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Characterization and preoperative risk analysis of leiomyosarcomas at a high-volume tertiary care center

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Abstract

Introduction—Uterine morcellation in minimally invasive surgery has recently come under scrutiny due to inadvertent dissemination of malignant tissue, including leiomyosarcomas commonly mistaken for fibroids. Identification of preoperative risk factors is crucial to ensure that oncologic care is delivered when suspicion for malignancy is high, while offering minimally invasive hysterectomies to the remaining patients.

Objectives—To characterize risk factors for uterine leiomyosarcomas by reviewing pre-, intra-, and postoperative data with an emphasis on the presence of concurrent fibroids.

Methods—A retrospective case-control study of women undergoing hysterectomy with pathologic diagnosis of uterine leiomyosarcoma at a tertiary care center between 1/2005 and 4/2014.

Results—31 women were identified with leiomyosarcoma and matched to 124 controls. Cases with leiomyosarcoma were more likely to have undergone menopause and to present with larger uteri (19 vs. 9 week sized) with the most common presenting complaint being a pelvic mass (35.5% vs. 8.9%). Controls were ten-times more likely to have undergone a tubal ligation (30.6% vs. 3.2%). Endometrial sampling detected malignancy preoperatively in only 50% of cases. Leiomyosarcomas were more commonly present when pelvic masses were identified in addition to fibroids on preoperative imaging. The majority of leiomyosarcoma cases (77.4%) were performed by oncologists via an abdominal approach (83.9%) with only 2/31 leiomyosarcomas being morcellated. Comparative analysis of preoperative imaging and postoperative pathology showed that in leiomyosarcoma patients, fibroids were misdiagnosed 58.1% of the time, and leiomyosarcomas arose directly from fibroids in only 6.5% of cases.

Conclusions—Leiomyosarcoma risk factors include older age/postmenopausal status, enlarged uteri >10 weeks and lack of prior tubal ligation. Preoperative testing failed to definitively identify

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leiomyosarcomas, although presence of synchronous pelvic masses in fibroid uteri should raise clinical suspicion. Given the difficulty of preoperative identification, future efforts should focus on the development of safer minimally invasive techniques for uterine morcellation.

Keywords

Hysterectomy; Preoperative risk stratification; Leiomyosarcoma; Morcellation

INTRODUCTION

Uterine leiomyosarcoma (LMS) is an aggressive smooth muscle tumor with poorly understood origins and risk factors.[1] Although rare, with a prevalence of only 1/498 to 1/568 in women undergoing hysterectomy, LMS recently gained widespread attention when the FDA issued warnings regarding the use of power morcellation devices to extract uterine specimens.[2] Undiagnosed LMS is of particular concern due to the risks of disseminating cellular debris within the peritoneal cavity resulting in higher recurrence and death rates.[3–9] Despite the clear advantages of minimally invasive hysterectomy over the abdominal approach, which include decreased rates of blood transfusions, venous thromboembolic events, wound infections, hernias and death,[10] this warning has lead to increased restrictions on power morcellation, leaving surgeons searching for ways to identify ‘at risk patients’ preoperatively. However, similarities in clinical presentation have limited our ability to definitively distinguish LMS from benign leiomyomas, despite utilization of tumor marker testing, various imaging modalities and endometrial sampling.[11–15] Previous studies have suggested that increasing age, African American race, and hormone replacement therapy are associated with higher rates of LMS, however, the origin of LMS and its relationship to benign leiomyomas is poorly understood.[16,17] It is now believed that only a minority of LMS cases arise in the background of fibroids, yet we lack adequate preoperative risk stratification and testing to reliably distinguish LMS from fibroids prior to hysterectomy.[18,19]

This case-control study aims to define pre-, intra-, and postoperative characteristics of LMS encountered at our tertiary academic institution over a 9-year time period compared to controls. Identification of LMS-associated characteristics may assist in risk stratification that would allow for safe, selective use of uterine morcellation in patients undergoing minimally invasive hysterectomies.

MATERIALS AND METHODS

A retrospective case-control chart review was performed of all patients diagnosed with LMS at Magee-Womens Hospital of UPMC between January 2005 and April 2014. Cases were identified through the pathology database and included only patients with a diagnosis of uterine LMS undergoing primary surgical management. Exclusion criteria included recurrent LMS, LMS of alternate soft tissue (not uterine primary) or surgery performance at another institution. LMS cases were temporally matched in a standard statistical 1:4 ratio to control subjects consisting of the next four hysterectomies performed for any indication to ensure a diverse range of hysterectomies for comparison. Controls were purposefully not matched by

any other criteria in order to capture the broadest constellation of pre-operative presentation and testing, as well as concurrent pathology for comparison to LMS cases.

Chart reviews extracted pre-, intra- and postoperative data. Preoperative information included age at time of surgery, gravity, parity, race, body mass index (BMI), tobacco use, menopausal status, history of hormone replacement therapy (HRT), tamoxifen use, cancer, chemotherapy, radiation, and prior pelvic surgery. Additionally, we collected data on presenting symptoms, LDH serum values, imaging findings, endometrial sampling and uterine size on physical examination. Operative information consisted of route of hysterectomy, specialty of primary surgeon, intraoperative consultations, length of surgery, estimated blood loss (EBL), performance of morcellation, and intraoperative complications. Lastly, the pathology details were abstracted.

The University of Pittsburgh Institutional Review Board approved this study.

Statistical Methods

Descriptive statistics are reported for both patient cohorts. Continuous variables are presented as means and standard deviations. Categorical variables are presented as percentages. For comparisons between cases and controls, the nonparametric Mann-Whitney U test was used for all continuous variables due to small group sizes, and the chi-squared or Fisher's exact test (as appropriate) were used for categorical variables. SPSS Statistics, Version 22.0, Armonk, NY:IBM Corp. was used for all analyses. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Out of 9,378 hysterectomies performed at Magee-Womens Hospital between January 2005 and April 2014, 31 patients with pathology-confirmed LMS met criteria. 124 controls were identified as described above for comparative analysis.

Population demographics were consistent among cases and controls with the exception of age and menopausal status; LMS cases were older and more likely to be postmenopausal (Table 1A). No other differences were identified between the groups in BMI, gravity, parity, tobacco use, race, hormone replacement therapy (HRT), tamoxifen use, or history of cancer, chemotherapy and pelvic radiation. Previous surgical history was remarkable for 30.6% of controls having undergone a bilateral tubal ligation (BTL) compared to only 3.2% of LMS cases (p=0.002) (Table 1B).

The primary presenting complaints in LMS cases included pelvic mass, abnormal uterine bleeding (AUB) and abdominal/pelvic pain (Table 2). Controls were more likely to report pelvic organ prolapse (POP) with no LMS cases presenting with prolapse.

51.6% of LMS patients had preoperative endometrial sampling (vs. 50.8% in controls, p=0.560) (Table 3). Of the 15 patients with sufficient endometrial sampling, 7 patients (46.7%) had pathology consistent with malignancy, of which 5 had either a preoperative sarcoma or LMS diagnosis. Only 14.3% of controls had malignancy on endometrial sampling (p=0.005). Uterine size on physical examination was significantly larger in LMS

(mean 19.0 vs. 9.2 weeks gestation, p<0.001). Small numbers of both case and control patients had lactate dehydrogenase (LDH) serum testing with no difference in percent of patients with abnormal values (48.4% vs. 31.3%, p=0.473).

All LMS patients (n=31) had preoperative imaging compared to 76.6% of control subjects (n=95) (Table 4A). Imaging modalities included transvaginal ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), or others (PET, abdominal or retroperitoneal ultrasound). Controls were less likely to have had multiple imaging modalities (23.4% vs 48.2%; p<0.001). Fibroids were documented on preoperative imaging (any type) in 51.6% of LMS and 46.3% of controls with no difference in the number of fibroid present per uterus (p=0.608). However, generalized adnexal, pelvic or uterine masses other than fibroids were detected in 25.8% of LMS vs. 8.4 % of control patients (p=0.004) (Table 4B). There were no differences in these additional imaging findings when no concurrent fibroids were identified. However, in the presence of fibroids, these concurrent pathologies were solely recognized in the LMS group (p<0.001).

Operative details are summarized in Table 5. The most common surgical route in LMS cases was via abdominal hysterectomy (83.9%) with the rest being performed either laparoscopically (12.9%) or vaginally (3.2%) (p<0.001). Controls had 62.9% of hysterectomies performed minimally invasively while 37.1% were performed via an abdominal approach. 77.4% of LMS cases were performed by a gynecologic oncologist with referral prompted primarily by preoperative diagnosis of malignancy or concerning imaging findings. Intra- and preoperative consultation with an oncologist occurred in an additional six patients leaving only one patient who was solely managed by a general gynecologist. Controls had less intraoperative consultations (General Surgery (n=2), Urology (n=1); p=0.002) and had 3 planned joint cases with plastic surgery and maternal fetal medicine. Lower urinary tract injuries were the most common complication (n=3) in LMS cases while hemorrhage/transfusion was more common in the control group (n=4), even though estimated blood loss was significantly higher in LMS cases (828 mL) than controls (253 mL) (p<0.001). No difference in operative time was observed. With regard to specimen retrieval, only two of the 31 LMS cases were morcellated compared to 24 controls (p=0.083). One LMS was vaginally morcellated at the time of the vaginal hysterectomy, and the second was power morcellated at the time of the laparoscopic supra-cervical hysterectomy. Uterine weight was significantly greater in LMS cases (1833g vs. 234g, p<0.001).

Postoperative pathology examination revealed that nearly all LMS patients (96.8%) had other reported pathology on the final specimen other than fibroids (Supplemental Table 1). However, no differences were noted between cases and controls in rates of endometriosis and cervico-, tubo- or ovarian pathology. Controls were more likely to have adenomyosis (41.9% vs. 19.4%, p=0.020), while LMS patients had increased numbers of endometrial polyps (32.3% vs. 14.5%, p=0.022). Interestingly, one LMS was reported to be arising from a polyp with only superficial endometrial involvement.

Given that LMS has also been proposed to arise from fibroids, we performed subgroup analyses on these cases. Only 12 LMS (38.7%) vs. 44 control (46.3%) patients had benign

leiomyomas reported on their pathology, and only two pathology reports specifically commented that the LMS was arising from a leiomyoma (6.5% of all cases). Moreover, as LMS are frequently misidentified preoperatively for benign fibroids (and vice versa), we performed further correlative studies comparing preoperative imaging vs. postoperative pathological examination to assess the accuracy of fibroid detection in the presence and absence of LMS (Table 6). 37 out of 44 control patients (84.1%) who had fibroids on imaging had correlative fibroids on final pathology, in contrast to LMS cases where correlation was noted only in 5 out of 16 subjects (31.3%) ($p<0.001$) (Table 6A). Overall discordance between imaging and pathology for the presence or absence of fibroids was observed in 58.1% (n=18/31) of LMS cases in contrast to only 24.5% (n=23/94) of controls ($p<0.001$). While there was no statistical difference in the absolute presence or absence of fibroids between cases and controls on imaging or final pathology, in LMS cases, mean maximum fibroid size was significantly larger on preoperative imaging than on postoperative pathology (Table 6B). However, when adjusted for the preoperatively misdiagnosed fibroids in LMS, which in the majority of LMS uteri represented a single fibroid, this trend was no longer statistically different (Table 6C).

DISCUSSION

Our review identifies and matches 31 cases of pathology-confirmed uterine LMS to control hysterectomies over the course of nine years at our institution. In this time frame, 9,378 hysterectomies were performed translating to an incidence of 1/303 (0.3%), which is consistent with published rates.[2] Only two of the 31 LMS cases were inadvertently morcellated. This is comparable with the rate of morcellated LMS in other recent studies.[20–22] It is important to differentiate the risk of LMS from the risk of inadvertent morcellation of LMS. In our series, the rate of LMS in patients undergoing hysterectomy was 31/9378 (0.3%) whereas the risk of inadvertently morcellating LMS was 2/9378 (0.02%). With appropriate patient selection, the risk of morcellating occult LMS appears to be quite low.

With recently implemented restrictions on power morcellation, redirecting focus toward identification of risk factors associated with LMS has become the key in continuing to safely offer patients minimally invasive hysterectomies. Patient demographics of increasing age and postmenopausal status did appear to be risk factors as suggested by previous authors.[16,23] African-American race has been associated with increased rates of LMS; however, this was not demonstrated in our series.[16,23] Previous studies have demonstrated that prior radiotherapy does not appear to be a risk factor for LMS (unlike typical sarcomas), which is supported by our cohort in which no patients had a history of pelvic radiation.[24,25] Hormone replacement therapy (HRT) was not shown in the Women's Health Initiative to increase rates of non-endometrial uterine cancers and indeed, no statistical difference was noted in our case series.[17]

Interestingly, in contrast to controls who underwent BTL near national rates, only one out of 31 women in the LMS group (3.2%) had a BTL.[26] Salpingectomy and BTL have been documented to decrease the odds of ovarian/fallopian tube cancer as well as reduce mortality in high-grade endometrial cancer.[27,28] Additional studies may support opportunistic

salpingectomies as LMS risk reducing strategy at the time of permanent sterilization or other adnexal surgeries.

Although no definitive presenting complaint identified LMS, a higher trend towards pelvic masses and AUB raised clinical suspicion, while those with POP lowered it. No cases of LMS in 1,196 women undergoing hysterectomy with concurrent POP procedures were noted at our institution. Although still at risk for other incidentally encountered non-LMS cancers (0.25%), patients undergoing urogynecologic procedures appear to represent an extremely low-risk cohort that would benefit from morcellation given higher medical comorbidities observed in this usually older patient population.[29]

To improve preoperative diagnosis of LMS a variety of testing strategies have been evaluated. Combination of LDH levels and dynamic MRI with apparent diffusion coefficient (ADC) value carry sensitivities and specificities of 94–100% in differentiating LMS from benign leiomyoma.[12,13] However, this is only useful in cases where clinical suspicion for LMS is already high with limited universal application for general preoperative screening. This is apparent in our series in which LDH values did not differ significantly between the two groups, and only a small fraction of LMS patients underwent MRI imaging. Similarly, little success has been demonstrated with endometrial sampling to detect LMS as would be expected unless the tumor had reached the endometrial surface.[14,15] In our cohort, when sufficient endometrial sampling was performed, 46.7% were positive for malignancy, leaving 53.3% of patients with unrecognized high-grade malignancy prior to hysterectomy. We hypothesized that larger tumor size and presence of LVSI might increase the likelihood of positivity on endometrial sampling; however, this was unable to be demonstrated on further sub-analysis (data not shown). Hence negative endometrial sampling should not be a reassuring feature for preoperative risk stratification of candidates considered for uterine morcellation. Furthermore, although LMS cases had larger uteri on pelvic exam (and pathological examination), large standard deviations suggest overlap with control uterine sizes. However, it should be noted that no LMS cases were observed in hysterectomies performed in uteri less than 10 weeks gestation. This is particularly important for women undergoing supracervical procedures in which uterine morcellation may be required for tissue extraction.

Despite having similar clinical presentations and tissue derivations, prior molecular studies have demonstrated stark differences in biomarker and microRNA expression that suggest that leiomyoma and LMS have separate origins or at least alternate transformation pathways.[31,32] In our present study, only 6.5% of LMS cases appeared to be arising within a benign leiomyoma and only 38.7% of patients had concomitant benign fibroids. These rates are low, which is consistent with other small studies that suggest LMS rarely arises within benign leiomyomas.[18] Yet, these two discrete entities continue to be midsdiagnosed preoperatively. This discrepancy is likely largely fueled by the lack of imaging modalities to reliably differentiate these pathologies, as demonstrated in our series where 35.5% of preoperatively identified “fibroids” in LMS uteri likely represent malignancy. Furthermore, the size of the preoperatively misidentified fibroid did not differ significantly from those that were labeled correctly, hence further supporting this notion. Interestingly, a trend towards diagnosis of LMS was noted in those patients diagnosed with fibroids who also had

synchronous adnexal, pelvic, or uterine masses. This finding may assist in preoperative risk stratification to avoid minimally invasive surgical approaches in patients with these imaging presentations.

Furthermore, we tried to establish additional trends from postoperative pathological examination. Although the majority of patients had other associated pathology on the final specimen, we were unable to identify a concomitant pelvic pathology consistently associated with LMS alone. However, 32.2% of LMS uteri had endometrial polyps, a rate much higher than controls (14.5%), and interestingly one LMS arose directly from a polyp. Similarly, approximately one-third of LMS patients had expression of estrogen and progesterone receptors (37.5% and 31.3% respectively) in their tumor (data not shown), suggesting a potential role of these hormones in the pathogenesis of LMS.

Weaknesses of this study are those inherent to a retrospective chart review, including missing or illegible data leading to limited datasets for some parameters, and/or errors in data collection. For this reason, pre-study power analysis was also impossible to assess leading to the standardized 1:4 case-control match we chose for this hypothesis generating retrospective study. Furthermore, given the nature of a retrospective review, there was a lack of standardized pre-operative testing (LDH, endometrial sampling, type of imaging modality) which somewhat limits generalizations about the current testing strategies. In light of this, we purposefully did not match controls to LMS cases by criteria other than time to account for surgical practices, while avoiding missing risk factors that may help distinguish these two groups preoperatively. In particular, case-control matching based on criteria such as fibroids or uterine size would have meant that we could not evaluate these variables as risk factors for LMS and would have represented a skewed patient population for other variables. Strengths of the study include its large sample size and case-control nature, as well as an array of preoperative testing, which allowed us to identify numerous preoperative risk factors. In addition, we highlighted an important discrepancy in the imaging findings of LMS cases commonly mistaken for fibroids. We demonstrate that fibroids are misidentified in nearly two-third of LMS cases, and only rarely give rise to LMS.

In summary, given the current lack of definitive preoperative risk stratification to diagnose or differentiate LMS from benign leiomyomas, physicians need to counsel their patients on the potential risks of uterine morcellation if desiring to undergo minimally invasive surgery. Additionally, with better pre-operative risk assessment, these candidates electing for morcellation can be more suitably chosen in an attempt to further minimize risk of malignant dissemination. Future efforts should also be directed towards delineating safer methods for contained uterine morcellation for those patients electing to undergo minimally invasive hysterectomies. Until these techniques have been perfected, suspicious cases should be performed via abdominal hysterectomy by or under consultation of a gynecologic oncologist, and uterine morcellation should be discouraged.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Preoperative Demographics

A. Description of patient characteristics in leiomyosarcoma vs. control subjects.
B. Description of past surgical history in leiomyosarcoma vs. control subjects.

A			
Characteristics	**LMS (n=31)**	**Control (n=124)**	**p-Value**
Age (years)	55.2	49.2	0.011
BMI (kg/m^2)	32.2	30.7	0.474
Gravity	2.3	2.5	0.265
Parity	1.9	1.9	0.617
Tobacco Use			0.206
Yes	7.1% (n=2)	20.2% (n=25)	
Former	21.4% (n=6)	14.5% (n=18)	
No	71.4% (n=20)	65.3% (n=81)	
Race			0.140
Caucasian	80.6% (n=25)	80.6% (n=100)	
African American	12.9% (n=4)	18.5% (n=23)	
Asian	6.5% (n=2)	0.8% (n=1)	
Menopause			0.006
Unknown	3.2% (n=1)	1.6% (n=2)	
Pre-menopausal	38.7 (n=12)	66.1% (n=82)	
Postmenopausal	58.1% (n=18)	32.3% (n=40)	
HRT Use	29.4% (n=5/17)	13.2% (n=5/38)	0.255
Tamoxifen Use	3.2% (n=1)	3.3% (n=4)	1.000
H/o any Cancer	6.5% (n=2)	9.7% (n=12)	0.737
H/o Chemotherapy	0% (n=0)	2.5% (n=3)	1.000
H/o Pelvic Radiation	0% (n=0)	0.8% (n=1)	1.000

B			
Prior Surgeries	**LMS (n=31)**	**Control (n=124)**	**p-Value**
Tubal			
BTL	3.2% (n=1)	30.6% (n=38)	0.002
Cannalization	0.0% (n=0)	0.8% (n=1)	1.000
Salpingectomy	3.2% (n=1)	2.4% (n=3)	1.000
Uterine			
Intracavitary			
D&C, D&E, Hysteroscopy	16.1% (n=5)	30.6% (n=38)	0.106
Endometrial Ablation	6.5% (n=2)	12.1% (n=15)	0.527
Extracavitary			
Cesarean Section	16.1% (n=5)	19.4% (n=24)	0.680

B

Prior Surgeries	LMS (n=31)	Control (n=124)	p-Value
Myomectomy	3.2% (n=1)	4.8% (n=6)	1.000
Uterine Artery Embolization	3.2% (n=1)	0.8% (n=1)	0.361
Ovarian			
Cystectomy	0.0% (n=0)	7.3% (n=9)	0.206
Oophorectomy	3.2% (n=1)	2.4% (n=3)	1.000
Cervical (LEEP, CKC)	3.2% (n=1)	9.7% (n=12)	0.467
Diag. Laparosocpy	0.0% (n=0)	4.8% (n=6)	0.600
Endometriosis Excision	0.0% (n=0)	4.0 % (n=5)	0.584
Bowel (Appendectomy, Small Bowel)	3.2% (n=1)	13.7% (n=17)	0.126
Vulvar/Vaginal	0.0% (n=0)	1.6% (n=2)	1.000

(n)=Number of subjects.

Table 2

Preoperative Patient Presentation

Symptoms experienced in leiomyosarcoma vs. control subjects experienced at the time of hysterectomy.

Symptoms	LMS (n=31)	Control (n=124)	p-Value
Pelvic Mass	35.5% (n=11)	8.9% (n=11)	0.001
Prolapse	0.0% (n=0)	18.5% (n=23)	0.008
AUB	32.3% (n=10)	51.6% (n=64)	0.054
PMB	9.7% (n=3)	11.3% (n=14)	1.000
Pain	32.3% (n=10)	38.7% (n=48)	0.507
Pelvic Pressure	6.5% (n=2)	8.9% (n=11)	1.000
Urinary	6.5% (n=2)	10.5% (n=13)	0.737
Gastrointestinal	3.2% (n=1)	4.8% (n-6)	1.000
Anemia	6.5% (n=2)	9.7% (n=12)	0.737
Other	25.8% (n=8)	21.0% (n=26)	0.560

(AUB=Abnormal uterine bleeding, PMB=postmenopausal bleeding, Other=back pain, pulmonary embolism, syncope, abnormal imaging, weight gain, pelvic infection).

(n)=Number of subjects.

Table 3

Preoperative Evaluation

Description of preoperative laboratory, pathology, and physical examination testing in leiomyosarcoma vs. control subjects.

Test	LMS	Control	p-Value
LDH	n=15/31	n=16/124	
Abnormal	46.7% (n=7)	31.3% (n=5)	0.473
Mean Value	217.0 +/− 23.6	222.5 +/− 30.0	0.861
95% CI	166.3 – 267.7	158.3 – 286.2	
Endometrial Sampling	n=16/31	n=63/124	0.560
EMB	29.0% (n=9)	31.5% (n=39)	
D&C	22.6% (n=7)	29.0% (n=22)	
Both	0.0% (n=0)	1.6% (n=2)	
Malignancy	46.7% (n=7/15)	14.3% (n=9/63)	0.005
Uterine Size (weeks)			
Mean	19.0 +/− 8.4	9.2 +/− 4.7	<0.001
95% CI	15.8 – 22.2	8.4 – 10.1	

(n)=Number of subjects with applicable testing performed.

n = number of patients per group who had testing performed

Table 4

Preoperative Imaging

Description of preoperative imaging including number and types of imaging modalities, as well as presence of benign leiomyomas and coexisting other pathology in leiomyosarcoma vs. control subjects.

A

Imaging Testor Finding	LMS (n=31)	Control (n=124)	p-Value
#of Patients with Imaging	N=31	N=95	
# of Modalities			<0.001
0	0.0% (n=0)	23.4% (n=29)	
1	51.6% (n=16)	53.2% (n=66)	
2	45.2% (n=14)	22.6% (n=28)	
3	3.2% (n=1)	0.8% (n=1)	
Ultrasound	64.5% (n=20)	68.5% (n=85)	0.668
CT	67.7% (n=21)	24.2% (n=30)	<0.001
MRI	16.1% (n=5)	5.6% (n=7)	0.065
Other	3.2% (n=1)	1.6% (n=2)	0.491
Fibroids			
Presence	51.6% (n=16)	46.3% (n=44)	0.608
Number			
1	62.5% (n=10)	31.8% (n=14)	
2	6.25% (n=1)	22.7% (n=10)	
3	6.25% (n=1)	6.8% (n=3)	
4	0.0% (n=0)	9.09 (n=4)	
5	0.0% (n=0)	4.5% (n=2)	
>5	6.25% (n=0)	13.6% (n=6)	
Not specified	18.75% (n=3)	11.4% (n=5)	

B

Other Imaging Pathology	LMS (n=31)	Control (n=95)	p-Value
----------	8	44	0.058
+Fibroids			
+Adx Mass	2	0	0.059
+Fibroids			
+Uterine Mass	2	0	0.059
+Fibroids			
+Pelvic Mass	3	0	0.014
+Fibroids			
----------	15	43	0.837
−Fibroids			
+Uterine Mass	1	4	1.000
−Fibroids			

B

Other Imaging Pathology	LMS (n=31)	Control (n=95)	p-Value
+Adx Mass	0	4	0.571
−Fibroids			

(n)=Number of subjects with imaging.

Table 5

Intra-operative Analysis

Description of operative details including surgeon and surgery type, consultations, complications, estimated blood loss (EBL), operative room (OR) time, specimen weight and use of morcellation in leiomyosarcoma vs. control subjects.

	LMS (n=31)	Control (n=124)	P-Value
Surgery Type			<0.001
Abdominal	83.9% (n=26)	37.1% (n=46)	
Laparoscopic	12.9% (n=4)	40.3% (n=50)	
Vaginal	3.2% (n=1)	22.6% (n=28)	
Surgeon			<0.001
Benign Gyn	22.6% (n=7)	77.4% (n=96)	
Gyn Onc	77.4% (n=24)	22.6% (n=28)	
Consultations			0.005
Intraop	12.9% (n=4)	4.1% (n=5)	
Gyn Onc Back-up	6.5% (n=2)	0.0% (n=0)	
Intra-operative Complications	16.1% (n=5)	8.9% (n=11)	0.319
EBL			<0.001
Mean +/− SD (mL)	828.3 +/− 134.3	252.8 +/− 26.4	
OR Time			0.544
Mean +/− SD (min)	170.3 +/− 88.8	150.85 +/− 61.3	
Uterine +/−Adnexal Weight	n=31	n=124	<0.001
Mean +/− SD (grams)	1833.8 +/− 411.3	234.0 +/− 24.2	
Morcellation	6.5% (n=2)	19.5% (n=24)	0.083

(n)=Number of subjects.

Table 6

Pre/Post-operative Analysis

A. Analysis of presence, number, and maximum sized fibroid on preoperative imaging compared to postoperative pathological examination in leiomyosarcoma vs. control subjects.

B. Correlative analysis between preoperative (Imaging) vs. postoperative (pathology) detection of fibroids in leiomyosarcoma vs. control subjects.

A

Analysis	+Pathology	−Pathology	−Pathology	+Pathology	p-Value
Subjects	**+Imaging**	**−Imaging**	**+Imaging**	**−Imaging**	
LMS (n=31)	16.1% (n=5)	25.8% (n=8)	35.5% (n=11)	22.6% (n=7)	<0.001
Control (n=94)	39.4% (n=37)	36.2% (n=34)	7.4% (n=7)	17.0% (n=16)	

B

	LMS	Control	p-Value
Pre-operative: Imaging	n=31	n=95	
Fibroid Presence	51.6% (n=16)	46.3% (n=44)	0.608
Max Fibroid Size	n=14/16 *	n=40/44	
Mean +/− SD (cm)	8.8 +/− 4.3	4.7 +/− 2.7	<0.001
Post-operative: Pathology	n=31	n=123	
Fibroid Presence	38.7% (n=12)	54.5% (n=67)	0.117
Max Fibroid Size	n=11/12 *	n=55/67 *	
Mean +/− SD (cm)	4.6 +/− 3.7	3.6 +/− 2.9	0.474

C	LMS	Control	p-Value
+Pathology / +Imaging	n=4/5 * 8.0 +/− 3.4 cm	n=27/37 * 4.8 +/− 3.2 cm	0.062
+Pathology / −Imaging	n=7/7 2.7 +/− 2.1 cm	n=14/16 * 2.2 +/− 1.3 cm	0.913
−Pathology / +Imaging	n=10/11 * 9.1 +/− 4.5 cm	n=5/7 * 3.1 +/− 2.2 cm	0.008

(n)=Number of subjects with imaging and intact pathology specimen available for review (i.e. unmeasured fibroids or morcellated specimen excluded for size measurements)

(n)=Number of subjects with imaging. Analysis of maximum sized fibroid depending on correspondence or discrepancy between preoperative (imaging) and postoperative (pathology) detection of fibroids in leiomyosarcoma vs. control subjects. (n)=Number of subjects with available date/ total number of subjects.

* Numerator reflects number of patient with fibroids measured/available for analysis