canine patients with SS/SH. Further exploration of the optimal cut-offs in qSOFA score may improve the performance of this scoring system, however, there will likely remain some limitations in extrapolating human scoring systems for use in veterinary medicine.

Finally, in this study, we combined patients with SS/SH. Because only seven dogs met the criteria for SH, we did not separate these two subgroups of patients and did not perform additional statistical analysis.

In conclusion, qSOFA score of at least 1, at least 2 or at least 3 demonstrated a poor ability to predict mortality and low sensitivity with fair specificity to detect dogs with SS/SH presented to the emergency service. Its performance has not improved when different respiratory rate cut-offs were used. Therefore, further studies are needed to understand whether the qSOFA score has any utility in risk stratification and timely sepsis identification in canine patients.

As per the data sharing policy, data associated with this paper are available.

Conflict of interest

None of the authors of this article has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

Data availability statement

As per the data sharing policy, data associated with this paper are available.

References

- Babayak, J. M. & Sharp, C. R. (2016) Epidemiology of systemic inflammatory response syndrome and sepsis in cats hospitalized in a veterinary teaching hospital. *Journal of the American Veterinary Medical Association* **249**, 65-71
- Boller, E. M. & Otto, C. M. (2014) Sepsis and septic shock. In: *Small Animal Critical Care Medicine*. 2nd edn. Eds D. C. Silverstein and K. Hooper. Saunders, St. Louis
- Bragg, R. F., Bennett, J. S., Cummings, A., *et al.* (2015) Evaluation of the effects of hospital visit stress on physiologic variables in dogs. *Journal of the American Veterinary Medical Association* **246**, 212-215
- Du, B. & Weng, L. (2017) Systemic inflammatory response syndrome, sequential organ failure assessment, and quick sequential organ failure assessment: more pieces needed in the sepsis puzzle. *Journal of Thoracic Disease* **9**, 452-454
- Evans, L., Rhodes, A., Alhazzani, W., *et al.* (2021) Surviving sepsis campaign: international guidelines for Management of Sepsis and Septic Shock 2021. *Critical Care Medicine* **49**, e1063-e1143
- Finkelsztain, E. J., Jones, D. S., Ma, K. C., *et al.* (2017) Comparison of qSOFA and SIRS for predicting adverse outcomes of patients with suspicion of sepsis outside the intensive care unit. *Critical Care* **21**, 73
- Freund, Y., Lemachatti, N., Krastinova, E., *et al.* (2017) Prognostic accuracy of Sepsis-3 criteria for in-hospital mortality among patients with suspected infection presenting to the emergency department. *JAMA* **317**, 301-308
- Hauptman, J. G., Walshaw, R. & Olivier, N. B. (1997) Evaluation of the sensitivity and specificity of diagnostic criteria for sepsis in dogs. *Veterinary Surgery* **26**, 393-397
- Haydar, S., Spanier, M., Weems, P., *et al.* (2017) Comparison of QSOFA score and SIRS criteria as screening mechanisms for emergency department sepsis. *The American Journal of Emergency Medicine* **35**, 1730-1733
- Hayes, G., Mathews, K., Doig, G., *et al.* (2010) The acute patient physiologic and laboratory evaluation (APPLE) score: a severity of illness stratification system for hospitalized dogs. *Journal of Veterinary Internal Medicine* **24**, 1034-1047
- Ho, K. M. & Lan, N. S. (2017) Combining quick sequential organ failure assessment with plasma lactate concentration is comparable to standard sequential organ failure assessment score in predicting mortality of patients with and without suspected infection. *Journal of Critical Care* **38**, 1-5
- Jiang, J., Yang, J., Mei, J., *et al.* (2018) Head-to-head comparison of qSOFA and SIRS criteria in predicting the mortality of infected patients in the emergency department: a meta-analysis. *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine* **26**, 56
- Kaukonen, K. M., Bailey, M. & Bellomo, R. (2015) Systemic inflammatory response syndrome criteria for severe sepsis. *The New England Journal of Medicine* **373**, 881
- Kenney, E. M., Rozanski, E. A., Rush, J. E., *et al.* (2010) Association between outcome and organ system dysfunction in dogs with sepsis: 114 cases (2003-2007). *Journal of the American Veterinary Medical Association* **236**, 83-87
- Moreno, R., Vincent, J. L., Matos, R., *et al.* (1999) The use of maximum SOFA score to quantify organ dysfunction/failure in intensive care. Results of a prospective, multicentre study. *Intensive Care Medicine* **25**, 686-696

- Ortolani, J. M. & Bellis, T. J. (2021) Evaluation of the quick sequential organ failure assessment score plus lactate in critically ill dogs. *The Journal of Small Animal Practice* **62**, 874-880
- Purvis, D. & Kirby, R. (1994) Systemic inflammatory response syndrome: septic shock. *The Veterinary Clinics of North America: Small Animal Practice* **24**, 1225-1247
- Puskarich, M. A. & Jones, A. E. (2020) Sepsis. In: Tintinalli's Emergency Medicine: A Comprehensive Study Guide. 9th edn. Eds J. E. Tintinalli, O. J. Ma, D. M. Yealy, G. D. Meckler, J. S. Stapczynski, D. M. Cline and S. H. Thomas. New York, NY, McGraw-Hill Education
- Quantz, J. E., Miles, M. S., Reed, A. L., et al. (2009) Elevation of alanine transaminase and gallbladder wall abnormalities as biomarkers of anaphylaxis in canine hypersensitivity patients. *Journal of Veterinary Emergency and Critical Care* **19**, 536-544
- Reineke, E. L., Rees, C. & Drobatz, K. J. (2015) Association of blood lactate concentration with physical perfusion variables, blood pressure, and outcome for cats treated at an emergency service. *Journal of the American Veterinary Medical Association* **247**, 79-84
- Ripanti, D., Dino, G., Piovano, G., et al. (2012) Application of the sequential organ failure assessment score to predict outcome in critically ill dogs: preliminary results. *Schweizer Archiv für Tierheilkunde* **154**, 325-330
- Sampson, H. A., Munoz-Furlong, A., Campbell, R. L., et al. (2006) Second symposium on the definition and Management of Anaphylaxis: summary report—Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. *Annals of Emergency Medicine* **47**, 373-380
- Seymour, C. W., Liu, V. X., Iwashyna, T. J., et al. (2016) Assessment of clinical criteria for sepsis: for the third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA* **315**, 762-774
- Sharp, C. R. (2019) Systemic inflammatory response syndrome, sepsis, and multiple organ dysfunction syndrome. In: Textbook of Small Animal Emergency Medicine, I & II. 1st edn. Eds K. J. Drobatz, K. H. E. Rozanski and D. Silverstein. Wiley Blackwell, Hoboken, NJ
- Simpson, S. Q. (2016) New sepsis criteria: a change we should not make. *Chest* **149**, 1117-1118
- Singer, M., Deutschman, C. S., Seymour, C. W., et al. (2016) The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA* **315**, 801-810
- Stastny, T., Koenigshof, A. M., Brado, G. E., et al. (2022) Retrospective evaluation of the prognostic utility of quick sequential organ failure assessment scores in dogs with surgically treated sepsis (2011-2018): 204 cases. *Journal of Veterinary Emergency and Critical Care* **32**, 68-74
- Stellato, A. C., Dewey, C. E., Widowski, T. M., et al. (2020) Evaluation of associations between owner presence and indicators of fear in dogs during routine veterinary examinations. *Journal of the American Veterinary Medical Association* **257**, 1031-1040
- Summers, A. M., Vezzi, N., Gravelyn, T., et al. (2021) Clinical features and outcome of septic shock in dogs: 37 cases (2008-2015). *Journal of Veterinary Emergency and Critical Care* **31**, 360-370
- Turner, K., Boyd, C., Stander, N., et al. (2021) Clinical characteristics of two-hundred thirty-two dogs (2006-2018) treated for suspected anaphylaxis in Perth, Western Australia. *Australian Veterinary Journal* **99**, 505-512
- Unterter, S., Busch, K., Leipzig, M., et al. (2014) Endoscopically visualized lesions, histologic findings, and bacterial invasion in the gastrointestinal mucosa of dogs with acute hemorrhagic diarrhea syndrome. *Journal of Veterinary Internal Medicine* **28**, 52-58
- Usman, O. A., Usman, A. A. & Ward, M. A. (2019) Comparison of SIRS, qSOFA, and NEWS for the early identification of sepsis in the emergency department. *The American Journal of Emergency Medicine* **37**, 1490-1497
- Vincent, J. L., Moreno, R., Takala, J., et al. (1996) The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the working Group on sepsis-related problems of the European Society of Intensive Care Medicine. *Intensive Care Medicine* **22**, 707-710
- Williams, J. M., Greenslade, J. H., McKenzie, J. V., et al. (2017) Systemic inflammatory response syndrome, quick sequential organ function assessment, and organ dysfunction: insights from a prospective database of ED patients with infection. *Chest* **151**, 586-596