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Outcome with surgical treatment of canine soft tissue sarcoma in the region of the ischiatic tuberosity: A veterinary society of surgical oncology retrospective study

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Abstract

The aim of this study was to determine the outcome of dogs with soft tissue sarcoma (STS) within the region of the ischiatic tuberosity (ITSTS) treated surgically. This was a multi-institutional retrospective study. Fifty-two dogs met the inclusion criteria, which were: histologically confirmed STS in the region of the IT treated with surgical resection between March 1st, 2009 and March 1st, 2021 with a minimum follow-up time of 6 months. Data collected included patient signalment, preoperative diagnostics, surgical intent/method, surgical complications, histopathology, margins, outcome and cause of death. Statistical analyses were performed to determine significant factors in the treatment and prognosis of ITSTS. Overall survival time (OST) and disease progression were negatively associated with tumour grade, while recurrence was positively associated with grade and incomplete margins. Of the 52 included dogs, there were 24 grade I, 20 grade II and 7 grade III tumours. Forty dogs had reported histopathologic margins of which 26 were reported to be complete and 14 were incomplete. OST and progression-free survival was not reached for tumours graded as I or II and was 255 and 268 days respectively, for grade III. Median time to recurrence was not reached for tumours excised with complete margins and was 398 days for those with incomplete margins. The surgical complication rate was 25%. ITSTS was not found to be a unique clinical entity in dogs as tumour behavior, treatment recommendations, and prognosis were similar to STS in other locations, with overall outcome and prognosis influenced by histologic grade and margins. While surgical complications were common, none resulted in significant morbidity or mortality.

KEYWORDS
dogs, oncology, sarcoma, soft tissue sarcoma, surgical oncology, veterinary

1 | INTRODUCTION

Soft tissue sarcoma (STS) is a spontaneously occurring connective-tissue tumour in animals and humans.[1] True incidence of STS in dogs is unknown but it has been previously suggested that these tumours account for 9%–15% of all cutaneous and subcutaneous canine tumours.[1] The underlying causes for sarcomas are varied and multifactorial.[2–28] In dogs, STS have been associated with radiation, trauma, chronic inflammation and parasitic infection.[2–6] In humans, STS has been associated with chronic inflammation, genetic predisposition, exposure to radiotherapy

and childhood cancer.[7–21] In human medicine, approximately 25% of malignancies have been associated with chronic inflammation.[17] Traumatic injury has also been suggested to predispose people to STS development.[18,19] In veterinary medicine, the relationship between inflammation and sarcomagenesis is associated with feline injection-site sarcomas[20–22] and fracture repair associated osteosarcoma (OSA) in dogs.[23–26]

In human medicine, a widely accepted nomogram is used that correlates prognosis with STS tumour location.[11] Approximately 40% of STS in humans occur in the extremities, with the thigh being the most common site.[12] STS of the buttocks (BSTS) specifically is a rare presentation, and these tumours have historically been categorized as both trunk and extremity sites.[13] However, humans with BSTS have been found to have poorer outcomes, including recurrence, progression and metastasis.[13,14] Independent predictors of disease-free interval (DFI) and survival time (ST) of BSTS include tumour size and grade.[14] Given the poorer prognosis, it has been proposed that BSTS should be categorized as its own clinical entity.[13]

In veterinary medicine, the equivalent anatomical location to the human buttock region is the caudodorsal region of the proximal pelvic limb where the gluteal musculature inserts, and major extensor muscles of the hip originate at the ischial tuberosity. Of significant importance, beyond the musculature of this region, is the proximity of the sciatic nerve, perineum and rectum. The recommendations for successful wide resection of canine STS are 2–3 cm radial margins and one facial plane deep.[29,30] Both the wide radial margins and removal of a complete fascial plane in this region are not always feasible as the critical structures in this region complicate wide tissue resection. In most cases, these tumours are removed with marginal excision. One reported method of reconstruction for a defect in this region after tumour resection is the lateral caudal axial pattern flap.[31] Beyond this reconstruction technique, there is no information in the literature about tumours in this region in dogs. Anecdotally, the authors have noted the IT region appears to have a predilection for the development of STS (ITSTS) in dogs.

The authors postulate that some dogs may develop ITSTS due to repeated, low-level trauma associated with increased pressure at this site. Dogs are prone to the formation of decubitus ulcers in regions of bony protuberances including the IT.[32] The prolonged pressure may cause chronic inflammation in this region, providing an environment for sarcomagenesis. To the authors' knowledge, there is no veterinary literature evaluating ITSTS as a potentially distinct clinical entity or the relationship between increased risk of chronic inflammation or tissue damage in this region with STS development.

The aim of this study was to evaluate ITSTS in dogs retrospectively and to evaluate factors that may influence oncologic outcome. The authors hypothesize that ITSTS is a distinct clinical entity, but unlike humans, dogs may have improved outcomes.

2 | MATERIALS AND METHODS

A request for case submissions was made through the Veterinary Society of Surgical Oncology (VSSO) listserv. Inclusion criteria for this study were dogs with histologically confirmed STS in the region of the IT treated with surgical resection between 1 March 2009 and 1 March 2021, and a minimum follow-up time of 6 months. Exclusion criteria included dogs with histologically confirmed STS subtypes of histiocytic sarcoma, hemangiosarcoma, rhabdomyosarcoma, osteosarcoma, lymphangiosarcoma, leiomyosarcoma and synovial cell sarcoma, as these specific STS subtypes are well documented to have a different biological behaviour than other STS.[30,33–35]

Data collected included signalment; preoperative bloodwork and imaging; tumour depth and location; maximum tumour diameter; preoperative tumour sampling (cytology and/or histopathology). Surgical intent (wide vs. marginal), reconstruction method, outcome and complications and histopathologic results were recorded. Additional information included adjunctive treatment and oncologic outcome, such as local recurrence, metastasis, disease progression, and ST including overall survival time (OST), DFI and cause of death. Besides the statistical data performed on the above information, all data was provided and reported by the submitting surgeon. Official reports for cytology, histopathology and imaging were used if included with the submission of data.

Surgical resection was defined as wide or marginal by the submitting surgeon. Surgical complications were categorized and graded using the Veterinary Cooperative Oncology Group-Common Terminology Criteria for Adverse Events (VCOG-CTCAE) guidelines.[36] (Table 1) Histologic results, including grade, subtype and margins (complete or incomplete), were based on the report of the attending pathologist assigned to each case. Given the retrospective and collaborative nature of the study, no independent histological review was performed.

When reporting pre and postoperative metastatic disease and tumour recurrence, the presence of multiple pulmonary nodules were interpreted as metastatic spread unless otherwise specified. The presence of solitary large masses within the thorax or abdomen were

TABLE 1 VCOG grading guidelines[a]

Grade	Description of adverse event
1	Mild; asymptomatic or mild symptoms; clinical signs or diagnostic observations only; intervention not indicated
2	Moderate; outpatient or non-invasive intervention indicated; moderate limitation of activities of daily living (ADL)
3	Severe or medically significant but not immediately life threatening; hospitalization or prolongation of hospitalization indicated; disabling; significantly limiting ADL
4	Life-threatening consequences; urgent interventions indicated
5	Death related to AE death can be defined as either euthanasia or natural death, according to the investigators' discretion

[a]Adapted from Veterinary Cooperative Oncology Group—Common Terminology Criteria for Adverse Event (VCOG-CTCAE v2) Grading Guidelines.[36]

assumed to be unrelated to ITSTS. Dogs with enlarged lymph nodes were not considered to have metastatic disease unless confirmed by cytology. Regional lymph nodes were defined as those lymph nodes associated with the structures in the IT region and included the inguinal, iliac, sacral and hypogastric lymphosomes. In those dogs with suspected metastatic disease at the time of diagnosis, any new lesions or progression of previously noted lesions were defined as progressive metastatic disease. Recurrence was defined as any new growth of a solid mass in the location of the originally excised tumour.

2.1 | Statistical analysis

Continuous variables were assessed for normality using the Shapiro–Wilk test. Normally distributed continuous variables were described using mean and SD, while non-normal continuous variables were described using median and range. [SO1] Survival was assessed using the Kaplan–Meier method. Differences in overall survival and progression-free survival (PFS) associated with histologic grade and differences in recurrence associated with histologic grade and histologic margins status (complete or incomplete) were assessed using the log-rank test. $p < .05$ was considered statistically significant. Statistical software (Prism 8, GraphPad, San Diego, CA) was used for all analyses. DFI is defined as the time from surgery to the time disease recurrence or metastatic disease was first noted. ST is defined as the time from surgery to the time of death, if reported. Dogs were censored from assessment of overall survival if they were alive at last follow-up or lost to follow-up. Death due to any cause was counted as an event. For the purposes of PFS, any known or suspected progression of disease was counted as an event. Dogs were censored if they had no evidence of progression at last follow-up. Dogs that died of known unrelated causes were censored but dogs that died of unknown causes were considered to have died due to their disease.

3 | RESULTS

Fifty-two dogs met the inclusion criteria. There were 25 (48.0%) castrated males, 23 (44.2%) spayed females, three (5.8%) intact males and one intact female. Numerous breeds were represented, including Labrador retrievers (9), golden retrievers (7), boxers (2), German shepherd dogs (2), flat-coated retrievers (2), Staffordshire terriers (2), English springer spaniels (2), 11 other breeds (1 each) and 14 mixed-breed dogs. The median age of dogs was 9 years old. The median weight was 29 kg. Forty-seven dogs had a complete blood count, and 49 dogs had a serum chemistry panel performed prior to surgery. Eighteen dogs had minor abnormalities noted but none were considered clinically significant.

Fifty-one dogs had preoperative thoracic imaging with radiographs ($n = 28$) or CT scan ($n = 31$). Three dogs had pulmonary masses or nodules detected on the pre-operative CT scans. One dog had a solitary mass in the left cranial lung lobe; another dog had multiple small

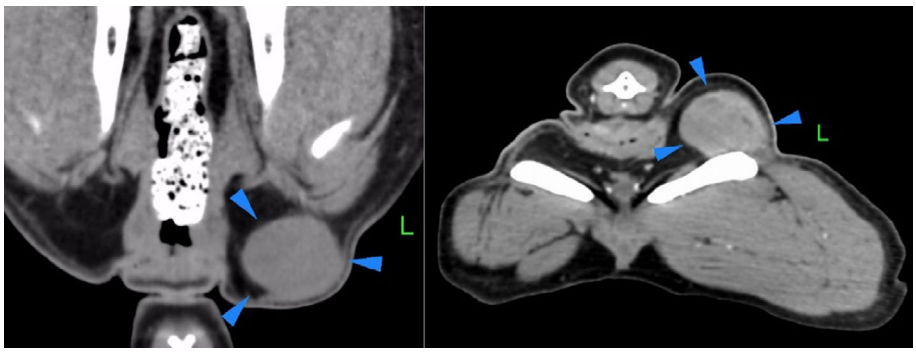

FIGURE 1 CT scan of a dog with an ischiatic tuberosity soft tissue sarcoma (ITSTS) in the region of the left IT. Blue arrows demarcate tumour. Image Credit: Dr. Sarah Boston

TABLE 2 Tumour pathology and outcomes

Case	FNA	FNA results	Incisional biopsy	Biopsy results	Pre-Op grade	Final grade	Subtype	Margin status	Recurrence
11	Yes	SpCT	Yes	STS	1	1		Incomplete	Yes
16	Yes	SA	No			1		Complete	Yes
35	No		Yes	STS	2	2	PWT/PNST	Complete	Yes
38	No		No			2		Incomplete	Yes
43	Yes	ND	No			2	PNST		Yes
46	No		Yes	HSA		3		Incomplete	Yes
48	Yes		Yes	STS		3		Incomplete	Yes
49	No		Yes	STS	2	3	FSA		Yes
51	No		Yes	SpCS	2	3		Complete	Yes

Abbreviations: HAS, hemangiosarcoma; ND, nondiagnostic; SA, sarcoma, unspecified; SpCS, spindle cell sarcoma; STS, soft tissue sarcoma.

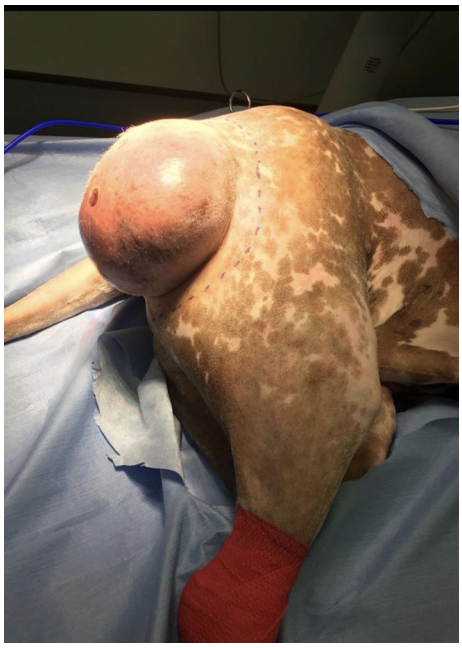

FIGURE 2 Dog with soft tissue sarcoma located within the region of the right ischiatic tuberosity. Photo Credit: Dr. Barnaby L. Dean

FIGURE 3 Surgical defect created by tumour excision, prior to reconstruction with a lateral caudal axial pattern flap procedure. Photo Credit: Dr. Barnaby L. Dean

pulmonary nodules reported as benign metaplasia; and the third dog had two soft-tissue attenuating nodules in the right cranial and left caudal lung lobes, as well as multiple smaller soft-tissue attenuating nodules throughout the entire lung field. Thirty-seven dogs had abdominal imaging performed with CT ($n = 32$) and ultrasound ($n = 5$) or both ($n = 9$). Based on CT scan, six dogs had evidence of enlarged regional lymph nodes. Tumour lateralization was 50% right- and 50% left-sided.

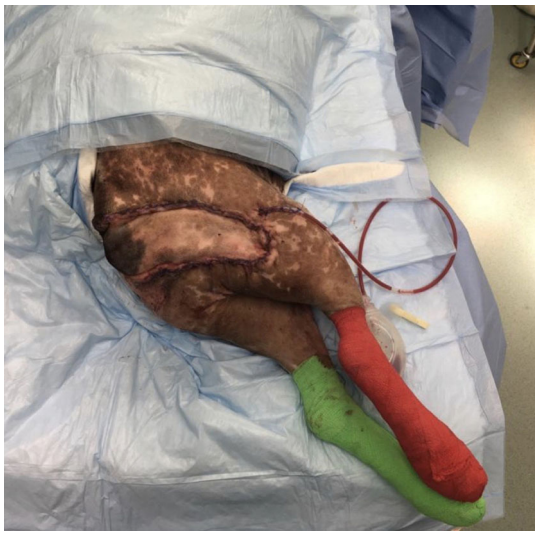

FIGURE 4 Immediate post-operative reconstruction using a lateral caudal axial pattern flap and closed suction drain. Photo Credit: Dr. Barnaby L. Dean

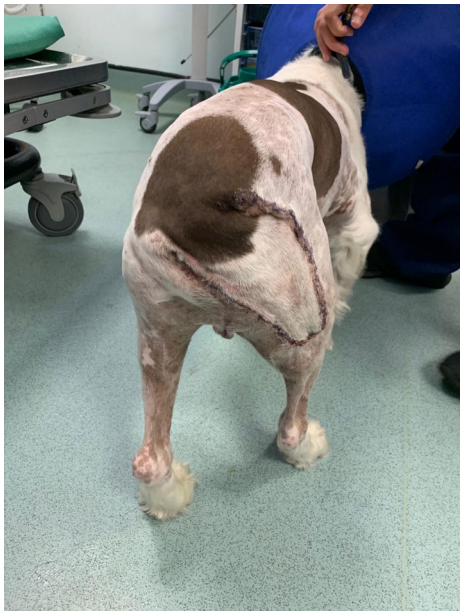

FIGURE 5 Result of lateral caudal axial pattern flap as seen at post-operative recheck exam. Photo Credit: Dr. Barnaby L. Dean

(Figure 1) Tumours measured 2.0–4.0 cm ($n = 14$), 4.1–6.0 cm ($n = 19$), 6.1–8.0 cm ($n = 9$), 8.1–10 cm ($n = 5$), 10.1–12 cm ($n = 2$), 12.1–14 cm ($n = 2$) and 14.1–16 cm ($n = 1$).

Fifty (96.2%) dogs had cytology and/or histopathology performed prior to surgery. Forty (80%) had cytology, 23 (46%) had an incisional biopsy and 13 (26%) of dogs had both performed. Of the 40 FNA cytology samples, 34 (85%) confirmed STS, four (10%) were non-diagnostic and two (5%) were reported as inflammatory. All 23 incisional biopsy samples confirmed STS. Of the 13 cases that had both an FNA and incisional biopsy, nine (69%) had agreement between the FNA cytology and biopsy results. (Table 2).

TABLE 3 Surgical reconstruction method and associated complications/VCOG grade

Case	Reconstruction method	Surgical intent	Surgical complications	Type of complication[a]	VCOG complication grade(s)
13	USF	Marginal	Yes	D, I	2, 2
19	IFTSF	Wide	Yes	D	2
23	LCAPF	Wide	Yes	I	1
26	PC	Wide	Yes	D	3
31	PC	Wide	Yes	D, N	3, 3
36	LCAPF	Wide	Yes	D	NP
39	DCISF	Wide	Yes	D	3
41	IFTSF	Wide	Yes	H	4
43	PC	Wide	Yes	TDI, D, I	3, 3, 3
49	LCAPF	Marginal	Yes	D, I	2, 3
50	IFTSF	Wide	Yes	D, I	2, 3
51	USF	Wide	Yes	N	3
52	DCISF	Wide	Yes	D	2

Abbreviations: DCISF, deep circumflex iliac skin flap; IFTSF, inguinal fold transposition skin flap; LCAPF, lateral caudal axial pattern flap; PC, primary closure; USF, unspecified skin flap.
[a]As defined by VCOG: D, dehiscence; H, haemorrhage; I, infection; N, necrosis; TDI: Tissue damage intraoperatively.

TABLE 4 Tumour grade for dogs with metastatic disease[a]

Case	Final grade	Subtype	Metastatic disease[a]	Location of Mets
44	2		Yes	RLN[b]
49	3	FSA	Yes	Lung
50	3	FSA	Yes	Lung
51	3		Yes	Lung[c], satellite lesion[c], RLN[b]
52		HPC	Yes	Lung

Abbreviations: FSA, fibrosarcoma; HPC, hemangiopericytoma; RNL, regional lymph node.
[a]Suspected metastatic spread.
[b]Confirmed with cytology.
[c]Metastatic disease present at time of diagnosis.

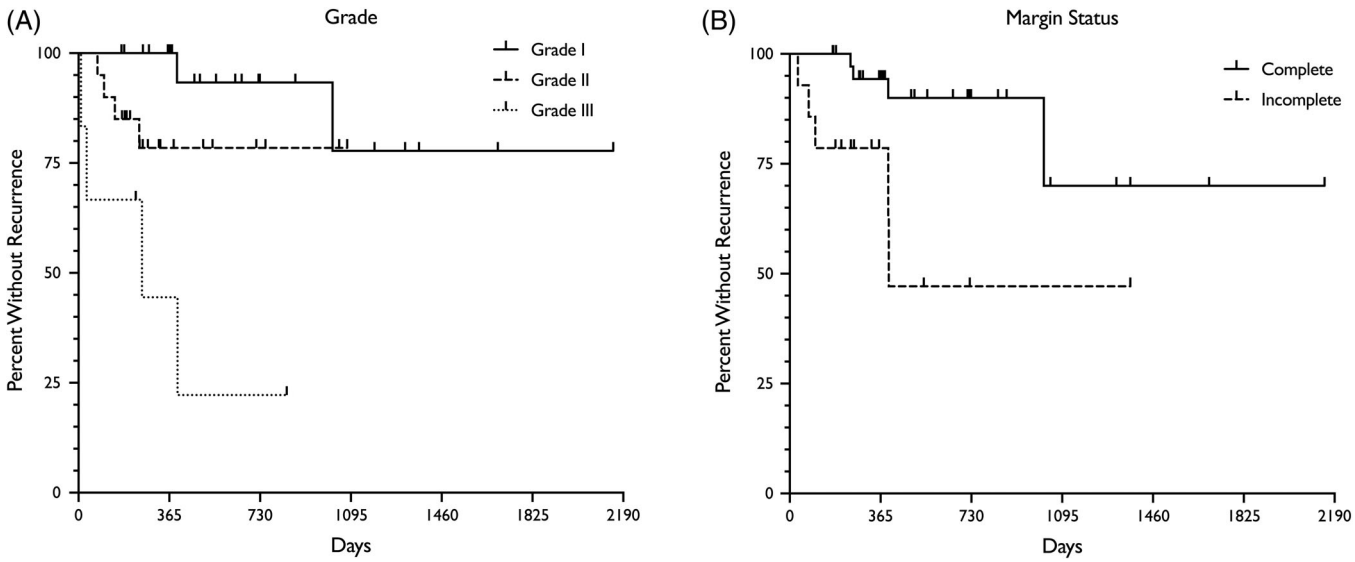

FIGURE 6 Kaplan–Meier curve showing ITSTS tumour recurrence based on grade (A) and completeness of excision (B). Censored patients are indicated by tick marks. Figures produced by Dr. Owen Skinner

Thirty-five (67.3%) surgeries were reported as wide excisions, while 16 (30.8%) were reported as marginal excisions. This information was not reported in one case. Sixteen (30.8%) dogs had a primary closure, while 36 (69.2%) dogs had the defect closed with various skin-flap techniques. The most commonly reported skin flaps were the lateral caudal axial pattern flap ($n = 14$) (Figures 2–5), caudal superficial epigastric axial pattern flap ($n = 7$) and the inguinal fold flap ($n = 6$). Thirteen dogs (25%) had a surgical complication during surgery or in the postoperative period. Intraoperative complications included iatrogenic rectal perforation ($n = 1$, VCOG grade 3) and haemorrhage requiring transfusion ($n = 1$, VCOG grade 4). Eleven dogs had postoperative incisional complications. (Table 3).

All tumours were confirmed as STS and assigned grade I ($n = 24$, 46.2%), grade II ($n = 20$, 38.5%), grade III ($n = 7$, 13.5%), and one tumour was not assigned a grade. A histologic subtype was reported in 21 (40.4%) dogs. Of the 20 dogs that had histologic grading of their preoperative incisional biopsy, there was a discrepancy between the incisional biopsy grade and the final histologic grade in eight cases (40%). Histopathologic margins were categorized in 40 (76.9%) cases. Of these, 26 (65.0%) were reported to have complete margins, while 14 (35.0%) were incomplete. Of the 51 cases that had a reported surgical intent, 56% of the marginal-intent surgeries were found to have incomplete margins, while 35% of the wide-intent surgeries had incomplete margins despite the surgeon's intent.

The two dogs with undefined preoperative lung nodules were reported to have a grade II and grade III STS respectively. Of the six dogs with enlarged lymph nodes, three had grade II STS, two had grade III STS, and one was not graded. No preoperative sampling was performed to assess the cause of the lymphadenopathy in any dog. (Table 4).

Twelve (23.1%) dogs were treated with adjuvant therapy after surgery, including systemic chemotherapy ($n = 6$), radiation therapy (RT) ($n = 4$), both RT and systemic chemotherapy ($n = 1$) and electrochemotherapy ($n = 1$). Chemotherapy agents used included doxorubicin, cyclophosphamide, carboplatin and vinblastine. The use of both selective and non-selective COX inhibitors was also reported as medical management, as was the use of oral steroids. Reported RT protocols ranged from 3 to 19 fractions.

Ten (19.2%) dogs had tumour recurrence. Median time to recurrence (MTR) was not reached for dogs with grade I and II STS and was 255 days for dogs with grade III STS. (Figure 6A) Of the 10 dogs with recurrence reported, five had incomplete margins, three had complete margins, and two were not categorized. The DFI was not reached for dogs with completely excised tumours and was 398 days for dogs with incomplete margins. (Figure 6B) Local tumour recurrence was significantly associated with margin status ($p = .01$) and histologic grade ($p = .0005$). Of the 10 dogs with reported disease recurrence, one dog had suspected metastatic disease prior to surgery, one had metastatic disease found along with recurrence of the primary tumour, and one dog had progression of preoperatively established metastatic disease. Overall, censored dogs separated by grade are as follows: grade I–22 censored, 2 recurrences, grade II–16 censored, 4 recurrences, grade III–2 censored, 4 recurrences. Those censored by margin status included 33 censored and 5 recurrences in those with complete margins and 9 censored and 5 recurrences in those with incomplete margins.

Five dogs had suspected metastatic disease including the dog with multiple pulmonary masses found at initial diagnosis and another with a suspected satellite lesion found on the initial CT scan. Three dogs had pulmonary nodules noted after surgery, one of which had confirmed progression of the nodules with repeated imaging 4 months after the initial finding. Two dogs had reported lymph node metastasis confirmed with cytology. Of these five dogs, there were three grade III STSs, one grade II STS and one was not graded.

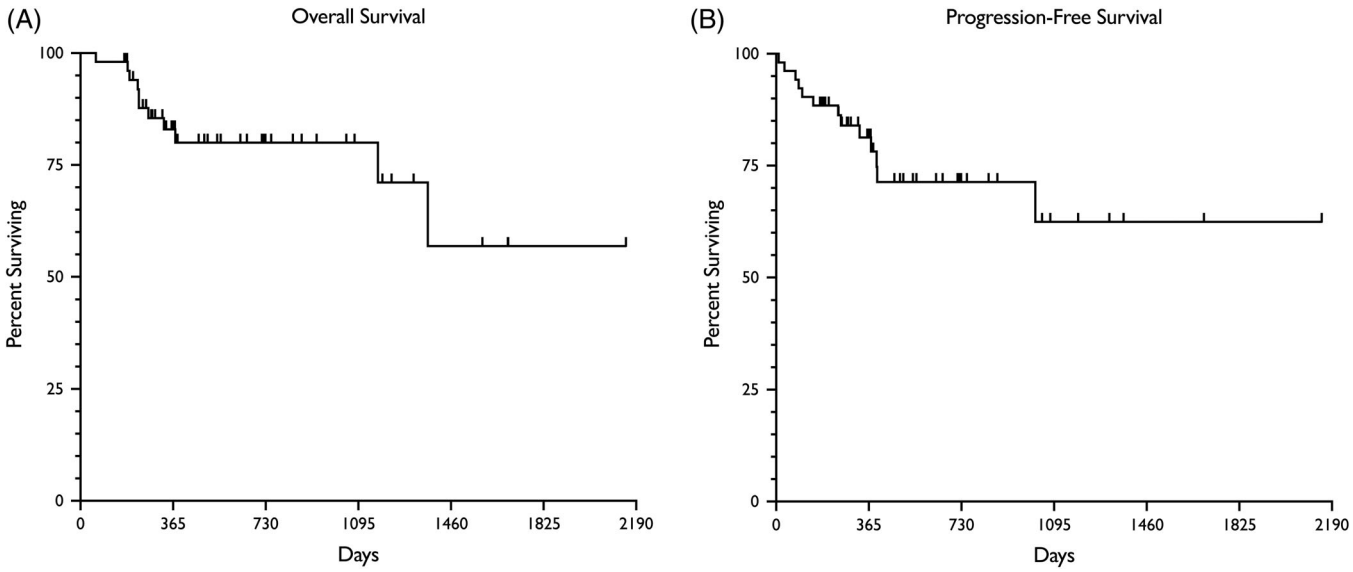

FIGURE 7 Kaplan–Meier curve showing overall survival (A) and progression-free survival (B) of dogs with ITSTS. Censored patients are indicated by tick marks. Figures produced by Dr. Owen Skinner

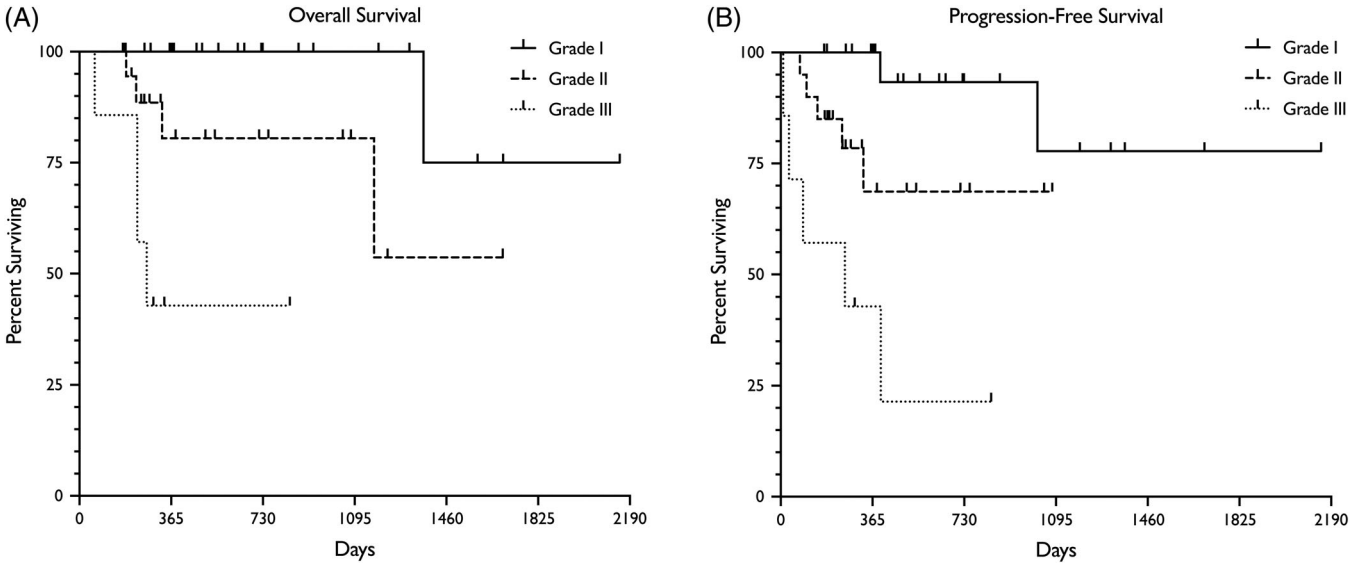

FIGURE 8 Kaplan–Meier curve showing overall (A) and progression-free survival (B) based on ITSTS tumour grade. Censored patients are indicated by tick marks. Figures produced by Dr. Owen Skinner

3.1 | Survival analysis

At the time of their last follow-up, 29 (55.8%) dogs were still alive. Of the 23 dogs that were dead, 10 died from ITSTS-related causes. Four were reported to have died from a secondary cancer including two diagnosed with lymphoma, one with a large thoracic mass of unknown origin, and one with suspected hemangiosarcoma. The remaining nine had deaths that were not related to neoplasia. OST and PFS were not reached. Dogs censored from the overall survival analysis (Figure 7A) were censored at a median of 501 days following surgery, resulting in a total of 41censored dogs and 11 deaths. Dogs censored from PFS analysis (Figure 7B) were censored at a median of 466 days following surgery with 39 censored and 13 deaths.

OST based on tumour grade for the dogs in this study was not reached for tumours classified as grade I or II and was 268 days for grade III tumours (Figure 8A). PFS based on tumour grade was not reached for tumours classified as grade I or II and was 255 days for grade III tumours. (Figure 8B) Median survival time (MST) was also not reached for dogs with grade I or II STSs; MST for dogs with grade III tumours was 268 days. Log-rank analyses identified significant differences in overall ($p = .0003$) and PFS ($p = .0001$) with histologic grade. When separated by grade, the number of censored dogs was as follows: grade I–23 censored, 1 death, grade II–15 censored, 4 deaths, grade III–3 censored, 4 deaths.

4 | DISCUSSION

Similar to previous canine STS studies, both tumour grade and margin status were found to be associated with overall prognosis in this study. Both OST and PFS were significantly influenced by histologic grade with grade III tumours having shorter STs. Disease recurrence was influenced by both tumour grade and margin status, with grade III tumours and those excised with incomplete margins more likely to return. This is consistent with behaviour of STS in other locations. Metastatic disease in this study was also similar to previous reports, with the lungs being the most common site of metastatic spread, with the exception of the dogs with cytologically confirmed metastatic disease in the lymph nodes. Surgical complications occurred in 25% of the cases in this study, though none were life-limiting. The most common complications were infection and skin-flap necrosis.

In humans, the most important prognostic indicators for STS are tumour location, histologic subtype and histologic grade.[14] Those STS with the best prognoses are located in the extremities with prognosis declining for STS located in the thoracic region, trunk and head/neck region,[13] as well as the uniquely aggressive BSTS.[15] There are no studies in veterinary medicine at this time that show tumour location alone is predictive of outcome for STS, though it has been suggested to play a role along with tumour grade and subtype in a few specific sarcomas, including oral FSA and PNST of the brachial plexus.[33] These tumours behave in a more aggressive manner and, therefore, have been designated as distinct clinical entities, separate from other STS.[33] Unlike BSTS in human medicine, ITSTS in this study had similar biologic behaviour and postoperative outcome to STS in other locations, suggesting canine ITSTS is not a distinct clinical entity. While the authors suspect the IT is a site that may have a predilection for STS formation due to increased inflammation and soft-tissue damage in this region, it was not evaluated further in this study.

While location alone is not predictive of outcome for STS, it does play a role when determining surgical approach, reconstruction method and feasibility of obtaining adequate margins during excision. In this study, the DFI was not reached for dogs with complete

margins, confirming previous reports that the ability to achieve complete margins plays a direct role in preventing local recurrence. Multiple surgical techniques were reported in this study for removal of ITSTS. While specific statistical analysis was not performed, the authors observed no obvious association between the type of reconstructive technique performed and association with tumour size, recurrence, margin evaluation or complications.

Of the 36 dogs who had reconstructive surgery using a flap technique, 10 (28%) had reported surgical complications. Despite the regional proximity to critical structures, only one case reported complications of this nature: a rectal perforation. Most of the complications reported were those previously noted for soft tissue, oncologic and reconstructive surgeries, including incisional dehiscence, infection and blood loss.[37,38] Ten dogs had reconstruction of the defect following tumour resection with a lateral caudal axial pattern flap, two of which had postoperative complications involving flap necrosis. This finding is similar to the previously reported 30% complication rate with lateral caudal axial pattern flaps, with flap necrosis being the most reported complication.[31] One of the dogs in this study experienced seroma formation along with flap necrosis. Seroma formation has been previously reported as a potential complication when using axial pattern flaps for reconstruction.[31,39] This complication has been previously mitigated with placement of drains.[31,39] The use of surgical drains in this region can be beneficial but caution should be taken given the proximity of this region to the anus and potential risk for infection. The authors of this paper encourage surgeons to consider the benefits and risks of drain use and placement, not only in the IT region, but with oncologic surgery in general. If needed, a closed-suction drain that exits adjacent to the incision site poses little risk of contamination of the tumour resection site.

The findings in this study support previous reports that the lateral caudal axial pattern flap, the caudal superficial epigastric flap or the ventral branch of the circumflex iliac axial pattern flap are good surgical options for large defects in the gluteal region.[31,39] The ventral branch of the deep circumflex iliac is a robust flap that can be transposed to the lateral pelvic area.[39] However, it may not be able to cover a skin defect caudal to the tuber ischii. The lateral caudal axial pattern flap would be most useful for those defects caudal to the ischium. The caudal epigastric axial pattern flap is particularly useful for perineal reconstruction and defects that are distal to the greater trochanter/tuber ischii on the thigh.

Margin assessment and categorization were performed by the reporting pathologist for 40 of the ITSTS cases. Of the 14 dogs that had incomplete margins reported, five (35.7%) had recurrence of the ITSTS while 11.5% of the dogs with complete margins had reported tumour recurrence. According to the VCS/ACVP Consensus on Grading Canine STS,[40] there is no literature defining sufficient surgical margins though 'complete' should be the overall goal of every surgery. Numerous studies exist evaluating the prognostic significance of margins in the setting of STS with conflicting reports on importance in terms of disease recurrence, metastatic spread and long-term survival.[30,33,41–44] This study supports the established dogma that those STS removed with incomplete margins are more likely to recur. In this study, 65% of the wide excisions were confirmed by the pathologist as having complete margins while 44% of the marginal excisions had complete margins. This finding suggests that removal of STS should still be attempted in regions where wide excision is not possible, as there is a chance of obtaining complete margins even with a narrow or marginal surgical intent.

In people, STS grade is the most important prognostic indicator but in veterinary medicine there remains debate about how grade plays into overall prognosis. Some studies report that overall grade is prognostic for recurrence but not for OST. These studies found that low-grade STS (grade I or II) are unlikely to recur, and when they do, the slow-growing nature of the tumours allows for more conservative management and less impact on overall patient quality of life. High-grade (grade III) STS are more likely to recur[1,42–44] and have increased risk for metastatic spread with reported rates of 22%–44%.[33–35,45] The findings of this study support previous reports of low-grade STS having a low risk of recurrence and metastatic spread as DFI and PFI were reached only with grade III tumours. Unlike the above reports, OST was found to be influenced by tumour grade; there was a significant difference between the OST for grade I and II tumours compared to grade III. This study reinforces the complications associated with discussing overall prognosis of STS, as both margin status and grade were determined to be significant. The reality is that it is unlikely that only one factor is responsible for prognosis and that multiple factors must be considered when assessing risk.

All but one of the cases in this study had pre-operative imaging performed. Two cases were found to have pulmonary nodules with one suspicious for metastatic disease. This finding is similar to previous reports that STS has a low rate of metastatic spread.[30,33–35,42] An interesting finding was that six cases had regional lymph node enlargement reported prior to surgery and two cases were cytologically confirmed to have metastatic spread to the regional lymph nodes post-operatively. Of those two cases, only one had reported pre-operative lymphadenopathy. Previously, STS has been reported to spread most commonly to the lungs and liver and rarely to the lymphatic system.[42] This finding supports that the lung is a more common site of metastasis than lymph nodes. Both cases with lymph node metastasis were grade III STS, which may suggest that higher grade ITSTS have an increased risk of spread to regional lymph nodes. Ultimately, the pre-operative finding of enlarged regional lymph nodes is not indicative of metastatic disease, but for those tumours found to be histologically high grade, close monitoring of the regional lymph nodes post-operatively may be useful for the early detection of disease recurrence or spread.

All but one of the cases reviewed in this study had pre-operative tumour sampling performed with FNA and/or incisional biopsy. Eighty-five percent of the FNA samples were consistent with STS and 100% of the incisional biopsies were diagnostic for STS. Thirteen cases had both techniques performed. This finding supports previous studies that the accuracy of FNA in STS diagnoses is from 60% to 90% when compared to histopathology.[46,47] Of the incisional biopsies that provided a tumour grade, 40% of the cases in this study showed disagreement between initial tumour grade and the final histopathology grade. This

finding is similar to previous reports of discordant grading that have found 41% of incisional biopsies to be different from the final histopathological grade given after review of the tumour as a whole.[48] Another similarity to the previous report was the finding that more of the ITSTS biopsies were underestimated in grade than were overestimated. While both FNA and incisional biopsies had high success in diagnosing STS, the 100% diagnostic success of incisional biopsies is superior. When options for treatment are between aggressive reconstructive surgical procedures or amputation and less invasive, marginal surgical approaches, an incisional biopsy may provide additional support for a more aggressive surgical procedure. While incisional biopsy is not benign, the information obtained from such a sample may be crucial in overall improved prognosis, surgeon success and client satisfaction.

Limitations of this study include the retrospective nature of the study, a relatively small sample population including low numbers of high-grade tumours, reporter (surgeon and pathologist) variability and lack of standardized screening, procedures and reporting of results. The small population and the low number of patients that developed recurrence or died during the follow-up period resulted in few events for statistical analysis. Given previous recommendations for at least 10 events per variable for Cox regression analysis,[49] we elected to forego more detailed statistical analysis. The relatively short follow-up time required to be included in this study is also a limitation. A larger, higher quality dataset with prospective and standardized reporting would allow for a more detailed analysis and might identify factors that could predict outcomes or identify treatment approaches that may result in a higher likelihood of success.

Another large limitation of this study is the lack of standardized assessment and reporting of tumour margins. This is a well-known controversy throughout the veterinary community with margin categorization and reporting being a topic of wide debate[50,51] with many different interpretations of how pathologists, surgeons and clinicians approach margin evaluation and use that information to guide therapy recommendations.[52] It is difficult to speak accurately about how therapeutic intervention affects long-term prognosis and overall survival, let alone make treatment recommendations, when there is little agreement amongst the most influential players about what the final goal should be.

5 | CONCLUSIONS

The ITSTS in dogs of this study appear to behave similarly to STS in other locations, suggesting that canine ITSTS is not a distinct clinical entity and, thus, the authors' hypothesis has been rejected. Treatment recommendations are similar to STS of other sites, including thorough staging with thoracic and abdominal imaging and tissue sampling of the tumour prior to surgical excision, ideally with incisional biopsy. Surgery should be performed with the goal of achieving complete histological margins. Outcome and prognosis of dogs diagnosed with ITSTS may be predicted by tumour grade and margin status postoperatively. Further studies are needed to assess whether the IT is a site with a predilection for STS formation as suspected by the authors of this paper.

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CONFLICT OF INTEREST

The authors declare no conflict of interest related to this report.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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