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Summary of **'Prognostic Factors for Cutaneous and Subcutaneous Soft Tissue Sarcomas in Dogs - M. M. Dennis, K. D. McSporran, N. J. Bacon, F. Y. Schulman, R. A. Foster and B. E. Powers - Vet Pathol 2011.**


## Abstract

Soft tissue sarcomas originate from mesenchymal elements of soft connective tissues and are frequently encountered in the canine skin and subcutis. Despite marked phenotypic diversity and often uncertain histogenesis, these tumours are commonly managed as a single diagnostic group because they share overlapping microscopic characteristics and comparable clinical behaviour. Following surgical excision, rates of local recurrence are generally low but vary according to histologic grade and the completeness of surgical margins, with complete excision being strongly associated with nonrecurrence. Even among grade I sarcomas, tumours excised with narrow margins infrequently recur, although the likelihood of recurrence increases with increasing grade. The true incidence of metastasis remains poorly defined; however, metastatic spread is believed to be uncommon in grade I tumours and most frequently associated with grade III lesions. Importantly, the occurrence of metastasis does not uniformly predict reduced survival. Elevated mitotic index has consistently been associated with shortened survival time. Additional investigation is required to refine estimates of recurrence and survival relative to surgical margin status and to clarify potential differences in metastatic frequency and median survival across histologic grades. Other candidate prognostic indicators requiring further validation include histologic subtype, tumour size, anatomic location, invasiveness, disease stage, cellular proliferation markers, and cytogenetic features. Common obstacles to prognostic evaluation include retrospective study design, small sample sizes, inconsistent confirmation of metastasis, variable classification and nomenclature, challenges in phenotypic differentiation, and heterogeneity of study populations.



**Keywords:** cancer, dog, neoplasia, sarcoma, prognostication, veterinary oncology


## Introduction

Canine soft tissue sarcomas are mesenchymal tumours arising from soft connective tissues and may develop at virtually any anatomic site, although the skin and subcutis are most commonly affected. These neoplasms account for approximately eight to fifteen percent of all cutaneous and subcutaneous tumours in dogs and are most frequently diagnosed in middle-aged to older animals of medium to large breeds (18,33). The majority demonstrate locally expansile growth, extending along fascial planes, and are typically surrounded by a pseudocapsule formed through compression of adjacent connective tissue, which may contain neoplastic cells. Reported postsurgical recurrence rates range from seven to thirty

percent (7,42), while metastatic spread is considered uncommon, with reported rates up to seventeen percent (11,32,33).

Surgical excision is the primary treatment modality for canine cutaneous and subcutaneous soft tissue sarcomas (17,19,22,33). Curative-intent procedures aim to remove the primary mass, its pseudocapsule, and a surrounding margin of normal tissue. Median survival times following excision are generally prolonged, reported between 1,013 and 1,416 days (11,32). Because affected dogs are often elderly, death from unrelated causes frequently precedes sarcoma-associated mortality (5,11,32,40,50).

Although overall prognosis is favourable, biological behaviour varies widely. Accurate prognostic assessment is therefore essential for guiding clinical decision-making, advising owners, and identifying patients that may benefit from aggressive local or adjunctive therapies such as radiation or chemotherapy. Numerous prognostic and predictive factors have been investigated, and several now inform routine clinical management. This review synthesizes current knowledge regarding prognostic indicators for canine cutaneous and subcutaneous soft tissue sarcomas while highlighting methodological limitations that constrain interpretation.

**STS Nomenclature**

Soft tissue sarcomas comprise a heterogeneous collection of mesenchymal neoplasms that may be categorized according to presumed tissue of origin based on dominant histologic features. Despite this diversity, these tumours are generally grouped together in dogs because of shared microscopic characteristics and comparable biological behaviour (7,11,32). While this collective approach simplifies diagnosis and management, inconsistent terminology and weak correlation between classification and histogenesis have contributed to diagnostic ambiguity.

Several mesenchymal tumours are conventionally excluded from the canine cutaneous and subcutaneous soft tissue sarcoma category, including histiocytic sarcoma, lymphangiosarcoma, hemangiosarcoma, synovial cell sarcoma, leiomyosarcoma, rhabdomyosarcoma, oral fibrosarcoma, and brachial plexus peripheral nerve sheath tumours. These neoplasms are excluded because they can usually be distinguished by histologic features or anatomic location and typically demonstrate more aggressive biological behaviour (8,11,17,19,32,33,35,40,50). As a result, the term soft tissue sarcoma in dogs has increasingly become a diagnosis of exclusion, contrasting with classification practices in human oncology (52).

Tumours typically included within the canine soft tissue sarcoma group encompass non-brachial plexus peripheral nerve sheath tumours, fibrosarcoma, myxosarcoma, liposarcoma, perivascular wall tumours, pleomorphic sarcoma (also termed malignant fibrous

histiocytoma), malignant mesenchymoma, and undifferentiated sarcoma. Peripheral nerve sheath tumours may represent the most common subtype (32). Historical terminology, particularly hemangiopericytoma, has been inconsistently applied and now largely overlaps with peripheral nerve sheath or perivascular wall tumours, although histogenesis remains debated (2,36,44).

At the light microscopic level, these tumours are difficult to distinguish because they commonly consist of spindle-shaped mesenchymal cells arranged in bundles, streams, or whorls within collagenous stroma (27,29). Immunohistochemistry and architectural patterns are used to infer phenotype, but overlap among tumour types is substantial, and no single marker reliably differentiates all categories (2,12,56). Consequently, some authors advocate collective classification as canine spindle cell tumours of soft tissue (11,26,44,56). This approach reflects both the uncertainty of histogenesis and the relatively indolent behaviour of many lesions traditionally labelled as sarcomas.

**Limitations of Canine STS Prognostic Studies**

Although numerous publications address prognostic and predictive factors for canine soft tissue sarcomas, few employ study designs specifically optimized for survival analysis. Much prognostic information has been derived from studies primarily designed to evaluate treatment efficacy rather than prognostic variables (11,23,28,38,46,48). Such studies are subject to selection and treatment biases that complicate interpretation.

Many investigations involve small cohorts, often fewer than one hundred dogs, limiting statistical power (3–6,8,23–25,28,32,34,36–39,45,46,49–51). In several cases, an excessive number of prognostic variables were examined relative to the number of outcome events, reducing the likelihood of detecting true associations (55). Estimates of recurrence and metastatic rates are therefore imprecise.

Retrospective design further limits interpretation due to incomplete follow-up, inconsistent treatment protocols, inability to confirm metastasis, and lack of standardized tumour measurements (3,5,7,11,23,32,46,48–50). Additionally, many studies rely on univariable analyses without adjusting for confounding factors (4,5,7,11,20,25,37,40,46,49,50). Heterogeneous grouping of tumours, including visceral sarcomas or biologically aggressive subtypes, further confounds results.

**Prognostic and Predictive Factors**

A range of clinical and histologic features have traditionally been considered when assessing prognosis, including histologic type, grade, tumour size, location, prior treatment, invasiveness, and surgical margin status (17,19,22,33). Evidence supporting the prognostic

relevance of these variables varies considerably, and no single factor reliably predicts outcome.

### Histologic Type

In human oncology, histologic subtype is increasingly recognized as prognostically relevant (9,15). In dogs, however, studies evaluating histologic type have not demonstrated consistent differences in survival or recurrence, likely due to limited sample sizes and imprecise classification (37,39,48,49). Associations between subtype and grade or mitotic index suggest that apparent behavioural differences may reflect differing propensities for high-grade disease rather than intrinsic differences (7,23,32). Consequently, histologic type currently has limited influence on clinical management.

### Degree of Resection and Completeness of Surgical Margins

Surgical recommendations are based on the Enneking system, with wide or radical excision pursued for curative intent (17,19,21,33). Recurrence rates appear lowest following wide or radical excision and highest after marginal excision, although statistically robust comparisons are lacking (6,11). While local recurrence following marginal excision is common, a clear association between extent of resection and survival has not been definitively established.

Completeness of surgical margins, assessed histologically, is a critical predictor of recurrence. However, margin classification varies widely across studies, limiting comparability. Definitions of incomplete, close, and complete margins differ substantially, and margin distance is rarely treated as a continuous variable. Evidence indicates that tumours excised with complete margins recur infrequently, whereas recurrence rates are higher for incomplete or close margins (11,32,40). Standardized margin evaluation and reporting practices are essential for improving prognostic precision.

### Histologic Grade

Histologic grading, adapted from human oncology, incorporates differentiation, mitotic index, and necrosis (53). Most canine soft tissue sarcomas are classified as grade I, which are associated with low recurrence and rare metastasis, particularly when margins are complete (6,40,50). Grade II tumours exhibit intermediate behaviour, with higher recurrence rates when margins are close. Grade III tumours, although less common, demonstrate the highest risk of recurrence and metastasis.

The relationship between grade and survival remains inconsistent across studies, likely due to limited numbers of grade III tumours and competing causes of death in older dogs.

Subjectivity and interobserver variability further limit reproducibility, particularly in assessment of differentiation.

### Mitotic Index and Proliferation Markers

Mitotic index independently provides strong prognostic information. High mitotic activity is consistently associated with increased recurrence, metastasis, and reduced survival (7,23,32,40,49). Although additional proliferation markers such as Ki-67 and AgNOR have demonstrated prognostic value, their clinical utility beyond mitotic index and grade remains uncertain given added cost and limited comparative data.

### Other Factors

Tumour size, location, invasiveness, recurrence status, and prior treatment have been variably associated with outcome, but evidence remains inconclusive. Larger tumours and invasive growth patterns may limit resectability, yet consistent prognostic significance has not been demonstrated. Oral soft tissue sarcomas represent an exception, exhibiting aggressive behaviour despite low-grade histology.

Emerging markers, including intratumoural microvessel density and molecular cytogenetic abnormalities, show promise but require further validation in canine populations.

### Consensus on Reporting of Prognostic and Predictive Factors for Canine STS of the Skin and Subcutis

Diagnostic reports should routinely include histologic type when possible, grade, mitotic index, and detailed margin assessment. Mitotic index should always be reported, as it provides critical survival information, while grade remains more informative for recurrence risk. Margin evaluation should follow standardized trimming and inking protocols, with explicit reporting of evaluation methods, tissue planes examined, and minimum distances between neoplastic cells and surgical margins. Ambiguous descriptors should be avoided in favour of precise measurements.

### Conclusion

Canine cutaneous and subcutaneous soft tissue sarcomas are common neoplasms characterized by diagnostic and prognostic complexity. Histologic grading, mitotic index, and surgical margin status provide the most reliable prognostic information currently available. Complete excision predicts nonrecurrence, recurrence risk increases with grade, and high mitotic index is associated with reduced survival. Continued research employing rigorous study design, standardized classification, and long-term follow-up is essential to refine prognostication and improve clinical management.

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