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What is the likelihood of non-pulmonary metastasis occurring in the absence of lung metastasis in bone and soft tissue sarcoma? A nested case control study from an ongoing prospective cohort.

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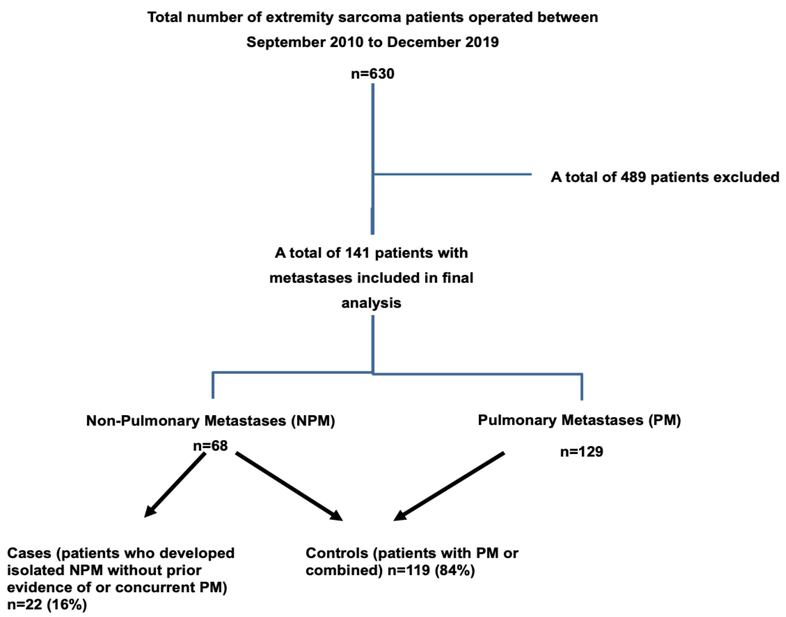
Background

- Pulmonary metastasis (PM) in bone and soft tissue sarcomas have a drastic effect on overall survival.
- Non-pulmonary metastases (NPM) (Visceral, nodal, and osseous) are rare and associated with poorer prognosis.
- Although the accepted clinical practice is to obtain chest imaging for sarcoma surveillance, there is paucity in literature on whether imaging of the lung alone is enough to identify the presence of overall metastasis in the body.
- The objectives of the study are to measure the incidence of isolated NPM, to determine if NPM occur in isolation or if they are predicted by the presence of synchronous or prior PM, and to identify the predicting factors for NPM.

Methods

- Investigators identified patients who developed NPM from an ongoing cohort of bone and soft tissue sarcoma patients.
- We retrospectively collected patient characteristics and tumor clinicopathological variables.
- Our population of interest was patients who developed isolated NPM without prior evidence of or concurrent PM. PM recognized within 3 months of NPM was considered concurrent.
- We analyzed the background characteristics and predicting factors.
- Non-parametric analysis was used followed by subgroup analysis.
- results were reported in-line with the criteria of Strengthening The Reporting of Cohort Studies in Surgery (STROCSS).

Figure: Patients' participation status flowchart.



Histological Dx	Total n (%)	Cases n (%)	Controls n (%)
Osteosarcoma	25 (18%)	2 (9%)	23 (19%)
Malignant Nerve sheath	7 (5%)	3 (14%)	4 (3%)
Solitary fibrous	1 (%)	0	1 (1%)
Epithelioid sarcoma	2 (1%)	0	2 (2%)
Clear cell sarcoma	2 (1%)	0	2 (2%)
Malignant GCT	1 (1%)	0	1 (1%)
Angiosarcoma	1 (1%)	1 (5%)	0
Sarcoma, NOS	3 (2%)	1 (5%)	2 (2%)
Rhabdomyosarcoma	3 (2%)	2 (9%)	1 (1%)
Chondrosarcoma	16 (11%)	5 (23%)	11 (9%)
Extra Skeletal sarcoma	1 (1%)	0	1 (1%)
Alveolar soft part	2 (1%)	0	2 (2%)
Ewing sarcoma	11(8%)	3 (14%)	8 (7%)
UPS	32 (23%)	2 (9%)	30 (25%)
Fibrosarcoma	1 (1%)	0	1 (1%)
Myxoid Liposarcoma	8 (6%)	2 (9%)	6 (5%)
Myxofibrosarcoma	8 (6%)	0	8 (7%)
Synovial sarcoma	6 (4%)	1 (5%)	5 (4%)
Leiomyosarcoma	11 (8%)	0	11 (9%)
Location			
Lower Limb	110 (78%)	15 (68%)	95 (80%)
Upper Limb	7 (5%)	3 (14%)	4 (3%)
Axial/Girdle	24 (17%)	4 (18%)	20 (17%)
Total	141 (100%)	22 (100%)	119 (100%)

Table: Histology subtypes and anatomical location among cases (isolated non-pulmonary metastasis) and controls (pulmonary metastasis or combined).

Results & Discussion

- From the overall cohort of 630 extremity sarcoma patients treated between September 2010 to December 2019, the overall incidence of metastasis was 141 (22%).
- Out of the 141 patients with metastasis, 129 (91%) patients had PM while 68 (48%) had NPM.
- Twenty-two patients (16%) demonstrated isolated NPM;

  7 patients later developed PM.
- The most common site for NPM was bone, followed by abdominal viscera and lymph nodes.
- Malignant peripheral nerve sheath tumor, angiosarcoma, rhabdomyosarcoma, synovial sarcoma, and myxoid liposarcoma were more likely to develop isolated NPM than other subtypes of soft tissue sarcoma (OR 12, 95% CI 3-46, p<0.001).
- Interestingly, isolated NPM were 3 times more likely to metastasize to a single site compared to the control group (PM or combined) (OR 3.2, 95%CI 1.1-10).

Conclusion

- Patients who develop isolated NPM, without prior or concurrent PM, are rare and demonstrate a predilection towards some subtypes of extremity sarcoma.
  - Patients diagnosed with malignant peripheral nerve sheath tumor, angiosarcoma, rhabdomyosarcoma, synovial sarcoma and myxoid liposarcoma have a higher incidence of isolated NPM and may require more than simple chest imaging for comprehensive surveillance.
- They are more likely to develop oligometastatic disease, which may be amenable for surgical excision.
- We recommend multicenter studies with larger sample size to further identify the predicting factors for isolated NPM.