■ ONCOLOGY

What factors differentiate early from late pulmonary metastases in soft-tissue sarcoma of the limbs?

A COMPARATIVE COHORT ANALYSIS

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Aims

It remains unclear what factors differentiate patients who present with early rather than late pulmonary metastases after resection of a soft-tissue sarcoma, and how their outcomes differ. The purpose of this study was to compare the survival of patients with early and late sarcoma metastases in the lungs, and to compare the differences between the two groups.

Methods

We carried out a retrospective review of a prospectively maintained database, between January 1992 and November 2020, for all patients with a soft-tissue sarcoma of the pelvis and limbs who developed pulmonary metastases after definitive resection. We compared patients with early and late metastatic disease, defined as presentation before or after two years, respectively.

Results

A total of 584 patients developed pulmonary metastases after surgical treatment of a soft-tissue sarcoma of the limb or pelvis. Overall, 79% had metastases within two years of surgery. The median time to pulmonary metastasis was nine months (IQR 4 to 20). The five-year disease-specific survival (DSS) from presentation was significantly worse for patients who developed early pulmonary metastases compared with those with late pulmonary metastases (12.2% (95% CI 9.2 to 16.0) vs 27.5% (95% CI 19.2 to 37.7), respectively; p < 0.001). Among patients undergoing surgical excision of pulmonary metastases, the five-year DSS from presentation was significantly worse for patients who developed early pulmonary metastases (27.2% (95% CI 19.8 to 36.1) vs 48.7% (95% CI 32.8 to 64.9); p = 0.014). Multivariable analysis revealed that older age (hazard ratio (HR) 1.02 (95% CI 1.01 to 1.03); p = 0.001), larger tumour size (HR 1.1 (95% CI 1.04 to 1.13); p < 0.001), and higher tumour grade (HR 2.0 (95% CI 1.26 to 3.1); p = 0.002) were associated with an increased risk of early pulmonary metastases, whereas previous local recurrence was associated with an increased risk of late pulmonary metastases (HR 3.3 (95% CI 1.8 to 5.4); p < 0.001).

Conclusion

DSS is poor after the development of pulmonary metastases from a treated limb or pelvic soft-tissue sarcoma, but survival is worse for patients who present early.

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Introduction

Soft-tissue sarcomas are a rare, heterogeneous group of cancers, making up fewer than 1% of new cancer diagnoses annually.[1] Despite this, they are disproportionately lethal, and the overall survival for high-risk tumours is estimated to be only 50% to 55%. Several factors have been reported as being associated with overall prognosis. These include age, tumour size, tumour location, histological grade, and histological subtype.[2-5] However, the most important prognostic factor is surgical stage and the presence of metas-

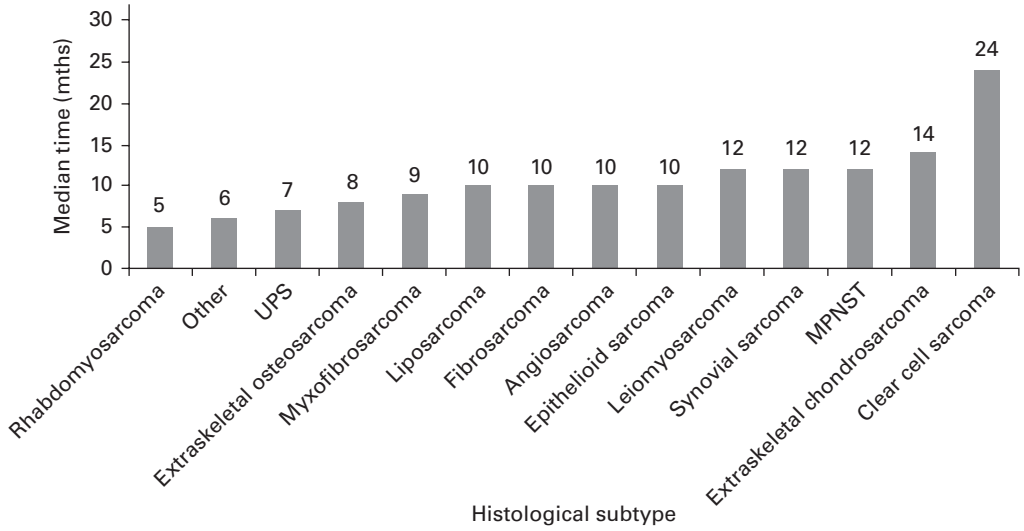

Fig. 1

Median time to pulmonary metastasis presentation by histological subtype of soft-tissue sarcoma. MPNST, malignant peripheral nerve sheath tumour; UPS, undifferentiated pleomorphic sarcoma.

Table I. Median time to metastatic disease presentation by histological subtype.

Subtype	Total, n (%)	Median time to metastasis, mths (IQR)
Rhabdomyosarcoma	12 (2.0)	5 (2 to 9)
Other	39 (6.7)	6 (3 to 22)
UPS	162 (27.6)	7 (4 to 15)
Extraskeletal osteosarcoma	11 (1.9)	8 (3 to 15)
Myxofibrosarcoma	62 (10.6)	9 (5 to 19)
Liposarcoma	120 (20.5)	10 (4 to 32)
Fibrosarcoma	11 (1.9)	10 (7 to 18)
Angiosarcoma	9 (1.5)	10 (5 to 17)
Epithelioid sarcoma	7 (1.2)	10 (4 to 43)
Leiomyosarcoma	59 (10.1)	12 (5 to 30)
Synovial sarcoma	55 (9.4)	12 (6 to 23)
MPNST	23 (3.9)	12 (4 to 39)
Extraskeletal chondrosarcoma (myxoid)	8 (1.4)	14 (2 to 52)
Clear cell sarcoma	8 (1.4)	24 (4 to 79)

MPNST, malignant peripheral nerve sheath tumour; UPS, undifferentiated pleomorphic sarcoma.

tasis at diagnosis, which is associated with less than 20% five-year survival.[6]

As many as 20% to 30% of patients who present with a localized soft-tissue sarcoma of the limbs will develop metastatic disease. Metastases occur most frequently within the first two years of follow-up, most commonly in the lungs.[7] Despite this, a subset of patients will develop metastatic disease after two years. It is understood that a short disease-free interval is associated with poorer survival.[8,9] An early study suggested that high grade of malignancy increases the risk for late metastasis after five years.[8] However, it remains unclear what factors differentiate patients who present with early rather than late pulmonary metastases, and how their outcomes differ.

When patients do develop metastatic disease, treatment varies. In cases of oligometastatic disease, pulmonary metastases may be considered for resection in the hope of prolonged survival.[10,11] Radiotherapy can also be effective in patients with a limited disease burden.[12] Generally, however, systemic therapy is considered the mainstay of treatment for metastatic soft-tissue sarcoma, and is typically used for patients with aggressive or progressive disease or for symptomatic control, but it is largely a palliative measure.[13,14] Nonetheless, there are few data to inform decision-making about treatment for patients with pulmonary metastases who present at different intervals after the initial diagnosis of a sarcoma.

The purpose of this study was to compare the survival of patients with early and late sarcoma metastases in the lungs, and to compare the relevant clinical differences between the two groups.

Methods

This study received institutional review board approval. A retrospective review of a prospectively maintained institutional database was carried out of all patients who had undergone surgical treatment of a soft-tissue sarcoma of the limbs or pelvis between 1 January 1992 and 15 November 2020. We included all patients with a soft-tissue sarcoma of the pelvis and limbs who developed pulmonary metastases after a definitive resection, defined as progressive pulmonary nodules > 1 cm on CT chest imaging or biopsy-proven pulmonary metastasis. Exclusion criteria included patients with metastatic disease at presentation.

Sarcomas were classified as grade 1, 2, or 3 according to the Federation Nationale des Centers de Lutte Contre le Cancer (FNCLCC) criteria.[15] Margins were characterized according to the R classification as negative (R0), microscopically positive (R1), and grossly positive (R2). A standardized follow-up protocol based on tumour size and grade was undertaken for five to ten years after surgical resection.[16] Typically, surveillance evaluations included physical examination and a chest radiograph.

Table II. Baseline patient, tumour, and treatment characteristics between patients presenting with early vs late pulmonary metastatic disease.

Variable	Overall	Early	Late	p-value
Patients, n	584	459	125	
Patient characteristics				
Mean age, yrs (SD)	57.9 (17.4)	59.2 (17.1)	52.9 (17.5)	< 0.001*
Sex, n (%)				0.042†
Female	257	192 (41.8)	65 (52.0)	
Male	327	267 (58.2)	60 (48.0)	
Prior surgery, n (%)				0.002†
Yes	121	82 (18.0)	39 (31.2)	
No	461	375 (82.0)	86 (86.8)	
Tumour characteristics				
Tumour depth, n (%)				0.518†
Deep	501	396 (86.3)	105 (84.0)	
Superficial	83	63 (13.7)	20 (16.0)	
Tumour grade, n (%)				0.001†
2	154	106 (23.8)	48 (38.7)	
3	416	340 (76.2)	76 (61.3)	
Tumour location, n (%)				0.027†
Upper	126	103 (22.6)	23 (18.4)	
Lower	399	303 (66.6)	96 (76.8)	
Central (paraspinal/ chest)	25	25 (5.5)	0 (0)	
Pelvic	30	24 (5.3)	6 (4.8)	
Mean size, cm (SD)	11.5 (6.7)	12.2 (6.8)	9 (5.7)	< 0.001*
Histological subtype, n (%)				< 0.001†
UPS	162	142 (30.9)	19 (15.2)	
Liposarcoma	120	82 (17.9)	38 (30.4)	
Myxofibrosarcoma	62	51 (11.1)	10 (8.0)	
Leiomyosarcoma	59	41 (8.9)	18 (14.4)	
Synovial sarcoma	55	42 (9.2)	13 (10.4)	
Other	39	31 (6.8)	8 (6.4)	
MPNST	23	16 (3.5)	7 (5.6)	
Rhabdomyosarcoma	12	12 (2.6)	0 (0)	
Extraskeletal osteosarcoma	11	11 (2.4)	0 (0)	
Fibrosarcoma	11	9 (2.0)	2 (1.6)	
Angiosarcoma	9	9 (2.0)	0 (0)	
Extraskeletal chondrosarcoma	8	5 (1.1)	3 (2.4)	
Clear cell sarcoma	8	4 (0.9)	4 (3.2)	
Epithelioid sarcoma	7	4 (0.9)	3 (2.4)	
Initial treatment characteristics				
Surgery type, n (%)				0.635†
Limb salvage	555	435 (95.0)	120 (96.0)	
Amputation	28	23 (5.0)	5 (4.0)	
Margin status, n (%)				0.664†
Negative	478	378 (82.4)	100 (80.6)	
Positive	105	81 (17.6)	24 (19.4)	
Radiation at time of initial surgery, n (%)				0.147†
Yes	479	382 (83.2)	97 (77.6)	
No	105	77 (16.8)	28 (22.4)	
Chemotherapy at time of initial surgery, n (%)				0.290†
Yes	31	22 (4.8)	9 (7.2)	
No	552	436 (95.2)	116 (92.8)	
Surgical complications, n (%)				0.650†
Yes	201	158 (37.8)	43 (35.5)	
No	338	260 (62.2)	78 (64.5)	
Metastasis treatment characteristics				
Surgery, n (%)				0.076†
Yes	178	132 (28.8)	46 (37.1)	
No	404	326 (71.2)	78 (62.9)	
Radiation to lung, n (%)				0.192†
Yes	53	38 (8.3)	15 (12.1)	
No	529	420 (91.7)	109 (87.9)	
Chemotherapy, n (%)				0.004†
Yes	187	160 (34.9)	27 (21.8)	
No	395	298 (65.1)	97 (78.2)	

*Mann-Whitney U test.
†Chi-squared test.
MPNST, malignant peripheral nerve sheath tumour; UPS, undifferentiated pleomorphic sarcoma.

Lesions of concern on chest imaging were confirmed with advanced cross-sectional imaging, typically a CT scan, with or without a biopsy for confirmation. Patients with metastatic disease were discussed at a weekly multidisciplinary tumour board to determine the optimal, patient-specific treatment plan. Patients with appropriate functional status and low metastatic burden were considered for pulmonary metastasectomy. For patients with greater disease burden and/or symptomatic disease, radiotherapy and systemic therapy were typically used rather than surgery.

The primary outcome measure was disease-specific survival (DSS) from the time of diagnosis of pulmonary metastatic disease. Comparisons were made between patients with early and late metastatic disease, defined as presentation before or after two years from the date of the definitive surgical resection of a primary soft-tissue sarcoma of the limb.

Statistical analysis. Survival analyses were performed utilizing the Kaplan-Meier method. Categorical (chi-squared test) and continuous (Mann-Whitney U test) variables were compared in univariate measures using parametric and non-parametric analyses as appropriate. Statistically significant variables from this were then used to construct a multivariable logistic regression analysis to control for potentially confounding variables. Statistical significance was set at a p-value < 0.05. All statistical analyses were performed using JMP Pro 15 software (SAS Institute, USA).

Results

A total of 2,263 patients who had presented with a primary, localized soft-tissue sarcoma of the limbs or pelvis and had undergone surgery with curative intent were identified from a prospectively maintained database. Of these, 705 (31%) developed metastatic disease to any site after surgical treatment of the primary tumour. Overall, 584 patients developed pulmonary metastases (26% overall (n = 152) and 83% of all metastases (n = 485). A total of 459 patients (79%) developed metastases within two years of surgery (early pulmonary metastasis), whereas 125 patients (21%) developed metastases more

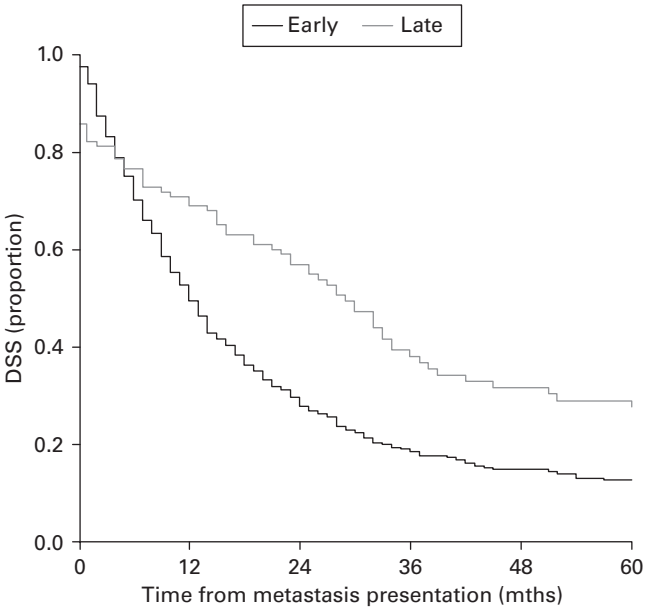

Fig. 2

Kaplan-Meier survival curve comparing early and late pulmonary metastatic disease-specific survival (DSS) from first pulmonary metastasis presentation (12.2% (95% CI 9.2 to 16.0) five-year DSS for early presentation vs 27.5% (95% CI 19.2 to 37.7) five-year DSS for late presentation).

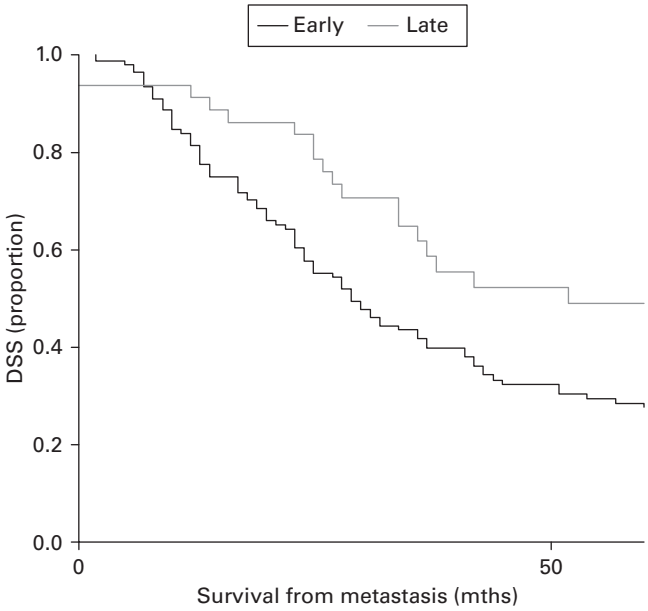

Fig. 3

Kaplan-Meier survival curve comparing surgical treatment of pulmonary metastases in early vs late pulmonary metastasis disease-specific survival (DSS) from first presentation (27.2% (95% CI 19.8 to 36.1) five-year DSS for early presentation vs vs 48.7% (95% CI 32.8 to 64.9) five-year DSS for late presentation).

than two years after surgery (late pulmonary metastasis). The median time to pulmonary metastasis was nine months (IQR 4 to 20). Overall, the five-year DSS from presentation of pulmonary metastasis was 15.2% (95% CI 12.2 to 18.8). Of patients with metastatic disease, the most common histological subtypes were undifferentiated pleomorphic sarcoma, liposarcoma, myxofibrosarcoma, and leiomyosarcoma (Figure 1 and Table I).

When comparing patient factors between groups, early pulmonary metastases tended to occur in older patients (59.2 years (SD 17.1) vs 52.9 years (SD 17.5); $p < 0.001$) and were more commonly associated with male sex (58.2% (n = 267) vs 48% (n = 60); $p = 0.042$) (Table II). Regarding tumour factors, late pulmonary metastases were associated with a histological diagnosis of clear cell sarcoma, leiomyosarcoma, and liposarcoma, whereas early pulmonary metastases were associated with angiosarcoma, soft-tissue osteosarcoma, and undifferentiated pleomorphic sarcoma (UPS) ($p < 0.001$). Early pulmonary metastases were associated with high-grade tumours (76.2% (n = 340) vs 61.3% (n = 76); $p = 0.001$) and with larger tumours (mean 12.2 cm (SD 6.8) vs 9 cm (SD 5.7); $p < 0.001$).

When considering treatment of the original primary tumour, surgery type, use of radiation therapy, and chemotherapy did not differ between patients who subsequently developed an early rather than late pulmonary metastasis. However, patients who developed a late pulmonary metastasis were more likely to have also developed a previous local recurrence than patients who developed an early pulmonary metastasis (25% (n = 31) vs 10% (n = 48); $p < 0.001$). When specifically investigating these local recurrences (LRs), we identified 80 LRs overall. A total of 32 patients (40%) developed a LR prior to the development of a metastasis, and 12 patients (15%) developed a LR after an initial metastasis: 36 patients (45%) developed a LR that was concurrent (i.e. presenting within three months of each other) with a metastasis. Most patients with concurrent metastasis and LR were in the early metastasis group, whereas most with a LR prior to metastasis were in the late metastasis group.

In terms of the treatment of pulmonary metastasis, patients who presented with early metastatic lung disease were more likely to receive chemotherapy than those presenting with late disease (34.9% (n = 160) vs 21.8% (n = 27); $p = 0.004$). There was no difference in the rates of surgical excision or use of radiotherapy.

The five-year DSS from presentation of pulmonary metastasis was significantly worse for patients who developed early pulmonary metastasis compared with those with late pulmonary metastasis (12.2% (95% CI 9.2 to 16.0) vs 27.5% (95% CI 19.2 to 37.7), respectively; $p < 0.001$) (Figure 2). Among patients who underwent surgical excision of pulmonary metastasis, the five-year DSS from presentation was significantly worse for patients who developed early pulmonary metastasis (27.2% (95% CI 19.8 to 36.1) vs 48.7% (95% CI 32.8 to 64.9); $p = 0.014$; Figure 3). Similarly, the five-year DSS from presentation was significantly worse for patients who developed early pulmonary metastasis, even when controlling for the use of chemotherapy (11.9% (95% CI 8.7 to 17.2) vs 29.3% (95% CI 19 to 40); $p = 0.017$; Figure 4) and radiotherapy (3.4% (95% CI 0.5 to 20.4) vs 43.1% (95% CI 20.8 to 68.9); $p = 0.007$; Figure 5).

Multivariable logistic regression analysis was conducted to identify risk factors for early and late pulmonary metastasis (Table III). Older age (hazard ratio (HR) 1.02 (95% CI 1.01 to

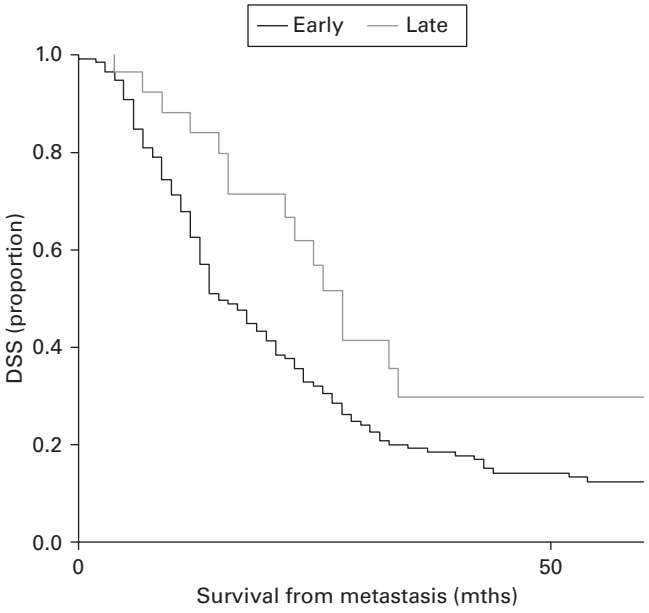

Fig. 4

Kaplan-Meier survival curve comparing treatment of pulmonary metastases with chemotherapy in early vs late pulmonary metastasis disease-specific survival (DSS) from first presentation (11.9% (95% CI 8.7 to 17.2) five-year DSS for early presentation vs 29.3% (95% CI 19 to 40) five-year DSS for late presentation).

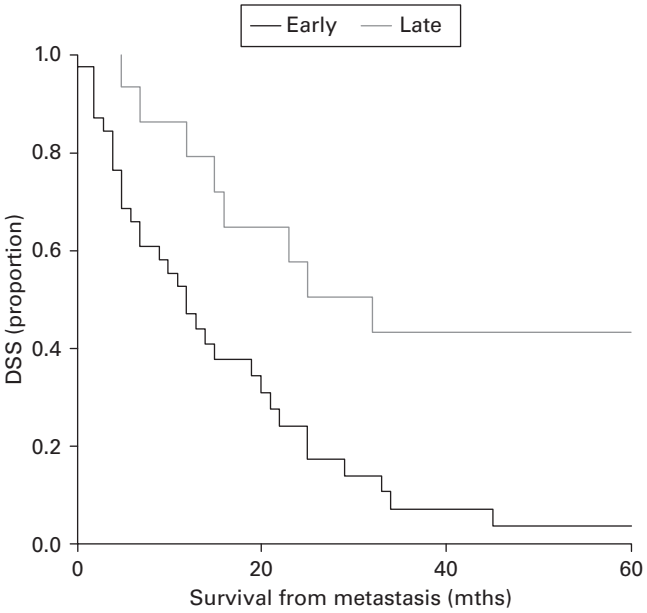

Fig. 5

Kaplan-Meier survival curve comparing treatment of pulmonary metastases with radiotherapy in early vs late pulmonary metastasis disease-specific survival (DSS) from first presentation (3.4% (95% CI 0.5 to 20.4) five-year DSS for early presentation vs 43.1% (95% CI 20.8 to 68.9%) five-year DSS for late presentation).

1.03); p = 0.001), larger tumour size (HR 1.1 (95% CI 1.04 to 1.13); p < 0.001), and higher tumour grade (HR 2.0 (95% CI 1.26 to 3.1); p = 0.002) were associated with an increased risk of early pulmonary metastasis, whereas previous local recurrence was associated with an increased risk of late pulmonary metastasis (HR 3.3 (95% CI 1.8 to 5.4); p < 0.001).

Discussion

Soft-tissue sarcomas are a rare, heterogeneous group of cancers. However, particularly for high-risk subtypes, sarcoma can be disproportionately deadly, and lethality is strongly associated with the development of metastatic disease. Metastases are most likely to occur early, and typically to the lungs. However, in a subset of patients, metastases will develop much later. Data are limited on the characteristics and treatment of early rather than late pulmonary metastases. More information is needed to determine treatment stratification by time of disease presentation, as well as translational studies into the biology of lung metastases in soft-tissue sarcoma. This study compared patients with early and late sarcoma metastases in the lung and found that known high-risk features, including older age, larger tumour size, and higher histological grade, were associated with an increased risk of developing early pulmonary metastasis. Patients who presented with local recurrence, however, were at risk of late metastasis.

Older age, higher tumour grade, and larger tumour size are poor prognostic factors associated with early disease presentation. Previously, these variables have been strongly associated with a poorer overall prognosis.[2–4,17,18] Pisters et al[4] found that several factors, including higher tumour grade and larger tumour size, were poor prognostic factors and were associated with poorer survival outcomes. In contrast, a study by von Konow et al[8] found that high tumour grade was associated with late metastatic disease. These differences may be explained by the way in which the statistical analyses were carried out, as the findings suggest that high-grade tumours account for a greater proportion of metastasis overall, regardless of whether they present early or late. We found similar results in our study: more patients with high-grade tumours presented with metastatic disease overall, regardless of whether they presented early or late. However, high-grade tumours were more likely to present early, whereas lower-grade tumours tended to present later. Nonetheless, these findings point to the importance of known prognostic risk factors for informing surveillance protocols and advising patients as to metastatic disease risk.

Historically, the treatment of soft-tissue sarcomas had been generalized across subtypes: recently, however, the importance of subtype-specific treatment and surveillance paradigms has increasingly been recognized.[19–21] The present study found a histological predisposition for early and late metastatic disease presentation. Rhabdomyosarcoma, UPS, and extraskeletal osteosarcoma tended to present with early metastasis: by contrast, patients with clear cell sarcoma, extra skeletal myxoid chondrosarcoma, and leiomyosarcoma tended to present with late metastasis. Our findings reflect trends shown previously in the literature. Gonzalez et al[7] found that metastatic presentation at the time of diagnosis varied considerably by sarcoma subtype. Interestingly, the study by von Konow et al[8] did not identify a histological predilection for early or late metastatic disease presentation. Nonetheless, it is increasingly

Table III. Multivariable logistic regression analysis identifying factors associated with risk of early metastasis.

Variable	Hazard ratio (95% CI)	p-value
Age		
Per-year increase	1.02 (1.01 to 1.03)	0.001
Sex		
Male	Reference	0.321
Female	1.24 (0.81 to 1.92)	
Size (per 1 cm increase)	1.1 (1.04 to 1.13)	
Grade		
2	Reference	
3	2.0 (1.26 to 3.1)	0.002
Local recurrence		
No	Reference	
Yes	0.027 (0.16 to 0.45)	< 0.001

acknowledged that certain histological subtypes of sarcoma have unique disease courses. These differences highlight the importance of subtype-specific surveillance and, potentially, treatment strategies.

Our study shows that survival was poor overall. However, patients who presented with late pulmonary metastases had improved survival outcomes compared to patients who presented with early pulmonary metastases. Additionally, patients who were suitable candidates for surgical resection of their pulmonary metastasis had the best overall outcome. Kim et al[22] investigated prognostic factors for patients undergoing pulmonary metastasectomy. They found that patients with a longer disease-free interval and a lower burden of disease survived longer. These findings confirmed those of an earlier study from Billingsley et al,[11] which found that the ability to perform a complete metastasectomy of pulmonary metastasis was the most important prognostic factor for survival in patients with metastatic sarcoma. Crucial in this decision-making, however, is the time interval to presentation as well as the burden of disease at presentation.[11,22,23] Our study findings reflect a treatment selection bias, as patients selected for pulmonary metastasectomy tended to have a lower burden of disease, whereas patients with a greater disease burden tended to be treated with either radiotherapy or systemic treatment options. Regardless, it is important to acknowledge that patients who present with metastatic sarcoma have a generally poor prognosis: as such, decision-making about treatment should only be decided after careful patient discussion and evaluation, as well as multidisciplinary input.

Our study found that local recurrence is associated with risk of the development of late metastasis. The relationship between local control in soft-tissue sarcoma of the limbs and DSS continues to be debated. Our findings suggest that tumour biology (grade, size, and histology) likely drives early metastasis. In contrast, it stands to reason that when a local recurrence occurs, the risk for systemic metastasis is again increased, which explains some of the late metastases. There is some precedent for this concept among other studies. Pisters et al[4] found that local recurrence was associated with an increased risk of death, while another study by Zagars et al[2] found that patients who had an isolated local recurrence had a lower DSS when compared with patients who presented with primary disease. Lewis et al[24] investigated 297 patients with a soft-tissue sarcoma of the limb and found that a high proportion of patients who presented with a local recurrence subsequently developed metastatic disease. This was particularly true in high-risk subgroups, such as high-grade, deep, and large tumours, calling into question whether tumour biology itself is the main driving factor, rather than local recurrence in and of itself. Several other studies have found a similar correlation between local recurrence and the risk of developing metastatic disease.[4,25,26] This supports the concept that surveillance should be 'reset' at the time of presentation with a local recurrence.

Taken in a broader context, our findings likely reflect the notion that metastatic presentation in soft-tissue sarcoma is shaped not only by clinicopathological factors, but also by underlying biological processes. The association of early metastasis with larger size, higher grade, and older age reflects an aggressive phenotype with rapid proliferation, early dissemination, and the capacity to colonize the metastatic niche.[27,28] In contrast, late metastasis in certain histological subtypes or after local recurrence is likely to follow a different trajectory influenced by tumour dormancy, angiogenic regulation, immune surveillance, and the microenvironment.[29–31] Disseminated cells may remain dormant for years through quiescence or balanced proliferation until a microenvironmental shift triggers outgrowth.[32] Similarly, immune surveillance may suppress metastatic progression until immune evasion occurs.[33] These mechanisms may explain why patients with lower-grade tumours or previous recurrence more often develop metastases after two years. Overall, the timing of metastases appears to reflect a biological continuum rather than simple disease chronology, with implications for surveillance, therapeutic decision-making, and translational strategies targeting metastatic progression.

This study has several limitations that are important to acknowledge. The first is that the study does not specifically account for indeterminate pulmonary nodules at presentation. In general, patients who present with indeterminate pulmonary nodules were considered to have localized disease to their primary sarcoma unless the indeterminate pulmonary nodule showed clear progression. Furthermore, given that this study was retrospective in nature, the treatment of PM was dictated by a multitude of factors decided in a multidisciplinary fashion. As such, direct comparisons in survival between treatment strategies fail to account for the nuances in this decision-making, such as isolated rather than multiple pulmonary nodules and patient-specific factors. Consequently, conclusions about the efficacy of various treatment methods should be considered in the context of these confounding factors. Finally, our institutional practice is to screen patients with a chest radiograph. As such, it is possible that the metastasis would have been detected earlier by high-resolution sequences, such as a CT scan of the chest which may influence the timing of what constitutes early and late metastases. However, pulmonary nodules of 1 cm in size and greater may be readily detected by routine radiographs, which aligns with our definition of what constitutes a 'pulmonary metastasis'.

This study confirms that DSS is poor after the development of pulmonary metastasis from limb or pelvic soft-tissue sarcomas. Nonetheless, survival is worst for patients who present early

with lung metastases (within two years of surgery of the primary tumour). Older age, larger tumour size, and higher tumour grade are independently associated with the development of early PM, whereas local recurrence increases the risk of late PM. Treatment factors did not appear to be associated with the risk of developing early rather than late metastatic lung disease.

Take home message

- This study demonstrates that the timing of pulmonary metastasis after resection of limb and pelvic soft-tissue sarcoma has important prognostic implications, with early metastasis associated with substantially worse disease-specific survival.
- Identification of clinical and tumour factors associated with early metastasis (including older age, larger tumour size, and higher grade) may help guide surveillance intensity, patient counselling, and risk stratification.
- Furthermore, the finding that patients with late metastasis have comparatively improved outcomes highlights the importance of individualized management strategies, and supports consideration of aggressive treatment, including metastasectomy, in appropriately selected patients.

Social media

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