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Review Article

Outcome and Management of Uterine Leiomyosarcoma Treated Following Surgery for Presumed Benign Disease: Review of Literature

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Abstract

Uterine leiomyosarcoma (uLMS) is a rare and aggressive cancer, usually diagnosed incidentally at the time of myomectomy or hysterectomy. There have been concerns for several years about the fact that the inadvertent disruption of occult uLMS may have a negative impact on patient outcome. This study reviews the outcome and management of patients with a diagnosis of uLMS after surgery for presumed benign disease. We conducted a literature search in which 47 published English-language articles were obtained for evaluation. A total of 23 studies with outcomes data were included. It is evidenced that patients who underwent surgery with tumor disruption resulted in poorer outcomes compared with *en bloc* tumor, especially by power morcellation. The power morcellation was associated with an increased risk of recurrence, shorten time to recurrence, and upstage after re-exploration. Early re-exploration and surgical staging are appreciated for better prognosis and may alter postoperative treatment. We also updated on the incidence and preoperative evaluation to assess the risk of patient and give an effective counseling.

Keywords: Hysterectomy, myomectomy, occult leiomyosarcoma, prognosis

Introduction

Leiomyoma is the most common type of pelvic tumor in women, with an approximately 70%–80% lifetime risk. Surgery is the mainstay of therapy for leiomyoma. The route of surgery can be performed by traditional laparotomy, vaginally or minimally invasive surgery (MIS). MIS is more common and its advantage compared to laparotomy has been well documented. It is associated with less postoperative pain, lower postoperative fever, and shorter hospital stay.[1] The ability to offer less invasive surgery often requires the removal of large tissue specimens through a small incision. It may be facilitated by either manual or electromechanically assisted morcellation. The morcellation should only be considered in women with low risk for gynecologic malignancy. Unexpected uterine sarcoma treated by surgery involving tumor disruption is associated with worse prognosis.[2]

Uterine leiomyosarcoma (uLMS) is a rare and aggressive cancer, encompassing 1% of all female genital tract malignancies.[3] Distinguishing uLMS from leiomyoma preoperatively is very difficult, and it is often diagnosed at the time of surgery. It is unclear and remains elusive that inadvertent disseminated occult uLMS in patients undergoing myomectomy may increase the risk of recurrence and disease-related mortality compared with women whose tumors were removed intact. A review of the outcome of occult uLMS after surgery for presumed fibroid in 2015 concluded that it is difficult to establish conclusion because of the small numbers of patients and heterogeneity of studies. In addition, whether power morcellation posed a danger to the patient is still questioned.[4] In the recent years, there are a number of studies published about the occult uLMS patients. We have

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collected a large number of patients in the similar conditions and reviewed more updated studies to clarify the outcome and to provide further guidance for optimal management.

Materials and Methods

We included studies those provided incidence and outcome data of patients with a diagnosis of occult LMS after surgery for presumed benign disease. The patients had undergone either total hysterectomy, subtotal hysterectomy, or myomectomy. Such outcomes included the evidence of recurrence and survival.

A broad-ranging search was undertaking on the PubMed and Cochrane database in the English language without time restriction. The search strategy used various combinations of the following keywords "hysterectomy," "myomectomy," "laparoscopy," "hysteroscopy," "inadvertent," "leiomyoma," "myoma," "leiomyosarcoma," "morcellation," "management," "outcome," "recurrence," and "survival." Based on keywords, 47 articles were evaluated thoroughly, and 23 with outcomes data were included. References from articles were further reviewed. Pertinent articles and reviews were used for the discussion.

Result and Discussion

The incidence of occult uterine leiomyosarcoma in presumed fibroid

The US Food and Drug Administration (FDA) published a total incidence of uterine sarcoma of 0.28% (1/352 cases) and uLMS of 0.20% (1/498 cases) based on nine studies of women undergoing hysterectomy or myomectomy for presumed benign leiomyoma.[5] We reviewed the recent data on the prevalence of occult sarcoma and focused on uLMS in presumed benign gynecological condition. In a total of 16 studies, 13 studies were retrospective case series in a single institution, one study was case report series, and two studies were meta-analysis studies.[6-21] All of the studies were conducted in the last 2 years with long study period. Eleven of the 16 studies had the population of over 1000 patients. The incidence of occult uterine sarcoma and uLMS varies from 0.06% to 1.4% and 0.05% to 0.4%, respectively [Table 1]. This review suggests that uLMS in women undergoing surgery for presumed benign disease is very rare. The incidence from several large studies is lower than quoted by the FDA.[4,7-9,13-15,20]

Preoperative evaluation

Risk factor and clinical presentation

Risk factors for uLMS are less well defined. In a recent retrospective study, Peters *et al*. reported that uLMS patients were more likely to be at old age or postmenopausal, presenting with a pelvic mass >10-week size and lacking of previous tubal ligation.[22] The rapidly growing leiomyoma does not substantiate the concept of increased risk of sarcoma.[23] Clinical manifestations are not useful to distinguish between leiomyomas and uterine sarcomas since both typically present with abnormal uterine bleeding, pelvic pain, pelvic pressure, and pelvic mass.

Imaging

There is no imaging modality that can differentiate uLMS from leiomyoma. Both conditions may potentially have similar imaging findings. Pelvic ultrasound is the first-line study to evaluate women with a pelvic mass. Sonographic features suggestive of sarcoma can appear as large, heterogeneous masses containing area with poor echogenicity central necrosis. Color Doppler findings show irregular vessel distribution, low impedance to flow, and high peak systolic velocity.[24] Magnetic resonance imaging (MRI) is helpful in women with suspicion of cancer. LMS typically demonstrates hyperintensity

Table 1: Incidence of occult uterine sarcoma and uterine leiomyosarcoma after surgery presumed uterine fibroid

Author	Year published	Study period	Number of patients	Number of uterine sarcoma	Uterine sarcoma rate	Number of uLMS (cases)	uLMS rate
Pritts *et al*.[6]	2015	1990-2014	NR	NR	NR	1 in 1960	0.051
Brohl *et al*.[7]	2015	1980-2014	-	6/2075	0.28	18/10,120	0.17
Bojahr *et al*.[8]	2015	1998-2014	10,731	6	0.06	2	0.02
Lieng *et al*.[9]	2015	2000-2013	4791	NR	NR	6	0.13
Cormio *et al*.[10]	2015	2000-2010	588	NR	NR	3	0.5
Tan-Kim *et al*.[11]	2015	2001-2012	941	6	0.6	3	0.3
Paul *et al*.[13]	2016	2004-2014	2678	8	0.29	5	0.17
Graebe *et al*.[12]	2015	2005-2014	1361	4	0.29	3	0.22
Zhang *et al*.[14]	2016	2009-2013	3021	18	0.6	5	0.17
Tan *et al*.[16]	2015	2009-2015	734	2	0.27	2	0.27
Rodriguez *et al*.[15]	2016	2002-2011	13,964	NR	NR	NR	0.13
Gao *et al*.[17]	2016	2005-2014	3986	59	1.4	17	0.4
Chin *et al*.[21]	2016	2004-2013	3013	3	0.1	2	0.06
Raine-Bennett *et al*.[18]	2016	2006-2013	34,728	125	0.36	81/34,706	0.23
Lee *et al*.[19]	2016	2006-2014	NR	45	NR	18	NR
Mettler *et al*.[20]	2017	2003-2015	2269	6	0.26	4	0.17

NR: Not reported, uLMS: Uterine leiomyosarcoma

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signal with fine granular appearance in T2-weighted or both T1/T2-weighted images. Irregular contours and areas of hemorrhage and necrosis are also observed. Nonetheless, benign leiomyomas with degeneration also share these findings.[25] In addition to morphological features, diffusion-weighted imaging and quantitative measurement of apparent diffusion coefficient values have a potential ability to differentiate the uterine sarcoma from benign leiomyoma.[26] Further studies evaluating role of MRI for this purpose are required.

Despite similar appearance to fibroids observed from ultrasonography or MRI, a >8 cm large, solitary, oval-shaped, highly vascularized (peripheral and central), and heterogeneous myometrial tumor with central necrosis, degenerative cystic changes, and absence of calcifications should warrant the suspicion of LMS.[27]

Computed tomography is ineffective in differentiating between leiomyoma and LMS.[24] Positron emission tomography (PET) with fluorodeoxyglucose (FDG) does not appear to be useful. Several reports of degenerating leiomyomas demonstrated an increased uptake in the FDG-PET scan as well as in uLMS. Furthermore, the FDG activity seems to be increase during the menstrual and ovulatory phases, increasing the risk of false-positive cases by FDG-PET alone.[28]

Tissue sampling

LMSs predominantly grow inside the myometrium and often do not reach the surface of the endometrial cavity. The predictive value of a negative biopsy is expectedly low because uLMS contains large areas of necrosis.[27] From previous studies, the histological diagnosis from endometrial sampling was only 37%–64% correct.[29,30]

Serum marker

There was a significant overlap in preoperative serum CA125 concentrations between the uterine leiomyoma and early-stage uLMS in which it limits the clinical use.[31] Goto *et al*. found that the combined use of dynamic MRI and serum measurement of LDH was useful in making a differential diagnosis of uLMS from degenerating leiomyomas.[25]

Outcome

The impact of morcellation on recurrent rate and survival

Most of the studies in this review are retrospective studies which compared between two divided groups according to the type of tissue removal. Some studies compared between nonmorcellation (*en bloc* uterine removal) and fragmentation (power or hand morcellation and tumor injury). The others compared between power and nonpower morcellation.

There were 40 patients from 14 studies in power morcellation group and 24 patients from seven studies in nonpower morcellation group. The characteristics of these patients were shown in Tables 2 and 3. When comparing between two groups, the tumor size and uterine weight in power morcellation group were similar to nonpower morcellation group (6.14 cm, 427 g and 6.4 cm, 585.5 g). After re-exploration was performed, 33% of patients of power morcellation group were in stage III, whereas there were only 7% in nonpower morcellation. The recurrent rates were high in both two groups. There was a minimal difference in total recurrence rate (58% and 55.5%) while the abdominal recurrence rate was much higher in power morcellation group (100% and 29%). Regarding the nonpower morcellation group, the intra-abdominal recurrence occurred more commonly in patients who had tumor injury during hand morcellation than one who morcellation had not been performed (33% vs. 25%). The mortality rate in the power morcellation group was also higher than the nonpower morcellation (27.5% vs. 14.9%). Nonetheless, it is very difficult to draw a definite conclusion due to a retrospective nature and heterogeneity among all studies.

Table 4 shows the survival outcome of patients with *en bloc* and morcellation tissue removal (either power/hand morcellation or tumor injury). These studies revealed that tumor injury during surgery increased the rate of abdominal disseminated and adversely affected disease-free survival and overall survival (OS) in patients with apparently early uLMS. This result was not consistent with some studies.[17,41] Gao *et al*. concluded that fibroid morcellation during laparoscopic surgery had no significant impact on recurrence-free survival and OS.[17] However, the study included patients with other types of uterine sarcoma (endometrial stromal sarcoma and malignant mixed Müllerian tumor); therefore, it might not represent the real outcome of the uLMS patient. Another study conducted by Lin *et al*. revealed that morcellation does not seem to be associated with a worse prognosis.[41] This study included only patients in stage I who tend to have a good prognosis. Compared to the other studies in Table 4, the number of patients in morcellation group of both studies (Lin's and Gao's) was less and thus did not have enough statistical power to demonstrate a significant difference. Due to the aggressive nature of uLMS, some studies reported that the recurrence rates and survival outcomes are poor even in the setting of early disease and uterus removed intact (recurrent rate 71%, mortality rate 40%).[17,18] The result of this review provides some evidence that patients who underwent power morcellation had a worse prognosis. The power morcellation is associated with an increased risk of recurrence, shorten time to recurrence, and a marked increased risk of peritoneal recurrence when compared to uLMS removed by nonpower morcellation or *en bloc* removal in the first surgery. It is obvious that power morcellation devices should not be used to remove uterine masses with potential malignancy.

No study compared the outcome directly between manual morcellation and *en bloc* removal. Balgobin *et al*. determined the safety of manual vaginal morcellation and concluded that it is safe with a low risk of incidental malignancy.[42] Any type of morcellation might results in spreading of tissue through

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Table 2: Characteristics of patients with power morcellated uterine leiomyosarcoma (40 patients from 14 studies)

Author	*n*	Initial operation	Tumor size (cm)	Uterine weight (g)	Re-exploration surgery	Final stage	Adjuvant	Recurrence	Site of recurrence	RFS (mon)	Follow-up time (month)	Final status
Tan-Kim *et al.*, 2015[11]	1	LSH BSO	5	285	Y: Trachelectomy	I	N	NR	-	-	31	NED
	2	LSH	NR	486	Y: BSO, resection of abdominopelvic mass	III	N	NR	-	-	51	NED
	3	LSH BSO	6	250	Y: Resection of pelvic mass appendectomy	II	CMT RT	NR	-	-	36	DWD
Seidman *et al.*, 2012[32]	4	LM	6.2	139	Y: Unspecified procedure	II	CMT	NR	-	-	39	NED
	5	LM	NR	NR	Y: Unspecified procedure	NR	N	NR	-	-	38	NED
	6	LM	NR	NR	Y: Unspecified procedure	III: DPC	CMT	NR	-	-	17	DWD
	7	LM	NR	NR	Y: Unspecified procedure	NR	N	NR	-	-	9	NED
	8	LM	NR	NR	Y: Unspecified procedure	III: DPC	CMT	NR	-	-	39	NED
	9	LM	NR	NR	Y: Unspecified procedure	III: DPC	Arom/RT	NR	-	-	27	DWD
	10	LM	NR	NR	Y: Unspecified procedure	III: DPC	CMT	NR	-	-	29	DWD
Bojahr *et al.*, 2015[8]	11	LSH	NR	567	Y: Cervical stump extirpation	I	NR	N		-	137	NED
	12	LSH	NR	1000	Y: Cervical stump extirpation	I	NR	Y	Ab	10	13	DWD
Graebe, *et al.*, 2015[12]	13	TLH	NR	NR	Y: Unspecified procedure	IV: Sigmoid peritoneum	NR	Y	Ab	3	5	AWD
	14	TLH	NR	NR	Y: Unspecified procedure	III: Adnexa, cervix omentum appendix	CMT	NR	-	-		AWD
	15	TLH	NR	NR	N	I	NR	N	-	-		NED
Cusidó *et al.*, 2015[33]	17	TLH	6.5	NR	N	NR	RT	Y	Ab	6	36	NED
	18	LM	5	NR	Y: TH	NR	NR	Y	Ab	26	27	NED
Cormio *et al.*, 2015[10]	19	LM	4	NR	Y: TH BSO OM PND PW resection of trocar ports	Ia	CMT	N	-	-	24	NED
	20	LM	5	NR	Y: TH BSO OM PND PW resection of trocar ports	Ia	CMT	N	-	-	22	NED
	21	LM	6	NR	Y: TH BSO OM PND PW resection of trocar ports	Ib	CMT	Y	Ab	42	64	DWD
Nappi *et al.*, 2008[34]	22	HM	4	NR	Y: TH BSO OM PND PW	I	CMT	N	-	-	36	NED
Chin *et al.*, 2016[21]	23	LM	5.7	NR	Y: TH BSO	I	N	N	-	-	100	NED
	24	LM	9	NR	Y: TH BSO	I	CCRT	Y	Ab	11	51	DWD
Lee *et al.*, 2016[19]	25	LM	NR	NR	Y: TH BSO OM PND PAND	I	NR	NR	-	-		AWD
	26	HM	NR	NR	Y: TH BSO PND	I	NR	NR	-	-		DWD
Zhang *et al.*, 2016[14]	27	TLH	NR	264	N	IB	CMT	NR	-	-	54	NED

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Table 2: Contd...

Author	*n*	Initial operation	Tumor size (cm)	Uterine weight (g)	Re-exploration surgery	Final stage	Adjuvant	Recurrence	Site of recurrence	RFS (mon)	Follow-up time (month)	Final status
Tan *et al.*, 2015[16]	28	LM	14	NR	NR	III	NR	Y	Ab	32	34	DWD
Oduyebo, *et al.*, 2014[35]	29	LSH	NR	NR	Y: Trachelectomy, excision of port sites BSO, OM, peritoneal biopsies	I	RT	Y	NR	NR	27	NED
	30	LSH	NR	NR	Y: Trachelectomy, BSO, PND, PW, peritoneal biopsies	I	N	N	-	-	38	NED
	31	LM	NR	NR	Y: TH BSO PND	I	CMT	N	-		48.7	NED
	32	LM	NR	NR	Y: TH BSO OM PLD debulking	III: Omentum	RT	Y	NR	NR	37.5	DWD
	33	LSH	NR	NR	Y: Lysis adhesion, cervical biopsy, resection of port sites multiple biopsies	I	N	N	-	-	20.2	NED
	34	RA-TLH	NR	NR	NA	NR	CMT	Y	NR	NR	15.3	NED
	35	LSH	NR	NR	Y: BSO, debulking trachelectomy, OM	III: Cancer in all specimens	CMT	Y	NR	NR	8.3	NED
Einstein *et al.*, 2008[36]	36	LSH	NR	NR	Y: Trachelectomy and staging	I	NR	NR	-	-	30	NED
	37	LM	NR	NR	Y: TAH BSO staging	III	NR	NR	-	-	61	NED
	38	SCH BSO Trachelectomy	NR	NR	Y: PLD and staging	III: Mesenteric nodule, pelvis vaginal cuff	NR	NR	-	-	31	AWD
	39	SCH BSO	NR	NR	Y: Trachelectomy with staging	I	NR	NR	-	-	37	NED
	40	SCH BSO	NR	NR	N	IV	NR	NR	-	-	6	AWD

Ab: Abdomen, Arom: Aromatase inhibitor, AWD: Alive with disease, BSO: Bilateral salpingo-oophorectomy, CMT: Chemotherapy, DPC: Disseminated peritoneal carcinomatosis, DWD: Dead with disease, HM: Hysteroscopy myomectomy, LM: Laparoscopic myomectomy, LSH: Laparoscopic supracervical hysterectomy, N: No, NED: No evidence of disease, NR: Not reported, OM: Omentectomy, PAND: Paroaortic node dissection, PND: Pelvic node dissection, PW: Peritoneal washing, RA-TLH: Robotic-assisted total laparoscopic hysterectomy, RT: Radiotherapy, SCH: Supracervical hysterectomy, TH: Total hysterectomy, Y: Yes, RFS: Recurrence-free survival, TAH: Total abdominal hysterectomy

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Table 3: Characteristics of patients with nonpower morcellated uterine leiomyosarcoma (24 patients from 7 studies)

Reference	*n*	Initial operation	Tumor size (cm)	Uterine weight (g)	Re-exploration surgery	Final stage	Adjuvant	Recurrence	Site of recurrence	RFS (mon)	Follow-up time (month)	Final status
Tan *et al*., 2015[16]	1	TLH	7	286	NR	NR	N	N	-	-	37	NED
	2	TLH	5.2	184	NR	NR	CMT	Y	NR	NR	23	DWD
Cusidó *et al*., 2015[33]	3	TAH	NR	NR	NR	NR	CMT	Y	Dt	12	14	NED
	4	TAH	NR	NR	NR	NR	CMT	Y	Dt	84	90	NED
	5	TAH	NR	NR	Y	NR	N	Y	Dt	14	16	NED
	6	TLH	9	NR	N	NR	N	Y	Dt	26	32	DWD
	7	TLH	10.8	NR	N	NR	NR	Y	Ab	10	22	DWD
	8	TAH	NR	NR	Y	NR	N	Y	Ab	1	12	NED
Mettler *et al*., 2017[20]	9	TAH	NR	1228	NR	Ia	CMT	Y	NR	NR		AWD
	10	TAH	NR	1118	NR	IIB	CMT	Y	NR	NR		AWD
	11	TAH	NR	840	NR	IIIA	CMT	NR	-	-		NR
	12	TAH	NR	308	NR	IIB	CMT	Y	NR	NR		AWD
Zhang *et al*., 2016[14]	13	TAH	NR	598	NR	IB	NR	NR	-	-		NR
	14	TAH	NR	298	NR	IIB	CMT	N	-	-	17	NED
	15	TAH	NR	410	NR	IB	NR		-	-		NR
Lee *et al*., 2016[19]	16	Myomectomy	NR	NR	NR	I	NR	N	-	-		NED
	17	Myomectomy	NR	NR	NR	I	NR	N	-	-		NED
	18	Myomectomy	NR	NR	NR	I	NR	N	-	-		NED
	19	Myomectomy	NR	NR	NR	I	NR	N	-	-		NED
	20	Myomectomy	NR	NR	NR	I	NR	N	-	-		NED
Oduyebo *et al*., 2014[35]	21	TVH	NR	NR	NR	I	CMT	Y	NR	NR	26	NED
	22	TLH	NR	NR	NR	I	N	N	-	-	1.8	NED
	23	LAVH	NR	NR	BSO OMX peritoneal biopsies PND	I	N	N	-	-	4.5	NED
Tan *et al*., 2015[16]	24	VH	NR	NR	NR	NR	NA	Y	Dt	21	60	AWD

Ab: Abdomen, AWD: Alive with disease, BSO: Bilateral salpingo-oophorectomy, CMT: Chemotherapy, Dt: Distant, DPC: Disseminated peritoneal carcinomatosis, DWD: Dead with disease, N: No, NED: No evidence of disease, NR: Not reported, OM: Omentectomy, PND: Pelvic node dissection, TLH: Total laparoscopic hysterectomy, VH: Vaginal hysterectomy, Y: Yes, RFS: Recurrence-free survival, TAH: Total abdominal hysterectomy, TVH: Total vaginal hysterectomy

the peritoneum. Regarding the FDA statement concerning malignancy spillage, in a bag or contained tissue, extraction techniques have been developed. Cohen *et al*. evaluated the safety of contained power morcellation utilizing both *in vivo* and *in vitro* studies. Although dye leakages were detected, power morcellation in an isolated bag was suggested as a feasible method with the needs for further studies to confirm the safety of current techniques and materials used.[43,44] Another study that evaluated the integrity of the endoscopic bag after transvaginal in-bag morcellation was conducted by Solima *et al*.[45] The containment bags were found to be ruptured in 4 of 12 cases after filling up with methylene dye, demonstrating a potential risk of cancer cells spreading. Authors addressed the importance of development of new, resistant, and durable materials and devices. Even in the absence of morcellation, there is some tissue disruption that seems to cause cell spread after myomectomy.[46] Although its clinical significance is still unclear, patients should be informed that there is a risk of cellular dissemination during myomectomy procedure despite no morcellation performed. The Clinical Practice–Gynaecology Committee of the Society of Obstetricians and Gynaecologists of Canada recommends that physicians should consider and employ techniques that minimize specimen disruption and intra-abdominal spread.[2]

Reproductive outcome after fertility-sparing surgery

The uLMS in young patients subjected to myomectomy for a presumed benign leiomyoma is rare. There are limited data concerning conservative management in this group. The role of conservative management is not well defined. Lissoni *et al*. studied the role of fertility-sparing surgery (myomectomy) in eight young women with a diagnosis of LMS. Three pregnancies (37%) were recorded. Two patients had a spontaneous delivery at term. A 21-year-old patient was found to have local recurrence in the uterus at the time of cesarean section (preterm delivery). A total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed in this case. Nonetheless, the patient developed multiple liver metastases; in which despite chemotherapy using adriamycin and ifosfamide, she died from disseminated disease at 26 months after the diagnosis.[47] The other study also reported failure of the conservative management whereas the patient died of the disease at 48 months after surgery.[10]

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Table 4: Survival outcome *en bloc* removal versus morcellation

Reference	Number of patients	Recurrence	RFS (months)	Abdominopelvic recurrence	Died of disease	Survival outcome
Perri *et al*., 2009[37]	21 *en bloc* 16 morcellation, power and hand/tumor injury	Morcellation 9 (56%)			*En bloc* versus morcellation 8 (38%) versus 10 (62%)	
Park *et al*., 2011[38]	31 *en bloc* 25 morcellation, power and hand	*En bloc* versus morcellation 7 (22%) versus 13 (52%); *P*=0.02*	*En bloc* versus morcellation 10 (3-68) versus 9 (1-102)	*En bloc* versus morcellation 12.9 versus 44%; *P*=0.032	*En bloc* versus morcellation 6 (19.4%) versus 11 (44%); *P*=0.04*	*En bloc* versus morcellation 5 years DFS: 65% versus 40%; *P*=0.04* 5 years OS: 73% versus 46%; *P*=0.04*
George *et al*., 2014[39]	39 *en bloc* 19 morcellation, power and hand	*En bloc* versus morcellation 20 (51%) versus 14 (73.7%)	*En bloc* versus morcellation 39.6 versus 10.8; *P*=0.02*	*En bloc* versus morcellation 4 (20%) versus 85.7; *P*=0.01* RR 3.1 (95% CI 1.5-6.5)	*En bloc* versus morcellation 13 (33.3%) versus 8 (42.1%)	*En bloc* versus morcellation 3 years OS: 73% versus 64%; *P*=0.21 Median OS: Not reach versus 48 months
Bogani *et al*., 2015[40]	127 *en bloc* 75 morcellation, power and hand	*En bloc* versus morcellation 39% versus 62%; *P*=0.007*		*En bloc* versus morcellation 9% versus 39%; *P*<0.01* OR 3.63 (95% CI 0.82–16.11)	*En bloc* versus morcellation 29% versus 48%; *P*=0.01* OR 2.4 (95% CI 1.2-4.8)	
Gao *et al*., 2016[17] include ESS MMMT	6 *en bloc* 11 morcellation, power and hand	*En bloc* versus morcellation 37.9% versus 50%; *P*=0.36	*En bloc* versus morcellation 90 versus 60 months	*En bloc* versus morcellation 5 (71%) versus 6 (66%); *P*=0.36		*En bloc* versus morcellation 5 years RFS 43.5% versus 24% OS 43% (50 months) versus 37.8% (60 months)
Lin *et al*., 2015[41]	29 *en bloc* 14 morcellation, power and hand	*En bloc* versus morcellation 48.3% versus 57.1%; *P*=0.83		*En bloc* versus morcellation 2 (14.2%) versus 3 (37.5%); *P*=0.3	*En bloc* versus morcellation 13 (44.8%) versus 7 (50%)	Morcellation group HR 2.16 (*P*=0.99) and 2.31 (*P*=0.84)
Raine-Bennett *et al*., 2016[18]	76 *en bloc* 35 morcellation, power and hand	*En bloc* versus morcellation 34 (53%) versus 18 (62%)		*En bloc* versus morcellation 14 (41%) versus 13 (72%); *P*=0.03*	*En bloc* versus morcellation 40% versus 37%; *P*=0.75	*En bloc* versus morcellation 5 years DFS: 54% versus 44%; *P*=0.27 OS: 64 versus 74%; *P*=0.89

**P*<0.05 - statistic significant. CI: Confidence interval, OR: Odds ratio, RR: Relative ratio, DFS: Disease-free survival, OS: Overall survival, HR: Hazard ratio, RFS: Recurrence-free survival

Management

The value of re-exploration

In the power morcellation group, we reviewed the data for women with presumed stage 1 uLMS comparing between patients who underwent completed surgical staging within or after 30 days [Table 5]. A quarter (10/38, 26%) of these patients were upstaged during re-exploration. Almost all (90%) were upstaged to stage 3. In a recent retrospective study, one patient was upstaged to stage 4 within 1 month although the re-exploration had taken place within 30 days.[12] The mortality rate of the patients with early restaging (within 30 days) was less than late re-staging (more than 30 days). Because the data were heterogeneous and a number of patients was small, it is very difficult to establish a guidance. However, it is plausible to conclude that surgical staging and time to re-exploration are valuable for prognosis and may alter postoperative treatment.

Fertility-sparing surgery

The uLMS is an aggressive tumor biologically and a relatively chemo-resistant disease; an effective therapy to achieve prolonged survival or cure in those presented with both early and advanced-stage disease has not been established. Failures of conservative management were observed in previous studies.[12,47] Survival outcome is poor despite in early stage and the uterus was removed intact. Table 5 shows that the time to re-exploration is negatively correlated with outcomes of the disease. Complete staging is essential when uterine malignant is found incidentally after morcellation. Therefore, the fertility-sparing surgery is not strongly recommended.

Conclusion

The incidence of LMS in women who underwent surgery for presumed benign disease is very rare. Distinguishing uLMS

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Table 5: Number of leiomyosarcoma patient upstaging after performed power morcellation

Author	Number of patient presumed Stage I	Re-staging ≤30 days	Final stage	Patient status	DFS (months)	Re-staging >30 days	Final stage	Patient status	DFS (months)
Graebe *et al*., 2015[12]	3	2	4	AWD	3, 5				
			3	AWD	NA				
Seidman *et al*., 2012[32]	7	1	3	DWD	17	3	3	AWD	39
							3	DWD	27
							3	DWD	29
Cormio *et al*., 2015[10]	3	0							
Lee *et al*., 2016[19]	2	0							
Einstein *et al*., 2008[36]	13	2	3	AWD	31				
			3	NED	61				
Oduyebo *et al*., 2014[35]	10	0				2	3	DWD	37.5
							3	AWD	8.3
Total (%)	38	5 (13)				5 (13)			

AWD: Alive with disease, DFS: Disease-free survival, DWD: Dead with disease, NED: No evidence of disease, NA: Not available

from benign leiomyoma preoperatively is very difficult. The patients should be assessed for risk of malignancy based on risk factors and preoperative imaging. Moreover, all patients should be counseled for incidental malignancy, risk of morcellation, alternatives for intact specimen removal, and risk of cellular dissemination. The outcome of patients treated by surgery involving tumor disruption is poorer than *en bloc* removal of tumor. The power morcellation yields a significant risk of recurrence, potential for intra-abdominal tumor spread, and upstaging after re-exploration. When uLMS is found incidentally after morcellation, re-exploration for complete staging is recommended.

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Conflicts of interest

There are no conflicts of interest.

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