

Soft-tissue Sarcoma Metastases Identified on Abdomen and Pelvis CT Imaging

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Abstract The current standard of care for patients with extremity soft-tissue sarcomas is to obtain imaging of the chest for staging and surveillance. Our institutional standard of care has been to obtain CT scans of the chest, abdomen, and pelvis to evaluate for metastatic disease. Cost and radiation risk led us to question the utility of the additional scans. We presumed abdomen and pelvic CT scans would not benefit this patient population. We retrospectively reviewed our sarcoma databases from 2000 to 2008. We included 124 patients with 15 types of extremity soft tissue sarcomas evaluated with CT of the C/A/P. Primary outcomes were (1) location of metastatic disease in relation to (2) sarcoma type. Twenty patients (16%) presented with or developed abdomen/pelvis metastases and 10 of the 15 types of soft tissue sarcomas had abdominal or pelvic metastases. A larger number of patients demonstrated metastatic disease in the abdomen and pelvis than

anticipated. We believe routine imaging of the abdomen and pelvic with CT for both staging and surveillance of all types of soft tissue sarcoma should be considered.

Level of Evidence: Level III, diagnostic study. See Guidelines for Authors for a complete description of levels of evidence.

Introduction

Soft tissue sarcomas comprise less than 1% of all malignancies and occur virtually anywhere throughout the body [5, 18, 20]. Most studies report that approximately 50% of soft tissue sarcomas occur in the extremities [14]. The prognosis for patients with soft tissue sarcomas depends on a number of factors including grade, size, location of tumor, and histologic type. Patients with large, deep, high-grade sarcomas can expect a risk of metastases of approximately 40% to 50% [14, 15, 18–20]. By far the most common route for metastatic spread is hematogenous [19]. Some subtypes such as synovial sarcoma, epithelioid sarcoma, and rhabdomyosarcoma have a relatively higher incidence of regional lymph node spread [6, 19]. Numerous investigations have demonstrated the lung to be the most common site for metastatic disease from extremity soft tissue sarcoma.

The incidence of lung involvement with disseminated disease has been estimated at approximately 70% to 80% [2, 5, 6, 13, 15, 18–20]. Approximately 30% of patients treated with complete removal of all metastatic lung lesions can expect to have meaningful long-term survival [2]. Traditional staging and surveillance recommendations have included chest imaging of some kind [1, 9, 14]. There has been little emphasis placed on imaging of the remainder of the body despite studies that have demonstrated 20% to 30% of metastatic disease will occur outside

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Each author certifies that his or her institution has approved the human protocol for this investigation and that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

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of the lung. Current National Comprehensive Cancer Network (NCCN) guidelines recommend abdomen and pelvis CT scans for the staging of only a subset of extremity soft tissue sarcomas including myxoid liposarcoma, leiomyosarcoma, epithelioid sarcoma, and angiosarcoma [11].

One of us observed a substantial number of soft tissue sarcoma patients developed extrapulmonary metastatic disease. This led to routine CT imaging of the lungs, abdomen, and pelvis for staging and surveillance of extremity soft tissue sarcoma patients. Recent attention on the radiation risk associated with diagnostic imaging, particularly CT scans [3, 7, 11, 17] as well as increased scrutiny of the cost of medical care called into question the additional benefit from imaging of the abdomen and pelvis.

We therefore asked whether: (1) the additional abdomen and pelvis CT scans would lead to the discovery of a substantial number of patients with extrapulmonary disease and (2) certain soft tissue sarcoma types such as myxoid liposarcomas or leiomyosarcomas would demonstrate disease outside of the lung.

Material and Methods

We identified all 213 patients with extremity soft tissue sarcomas evaluated by the authors at the home institution from January 2000 to June 2008. To identify all patients our radiology database was cross-referenced with the prospective databases of the musculoskeletal oncologists. Extremity lesions included buttock and nonretroperitoneal pelvic tumors. Patients were included in the study even if they did not have definitive surgery at our institution. Of the 213 patients 124 were adult patients who had CT C/A/P imaging performed at our institution for staging and surveillance of sarcomas with metastatic potential. Twenty-two patients younger than 18 years of age at the time of diagnosis were excluded. We excluded seven patients with dermatofibrosarcoma protruberans and five patients with unclear or indeterminate sarcoma diagnoses. Five patients did not have adequate records to accomplish both aims of the study. Fifty patients were excluded who were referred by outside oncologists who continued surveillance imaging at outside institutions for reasons of patient convenience or insurance requirements; these patients were excluded due to IRB concerns. There were 15 types of soft tissue sarcoma included in the study (Table 1). One hundred nine of the 124 patients (88%) had high-grade lesions. We included all patients regardless of the length of followup; the minimum followup was 0 months (mean, 22 months; range, 0 to 94 months). Six of the 124 patients (5%) were lost to followup with their current disease status unknown. IRB approval was obtained prior to initiating the study.

The surveillance regimen for high-grade, deep, large soft tissue sarcomas included CT scans of the chest, abdomen, and pelvis (CT C/A/P) every 4 months for the first 2 years, then every 6 months for the subsequent 3 years. Patients more than 5 years from diagnosis were evaluated with yearly PA and lateral chest xray (CXR) or CT C/A/P at the discretion of the treating physician. Some patients received imaging at the home institution as well as at outside facilities. Followup was determined as the amount of time from the initial CT C/A/P scan to the final CT C/A/P. All scans at the home institution were performed on a 64-slice multidetector CT unit (GE BCT Lightspeed) with a pitch setting of 1.375:1, table speed of 55 mm per rotation, and helical scan thickness of 2.5 mm. Intravenous contrast was administered at a dose of 150 ml. at 4 ml. per second with a 70 second scan delay. Oral contrast was also administered as part of the surveillance protocol. All scans were interpreted by a radiologist with Body Imaging subspecialty training.

Primary endpoints included (1) the location of metastatic disease identified on staging or surveillance CT scans of the C/A/P and (2) sarcoma type. Secondary endpoints included incidental findings and patients lost to followup, as well as the number of patients who died of their disease. Patients with high-grade, pleomorphic, or undifferentiated sarcomas without further classification were assigned to the pleomorphic sarcoma NOS (not otherwise specified) category. This included sarcomas that would have in the past been called malignant fibrous histiocytoma lesions.

Results

Seven patients had abdominal or pelvic metastases identified on the initial CT scan and 13 on subsequent surveillance scans for a total of 20 of the 124 (16%) patients (Tables 1, 2). Six of the 20 patients with abdomen/pelvis metastases had isolated abdomen/pelvis metastases (5%) without the development of pulmonary disease during the study period. Thirteen patients developed both pulmonary and abdomen/pelvis metastases. Of the 30 patients with pulmonary metastases, 17 had isolated pulmonary metastases (14%). Of the 13 patients with both pulmonary and abdomen/pelvis metastases, six patients developed pulmonary metastases prior to the development of abdomen/pelvis metastases and seven patients had both pulmonary and abdomen/pelvis metastases identified for the first time on the same CT scan.

Ten of the 15 different sarcoma types developed extrapulmonary metastatic disease. Types with a higher percentage of abdomen and pelvic metastases were leiomyosarcomas, MPNST, myxofibrosarcoma and pleomorphic sarcoma NOS (Tables 1, 2). No patients with

Table 1. Summary of sarcoma types and location and timing of metastatic disease

Sarcoma type	Number of patients	Total patients with Mets	Lung Mets staging	Lung Mets surveillance	A/P Mets staging	A/P Mets surveillance
Pleomorphic sarcoma NOS	30	8	3	3	1	2
Myxofibrosarcoma	20	5	3	1	2	2
Liposarcoma						
High-grade	5	3	0	3	0	2
Myxoid	13	0	0	0	0	0
Synovial sarcoma	14	6	1	4	1	1
Leiomyosarcoma						
High-grade	11	7	3	3	0	3
Intermediate-grade	1	0	0	0	0	0
MPNST	8	2	1	1	0	2
Extraskeletal myxoid chondrosarcoma	4	1	0	1	0	0
Solitary fibrous tumor	4	1	0	1	0	0
Fibromyxoid sarcoma	4	0	0	0	0	0
Rhabdomyosarcoma	3	1	1	0	0	0
Epitheloid sarcoma	2	1	0	0	0	1
Fibrosarcoma						
Intermediate-grade	1	1	0	0	1	0
Low-grade	1	0	0	0	0	0
Epitheloid hemangioendothelioma	1	1	1	0	1	0
Alveolar soft parts sarcoma	1	1	0	0	1	0
Giant cell type osteosarcoma of soft tissue	1	0	0	0	0	0
Totals	124	38	13	17	7	13
Percentages		31%	11%	14%	6%	11%

Mets = metastatic disease.

myxoid liposarcomas developed disease in the abdomen and pelvis.

Thirteen patients had pulmonary metastases on the initial CT scan and 17 had pulmonary metastases identified on subsequent surveillance scans; thus 30 of 124 (24%) patients had or developed pulmonary metastases. One patient had a non-pulmonary metastasis found on a chest CT scan (thoracic paraspinal muscle).

Twenty-one of the 124 patients (17%) died of their disease. Of the six patients lost to followup, one patient had pulmonary metastases and one patient had extrapulmonary metastases at last study. There were numerous incidental findings noted on the abdomen and pelvic CT scans. The most common were liver, kidney, and adrenal lesions (Table 3). Three primary carcinomas were incidentally discovered on CT of the abdomen and pelvis.

Discussion

Patients with soft tissue sarcoma of the extremities treated at our institution have been evaluated with CT of the chest, abdomen, and pelvis for staging and surveillance for the

past eight years. Increasing concerns regarding both the cost of these scans as well as the radiation exposure to these patients led us to question the current standard of care at our institution [3, 17]. We questioned whether the addition of abdomen and pelvis CT imaging would lead to the discovery of a clinically important number of sarcoma patients identified with extrapulmonary disease. We also wondered whether certain sarcoma subtypes would demonstrate a higher incidence of extrapulmonary disease and provide justification for additional abdomen and pelvis imaging for staging and surveillance.

There are a number of limitations to our study. First, we had a limited number of patients. Fifty patients with CT imaging performed solely at outside facilities were dropped from the study due to institutional review board concerns. Despite this omission, there is no reason to suspect that the two patient populations would differ in the pattern of metastatic disease. However, we did not have an adequate number of patients to determine with any statistical confidence which types of sarcoma might have an increased risk of metastatic spread to extrapulmonary sites. Second, the short followup interval for some patients may also be a concern. Longer followup might actually increase the

Table 2. Type and location of abdomen and pelvis metastatic disease

Patient #	Sarcoma subtype	A/P Mets at staging? (Y/N)	Location of Mets	A/P Mets on surveillance? (Y/N)	Time to Mets (months)	Location of Mets	Lung Mets on staging? (Y/N)	Lung Mets surveillance (Y/N)	Patient status
5	myxofibrosarcoma	Y	liver	N	0		Y		DOD
11	MPNST	N		Y	25	Ilium	N	Y	DOD
13	Leiomyosarcoma	N		Y	6	Lumbar Spine and ilium	N	Y	AWD
18	Leiomyosarcoma	N		Y	67	Sartorius & pelvic wall	N	N	AWD
19	Myxofibrosarcoma	Y	Retroperitoneum (iliacus)		0		Y		DOD
22	MPNST	N		Y	21	Adrenal	N	Y	DOD
26	Malignant epithelioid hemangioendothelioma	Y	liver		0		Y		AWD
38	Myxofibrosarcoma	N		Y	21	Inguinal region (node)	N	Y	AWD
40	Round cell liposarcoma	N		Y	21	Intra-abdominal	N	Y	DOD
41	Dediff liposarcoma	N		Y	50	Psoas	N	Y	DOD
44	Pleomorphic sarcoma NOS	N		Y	10	Intra-abdominal	N	Y	DOD
46	Epithelioid	N		Y	45	Inguinal nodes	N	N	DOD
50	Alveolar soft parts sarcoma	Y	acetabulum	N	0		N	N	AWD
53	Synovial sarcoma	Y	Femoral neck	N	0		N	N	AWD
67	Synovial sarcoma	N		Y	23	Inguinal node	Y		AWD
68	Myxofibrosarcoma	N		Y	25	Intra-abdominal	N	N	AWD
97	Leiomyosarcoma	N		Y	26	Retroperitoneum	N	Y	AWD
99	Pleomorphic sarcoma NOS	Y	Widespread		0		Y		DOD
105	Pleomorphic sarcoma NOS	N		Y	16	Abdominal wall	N	Y	DOD
118	Fibrosarcoma	Y	Lumbar paraspinal muscle	N	0		N	N	NED

Mets = metastatic disease.

Table 3. Incidental findings noted on abdomen/pelvis imaging

Incidental finding on A/P CT scan	Number of cases
Liver lesions	
Hemangiomas	6
Focal nodular hyperplasia	2
Cysts	14
Granuloma	1
Kidney lesions	
Renal cyst	15
Renal cell carcinoma	2
Transitional cell carcinoma	1
Adrenal lesions	
Adrenal cyst	8
Adrenal nodule	1
Adrenal adenoma	7
Splenic lesions	
Splenic mass	1
Splenomegaly	1
Spleen granuloma	1
Iliac bone island	1
Vertebral hemangioma	1
Ovarian lesions	
Ovarian fibroids	1
Ovarian cyst	1
Pancreatic lesions	1
Pelvic cyst	1
Enlarged inguinal nodes	1
Sarcoidosis	1

strength of the study by the identification of additional patients with extrapulmonary disease. Many patients developed metastatic disease in the abdomen and pelvis after first being diagnosed with metastatic disease to the lungs. In addition, no patients with myxoid liposarcoma in our study developed extrapulmonary disease despite numerous reports of an increased risk of extrapulmonary disease in this patient population. The lack of metastatic disease in this cohort is likely due to the short followup interval in the study for a lower-grade neoplasm. Third, while this was a retrospective study we do not believe the findings and conclusions would be substantially affected because the information was drawn from a prospectively collected database of sarcoma patients with a low percentage of patients (5%) lost to followup. Nevertheless, a prospective study with more stringent adherence to protocol would undoubtedly strengthen the conclusions and allow for an improved temporal understanding of the disease process.

The primary purpose of the study was to determine whether additional abdomen and pelvic CT imaging for patients with extremity soft tissue sarcoma would identify a

substantial number of patients with extrapulmonary disease. A review of the literature revealed no justification for additional abdomen and pelvis imaging [8, 11, 14, 20]. Society of Surgical Oncology practice guidelines for soft tissue sarcoma were last published in 1997 [14]. The guidelines recommend CT of the chest for intermediate or high grade lesions >5 cm and CT scan of the chest, abdomen, and pelvis for myxoid liposarcoma patients with tumors >5 cm as initial staging. Recommendations for surveillance scanning are not provided. The most commonly referenced current guidelines are from the National Comprehensive Cancer Network (NCCN) staging guidelines for extremity soft tissue sarcoma [11]. The NCCN recommends imaging of the chest without specifying CT versus CXR. They also recommend that abdominal/pelvic CT should be considered for myxoid liposarcoma, leiomyosarcoma, epithelioid sarcoma or angiosarcoma. The surveillance guidelines are provided with the caveat that very limited data are available in the literature regarding effective surveillance strategies and that the recommendations outline a “prudent followup schedule that avoids excessive testing”. Recommendations include consideration of CXR every 6 to 12 months for Stage I tumors. Stage II and III tumors should have chest imaging (plain radiograph or chest CT) every 3 to 6 months for 2–3 years, then every 6 months for the next 2 years, and then annually. They indicate there has never been a study demonstrating improved clinical outcomes with more sensitive CT scans as opposed to CXR. Surveillance imaging for the subset of sarcomas for whom abdomen and pelvis imaging was suggested for staging is not discussed. Concerns regarding the additional cost of the scans as well as the additional radiation burden to these patients led us to evaluate the utility of our current institutional practice. The results of our investigation were surprising. We identified a substantial percentage (16%) of extremity soft tissue sarcoma patients who either presented with or developed metastatic lesions to the abdomen and pelvis. Most of the large outcome studies of soft tissue sarcoma patients have reported the primary site of metastatic disease as the lung without further discussion or reporting of sites of extrapulmonary metastatic disease [2, 13, 15, 19, 20]. Many older studies, particularly from the surgical oncology literature, recommend CXR alone as a screening study for metastatic disease [1, 8, 20]. Despite multiple studies indicating that 20 to 30% of soft tissue sarcoma metastases will occur outside of the lungs, to our knowledge, there is no study examining the role of CT of the C/A/P as routine staging and surveillance in this patient population.

The second aim of the study was to determine whether certain sarcoma types would demonstrate an increased incidence of extrapulmonary metastatic disease to justify abdomen and pelvis imaging. Ten of the 15 sarcoma types

in the study included patients who either presented with or developed metastatic disease to the abdomen and pelvis (Tables 1, 2). Sarcoma types demonstrating more prevalent extrapulmonary metastases included leiomyosarcomas, MPNST, myxofibrosarcoma, and pleomorphic sarcoma NOS. A review of the literature reveals a number of studies documenting the increased incidence of extrapulmonary disease in patients with myxoid liposarcoma [4, 12]. NCCN guidelines advocate abdomen and pelvic imaging for the initial staging of patients with myxoid liposarcoma, epithelioid sarcoma, angiosarcoma, and leiomyosarcoma [11]. It is not clear from the NCCN guidelines or the references provided with the guidelines, the justification for the recommendations for the select subset of sarcoma types. While the study does not include enough patients to determine the validity of those recommendations, the demonstration of 10 of 15 types of metastatic disease outside of the lung would suggest that additional imaging may be warranted for additional sarcoma types beyond those recommended by the NCCN. The evaluation of a larger database of patients may be helpful in elucidating differences in metastatic patterns related to sarcoma type.

When we formulated the study, we anticipated additional scans of the abdomen and pelvis would not be beneficial in the management of soft tissue sarcoma patients. We planned to determine the additional costs associated with the scans as another reason to abandon the practice. Our combined institution and radiologist charges for a CT of the chest with contrast are \$1600. The abdomen and pelvis scans if performed with and without contrast each add \$1800 to the bill. The total charged to the patient for all three scans is approximately \$5000. The additional abdomen and pelvis scans add an additional \$3600 for each surveillance visit. An individual sarcoma patient completing all of their surveillance imaging would generate an estimated \$65,000 in charges. Clearly, reimbursement rates and actual costs are much less than these numbers. Additional costs would be incurred in a number of patients in the further workup of incidentally noted abnormalities unrelated to the sarcoma (Table 3). A cost analysis portion of the study was abandoned when we identified a substantial number of patients with metastatic disease of the abdomen and pelvis. We believe the number of patients identified with extrapulmonary disease justifies additional costs associated with abdomen and pelvis imaging. We found that incidentally noted abnormalities were uniformly observed outside of the three patients who were identified as having kidney and transitional cell carcinomas on their staging work-up. Future studies that include cost analysis would be important to determine whether the added information changes the treatment, the outcome, or the prognosis; such information would likely add to the complexity of the decision-making process. The individual physician caring

for the extremity sarcoma patient will need to determine whether the earlier identification of extra-pulmonary metastatic disease is worth the additional cost.

The long-term consequences of radiation from diagnostic radiology scans has become a topic of concern in the literature and media [3, 17]. In our institution, radiation doses for specific patients are not estimated or tracked. All CT scans were performed using scanners that meet current ACR accreditation effective dose limits, and an automatic exposure control (Smart mA, GE Corp.) was applied during all scans. In the absence of specific patient dose information, the risk of incurring a fatal cancer can be estimated by using average effective doses for CT of the chest (7 mSv), abdomen (8 mSv) and pelvis (6 mSv) [10, 16]. The effective dose for the chest, pelvis and abdomen is equal to approximately 21 mSv. If a patient were to follow the protocol at our institution they would receive a total of 12 surveillance scans in addition to the staging scan. The total effective dose for 13 examinations is approximately 273 mSv during the 5 year surveillance period. Dose modifiers of age, gender, and previous cancer history as well as exam interval can be applied, but exclusive of these modifiers, using the fatal cancer risk estimate of 0.04 per Sv, the risk of the surveillance scans calculates to be $(0.273 \text{ mSv} \times 0.04 \text{ per Sv}) = 0.001009$, or about 1%. This should be taken in the context of the natural cancer risk for the adult human population of about 20%. Longer followup will be necessary to determine the incidence of radiation-induced secondary cancers or other complications related to the additional radiation burden. Particularly in the young patient [17], where the impact of radiation is greater, caution may be indicated in the selection of a surveillance regimen. Ultimately, decisions on surveillance will come down to a risk benefit analysis encompassing both tumor and patient dependent factors. Ongoing study of radiation-limiting techniques for CT scanning will also provide opportunities for improving the risk of radiation exposure.

Our study demonstrates metastases to the abdomen and pelvis in 16% of our patients with extremity soft tissue sarcomas. Perhaps more compelling are the 5% of patients who developed metastatic disease to the abdomen or pelvis without pulmonary disease. The findings raise a number of issues. It is unclear from the literature whether extrapulmonary disease in addition to lung metastases affects a patient's prognosis. Studies have demonstrated relatively long-term survival of a subset of patients treated with complete metastatectomy [2, 6, 18]. Are we potentially subjecting 20% of our patients with presumed isolated lung disease to surgical resection that will not be curative and is unwarranted? If we do identify extrapulmonary disease, is there a role for attempting complete and radical resection of all metastatic lesions in the hopes of prolonging survival? The findings could also influence how patients are

staged as 6% of patients in our study had disease outside of the lungs identified at initial staging. The results of outcome studies and clinical trials could be affected if a substantial number of patients with metastatic disease are not identified. Perhaps the most important question to ask is whether it matters if we identify patients with asymptomatic abdomen and pelvis disease earlier. Many would argue that we are overevaluating these patients by obtaining CT scans of the lungs. They would also argue that the addition of abdomen and pelvis scans will only serve to increase cost to society and the patient, increase anxiety for the patient and physician, and increase the risk of radiation-related complications. Our hope is that future development of meaningful curative options for this patient population will eliminate this argument.

The optimal schedule and imaging modalities for sarcoma staging and surveillance have not been identified at this time. We found only 5% of patients developed metastatic disease to the abdomen and pelvis in the absence of pulmonary disease. One strategy could therefore be to obtain routine chest CTs for staging and surveillance and add abdomen and pelvic scans only for those patients who demonstrate metastatic disease to the lungs. Based on the considerable number of sarcoma types that developed extra-pulmonary disease we advocate all soft tissue sarcoma types be considered for abdomen and pelvis imaging until further data are available. Our current approach involves an honest discussion with patients explaining that the optimal surveillance recommendations are not clear and that we do not know whether earlier detection will have any impact on their survival. We recommend CT of the C/A/P at staging and every 4 months for 2 years following the resection date. We then recommend C/A/P scans every 6 months for an additional 3 years followed by yearly CXR for 5 additional years for a total of 10 years of surveillance. If patients have concerns with cost or radiation burden we modify the plan according to their wishes. The role of developing imaging modalities such as PET/CT in evaluating metastatic disease in sarcoma populations is not fully understood, and may influence future staging and surveillance regimens.

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