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RETROSPECTIVE STUDY

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Retrospective evaluation of the prognostic utility of quick sequential organ failure assessment scores in dogs with surgically treated sepsis (2011-2018): 204 cases

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Abstract

Objective: To assess the prognostic utility of admission quick Sequential Organ Failure Assessment (qSOFA) scores for in-hospital mortality in a population of dogs with surgically treated sepsis.

Design: Retrospective cohort study of dogs from January 2011 to January 2018.

Setting: University teaching hospital.

Animals: One thousand three hundred nine cases were identified with a clinical diagnosis of sepsis requiring surgical source control. Two hundred and four dogs with surgically treated sepsis met inclusion criteria, defined as: meeting 2 or more systemic inflammatory response syndrome (SIRS) criteria with a documented source of infection. One hundred and forty-three cases of septic peritonitis, 26 cases of septic soft tissue infection, 20 cases of pyometra, and 15 cases of pyothorax were evaluated.

Interventions: None.

Measurements and main results: Overall in-hospital mortality was 63 of 204 (30.9%). Patients with a qSOFA ≥ 2 were more likely to die or be euthanized (odds ratio [OR] 7.1, 95% confidence interval [CI] 2.9-16.4; $P < 0.0001$). Survivor and nonsurvivor qSOFA scores were significantly different in all categories. Dogs with septic peritonitis and a qSOFA ≥ 2 had an increased risk of postoperative complications (OR 3.9; 95% CI 1.3-11.1; $P = 0.02$). qSOFA scores were correlated with length of hospitalization in survivors of all-cause surgical sepsis ($r = 0.28$, $P = 0.0007$), septic peritonitis ($r = 0.33$, $P = 0.001$), and septic soft tissue infection ($r = 0.59$, $P = 0.004$).

Conclusions: This was the first study to retrospectively evaluate the prognostic utility of qSOFA scores in dogs surgically treated for sepsis. Dogs diagnosed with septic peritonitis and other causes of surgically treated sepsis with a qSOFA ≥ 2 may have a higher risk of in-hospital mortality, although future prospective studies are necessary.

Abbreviations: APPLE, score Acute Patient Physiologic and Laboratory Evaluation score; ATT, Animal Trauma Triage; AUROC, area under the receiver operating characteristic curve; CI, confidence interval; LOH, length of hospitalization; mGCS, modified Glasgow Coma Scale; OR, odds ratio; qSOFA, quick Sequential Organ Failure Assessment; SIRS, systemic inflammatory response syndrome; SOFA, Sequential [Sepsis-related] Organ Failure Assessment; SSTI, septic soft tissue infection

KEYWORDS
canine, infection, organ failure, postoperative complications, SIRS

1 | INTRODUCTION

Sepsis is a significant cause of morbidity and mortality, accounting for over 5 million patient deaths annually and mortality rates that range from 34% to 56% in people.[1–6] In veterinary medicine, the incidence of sepsis is poorly described, with reported mortality rates of 20% to 71%.[7–10] Recent focus in human medicine has been on early detection and intervention in septic patients, as increases in sepsis-related mortality are associated with delays in treatment.[1,11–15]

Sepsis has previously been defined as documented infection with systemic inflammatory response syndrome (SIRS). In people, at least 2 of the 4 SIRS criteria must be met: tachypnea (respiratory rate > 20/min); tachycardia (heart rate > 90/min); leukopenia or leukocytosis (leukocyte count > 12×10^9/L or < 4×10^9/L [> 12,000 cells/μL or < 4,000/μL]; and fever or hypothermia (body temperature > 38°C or < 36°C, respectively).[1,16] However, this original concept of sepsis focused solely on the identification of patients with an inflammatory excess and was critiqued for lacking sensitivity and specificity.[13,17,18] The Third International Consensus Definitions for Sepsis (Sepsis-3) task force was assembled to develop more precise clinical criteria that would more accurately identify all the elements of sepsis (infection, host response, and organ dysfunction) and offer increased uniformity in identifying the syndrome.[13,19]

In 2016, the Sepsis-3 task force redefined the syndrome of sepsis as "life-threatening organ dysfunction caused by a dysregulated host response to infection."[13] In the Sepsis 3.0 definition, a patient must have 2 or more points elevated in the Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score, based on the categories: respiration (PaO_2/FiO_2 ratio), coagulation (platelet count), liver (blood bilirubin concentration), cardiovascular (mean arterial pressure), central nervous system (Glasgow Coma Scale score), and renal (blood creatinine concentration, urine output).[11,13] Additionally, the Sepsis-3 task force recommended the use of a novel screening tool, the quick Sequential Organ Failure Assessment (qSOFA) to facilitate rapid risk stratification of patients at greatest risk of poor outcomes.[12,13,20] The qSOFA score assigns 1 point each for systolic blood pressure < 100 mm Hg, altered mental status, and respiratory rate > 22/min.[12,13,20] The added value of these new criteria in the emergency department and specific clinical settings remains unclear in human medicine and is the basis of continued investigation.[11,14,18,21]

In human medicine, illness severity scores are used for research purposes as well as to help predict outcomes in individual patients with an estimated probability. Scoring systems are underused in veterinary medicine, with few scoring systems having been developed and validated for veterinary patients.[22] The Animal Trauma Triage (ATT) and modified Glasgow Coma Scale (mGCS) scores are trauma-specific illness severity scores that allow objective quantification of injury severity.[22] There is 1 study that assessed SOFA in a population of dogs with sepsis and SIRS and showed that SOFA scores during the first 3 days of hospitalization significantly correlated with outcome, and an increased SOFA score was predictive of mortality.[23]

To date, the utility of qSOFA in veterinary sepsis has not been specifically evaluated. The purpose of this study was to assess the prognostic utility of admission qSOFA scores for in-hospital mortality in a large population of dogs with surgically treated sepsis. Our hypothesis was that qSOFA scores ≥ 2 would identify patients more likely to die or be euthanized in this population of dogs with surgically treated sepsis.

2 | METHODS

A medical record search was performed for all dogs coded with a clinical diagnosis of sepsis between January 2011 and January 2018, as identified by specific codes assigned to each case at the time of discharge or death. This search included cases coded specifically for septic peritonitis/abdomen, intra-abdominal abscess (including renal, hepatic, lymph node), septic bite wounds, necrotizing fasciitis, pyometra, and pyothorax.

Cases were included if they had a surgical source of sepsis and definitive surgical treatment was pursued, a complete medical record documenting evidence of infection (intracellular bacteria identified on cytology, positive bacterial culture, or gross diagnosis at time of surgery), and met 2 or more canine SIRS criteria: rectal temperature < 38.1°C or > 39.2°C; heart rate > 120/min; respiratory rate > 20/min; WBC < 6×10^9/L or > 16×10^9/L or > 3% band neutrophils (< 6,000/μL or > 16,000/μL).[24]

Cases were excluded if they left to pursue treatment elsewhere or were euthanized prior to treatment, did not have a documented source of infection, had a respiratory rate recorded as "panting," or did not meet SIRS criteria.

Data for the determination of SIRS and qSOFA scores were collected from parameters documented at the time of admission. For assignment of the mentation score for qSOFA, 1 point was assigned for any abnormal mentation, including those recorded as dull, obtunded, or stuporous. One point was assigned for a respiratory rate > 22/min, and 1 point was assigned for a Doppler blood pressure < 100 mm Hg, resulting in scores ranging from 0 to 3. Patients were further subcategorized into ≥ 2 qSOFA score and < 2 qSOFA score.

Additional data collected included signalment, source of sepsis, length of hospitalization (LOH), clinicopathological data including leukogram data and plasma lactate concentration, vasopressor requirement, and outcome (alive at discharge, euthanized, died). Cases were also evaluated for postoperative complications, including aspiration, dehiscence, and newly acquired hospital infections such as

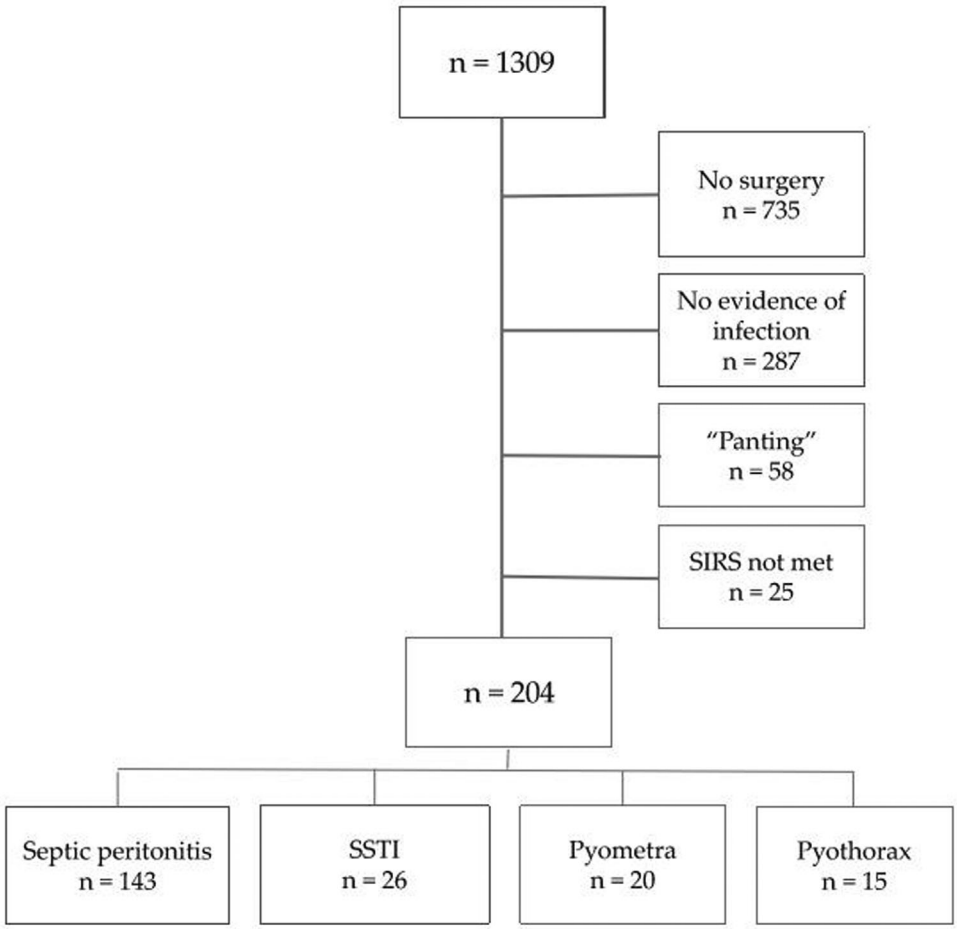

FIGURE 1 Flow diagram of case selection of dogs with surgically treated sepsis

incisional infections, catheter site-related infections, and urinary tract infections. If the record indicated a complication that fell into 1 of these 3 categories, the patient was classified as having had a "complication." The number of complications per category and association with qSOFA score was then evaluated.

2.1 | Statistical analysis

Data were assessed for normality using D'Agostino–Pearson omnibus normality test. Statistical analysis was performed using commercially available software,[a] with Bonferroni-corrected Mann–Whitney testing used where appropriate ($P < 0.01$ was considered significant). Spearman's rank correlation testing was used to assess qSOFA scores with plasma lactate concentrations and length of hospitalization and is reported using the following criteria for subjective terms of correlation: 0.10 to 0.39 weak, 0.40 to 0.69 moderate, > 0.7 strong.

Descriptive statistics were used for continuous population data and are reported as medians and interquartile ranges. The area under the receiver operating characteristic curve (AUROC) was calculated for the categories of all-cause surgical sepsis and septic peritonitis, with data reported as AUROC (95% confidence interval [CI]). Odds ratios (OR) were calculated using the Fisher's exact tests with Baptista–Pike method to calculate CI, with data reported as OR (95% CI).

3 | RESULTS

There were 1,309 cases identified with a clinical diagnosis of sepsis with a source requiring surgical intervention. There were 735 patients excluded because they did not pursue surgery, 287 excluded because no evidence of infection was identified, 58 excluded because of respiratory rates recorded as "panting," and 25 excluded because they did not meet SIRS criteria (Figure 1). The median age of the 204 dogs included in the study was 6 years old (range, 1 month-15 years). Ninety-nine (48.5%) dogs were females, and 105 (51.5%) were males. Thirty-two (15.6 %) were mixed breed dogs, 26 were Labrador Retrievers (12.7%), 15 were Golden Retrievers (7.3%), 5 were German Shepherd Dogs (2.5%), and the remaining 126 (61.8%) comprised other purebred dogs.

There were 204 patients included for analysis, with 143 (70.1%) cases of septic peritonitis, 26 (12.7%) cases of septic soft tissue infection (SSTI), 20 (9.8%) cases of pyometra, and 15 (7.3%) cases of pyothorax (Figure 1). Overall in-hospital mortality was 63 of 204 (30.9%).

TABLE 1 Patients categorized by source of sepsis and number of qSOFA criteria met

	qSOFA < 2	qSOFA ≥ 2
All-cause surgical sepsis	104/204 (51%)	100/204 (49%)
Septic peritonitis	71/143 (49.7%)	72/143 (50.3%)
SSTI	16/26 (61.5%)	10/26 (38.5%)
Pyometra	10/20 (50%)	10/20 (50%)
Pyothorax	7/15 (46.7%)	8/15 (53.3%)

Abbreviations: qSOFA, quick Sequential Organ Failure Assessment; SSTI, septic soft tissue infection.

Overall in-hospital mortality in septic peritonitis cases was 50 of 143 (35%), 4 of 26 (15.4%) in SSTI cases, 2 of 20 (10%) in pyometra cases, and 7 of 15 (46.7%) in pyothorax cases. Patients were further subcategorized into ≥ 2 qSOFA score and < 2 qSOFA score (Table 1). Similar numbers of patients with qSOFA < 2 or ≥2 were found in each category of sepsis except SSTI, in which only 38.5% had a qSOFA ≥ 2 (Table 1). The qSOFA score provided good discrimination between survivors and nonsurvivors for cases of all-cause surgical sepsis (AUROC 0.81 [95% CI 0.75-0.87]) and was fair for cases of septic peritonitis (AUROC 0.78 [95% CI 0.7-0.86]).

Sixty-three patients had a qSOFA ≥ 2 and, of these, 43 of 63 (68.3%) did not survive. Patients with a qSOFA ≥ 2 were significantly more likely to die or be euthanized (OR 7.1 [95% CI 6.1-34.3]; $P < 0.0001$). Thirty-five of 63 (55.6%) nonsurvivors received vasopressors, and 10 of 63 (15.9%) survivors received vasopressors. Plasma lactate concentration and qSOFA scores were weakly correlated in all-cause sepsis ($r = 0.16$, $P = 0.03$) and septic peritonitis ($r = 0.39$, $P < 0001$). Length of hospitalization and qSOFA scores were weakly correlated in survivors of all-cause surgical sepsis ($r = 0.28$, $P = 0.0007$) and septic peritonitis ($r = 0.33$, $P = 0.001$) and were moderately correlated with survivors of dogs with SSTI ($r = 0.59$, $P = 0.004$).

Survivor and nonsurvivor qSOFA scores were significantly different in all categories (Table 2). Median plasma lactate concentrations were higher in nonsurvivors when compared to survivors in the all-cause surgical sepsis and septic peritonitis patients ($P = 0.002$ and $P = 0.006$, respectively), although not different in patients with SSTI, pyometra, or pyothorax (Table 2). Median Doppler blood pressure between survivors and nonsurvivors was significantly different in all categories except for pyometra and pyothorax (Table 2).

All-cause surgical sepsis had a total complication rate of 21 of 204 (10.2%); septic peritonitis of 19 of 143 (13.3%); SSTI of 0 of 26 (0%); pyometra of 1 of 20 (5%); and pyothorax 1 of 15 (6.7%). Dogs with septic peritonitis and a qSOFA ≥ 2 had an increased risk of postoperative complications (OR 3.9 [95% CI 1.3-11.1]; $P = 0.02$).

4 | DISCUSSION

The use of SOFA and qSOFA scores have been proposed in human medicine for rapid and objective identification of septic patients while, to date, qSOFA has been utilized infrequently in published veterinary studies.[b,c,d] Results of the present study indicate that qSOFA may be helpful in identifying patients at risk for death or euthanasia, as patients with a qSOFA score of ≥2 were 7.1 times more likely to die or be euthanized compared with dogs with a qSOFA < 2. Without the need for any laboratory data, the use of qSOFA for initial patient screening is attractive because of its easy and rapid application.

Studies in people have demonstrated mixed results regarding the utility of the qSOFA when evaluating patients at risk for sepsis.[10,11,14,15,17,18,25] Freund et al found that ≥ 2 qSOFA was a better predictor of in-hospital mortality among patients with suspected sepsis presenting to the emergency department (AUROC 0.80) vs SIRS (AUROC 0.65) and severe sepsis (AUROC 0.65).[11] The qSOFA score performed similarly in the present population of dogs with surgically treated sepsis (AUROC 0.81 [95% CI 0.75-0.87] and 0.78 [95% CI 0.7-0.86] for all-cause sepsis and septic peritonitis, respectively).

In the present study, sepsis was defined in patients with a documented source of infection and 2 or more SIRS criteria, which precluded a direct comparison between SIRS and qSOFA in this population. In each individual category of surgical sepsis (septic peritonitis, SSTI, pyometra, and pyothorax), there was no difference in the number of SIRS criteria met between survivors and nonsurvivors; however, qSOFA scores were significantly different in each category, suggesting an added benefit for using qSOFA in patients diagnosed with sepsis based on meeting SIRS criteria with a source of infection.

There was a weak correlation between qSOFA scores and LOH in survivors of all-cause surgical sepsis and septic peritonitis survivors and a moderate correlation between qSOFA scores and LOH in SSTI survivors. One explanation for this would be that patients with higher qSOFA scores that survived the perioperative period may have required more intensive care and longer hospital stays.

Increased plasma lactate concentrations are associated with worse outcomes in people with sepsis.[26,27] Similarly, the inability to normalize plasma lactate concentration in dogs with septic peritonitis, as well as a variety of other diseases, has been shown to be predictive of mortality in several retrospective veterinary studies.[28,29] The findings of the present study are in agreement, with nonsurvivors in all-cause surgical sepsis and septic peritonitis categories having significantly increased plasma lactate concentrations when compared to survivors. A difference was not noted in the SSTI, pyometra, and pyothorax groups, which may be due in part to the smaller number of patients available for analysis in these groups. Serial plasma lactate concentration and plasma lactate clearance were not assessed in the present study, limiting the

TABLE 2 Comparison of population data (case numbers, SIRS and qSOFA criteria, plasma lactate concentration, Doppler blood pressure, and length of hospitalization) between survivors and nonsurvivors in each category of surgical sepsis

Clinical diagnosis	All-cause surgical sepsis			Septic peritonitis			SSTI			Pyometra			Pyothorax		
	S[a]	NS[b]	*P*-value	S	NS	*P*-value	S	NS	*P*-value	S	NS	*P*-value	S	NS	*P*-value
n(%)	141(69.1)	63(30.9)		93(65.0)	50(35.0)		22(84.6)	4(15.4%)		18(90.0)	2(10.0)		8(53.3)	7(46.7)	
SIRS(out of 4)	3(2-4)	3(3-4)	0.03	3(2-4)	3(3-4)	0.06	3(2-4)	3(3-3.75)	0.72	3(2.75-3.25)	3.5(3-4)	0.61	3.5(3-4)	3 (3-4)	0.97
qSOFA(out of 3)	1(1-2)	3(2-3)	< 0.0001	1(1-2)	3(2-3)	< 0.0001	1(1-2)	2.5(2-3)	0.008	1(1-2)	3(3-3)	0.02	1(1-1.175)	3 (3-3)	0.001
Lactate (mmol/L)	2.6(1.5-2.5)	3.6(2.3-5)	0.002	2.5(1.5-3.5)	3.4(2.2-4.9)	0.006	3(1.5-4.5)	4.4(2.3-6.4)	0.54	3.01(2.4-4.3)	7.8(6.8-8.8)	0.07	1.7(0.9-2.9)	3.7(2.7-4.4)	0.05
Doppler blood pressure(mm Hg)	120(96-141)	80(60-90)	< 0.0001	110(90-139)	80(60-98)	< 0.0001	130(96-148)	70(50-90)	0.002	130(115-160)	65(60-70)	0.03	130(124-195)	65 (70-80)	0.03
Length of hospitalization (days)	5(4-7)	3(1-5)	< 0.0001	6(4-7)	3(2-6)	< 0.0001	5(3-8.25)	4(1-13)	0.31	3(2-4)	2(1-3)	0.29	3(6-9)	1 (1-4)	0.05

Data are median (25-75% interquartile range). Abbreviations: qSOFA, quick Sequential Organ Failure Assessment; SIRS, severe inflammatory respiratory infection; SSTI, septic soft tissue infection.
*Significant at $P < 0.01$.
[a]Survivors.
[b]Nonsurvivors.

conclusion that can be drawn from admission plasma lactate concentration.

Septic peritonitis was the largest contributor to the all-cause surgical sepsis population, which may have created an inherent population bias in the all-cause group. However, as septic peritonitis is the most common cause of surgically treated sepsis in dogs, this is likely representative of all-cause surgical sepsis in dogs as a whole.[7–9,30–32] Septic peritonitis cases also had the highest complication rates within our study population (19.0%), which may be attributed, at least in part, to the fact that septic peritonitis comprised the bulk of the cases. Additionally, septic peritonitis cases requiring intestinal resection and anastomosis are at risk for postoperative dehiscence, which was 1 of 3 complications recorded (dehiscence, aspiration pneumonia, newly acquired hospital infection).[31–34] Although superficial incisional dehiscence was also included in this category, no cases were identified with only superficial incisional dehiscence.

There are several limitations to the present study. First, a large number of cases were excluded due to inadequate medical records as well as absence of evidence of documented infection (intracellular bacteria identified on cytology, positive bacterial culture, or gross diagnosis at time of surgery). This likely created an inherent population bias that may or may not have accurately identified our septic patients. For example, the exclusion of dogs with mild clinical signs that did not have cultures submitted may have inadvertently been selected for a proportion of dogs with higher qSOFA scores. In contrast, the exclusion of dogs that were euthanized without medical or surgical treatment may have excluded a comparatively more critically ill subpopulation of dogs and artificially decreased the overall mortality rate. The retrospective nature of this study also made it difficult to determine if patients were euthanized due to financial constraints or perceived poor prognosis, which further confounds conclusion regarding qSOFA scores and mortality prediction in veterinary medicine.

Another limiting factor was the exclusion of records that had respiratory rates recorded as "panting." A panting dog's respiratory rate may range from 120 to > 300/min, depending on body temperature.[35] Additionally, true physiological panting is rapid shallow breathing and, as such, it is unlikely that the majority of these dogs were truly panting. These records were excluded, as this precluded accurate qSOFA scoring and further limited sample size.

The inherent subjectivity in assessing mentation in veterinary medicine is another limitation of this study, especially when assessed retrospectively via a review of medical records. Given that the qSOFA score was developed for human patients, a possible future direction would be to develop criteria more specific to veterinary patients with quantifiable parameters to decrease subjectivity.

The lack of a control population comparing qSOFA scores between healthy patients and patients with surgically treated sepsis was another limitation. Given that the qSOFA score has not previously been validated for use in dogs, a control population or, alternatively, the use of another validated veterinary scoring system (eg, Acute Patient Physiologic and Laboratory Evaluation [APPLE] score) would have been useful. Unfortunately, a database of healthy dogs' records was not available at the authors' institution. Similarly, parameters such as body fluid scores, as part of the APPLE score, were inconsistently documented in the retrospective data analyzed.

The principal reason behind developing the qSOFA score in human medicine was to aid in rapid risk stratification and to improve on the preexisting SIRS criteria for sepsis identification.[11] The added value of qSOFA scoring remains unclear in human medicine and is the source of continued research. This is the first study to retrospectively evaluate the prognostic utility of qSOFA scores in canine surgically treated sepsis. Dogs diagnosed with septic peritonitis and other causes of surgically treated sepsis with a qSOFA $\geq$ 2 may have a higher risk of in-hospital mortality, although future prospective studies are necessary.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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ENDNOTES

[a] GraphPad Prism, version 8.1.2 for Windows, GraphPad Software, La Jolla, CA, www.graphpad.com.

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