Retrospective Study

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Severe soft tissue infections in dogs: 47 cases (1996–2006)

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Abstract

Objective – To describe the patient population, microbiological findings, treatment and outcome in dogs with severe soft tissue infections (SSTIs) and to compare survivors to nonsurvivors.
Design – Retrospective study.
Animals – Forty-seven dogs with confirmed soft tissue infections originating from the SC tissues, muscle or fascia.
Interventions – None.
Measurements and Main Results – Physical and clinicopathologic data on presentation, microbiological and histopathological findings, antimicrobial treatment and outcome. Dogs with SSTIs were predominantly large breed dogs with a median body weight of 35.6 kg. Incidence of pre-existing conditions (immunomodulating diseases, blunt trauma, injections, clean surgical procedures) that could have contributed to development of SSTIs was 34%. Abnormal physical examination and diagnostic parameters on presentation included increased body temperature (median temperature 39.5 °C [103.1 °F]) and low arterial blood pressure (median systolic blood pressure 103.5 mm Hg). While *Streptococcus* species were the most commonly isolated bacteria, the incidence of polymicrobial infections differed between antemortem (38.7%) and postmortem (57.1%) cultures. The overall survival rate was 46.8%. Survivors had a higher body weight and higher respiratory rate on presentation than nonsurvivors. Nonsurvivors had a significantly lower WBC count and higher lactate, BUN, aspartate aminotransferase, and bilirubin concentrations. Histopathologic examination of tissue specimens showed that the degree of necrosis was higher in survivors compared with nonsurvivors.
Conclusions – SSTIs in dogs are serious conditions associated with high mortality, significant inflammatory changes, and cardiovascular compromise. A number of conditions, including those that compromise skin integrity and immunomodulating diseases have been identified in our patient population and could have contributed to development of SSTIs. Polymicrobial infections occurred in many cases, necessitating broad-spectrum antimicrobial coverage.

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Introduction

Skin and soft tissue infections are prevalent in both human and veterinary medicine. These infections vary in degree of severity, ranging from involvement of only superficial tissues, requiring minimal treatment, to extensive infections, which cause severe illness and may have high mortality rates.[1] Reports of severe or necrotizing soft tissue infections (NSTIs) in dogs in the veterinary literature include a case series of 8 animals with necrotizing fasciitis secondary to β hemolytic streptococcal infections,[2] as well as several isolated case reports of NSTIs caused by a variety of bacteria.[3–6]

Soft tissue infections are commonly described according to their anatomic origin and degree of severity. However, the nomenclature of soft tissue infections is confusing and inconsistent, making it a challenge for them to be accurately described and compared. In human medicine, the term cellulitis describes an infectious process that involves the deep dermis and SC tissues.[1] However, it is possible for inflammation to be present without an infectious organism, and therefore the term cellulitis may also be used to describe a sterile

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process, as occurs with immune-mediated disorders.[7] Necrotizing fasciitis has traditionally been defined as necrotizing infection that involves superficial fascia.[8–10] Others have defined necrotizing fasciitis as inflammation and necrosis of the SC tissues or muscle,[3,4,11] which may or may not include fascial involvement. Frequently multiple soft tissues are involved at the time of diagnosis, making it difficult to establish the origin of the process. Recently, Anaya and colleagues proposed that the term NSTIs be used to describe any human soft tissue infection with necrosis, as all necrotic processes share common characteristics.[12]

NSTIs present a specific diagnostic challenge that can result in delay of appropriate treatment and increase mortality. A number of attempts have been made in human medicine to aid in the early identification of an NSTI. These include physical exam findings of pain out of proportion to the clinical findings, hemorrhagic bullae, and crepitus at the affected site.[13] Evaluation of clinicopathologic data, specifically the laboratory risk indicator for necrotizing fasciitis (LRINEC),[14] as well as use of imaging modalities to detect SC gas, tissue necrosis, and abscess formation may also aid in the diagnosis of NSTIs.[12–14] Optimal treatment of NSTIs in humans includes appropriate antimicrobial therapy, immediate and often aggressive surgical debridement and intensive supportive care. This differs markedly from the approach to soft tissue infections without necrosis, where medical management alone is often sufficient to treat the condition.[7,12]

Risk factors for development of NSTIs that have been identified in humans include immunosuppressed states, trauma, alcohol or IV drug use, peripheral vascular disease, and obesity.[8,15] In addition, the use of nonsteroidal anti-inflammatory drugs (NSAIDs) has been implicated as a risk factor,[16] although this has not been reliably substantiated.[8] Risk factors for development of NSTIs have not been investigated in veterinary medicine.

In the last decade, the authors have observed an increase in the number of dogs that presented with severe or NSTIs at one or more anatomic locations. These infections developed with no or minimal inciting cause and resulted in significant morbidity and mortality. The incidence of severe or NSTIs in veterinary medicine, bacterial species involved, clinical course, and risk factors for development of these infections have not been investigated. The primary objective of this study was to identify and describe a population of dogs with severe soft tissue infections (SSTIs) with respect to the clinicopathologic findings, etiologic agents, therapeutics utilized, and outcome. The secondary objective was to determine if there were any pre-existing or concurrent conditions in these dogs that could contribute to the development of SSTIs and affect mortality.

Materials and Methods

The computerized medical record and Department of Pathobiology databases at the Veterinary Hospital of the University of Pennsylvania were searched to identify dogs that were presented to our veterinary hospital between January 1996 and July 2006 with a primary diagnosis of inflammation of soft tissues. Cases were included in the study when a diagnosis of a soft tissue infection was made based upon evidence of inflammation or necrosis of SC tissues, muscle, or fascia. Inflammation or necrosis could be documented by any of the following means: histopathologic examination of biopsy specimens, cytologic examination of aspirates or direct impression smears, or gross examination during surgery. In all cases the concurrent presence of bacteria in the affected site as documented by cytologic or histopathologic examination, or by bacterial growth in either aerobic or anaerobic (or both) bacterial culture. Cases were excluded from the study if the inflammation or necrosis was confined to the dermis; was present without confirmation of infection; was characterized as chronic or pyogranulomatous; was a direct result of sterile inflammatory condition; was inflicted by penetrating trauma, such as a bite wound or a foreign object (where inflammation could have been caused by direct trauma); was initiated or localized to an area other than the SC tissues, muscle, or fascia (eg, joint, organ, esophagus, salivary gland, dermis, bone); was associated with fungal infection; was associated with a previous procedure where inflammation was expected but was not inappropriate to the injury (such as external fixator placement). Records that did not provide sufficient information about the cases were also excluded.

Parameters examined included: month of diagnosis; age; gender; body weight (kg); body condition (defined as underweight, normal, overweight, or obese); area of the body affected; the presence of concurrent illness or pre-existing conditions; type and duration of clinical signs; medications taken within 1 month before presentation; temperature, pulse, respiration, physical examination abnormalities, diagnostic imaging, and laboratory findings from presentation or the first available data after presentation. Prothrombin time (PT)[a] and activated partial thromboplastin time (PTT)[a] were expressed as percent prolongation above mean of the normal range or a single reference value, if that was provided. Fibrinogen split products (FSPs)[b] were scored from normal ($0; < 5\,\mu g/mL$) to severely elevated ($3; > 20\,\mu g/mL$). Microbiological cultures were evaluated and described as being obtained antemortem or postmortem, and either monomicrobial or polymicrobial. Surgical interventions, the time from admission to surgery, the duration of hospitalization, antimicrobials

used during hospitalization, and the mortality rate were documented. All of the available biopsy specimens were reviewed by a single board-certified pathologist to determine the anatomic site involved and to assess for presence of infectious organisms, degree of inflammation, and necrosis. The severity of inflammation and necrosis in histopathologic specimens was evaluated and graded from mild to severe using a subjective numeric scale with increasing degree of severity from 1 to 4. Cases were classified as NSTIs if objective evidence of necrosis was identified on histopathology. The term SSTIs combined all of the NSTIs and the cases in which necrosis was highly suspected, but histopathology was not performed. The survivors were compared with the nonsurvivors for all the above-described parameters.

The Shapiro-Wilks test was used to assess the distribution of continuous variables for normality. Continuous variables are reported as median (25th, 75th percentiles). The unpaired *t*-test was used to compare normally distributed continuous variables between survivors and nonsurvivors while the Mann-Whitney test was used for the non-normally distributed variables. Categorical variables are reported as proportions (%) and the χ^2 test or Fisher's exact test (if the expected value within a cell was <5) were used to compare these variables between outcome groups. A *P*-value <0.05 was considered significant. All statistical evaluations were performed using a computer software program.[c]

Results

Signalment and history

Three hundred and eighty-five records were identified. Of these, 47 (12%) dogs met the inclusion criteria. Forty (85%) of these dogs had lesions that were classified as NSTIs based on evidence of necrosis diagnosed either on histopathologic examination of tissue specimens or grossly at surgery. Seven (15%) were classified as SSTIs, as no objective evidence of necrosis was identified. The remaining 338 (88%) records were excluded: 73 (19%) due to sterile inflammatory conditions; 69 (18%) did not have enough information or incomplete medical records; 47 (12%) due to the presence of inflammation only in the dermis; 42 (11%) due to bite wounds or severe penetrating trauma; in 42 (11%) inflammation in a site other than the SC tissues or muscle; 35 (9%) due to presence of chronic or pyogranulomatous inflammation; 3 (1%) presence of fungal infection; and 27 (7%) had inflammation that was associated with a previous procedure, but was not inappropriate to the injury.

Of the 47 dogs included in the study, 22 (46.8%) survived to discharge from the hospital, while 25 (53.2%) dogs were either euthanatized (23/25) or died (2/25). There was no apparent breed predisposition, with the following breeds represented: Labrador Retriever (8 of 47 [17%]), mixed breed (7 of 47 [15%]), German Shepherd (4 of 47 [8.5%]), Mastiff (4 of 47 [8.5%]), Boxer (4 of 47 [8%]), Sharpei (3 of 47 [6%]), Rottweiler (3 of 47 [6%]), Akita (2 of 47 [4%]), Doberman Pinscher (2 of 47 [4%]), and 1 each of 10 different breeds: Bull Terrier, Toy Poodle, Italian Greyhound, Shetland Sheepdog, Saluki, German Shorthaired Pointer, Lhasa Apso, Standard Poodle, Maltese, and Saint Bernard.

The body weight, signalment, and body condition score of the dogs included in the study are presented in Table 1. Signalment parameters and body condition score were not associated with outcome, but survivors had significantly greater median body weight (39.3 kg) than nonsurvivors (27.0 kg) ($P = 0.046$).

The mean duration of clinical signs before presentation was 3.9 ± 4.5 days; there was no difference between survivors (4.4 ± 5.7 days) and nonsurvivors (3.4 ± 3.0 days). Twenty-nine of 47 dogs (61.7%) were treated by another veterinarian for this condition before being referred to our hospital. The most common clinical signs included swelling (28/47), lameness or difficulty ambulating (26/47), inappetence or anorexia (17/47), lethargy (10/47), diarrhea (11/47), vomiting (8/47), discharge from the affected area (7/47), and acting painful (6/47).

Nine of 47 (19%) dogs were diagnosed with, or suspected to have 1 or more immunomodulating condition(s) before presentation (3 survivors, 5 nonsurvivors), including immune-mediated polyarthritis ($n = 2$), meningitis and vasculitis ($n = 1$), hyperadrenocorticism ($n = 1$), hypothyroidism ($n = 1$), immune-mediated hemolytic anemia ($n = 1$), concurrent immune-mediated hemolytic anemia and thrombocytopenia ($n = 2$), mast cell tumor ($n = 1$), gastrointestinal lymphoma ($n = 1$) and chronic urinary tract infections ($n = 1$). Necropsy revealed a pheochromocytoma in 1 dog and a left thyroid gland carcinoma in another dog; both were distant from the NSTI and were not thought to be the cause of clinical signs in these dogs.

Eight of 47 (17%) dogs had an event that could have compromised skin integrity (4 survivors, 4 nonsurvivors). One dog had received SC fluids 1 day before onset of clinical signs: the area affected by cellulitis included the ventral thorax and abdomen. One dog was reported to have an allergic reaction characterized by facial swelling, for which it was administered a SC injection of dexamethasone several hours before onset of clinical signs. The left hind limb was affected in this dog (the location of the injection was not available). One dog was vaccinated for rabies <24 hours before onset of clinical signs; the vaccine was given into the

Table 1: Signalment, age, and body condition score of dogs with necrotizing soft tissue infections

Parameter	Survivors ($n = 22$)	Nonsurvivors ($n = 25$)	Overall ($n = 47$)
Sex			
Intact female	3	4	7
Spayed female	6	6	12
Intact male	7	7	14
Neutered male	6	8	14
Age (y)*	5.5 (1.1, 5.2)	6.0 (0.7, 5.1)	5.8 (0.9, 5.5)
Body weight (kg)*	39.3 (27.0, 38.1)§	27.0 (15.0, 26.1)§	35.6 (17.2, 34.1)
Body condition score			
Underweight	2	5	7
Normal	12	13	25
Overweight	8	3	11
Obese	0	1	1

*Age and body weight are reported as median values (25th; 75th percentiles), while sex and body condition score are reported as absolute numbers.
§Significant difference between survivors and nonsurvivors ($P = 0.046$).

affected limb. Two dogs had surgery at a site distant to the affected area within 1 week of onset of clinical signs (entropion surgery, 6 days prior; ovariohysterectomy, 7 days prior) and 2 at the site affected (bilateral cryptorchid castration, 1 day prior; ovariohysterectomy, 1 day prior). One dog had been hit by a car and underwent 2 surgeries and management of cutaneous wounds on the 3 limbs other than the 1 affected 26 and 18 days before onset of clinical signs. The affected limb had minor abrasions that did not require surgical care at the time of previous surgeries. One dog had history of blunt trauma (caught hanging over the edge of the whelping box) within 24 hours of onset of clinical signs. One dog had been boarded at a kennel until 1 day before onset of clinical signs, and 1 dog was groomed 13 days before onset of clinical signs with reported razor burn.

Twelve of 47 (25%) dogs (7 survivors, 5 nonsurvivors) were administered NSAIDs before presentation. Of these, 8 dogs (6 survivors and 2 nonsurvivors) were administered NSAIDs for a different medical problem before onset of clinical signs. Two of the dogs received unknown pain medications for an unknown period of time. Eighteen of 47 (38%) dogs (8 survivors, 10 nonsurvivors) were given corticosteroids before presentation; 6 were receiving corticosteroids for a pre-existing condition before onset of clinical signs. One dog received concurrent corticosteroids and NSAIDs; both were prescribed before onset of presenting clinical signs. Twenty of 47 (42%) dogs received antimicrobials before presentation (10 survivors, 10 nonsurvivors); 18 dogs received antimicrobials for the current presenting complaint. There was no significant difference between survivors and nonsurvivors with respect to administration of NSAIDs, corticosteroids or antimicrobials or duration of administration of those medications before presentation to our hospital.

Physical examination findings

Body temperature and heart rate were available in 43 of 47 (91%) dogs. Median temperature was 39.5 °C (103.1 °F) (39.1 °C [102.4 °F], 40.1 °C [104.2 °F]), with 27 dogs being above reference interval (37.5–39.1 °C [99.5–102.4 °F]). Median heart rate was 140/minute (120, 160/min), with 30 of 43 (69.7%) dogs being above reference interval (80–120/min). Respiratory rate was recorded in 42 of 47 (89%) dogs; the median respiratory rate was 60/minute (36, 70/min), with 34 of 42 (81%) dogs being above reference interval. Respiratory rate was significantly faster in survivors compared with nonsurvivors ($P = 0.04$) (Table 2).

Mean arterial blood pressure at hospital admission was available in 20 of 47 (42%) dogs (performed by an oscillometric method[d]), and the median value was 71 mm Hg (63, 102 mm Hg). Systolic blood pressure was available in 26 of 47 (55%) patients (performed using a Doppler ultrasonic flow detector[e] or oscillometry)

Table 2: Initial physical examination and diagnostic findings in dogs with SSTIs*

Parameter†	Survivors	Nonsurvivors
Temperature (°C) (S = 21, N = 22)	39.4 (39.1, 40.0)	39.6 (38.9, 40.3)
Heart rate (/min) (S = 21, N = 22)	130 (120, 144)	155 (132, 166)
Respiratory rate (/min) (S = 21, N = 21)	70 (40, 70) ‖	48 (36, 70) ‖
Systolic arterial pressure (mm Hg) (S = 8, N = 12)	112 (98, 148)	100 (86, 139)
Mean arterial pressure (mm Hg) (S = 10, N = 16)	87 (70, 103)	69 (60, 100)

*Parameters are reported as median value (25th, 75th percentile).
†S, survivors; N, nonsurvivors; the values for survivors and nonsurvivors represent the number of dogs for which these data were available.
‖ Values that are significantly different ($P = 0.04$).
SSTIs, severe soft tissue infections.

and the median value was 104 mm Hg (86, 149 mm Hg) (Table 2).

Soft tissue infections were localized to the appendicular skeleton (1 or more limbs) in 30 dogs and axial skeleton in 17 dogs. Areas affected on the axial skeleton included ventral thorax, abdomen, inguinal area, flanks, dorsum, muzzle, and prepuce. There was no difference in outcome between dogs in which an extremity was primarily affected as opposed to the axial skeleton. Likewise, survival did not differ in dogs in which single (15 survivors, 22 nonsurvivors) as opposed to multiple (7 survivors, 3 nonsurvivors) areas of the body were affected.

Laboratory findings

CBCs were available in 34 of 47 (72%) dogs. In these animals, the median neutrophil count (15,000 cells/μL [6,775, 18,280 cells/μL]; reference interval 3,100–14,400 cells/μL) and median platelet count (160,000 cells/μL [65,375, 212,750 cells/μL]; reference interval 177,000–398,000 cells/μL) were outside of the reference interval. Leukocytosis was identified in 12 of 34 (35%) dogs (10 survivors, 2 nonsurvivors) and leukopenia was identified in 5 of 34 (14.7%) dogs (2 survivors, 3 nonsurvivors). A left shift (defined as >200 bands/μL) was present in 12 of 34 (35%) dogs (4 survivors, 8 nonsurvivors); degenerative left shift (defined as a normal WBC count with >200 band neutrophils/μL) was identified in 6 dogs.

Serum chemistry panels were available in 32 of 47 (68%) dogs. In these dogs, the following laboratory values were outside of the reference interval: serum albumin (median 22.5 g/L [2.25 g/dL], 25th percentile 20.7 g/L [2.07 g/dL], 75th percentile 27.0 g/L [2.70 g/dL]; reference interval 25.0–37 g/L [2.5–3.7 g/dL]), aspartate aminotransferase (AST) (median 73 U/L [38, 152 U/L]; reference interval 23–65 U/L), alkaline phosphatase (ALP) (median 255.5 U/L [128.5, 635 U/L]; reference interval 20–155 U/L). In 19 of 47 (59%) dogs, the albumin value was below reference interval; 18 of 32 (56%) patients had elevated AST and 21 of 32 (65%) had elevated ALP.

PT and PTT were available in 26 of 47 (55%) patients (12 survivors, 14 nonsurvivors). Median PT prolongation was 0% (0%, 11.8%), and median PTT prolongation was 14.2% (2.6%, 52.6%). FSP information was available in 22 of 47 (47%) patients. FSPs were mildly elevated in 11 patients, moderately elevated in 5 patients and severely elevated in 6 patients. None of the coagulation parameters were different between the survivors and nonsurvivors.

Clinicopathologic data obtained at presentation to the hospital that were significantly different between survivors and nonsurvivors are summarized in Table 3. With the exception of the neutrophil count, all of these values were within normal reference interval for the study population as a whole. In nonsurvivors, lactate and AST were above the reference interval and lymphocyte count was below the reference interval.

Twenty-three of 47 (48.9%) dogs had radiographs of the affected area performed and 16 of 47 (34%) had an ultrasonographic examination of the area performed. Periosteal reaction of the bones in the affected area was noted in 2 dogs and significant degenerative joint disease was noted in 4 dogs on radiographs. In 11 of 16 (68.7%) cases that had the affected area examined by ultrasound, fluid pockets were identified. SC edema was noted in all of the dogs that had an ultrasonographic examination performed.

Table 3: Clinicopathologic data different between survivors and nonsurvivors on presentation*

Parameter†	Survivors	Nonsurvivors	*P* value	Reference interval
Na^+ (mmol/L) (S = 17, N = 15)	148 (144, 150)	142 (138, 145)	0.02	140–150
Cl^- (mmol/L) (S = 16, N = 14)	113 (112, 114)	109 (106, 113)	0.006	109–120
Total Mg (mg/dL) (S = 5, N = 7)	1.8 (1.8, 1.9)	2.1 (2.0, 2.4)	0.04	1.6–2.5
Total Mg (mmol/L)	0.78 (0.78, 0.78)	0.86 (0.82, 0.99)	0.04	0.65–1.03
Lactate (mmol/L) (S = 17, N = 15)	2.1 (1.3, 2.3)	4.6 (2.2, 7.6)	0.008	<2.5
BUN (mg/dL) (S = 11, N = 14)	10.5 (6.8,14.5)	28.5 (20.8, 59.0)	0.002	5–30
BUN (mmol/L)	3.7 (2.4, 5.2)	10.2 (7.4, 21.1)	0.002	1.8–10.7
BUN/creatinine ratio (S = 19, N = 13)	12.6 (9.9, 17.9)	29.9 (16.1, 36.8)	0.003	9–33
AST (U/L) (S = 19, N = 13)	54 (34, 76)	158 (66, 286)	0.01	23–65
Total bilirubin (mg/dL) (S = 19, N = 13)	0.3 (0.2, 0.6)	0.8 (0.3, 1.2)	0.05	0.3–0.9
Total bilirubin (μmol/L)	5.1 (3.4, 10.3)	13.7 (5.1, 20.5)	0.05	5.1–15.4
WBC count (cells/μL) (S = 20, N = 14)	19,850 (17,100, 25,625)	9,350 (5592, 16,100)	0.02	5300–19,800
Neutrophils (cells/μL) (S = 20, N = 14)	15,500 (14,000, 23,000)	6,850 (3525, 14,312)	0.02	3100–14,400
Lymphocytes (cells/μL) (S = 20, N = 14)	1,195 (645, 1925)	690 (362, 1060)	0.03	900–5500

*Parameters are reported as median value (25th, 75th percentile).

†S, survivors; N, nonsurvivors; the values for survivors and nonsurvivors represent the number of dogs for which these data were available.

AST, aspartate aminotransferase.

Table 4: Bacterial cultures obtained antemortem and postmortem in survivors compared with nonsurvivors

	Antemortem ($n = 31$)		Postmortem ($n = 14$)	
Bacterium cultured	**Survivors ($n = 22$*)**	**Nonsurvivors ($n = 9$)**	**Survivors ($n = 0$)**	**Nonsurvivors ($n = 14$)**
Pure culture	14	4	0	6
Multiple bacteria	7	5	0	8

*One culture yielded no growth.

Fine needle aspirates of the limb were performed in 23 of 47 (48.9%) dogs. Eleven aspirates were performed using ultrasonographic guidance, while the remainder were performed blindly. Cytologic evaluation of the samples obtained by fine needle aspirate yielded a diagnosis of inflammation with evidence of bacterial infection in 15 of 23 (62%) dogs; the other samples were either nondiagnostic or revealed inflammation without evidence of infection.

Seventeen of 47 (36%) dogs had surgical exploration of the NSTI. Surgical procedures included exploration of the abnormal area, debridement of the necrotic tissue, abscess or fluid pocket drainage, lavage, biopsies, drain placement, wound closure, or management as an open wound. The median time from admission to the hospital to surgery was 18 hours (10, 26 h), which did not differ between survivors (18 h [11, 26 h]) and nonsurvivors (14 h [7, 25 h]). Dogs that had surgery were less likely to die or be euthanized compared with the dogs that did not (OR, 0.14; 95% CI, 0.03–0.67; $P = 0.004$). Of the 17 dogs that had surgery, 4 (23.5%) did not survive; 1 dog suffered a cardiopulmonary arrest and 3 dogs were euthanized. All of the nonsurvivors that had surgery died or were euthanized within 24 hours of surgical procedure. Median duration of hospitalization was 4.5 days (3.3, 5.8 d) in survivors and 0.5 days (0, 1.0 d) in nonsurvivors. The duration of hospitalization was shorter in nonsurvivors ($P < 0.001$), with 9 of 25 (36%) nonsurvivors euthanized within 8 hours of presentation. For 26 of 47 (55%) patients that were hospitalized for more than 1 day, survival did not differ between those dogs that had surgery compared with the dogs that did not.

Aerobic and anaerobic bacterial cultures were performed on the fluid obtained from either fine needle aspirate, direct culture obtained at surgery or on postmortem examination in 42 of 47 (89%) dogs. In the remaining 5 dogs, bacterial infection was confirmed by visualizing bacteria in the sample submitted for histopathology or by a positive Gram stain. Two or more bacterial species were identified in 12 of 31 (38.7%) samples obtained as antemortem cultures and 8 of 14 (57.1%) samples obtained as postmortem cultures. No difference was detected when antemortem and postmortem cultures were compared for presence for monomicrobial or polymicrobial infections (Table 4).

Antemortem and postmortem culture results are summarized in Tables 5 and 6. Antemortem, β-hemolytic *Streptococcus* species were cultured in 11 survivors (7 in pure culture) and 2 nonsurvivors (both in pure culture). Postmortem, β-hemolytic *Streptococcus* species were cultured in 5 non-survivors (2 in pure culture). Survivors did not differ significantly from nonsurvivors in the frequency of positive *Streptococcus* cultures.

Antimicrobial susceptibility results were available for 28 (21 survivors, 7 nonsurvivors) patients. Two of the *Staphylococcus* isolates were phenotypical methicillin-resistant strains (*Staphylococcus intermedius* and coagulase negative *Staphylococcus*); both dogs had a history of antimicrobial treatment before culture. Four (2 survivors, 2 nonsurvivors) of the β-hemolytic *Streptococcus* isolates were resistant to penicillin. Two of these isolates were shown to belong to Lancefield group G (*S. canis*). This is the first report of penicillin-resistant *S. canis* from dogs. One of these patients had been treated with an unknown antimicrobial for an unknown duration of time before the culture. Both of the *Escherichia coli* isolates for which sensitivity results were available, were multidrug-resistant as defined at our hospital.[17] One of the animals had an episode of NSTI in a different

Table 5: Antemortem bacterial culture results

Bacterium cultured	**Survivors**	**Nonsurvivors**
β-hemolytic *Streptococcus spp*	11	2
Escherichia coli	2	4
Staphylococcus intermedius	5	0
Coagulase negative *Staphylococcus spp*	3	0
Clostridium spp	2	1
Pseudomonas aeruginosa	2	0
S. aureus	2	0
Serratia spp	1	0
Klebsiella pneumoniae	1	0
Enterococcus faecalis	0	1
Pasteurella multocida	0	1
Peptostreptococcus spp	0	1
Streptopeptococcus spp	0	1
Propionbacterum spp	0	1
Enterobacter cloacae	1	0

Table 6: Postmortem bacterial culture results

Bacterium cultured	Nonsurvivors
β-hemolytic *Streptococcus spp*	5
Escherichia coli	6
Staphylococcus intermedius	3
Clostridium spp	3
Pseudomonas aeruginosa	2
Enterococcus spp	2
α-hemolytic *Streptococcus spp*	2
Propionbacterum spp	2
Acinetobacter spp	1
Enterobacter cloacae	1
Stenotrophomonas maltophilia	1
Coagulase negative *Staphylococcus spp*	1

limb 4 weeks prior and had finished a course of antimicrobial treatment (amoxicillin-clavulanic acid[f] and enrofloxacin[g]) 2 days before this presentation. The other dog had a cryptorchid castration and was being treated with the antimicrobials enrofloxacin and cefazolin[h] for 3 days before the culture.

Antimicrobials were used in 36 of 47 (76.6%) cases (Table 7). All 11 cases that did not receive antimicrobials were in the nonsurvivor category; 9 of these cases were euthanized shortly after presentation to the hospital, and 2 were hospitalized for 8 and 24 hours before euthanasia. Antimicrobial combinations were used in 31 of 36 (86%) dogs. When combinations were used, the following were the most common: ampicillin[i] and enrofloxacin ($n = 9$), ampicillin and cefoxitin[j] ($n = 4$), ampicillin, metronidazole[k] and enrofloxacin ($n = 3$), ampicillin, metronidazole and gentamicin[l] ($n = 2$), clindamycin[m] and enrofloxacin ($n = 2$). Antimicrobial therapy was appropriate in 22 of 27 (81.4%) cases for which culture and sensitivity results were available (17/20 [85%] survivors and 5/7 [71.4%] nonsurvivors). The doses of antibiotics administered were within the described range for treatment of bacteria they were prescribed for.

Table 7: Antimicrobials used as a part of treatment

Antimicrobial	Survivors	Nonsurvivors	Total
Ampicillin	12	10	22
Enrofloxacin	11	10	21
Metronidazole	3	6	9
Cefoxitin	4	4	8
Clindamycin	3	2	5
Cefazolin	4	1	5
Amoxicillin/clavulanic acid	3	0	3
Gentamicin	3	0	3
Ticarcillin/clavulanic acid	0	3	3
Doxycycline	1	1	2
Cephalexin	1	0	1
Amikacin	1	0	1

Enrofloxacin was used in 22 of 36 (61%) cases that had antimicrobial treatment (12 survivors, 10 nonsurvivors). There was no association between enrofloxacin usage and survival. In 16 patients in which enrofloxacin was used, culture and sensitivity results were available. In 8 of 16 (50%) cases, at least one isolate was resistant to enrofloxacin.

Histopathology was available for 37 of 47 (78%) dogs (12/22 [54%] survivors and 25/25 [100%] nonsurvivors). The anatomic localization of inflammation is reported in Table 8. The severity of inflammation was not associated with outcome. However, when the severity of necrosis was compared, survivors were found to have a significantly higher degree of necrosis compared with nonsurvivors ($P = 0.007$) with a median degree of necrosis of 3.5 (2.8, 4.0) in survivors and 2.0 (2.0, 3.0) in nonsurvivors. In addition, dogs in which myositis was noted on histopathologic evaluation were significantly more likely to be in the nonsurvivor group ($P = 0.002$).

Discussion

Severe or NSTIs are infrequent, but potentially life-threatening conditions of both humans and animals that require prompt identification and aggressive treatment to result in successful outcome. The goal of this study was to describe a population of dogs with SSTIs in the absence of overt penetrating trauma and to determine if any variables could distinguish dogs that survived from those that did not survive. The mortality rate for dogs with SSTIs in the current study was 53%, confirming the critical nature of this disease. Eighty-five percent of dogs in this study population had NSTIs, defined by presence of necrosis on histopathology or at surgery. It is possible that in the remainder of the population necrosis was present; however, no objective evidence of that was present in the medical record.

Numerous predisposing conditions that have been reported in association with NSTIs in humans include immunosuppressive diseases, such as diabetes and HIV, surgery, blunt and penetrating trauma, obesity, peripheral vascular disease, alcohol abuse and

Table 8: Anatomic localization of infection on histopathologic samples

Site	Survivors ($n = 12$)	Nonsurvivors ($n = 25$)
Fascia	7	24
Skin	4	8
Joints	0	4
Muscle	2	17
Vasculitis	0	7
Thombosis	3	9

injectable drug use.[1,12] Over 30% of the dogs in the current study had a pertinent history that involved an immunosuppressive condition, recent trauma, surgery, injections, or SC fluid administration, frequently at the site that was affected and within the month before developing a SSTI. All of these conditions could have predisposed the dogs to development of an SSTI. Largely due to the small sample size and the heterogeneity of predisposing causes, it was not possible to determine whether survivors differed from nonsurvivors in the type and duration of these concurrent conditions.

Body temperature was significantly elevated in the present study population (median 39.5 °C), most likely due to inflammation associated with an infectious process. The degree of pyrexia was not different between survivors and nonsurvivors. This is in contrast to a study of primary cellulitis in horse limbs, in which febrile horses were less likely to survive.[18] In our study, a larger proportion of survivors were febrile than nonsurvivors (50% versus 32%). The respiratory rate was found to be significantly higher in survivors (70/min) compared with nonsurvivors (48/min). This could be due to the fact that the survivors may be less systemically ill and therefore more alert and responsive to pain or fear, or could be a result of their elevated body temperature. In one study of necrotizing fasciitis in children, those with necrosis were more likely to have a higher respiratory rate than those with infections without necrosis.[11] Children in this group had a significantly higher temperature, which could be responsible for an increase in respiratory rate. This is similar to the dogs in our population.

Obesity is one of the reported risk factors for development of NSTIs in humans.[8,12,19] In our population, dogs with a normal body condition score comprised 53% of the population, and only 23% were reported to be overweight. Interestingly, in our study, dogs that weighed more were more likely to survive. It is possible that the affected area in these dogs was comparatively smaller, which resulted in less systemic involvement. We compared body weight to body condition score in order to ascertain if the higher weight was related to being overweight or related to breed size. In this group of patients, weight was not correlated to body condition; therefore, the larger dogs were not more obese. Although not statistically significant, a noteworthy point is that there were 5 nonsurvivors in the underweight category, as opposed to 2 survivors. This could be due to the fact that underweight dogs are more debilitated and have less reserve to defend against a significant insult.

Systolic and mean arterial blood pressures were decreased in our study population compared with normal range. This confirms the clinical impression that the dogs presenting with a SSTI frequently suffer from cardiovascular compromise.

A number of diagnostic tests have been evaluated in humans in order to accurately identify a NSTI in a timely manner.[13,14] A LRINEC score was developed with the purpose of distinguishing necrotizing fasciitis from other soft tissue infections.[14] Significant predictors of a diagnosis of necrotizing fasciitis were determined to be leukocytosis, low hemoglobin concentration, hyponatremia, hyperglycemia, elevated serum creatinine, and elevated C-reactive protein concentration when patients with confirmed diagnosis of necrotizing fasciitis were compared with controls that did not have tissue necrosis as a part of their soft tissue infection. Although the current study does not have a control group, similar laboratory parameters may be useful adjuncts when prognosis for survival is being evaluated. In this population, the median WBC count was higher than the normal range, which correlates to the LRINEC score, where a higher WBC count is a significant predictor of necrosis, and therefore, a more severe or life-threatening soft tissue infection. In contrast to the LRINEC scoring system, however, nonsurvivors in our study had significantly lower WBC counts compared with survivors. Three of 12 of the patients in the nonsurvivor group were neutropenic, which likely decreased the median neutrophil count in that group. Six of the patients in this study also had a degenerative left shift. Neutropenia or degenerative left shift may be related to the patients' ability to appropriately respond to an insult, and may reflect the severity of disease. Twelve dogs in this study had evidence of significant soft tissue inflammation and necrosis despite having a WBC count within the reference interval. Therefore, the presence of a normal WBC count should not create a false sense of having successfully ruled out a significant inflammatory process. Blood smear evaluation to determine the degree of left shift and toxic change may be a more useful aid to determine the level of inflammation. Increased lactate and BUN noted in nonsurvivors may reflect worse tissue perfusion, localized necrosis, and more severe dehydration, respectively. Nonsurvivors had a significantly higher AST than survivors. As AST may be elevated due to muscle damage, a higher value may represent a more significant muscle involvement in nonsurvivors. One study reported myonecrosis as a negative prognostic indicator in humans with necrotizing fasciitis and myositis,[15] which was similar to results of our study, where nonsurvivors were significantly more likely to have had myositis diagnosed on histopathologic evaluation. Measurement of creatinine kinase may be a more reliable and useful indicator of myonecrosis; this value was not available in our study. In our study the degree of necrosis was higher in sur-

vivors, which is in contrast to the AST findings. Alternatively, the higher AST in nonsurvivors could be attributed to more severe hypoxia of the liver parenchyma secondary to cardiovascular compromise. Significantly elevated serum bilirubin level in nonsurvivors compared with survivors may be representative of liver dysfunction or hyperbilirubinemia of sepsis, thus reflecting a more severe inflammatory process in that population. Clinicopathologic data were not available for approximately 45% of nonsurvivors, likely because they were euthanized or died before obtaining that information. This could have affected the results and biased the study leading to inaccurate comparisons between the groups.

A number of imaging modalities for determination of NSTIs have been evaluated in humans, including radiography, ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI).[7,8,9,12] Radiographs may be useful in visualizing gas in the SC tissues in the event of gas producing anaerobic pathogens. This modality did not prove useful in our study, as SC gas was only identified in 1 dog, and that dog had undergone a recent surgery in the location where area of gas accumulation was noted.

Ultrasonography was used frequently in the cases of this study and aided in identifying pockets of fluid, which were subsequently aspirated or surgically explored in the majority of patients. Aspirates of the affected area and fluid pockets yielded positive results in identifying a bacterial infection in 62% of the cases in which they were performed. Cytologic evaluation of aspirates is a cost effective and quick method that could be valuable, but has low sensitivity and may not predict the extent of infection well.[8] The disadvantage of this method is that it does not distinguish a soft tissue infection with necrosis from one without necrosis, and therefore may not yield a desired answer of whether a particular patient should have a surgical exploration. Identification of a purulent fluid pocket may prompt surgical exploration, nonetheless. In human medicine, CT and MRI are used as adjunctive tests to help diagnose NSTIs. MRI is considered superior to CT for identification of necrotic areas; however, MRI is more sensitive than specific.[8,9] None of the patients in this study had MRI or CT performed as a part of their diagnostic work-up.

Early recognition and prompt surgical debridement of the necrotic tissue is one of the mainstays of therapy for NSTIs in human medicine.[12,20,21,22] Surgical exploration has also been advocated as a diagnostic tool to confirm presence of an NSTI. While our study found that survivors were significantly more likely to have had surgery, we cannot say that surgery directly resulted in increased survival, as a number of confounding factors are present. Many of the nonsurvivors may have been euthanized shortly after presentation due to the severity of their illness or due to financial constraints. This is also supported by our finding that there was no difference in survival between surgical and nonsurgical cases in dogs that were hospitalized for more than 1 day. Dogs that presented with severe clinical signs of shock may have been perceived to have a worse prognosis and be inferior surgical candidates. Decisions to euthanize could have been made due to financial limitations or due to concurrent illness before surgery. Nevertheless, surgery should be strongly considered in any patient with an SSTI where a necrotic process is suspected or an abscess is identified. Prospective studies are needed to identify whether surgical debridement affects mortality in patients with SSTIs in veterinary medicine.

The time elapsed from hospital admission to surgery is another important factor that is thought to carry prognostic significance. In a human study that evaluated prognostic factors in necrotizing fasciitis and myositis, patients that were operated more than 48 hours after admission had the best survival rate; this was likely related to less severe necrotizing fasciitis in these patients.[15] In the present study, time from admission to surgery did not differ between survivors and nonsurvivors.

A wide range of bacteria are usually recovered from NSTI sites. Polymicrobial infections are common and have been reported to occur in 55–85% of human NSTIs.[12,21] Most of the monomicrobial infections in humans are caused by Gram-positive cocci, commonly *Streptococcus* species.[12] In veterinary medicine, most reports of necrotizing fasciitis involve infection with a single bacterial species, although a variety of etiologic agents have been described.[2–5,23] The incidence of polymicrobial infections in our study was 38.7% based on antemortem cultures and 57.1% on postmortem cultures. Six patients in our study were diagnosed with bacterial infection based only on histopathology and Gram stain results rather than by aerobic or anaerobic culture. Four of these patients had a single bacterial strain identified microscopically; therefore, the incidence of polymicrobial infections may be underestimated. Fourteen dogs had positive cultures obtained from tissues following postmortem examination. Necropsies are frequently performed up to 24 hours after death; therefore, various opportunistic bacteria that were not responsible for infection can proliferate. These organisms will be cultured from tissues submitted following postmortem examination and these animals will be defined as having a polymicrobial infection, whereas a single microorganism could have been responsible. Consequently, caution should be applied when interpreting the results from cultures obtained postmortem.

Streptococcus species were the most common organism isolated in our population. Therefore, when an SSTI is suspected, it is imperative to ensure that empiric antimicrobial therapy includes agents appropriate for the treatment of infection caused by *Streptococcus* species. Our results also indicate that broad-spectrum coverage may be warranted as polymicrobial infections are common. Proposed agents for NSTIs in human medicine include single agents, such as imipenem or meropenem, combination therapy of high-dose penicillin or clindamycin with a fluoroquinolone or an aminoglycoside.[12] Eighty-six percent of the patients that were administered antimicrobials in the current study received combination antimicrobial therapy geared for broad spectrum coverage. Use of protein synthesis inhibitors, such as clindamycin has also been advocated in NSTIs, as it may help inhibit toxin production, especially in patients infected with *Streptococcus* and *Clostridium* species.[12] One study has shown that enrofloxacin can induce bacteriophage lysis in *S. canis* which can lead to necrotizing fasciitis.[24] In our study the use of enrofloxacin was not associated with outcome; nevertheless, half of the bacteria for which culture and sensitivity were available were resistant to enrofloxacin, indicating that it may not be the best empiric choice when a NSTI is suspected. Empiric antimicrobial therapy was inadequate in 18.6% of cases, which is similar to reports in human medicine.[25]

Isolates of methicillin-resistant *Staphylococcus*, penicillin-resistant *Streptococcus* and MDR *E. coli* were identified in this study. All of these patients were treated with antimicrobials before collection of specimens for culture. Methicillin-resistant staphylococci are becoming increasingly common in veterinary medicine and a recent retrospective study demonstrated that methicillin-resistant staphylococcal infections in dogs and cats are frequently resistant to many other antimicrobials; most commonly the fluoroquinolones and macrolides.[26]

NSAIDs have been implicated in increasing the risk of NSTI development in humans, although controlled studies have failed to show that this is in fact the case.[10] The present study was not designed to determine if the use of NSAIDs is a risk factor for developing SSTIs. However, while 25% of the dogs in this study had received NSAIDs before hospitalization, our study did not find an association between NSAID use and survival.

Some degree of necrosis was present in the majority of the soft tissue infections in this study. Interestingly, the survivors in our population had a significantly higher degree of necrosis compared with nonsurvivors. Typically, in the animals that were necropsied, the whole lesion or affected area is available for evaluation by a pathologist, and the degree of necrosis may not be uniform; thus, the degree of necrosis may be judged by evaluating several different locations. In contrast to that, only a small fragment of tissue is available for evaluation when a biopsy is performed during surgery. The area that is most severely affected may be biopsied, which would explain the more severe degree of necrosis in survivors. Also, histopathology samples were not available in 45% of the survivors. It is possible that only the survivors that were more severely affected and had the most devitalized necrotic tissue were the ones in which a biopsy was performed, thus confounding our results.

One of the major limitations of the study is its retrospective nature and a small number of animals included in the study. This prevented a reliable interpretation of a number of important variables, such as reasons for euthanasia of nonsurvivors, or decisions of whether to treat a particular patient surgically or medically. Because euthanasia is common and acceptable in veterinary medicine, and the vast majority of nonsurvivors were euthanized, this precludes evaluation of the true mortality rate, as it is defined in human medicine. In addition, clinicopathologic and microbiologic data were not available for all dogs, particularly for those that were euthanized soon after admission, which could have biased our results.

In conclusion, SSTI in dogs is a potentially life-threatening disease process that is associated with significant cardiovascular compromise and a considerable mortality rate due to the systemic inflammatory response. Several conditions that compromise skin integrity and diseases that may affect the immune system have been identified in our patient population and could have contributed to development of SSTIs, although case-control studies are required to accurately identify risk factors for development of SSTIs in dogs. Ultrasound of the affected area was useful in the majority of patients in identifying fluid pockets that could be aspirated to achieve a diagnosis or surgically explored. Many of our patients suffered from polymicrobial infections, in which broad-spectrum antimicrobial therapy was essential. Prospective studies are needed to more accurately characterize this condition in veterinary medicine and appropriate treatment methods to maximize the survival rate.

Footnotes

[a] STA Compact, American Bioproducts, Parsippany, NJ.
[b] Fibrinogen, American Bioproducts.
[c] Stata 8.0 for Windows, College Station, TX.
[d] Dinamap 8100 VSM Vital Signs Monitor, Model 68100T, Critikon, Tampa, FL.
[e] Ultrasonic Doppler Flow Detector, Model 811-BL, Parks Medical Electronics Inc, Aloha, OR.
[f] Clavamox, SmithKline Beecham Pharmaceuticals, Philadelphia, PA.

[g] Baytril, Bayer Healthcare Product, Shawnee Mission, KS.
[h] Cefazolin, Westward Pharmaceutical Corp, Eatontown, NJ.
[i] Ampicillin, Sandoz Inc, Princeton, NJ.
[j] Cefoxitin, Apotex Corp, Weston, FL.
[k] Flagyl, Hospira Inc, Lake Forest, IL.
[l] GentaMax 100, AMtec Group Inc, MO.
[m] Clindamycin, Hospira Inc.

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