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The Value of Perioperative Imaging in Patients with Uterine Sarcomas

Elizabeth K Nugent, MD^a, Israel Zigelboim, MD^a, Ashley S Case, MD^a, Feng Gao, MD, PhD^b, Premal H Thaker, MD^a, Janet S Rader, MD^a, David G Mutch, MD^a, and L Stewart Massad, MD^a

^aDivision of Gynecologic Oncology, Department of Obstetrics and Gynecology, Washington University School of Medicine and Siteman Cancer Center

^bDivision of Biostatistics, Washington University School of Medicine and Siteman Cancer Center

Abstract

Objective—To explore the yield and impact of perioperative imaging on management among patients undergoing surgical resection and treatment of uterine sarcomas.

Methods—A retrospective chart review was done for women with histologically confirmed uterine sarcomas treated at Barnes Jewish Hospital/Washington University from 2001–2007. Descriptive statistics, Cox multivariate models, and Kaplan-Meier plots were used to evaluate associations and survival.

Results—A total of 92 patients were identified and 55(60%) were diagnosed with stage III–IV disease. Perioperative imaging was obtained in 84 (91%) cases, including chest x-ray in 66 (72%), computerized tomography (CT) of the abdomen and pelvis in 59 (64%), chest CT in 33 (36%), positron emission tomography (PET) in 8 (9%), and CT of the head, pelvic magnetic resonance imaging (MRI), or bone scan in a total of 2 (2.2%). Imaging identified abnormalities concerning for metastases in 30 (32%) studies. Thirty-four recurrences have been documented, and 21 (62%) of these treatment failures were extrapelvic. Multivariate analysis of this series noted that tomographic evidence of extrauterine disease predicted recurrence ($p=0.028$) and incomplete surgical resection ($p=0.003$, HR 6.0 95% CI 1.9–19.9) predicted disease free survival. Imaging contributed to change in surgical and postsurgical treatment decisions in 8 (9%) patients.

Conclusion—Pretreatment imaging studies change management in a minority of patients with newly diagnosed uterine sarcomas.

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Corresponding author: L. Stewart Massad, MD, Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, 660 S Euclid Ave Box 8064, Saint Louis, MO 63110-1010, Telephone: 314-362-3181, Fax: 314-362-2893, massadl@wudosis.wustl.edu.

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INTRODUCTION

Uterine sarcomas represent less than 5% of uterine cancer but demonstrate a pattern of frequent early metastasis, relative resistance to both chemotherapy and radiation, and a high risk for distant failure (1, 2). The optimal initial evaluation of gynecologic sarcomas is unknown. At present, national guidelines recommend CT or MRI during initial evaluation only if disease is suspected or patient is symptomatic (3). Initial surgical excision and extent of residual disease are associated with disease-free and overall survival (4,5). Small burden metastatic disease may be underdiagnosed in patients not undergoing imaging of distant sites. Though they may benefit from debulking, women with undiagnosed distant disease do not benefit from surgical staging and are at risk for early failure.

Increasing use of imaging has been blamed for a disproportionate share of rising health care costs (6). Policy experts have argued that expanded imaging strategies should be evidence-based. We sought to review imaging findings in patients with uterine sarcomas undergoing surgical excision to assess the impact of imaging on treatment, outcomes, and recurrences.

MATERIALS AND METHODS

We reviewed the medical records of patients diagnosed with uterine sarcomas at Washington University/Barnes Jewish Hospital between January 1, 2001 and December 31, 2007. Data was abstracted from hospital charts and outpatient medical, pathologic, and tumor registry records.

All patients entered in the study had histologically confirmed uterine sarcomas and were surgically treated for their malignancies at Washington University/Barnes Jewish Hospital. Available pre-treatment imaging and follow-up records were also necessary for inclusion. Exclusion criteria include presence of synchronous or metachronous malignancies and incomplete documentation. Patients were excluded if histology was not institutionally reviewed, for lack of surgical procedure documentation if a procedure was performed, for complete lack of follow up information after surgery. Patients were followed from time of initial diagnosis until death, loss to follow-up, or completion of study. The Washington University Human Research Protection Office deemed this study appropriate for expedited review since no patient contact was necessary (HRPO#08-0516).

Reports of all imaging studies obtained within 30 days of patient's histologic diagnosis were reviewed, as were imaging studies obtained during the disease course. Outcome measures including recurrence and treatment for recurrence were collected. Management changes were determined from documented treatment plans. Recurrence was defined as any histologically confirmed disease recurrence as well as any imaging recurrence for which patient was treated or offered treatment. Death from disease was defined as any death from complications associated with cancer as well as strict disease mortality.

Descriptive statistics were used to characterize the clinical and demographic variables of the study sample. The associations between imaging and clinical/demographic characteristics were evaluated using Fisher's exact test or Kruskal-Wallis' rank sum test as appropriate. Overall survival (OS) and disease-free survival (DFS) were described by Kaplan-Meier

product limit method and compared using log-rank test. Cox multivariate proportional hazard models were also fitted to assess the associations between each of the imaging variables and survival, while adjusting the clinical and demographic variables that were significant in the univariate survival analysis. All analyses were two-sided and significance was set at a p-value of 0.05. Statistical analyses were performed using SAS (SAS Institutes, Cary, NC). A smaller cohort of women were identified who had alterations in surgical or post surgical treatment care as determined by senior faculty members based on imaging in order to calculate number needed to treat.

RESULTS

A total of 105 patients diagnosed with uterine sarcoma treated between 2001–2007 were identified and met inclusion criterion. Ten patients were excluded because of incomplete documentation and 3 were excluded for synchronous primary tumors, leaving 92 for evaluation. Median age at diagnosis was 63.1 with a range of 23–89 years. Most patients (78%) were Caucasian, and approximately 20% were African American. The median body mass index (BMI) of those undergoing surgery was 28.8 with a range of 16.9 to 111.6 and the median CA-125 was 23.5 units/mL with a range of 3.4 to 1408.0 units/mL. The most common histological types were carcinosarcoma (52%), leiomyosarcoma (27%), endometrial stromal sarcoma (11%), uterine sarcoma (4%), and other less common uterine sarcoma types (4%). Sixty percent were diagnosed with stage III–IV disease.

Perioperative imaging was obtained in 91% of cases including chest x-ray in 72%, CT of the abdomen and pelvis in 64%, chest CT in 36%, PET scan in 9%, and 2.2% of patients had a head CT, pelvic MRI, or bone scan. Imaging identified abnormalities concerning for metastases in 30 cases (32%). Pelvic metastatic disease was examined on pathological specimens to correlate with radiologic findings. Pelvic metastatic disease was confirmed on pathological specimens from patients' surgical procedures. Metastatic disease in the chest was confirmed by thoracentesis only if pleural effusions were present. Metastatic disease was noted on imaging in the chest in 7 patients and the abdomen in 22 patients.

Indeterminate lesions and questionable metastatic disease were noted on initial imaging in 16 (18%) women. These women were followed. Of 11 patients with indeterminate lung lesions, 8 were eventually diagnosed with chest metastasis of their sarcomas, while 3 individuals had stable unknown abnormalities of the lung for a positive predictive value of 83%. Five patients were diagnosed with liver abnormalities on initial imaging; of these, one had confirmed liver metastasis of her sarcoma for a PPV of only 20%. Seven patients had negative chest x-ray and a positive CT scan of the chest. Of the 7 positive results, 4 were indeterminate lung lesions on CT scan. Of those indeterminate lesions with negative chest x-rays, three of them were diagnosed with stable abnormalities of the lung, representing all the individuals with stable lung abnormalities.

Seventy-five patients received a consultation for uterine sarcomatoid malignancy on biopsy at Washington University during the study period with 68 patients undergoing surgery (91%). Ninety percent of patients had a surgical procedure involving a total abdominal hysterectomy at minimum and approximately 8% of patients had a biopsy with or without

an exploratory laparotomy. The most common surgical treatment involved hysterectomy, with or without bilateral salpingo-oophorectomy and lymph node dissection (49%). Approximately 20% of patients' surgical treatments involved resection of bowel, bladder, or liver, splenectomy, or other radical tumor debulking procedure.

Forty-nine percent of patients in the study group received chemotherapy and 24% received radiation therapy. Of those receiving chemotherapy, 47% of patients were started on an initial chemotherapeutic regimen of a platinum agent and a taxane, 29% initially received a platinum agent and gemcitabine, and 16% were treated with a taxane and ifosfamide/mesna. Two patients were treated hormonally and 7 patients received various other agents. Of those patients receiving radiotherapy, 81% received pelvic radiation and 45% received brachytherapy.

Eight (9%) of the 92 patients included in the study had a change in surgical or post surgical treatment due to their imaging studies, all based on CT scan results. Five of 8 patients had a less aggressive surgical procedure performed and the remaining 3 patients had a plan for post surgical chemotherapy or radiation therapy added to or deleted from management plans. This resulted in approximately 9% patients having a change in surgery performed or post surgical care after a CT scan of the abdomen/pelvis, with or without a chest CT scan. The number of CT scans needed to change treatment for one patient was 12. Results of chest x-ray, head CT, MRI, and bone scans did not impact therapy.

In this series, perioperative tomographic evidence of extrauterine disease predicted recurrence ($p=0.028$). In univariate analysis, advanced stage and incomplete surgical resection predicted overall or disease free survival. In multivariate analysis, only advanced stage ($p=0.001$ HR=1.8 95% CI 1.3–2.5) predicted overall survival, and advanced stage ($p=0.001$ HR=1.8 95% CI 1.2–2.5) and incomplete surgical resection ($p=0.003$, HR 6.1 95% CI 1.8–19.9) predicted disease free survival. Age, race, BMI, CA125, disease histology, chemotherapy, and radiation therapy did not predict overall survival and disease free survival. Imaging did not significantly affect overall or disease free survival in multivariate analysis, nor did univariate analysis of possible correlation between OS/DFS and any imaging variable reach significance.

Median patient follow-up was 21.8 months (range 0.3–95.7) and the rate of patients lost of follow up was 9%. To date 34 (37%) of 92 patients have recurrent disease; of these 34, 21 (62%) tumors recurred in the abdomen or chest and 13 (38%) tumors recurred in the pelvis. At the end of the study period, 44 (49%) patients had no evidence of disease, 8 (9%) patients were alive with disease, 38 (44%) patients had succumbed to their disease, and 2 (2%) patients died from treatment or intercurrent disease. The mortality rate for stage I and II disease was 26% while the mortality rate for stage III and IV disease approached 73% by the end of the study period. The mortality rate for patients with very likely metastatic disease was 85% and the mortality for patients in the study cohort with indeterminate or questionable metastatic disease was 48%.

DISCUSSION

The use of perioperative imaging in the evaluation of patients with newly diagnosed uterine sarcomas has not been standardized. This investigation suggests that perioperative imaging, especially CT scanning, is very common and has a substantial yield. However, only a small minority of women with uterine sarcomas benefit from a change in management following imaging. The utility of imaging will depend on how clinicians and patients value these changes.

Two papers published in the radiology literature about CT scan identification of uterine sarcomas reported that metastases are frequent, with the most common sites being pulmonary (32%) followed by retroperitoneal lymph nodes, (21%) liver (16%), and omentum (11%) (7, 8). Although the radiology literature suggests that large heterogeneous primary tumors may be difficult to definitively identify as sarcomatoid in nature, early metastasis may be frequent and easier to recognize. Widely metastatic disease discovered prior to definitive surgical management is clearly important for treatment planning as well as necessary for full disclosure to a patient about their condition.

A recent study assessed the utility of CT scans in the preoperative management of uterine carcinoma. It suggested that management was altered in only 4% of the study population (9). It did find that high risk histologic subtypes such as sarcoma may benefit from preoperative imaging because of their propensity for early metastasis (9). Our study examining only sarcomas demonstrates a 9% change in patient management if surgical and post-surgical management are taken into account.

Historically, patients with uterine sarcomas have a significant risk of distant disease at the time of diagnosis, recurrent disease after cytoreduction, and minimal response to chemotherapy and radiation therapy (10, 11). The mainstay of treatment for gynecologic sarcoma patients remains optimal cytoreduction and potentially secondary cytoreduction after recurrence (12). Our study as well as others demonstrated that incomplete surgical resection rather than treatment with chemotherapy or radiation predicted disease free survival (5, 12, 13). Thus the importance of complete removal of visible disease in sarcoma patients cannot be understated. As Bansal and colleagues have noted, preoperative imaging may aid in determining whether a patient has unresectable disease, such as pulmonary, hepatic, or high retroperitoneal disease (9).

Small nodules identified on chest CT scans usually reflect metastatic disease and merit close observation with frequent repeat scans, while equivocal liver lesions are less likely to represent metastatic sarcoma and may be followed less often. Chest radiographs may help with the perioperative assessment of sarcoma patients but do not appear to alter cancer treatment plans. We had too few head CT, PET, MRI, or bone scans to draw conclusions about their utility. In an environment of increasingly constrained resources, our finding that imaging infrequently changes management of women with uterine sarcomas despite their relatively poor prognosis suggests that larger databases should be used for a formal cost-benefit assessment of the value of imaging in uterine cancers.

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Table 1

Demographic characteristics of the study population

	N	%
Age		
Median	63	
Range	23–89	
Race		
White	70	77%
African American	20	22%
Other	1	1%
Stage		
I	30	33%
II	7	8%
III	27	29%
IV	28	30%
Histology		
Leiomyosarcoma	25	27%
Carcinosarcoma	48	52%
Endometrial Stromal Sarcoma	10	11%
Sarcoma	4	5%
Other	4	5%
Surgical procedure		
Biopsy	7	8%
TAH +/- BSO +/- OMY	20	22%
Complete staging procedure	45	49%
Extended surgical procedure	20	21%
Chemotherapy received	45	49%
Radiotherapy received		
Pelvic radiation	18	81%
Brachytherapy	10	45%

Table 2

Sites of sarcoma metastasis by imaging modality

Modality	Total performed	Positive for malignancy	Indeterminate for malignancy	Negative for malignancy	Location of disease
Chest X-ray	66	7	3	56	2 pleural effusions 7 lung parenchyma masses
Chest CT	33	7	7	19	3 pleural effusions 13 pulmonary nodules 5 mediastinal lymphadenopathy
Abdomen/Pelvis CT	59	22	7	30	5 liver lesions 3 small bowel/mesentery lesions 4 omental/peritoneal lesions, 11 pelvic lymphadenopathy, 3 kidney lesions 4 bladder/rectum lesions 5 adnexal masses
MRI	2	0	0	2	NA
PET	8	3	2	3	1 pleural effusion 2 pelvic lymphadenopathy 2 periaortic lymphadenopathy
Bone scan	2	0	0	2	NA
Head CT	2	0	0	2	NA

Table 3

Characteristics of patients in who CT findings altered management

Imaging performed	Perioperative Imaging findings	Management	N
CT chest	Multiple lung nodules	Chemotherapy rather than a debulking procedure	1
	Pleural effusion	Thoracentesis positive for malignancy, chemotherapy given	2
	Concerning for metastatic disease prior to debulking surgery for IC disease	Chemotherapy received rather than surveillance	3
CT abdomen and pelvis	Large pelvic disease burden	TAH/BSO performed for palliation, no debulking procedure performed	4
	Large chest and pelvic disease burden	Biopsy rather than surgical procedure performed	5
	Large chest and pelvic disease burden	Chemotherapy and radiation rather than debulking performed	6
	Multiple chest lesions	No cuff radiation was performed, chemotherapy given	7
	Extensive chest and pelvic disease burden	Biopsy and chemotherapy performed rather than aggressive surgical management	8

Table 4

Multivariate analysis of prognostic factors

Prognostic factor	Disease free survival			Overall survival		
	HR	95% CI	P value	HR	95%CI	P value
Histology	1.93	0.55–6.74	0.31	1.46	0.60–3.55	0.40
FIGO stage	1.8	1.2–2.5	0.001	1.8	1.3–2.5	0.001
Surgical resection	6.1	1.8–19.9	0.003	1.83	0.50–2.34	0.83
Imaging	1.33	0.49–3.66	0.58	0.99	0.50–1.99	0.99