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

Tanitra Tantitamit¹, Kuan-Gen Huang²,³, Manatsawee Manopunya⁴, Chih-Feng Yen²,³

¹Department of Obstetrics and Gynecology, Faculty of Medicine, Srinakharinwirot University, Nakhonnayok, ²Department of Obstetrics and Gynecology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand, ³Department of Obstetrics and Gynecology, Linkou Chang Gung Memorial Hospital, ⁴Department of Obstetrics and Gynecology, Chang Gung University College of Medicine, Taoyuan, Taiwan

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, shorter 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...
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

| Author          | Year published | Study period | Number of patients | Number of uterine sarcoma | Uterine sarcoma rate | Number of uLMS (cases) | uLMS rate |
|-----------------|----------------|--------------|--------------------|---------------------------|----------------------|------------------------|------------|
| Pritts et al.\[9\] | 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       |
| Bojaht 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       |
| Corios 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       |
| Grecio 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.\[13\] | 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         |
| Metluer et al.\[20\] | 2017        | 2003-2015    | 2269               | 6                         | 0.26                 | 4                      | 0.17       |

\[NR: Not reported, uLMS: Uterine leiomyosarcoma]
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. 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. 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.

Computed tomography is ineffective in differentiating between leiomyoma and LMS. 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.

**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. From previous studies, the histological diagnosis from endometrial sampling was only 37%–64% correct.

**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. 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.

**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. Gao et al. concluded that fibroid morcellation during laparoscopic surgery had no significant impact on recurrence-free survival and OS. 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. 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%). 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, shorter 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. Any type of morcellation might results in spreading of tissue through
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 | 1   | LSH BSO           | 5               | 285                | Y: Tracheectomy        | 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 | 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 | 11  | LSH               | NR              | 567                | Y: Cervical stump extirpation | I           | NR       | N          | -                 | -          | 137                    | NED          |
|                    | 12  | LSH               | NR              | 1000               | Y: Cervical stump extirpation | I           | NR       | Ab 10      | 13                | 13         | DWD                    |             |
| Graebe, et al., 2015 | 13  | TLH               | NR              | NR                 | Y: Unspecified procedure | IV: Sigmoid peritoneum | NR         | Y Ab 3      | 5                 | 5          | AW D                   |             |
|                    | 14  | TLH               | NR              | NR                 | Y: Unspecified procedure | III: Adnexa cervix omentum appendix | CMT      | NR         | -                 | -          | AWD                    |             |
| Cusidó et al., 2015 | 15  | TLH               | NR              | NR                 | N                       | I           | NR       | N          | -                 | -          | NED                    |             |
|                    | 16  | TLH               | 6.5             | NR                 | N                       | NR          | RT       | Y Ab 6     | 36                | 36         | NED                    |             |
| Cormio et al., 2015 | 17  | LM                | 4               | NR                 | Y: TH                        | Ia          | CMT      | N          | -                 | -          | 24                     | NED          |
|                    | 18  | LM                | 5               | NR                 | Y: TH BSO OMPND PW resection of trocar ports | Ia          | CMT      | N          | -                 | -          | 22                     | NED          |
|                    | 19  | LM                | 4               | NR                 | Y: TH BSO OMPND PW resection of trocar ports | Ia          | CMT      | Y Ab 42    | 64                | 64         | DWD                    |             |
| Nappi et al., 2008 | 20  | LM                | 6               | NR                 | Y: TH BSO OMPND PW resection of trocar ports | Ia          | CMT      | N          | -                 | -          | 36                     | NED          |
| Chin et al., 2016 | 21  | LM                | 9               | NR                 | Y: TH BSO                   | I           | N        | N          | -                 | -          | 100                    | NED          |
| Lee et al., 2016   | 22  | HM                | 4               | NR                 | Y: TH BSO                   | I           | CCRT     | Y Ab 11    | 51                | 51         | DWD                    |             |
| Zhang et al., 2016 | 23  | LM                | 5.7             | NR                 | Y: TH BSO                   | I           | N        | NR         | -                 | -          | AW D                   |             |
|                    | 24  | LM                | 9               | NR                 | Y: TH BSO                   | I           | CCRT     | Y Ab 11    | 51                | 51         | DWD                    |             |
|                    | 25  | LM                | NR              | NR                 | Y: TH BSO OMPND PAND        | I           | NR       | NR         | -                 | -          | AW D                   |             |
|                    | 26  | HM                | NR              | NR                 | Y: TH BSO OMPND PND         | I           | NR       | NR         | -                 | -          | DWD                    |             |
|                    | 27  | TLH               | NR              | 264                | N                       | IB          | CMT      | NR         | -                 | -          | 54                     | NED          |

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<sup>[16]</sup> | 28 | LM | 14 | NR | NR | III | NR | Y | Ab | 32 | 34 | DWD |
| Oduyebo et al., 2014<sup>[35]</sup> | 29 | LSH | NR | NR | Y: Tracheectomy, excision of port sites BSO, OM, peritoneal biopsies | I | RT | Y | NR | NR | 27 | NED |
| | 30 | LSH | NR | NR | Y: Tracheectomy, 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 | Y: TAH BSO staging | II: Cancer in all specimens | CMT | Y | NR | NR | 15.3 | NED |
| | 35 | LSH | NR | NR | Y: BSO, debulking tracheectomy, OM | III: Cancer in all specimens | CMT | Y | NR | NR | 8.3 | NED |
| Einstein et al., 2008<sup>[36]</sup> | 36 | LSH | NR | NR | Y: Tracheectomy and staging | I | NR | NR | - | - | 30 | NED |
| | 37 | LM | NR | NR | Y: TAH BSO staging | III | NR | NR | - | - | 61 | NED |
| | 38 | SCH BSO | NR | NR | Y: PLD and staging | III: Mesenteric nodule, pelvis vaginal cuff | NR | NR | - | - | 31 | AWD |
| | 39 | SCH BSO | NR | NR | Y: Tracheectomy 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: Paraaortic 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.
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.\textsuperscript{[43,44]} Another study that evaluated the integrity of the endoscopic bag after transvaginal in-bag morcellation was conducted by Solima et al.\textsuperscript{[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.\textsuperscript{[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.\textsuperscript{[42]}

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; bilateral salpingo-oophorectomy was performed in this case.

### 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\textsuperscript{[16]} | 1 | TLH | 7 | 286 | NR | NR | N | N | - | - | 37 | NED |
| 2 | TLH | 5.2 | 184 | NR | NR | CMT | Y | NR | NR | 23 | DWD |
| 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 | 12 | NED |
| Mettler et al., 2017\textsuperscript{[19]} | 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\textsuperscript{[33]} | 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\textsuperscript{[16]} | 16 | Myomectomy | NR | NR | NR | I | NR | N | - | - | NED |
| 17 | Myomectomy | NR | NR | NR | NR | I | NR | N | - | - | NED |
| 18 | Myomectomy | NR | NR | NR | NR | I | NR | N | - | - | NED |
| 19 | Myomectomy | NR | NR | NR | NR | I | NR | N | - | - | NED |
| 20 | Myomectomy | NR | NR | NR | NR | I | NR | N | - | - | NED |
| Oduyebo et al., 2014\textsuperscript{[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 | I | N | N | - | - | 4.5 | NED |

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
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. 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. 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
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[22] | 3                                 | 2                   | 4           | AWD            | 3, 5         |                     |             | AWD            | NA          |
| Seidman et al., 2012[22] | 7                                 | 1                   | 3           | DWD            | 17           | 3                   | 3           | AWD            | 39          |
| Cormio et al., 2015[20] | 3                                 |                     |             |                |              | 3                   | 3           | DWD            | 27          |
| Lee et al., 2016[19]   | 2                                 |                     |             |                |              | 3                   | 3           | DWD            | 29          |
| Einstein et al., 2008[30] | 13                             | 2                   | 3           | AWD            | 31           |                     |             |                |             |
| Oduyebo et al., 2014[33] | 10                             | 0                   | 3           | NED            | 61           |                     |             |                |             |
| 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.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References
1. Bhave Chittawar P, Franik S, Pouwer AW, Farquhar C. Minimally invasive surgical techniques versus open myomectomy for uterine fibroids. Cochrane Database Syst Rev 2014;(10):CD004638.
2. Singh SS, Scott S, Bougie O, Leyland N; SOGC Clinical Practice-Gynaecology Committee, Leyland N, Wolfman W, et al. Technical update on tissue morcellation during gynaecologic surgery: Its uses, complications, and risks of unsuspected malignancy. J Obst Gynaecol Can 2015;37:68-81.
3. D’Angelo E, Prat J. Uterine sarcomas: A review. Gynecol Oncol 2010;116:131-9.
4. Pritts EA, Parker WH, Brown J, Olive DL. Outcome of occult uterine leiomyosarcoma after surgery for presumed uterine fibroids: A systematic review. J Minim Invasive Gynecol 2015;22:26-33.
5. Updated Laparoscopic Uterine Power Morcellation in Hysterectomy and Myomectomy: FDA Safety Communication; 2014. Available from: https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/SurgeryandLifeSupport/ucm584463.htm [Last accessed on 2018 Feb 16].
6. Pritts EA, Vanness DJ, Berek JS, Parker W, Feinberg R, Feinberg J, et al. The prevalence of occult leiomyosarcoma at surgery for presumed uterine fibroids: A meta-analysis. Gynecol Surg 2015;12:165-77.
7. Brohl AS, Li L, Andikyan V, Obicán SG, Cioffi A, Hao K, et al. Age-stratified risk of unexpected uterine sarcoma following surgery for presumed benign leiomyoma. Oncologist 2015;20:433-9.
8. Bojahr B, De Wilde RL, Chhartchian G. Malignancy rate of 10,731 uteri morcellated during laparoscopic supracervical hysterectomy (LASH). Arch Gynecol Obstet 2015;292:665-72.
9. Lieng M, Berner E, Busund B. Risk of morcellation of uterine leiomyosarcomas in laparoscopic supracervical hysterectomy and laparoscopic myomectomy, a retrospective trial including 4791 women. J Minim Invasive Gynecol 2015;22:410-4.
10. Cormio G, Loizzi V, Ceci O, Leone L, Selvaggi L, Bettocchi S, et al. Unsuspected diagnosis of uterine leiomyosarcoma after laparoscopic myomectomy. J Obstet Gynaecol 2015;35:211-2.
11. Tan-Kim J, Hartzell KA, Reinsch CS, O’Day CH, Kennedy JS, Menefee SA, et al. Uterine sarcomas and parasitic myomas after laparoscopic hysterectomy with power morcellation. Am J Obstet Gynecol 2015;212:594.e1-10.
12. Graebe K, Garcia-Soto A, Aziz M, Valarezo V, Heller PB, Tchabo N, et al. Incidental power morcellation of malignancy: A retrospective cohort study. Gynecol Oncol 2015;136:274-7.
13. Paul PG, Rengaraj V, Das T, Garg R, Thomas M, Khurd AS, et al. Uterine sarcomas in patients undergoing surgery for presumed leiomyomases: 10 years’ experience. J Minim Invasive Gynecol 2016;23:384-9.
14. Zhang J, Li T, Zhang J, Zhu L, Lang J, Leng J, et al. Clinical characteristics and prognosis of unexpected uterine sarcoma after hysterectomy for presumed myoma with and without transvaginal scalpel morcellation. Int J Gynecol Cancer 2016;26:456-63.
15. Rodriguez AM, Asoglu MR, Sak ME, Tan A, Borahay MA, Kilic GS, et al. Incidence of occult leiomyosarcoma in presumed morcellation cases: A database study. Eur J Obstet Gynecol Reprod Biol 2016;197:31-5.
16. Tan A, Saltfinger S, Tan J, Cohen P. Morcellation of occult uterine malignancies: An Australian single institution retrospective study. Aust NZ J Obstet Gynaecol 2015;55:503-6.
17. Gao Z, Li L, Meng Y. A retrospective analysis of the impact of myomectomy on survival in uterine sarcoma. PLoS One 2016;11:e0148050.
18. Raine-Bennett T, Tucker LY, Zaratisky E, Littell RD, Palen T, Neugebauer R, et al. Occult uterine sarcoma after laparoscopic myomectomy: Incidence and survival associated with morcellation. Obstet Gynecol 2016;127:29-39.
19. Lee JY, Kim HS, Nam EJ, Kim SW, Kim S, Kim YT, et al. Outcomes of uterine sarcoma found incidentally after uterus-preserving surgery for presumed benign disease. BMC Cancer 2016;16:675.
20. Mettler L, Maass N, Abdusattarova K, Dempfle A, Alkatout I. Frequency of uterine sarcomas in patients admitted for uterine fibroid surgery. J Turk Ger Gynecol Assoc 2017;18:62-6.
21. Chin H, Ng XH, Chern SM. Power morcellation&#8211;an emerging risk complicating minimally invasive surgery for uterine mesenchymal neoplasms. Gynecology and Minimally Invasive Therapy 2016;5:109-11.
22. Peters A, Sadecky AM, Winger DG, Guido RS, Lee TT,
Mansuria SM, et al. Characterization and preoperative risk analysis of leiomyosarcomas at a high-volume tertiary care center. Int J Gynecol Cancer 2017;27:1183-90.

23. Parker WH, Fu YS, Berek JS. Uterine sarcoma in patients operated on for presumed leiomyoma and rapidly growing leiomyoma. Obstet Gynecol 1994;83:414-6.

24. Amant F, Coosemans A, Debiec-Rychter M, Timmerman D, Vergote I. Clinical management of uterine sarcomas. Lancet Oncol 2009;10:1188-98.

25. Goto A, Takeuchi S, Sugimura K, Maruo T. Usefulness of gd-DTPA contrast-enhanced dynamic MRI and serum determination of LDH and its isozymes in the differential diagnosis of leiomyosarcoma from degenerated leiomyoma of the uterus. Int J Gynecol Cancer 2002;12:354-61.

26. Tamai K, Koyama T, Saga T, Morisawa N, Fujimoto K, Mikami Y, et al. The utility of diffusion-weighted MR imaging for differentiating uterine sarcomas from benign leiomyomas. Eur Radiol 2008;18:723-30.

27. Brölmann H, Tanos V, Grimbizis G, Ind T, Philips K, van den Bosch T, et al. The value of re-exploration in patients with inadvertently morcellated uterine sarcoma. Gynecol Oncol 2016;142:95-100.

28. Cui RR, Wright JD. Risk of occult uterine sarcoma in presumed uterine fibroids. Clin Obstet Gynecol 2016;59:103-18.

29. Bansal N, Herzog TJ, Burke W, Cohen CJ, Wright JD. The utility of preoperative endometrial sampling for the detection of uterine sarcomas. J Minim Invasive Gynecol 2008;15:380-3.

30. Leibsohn S, d’Ablaing G, Mishell DR Jr., Schlaerth JB. Leiomyosarcoma in a series of hysterecomies performed for presumed uterine leiomyomas. Am J Obstet Gynecol 1990;162:968-74.

31. Juang CM, Yen MS, Horng HC, Twu NF, Yu HC, Hsu WL, et al. Potential role of preoperative serum CA125 for the differential diagnosis between uterine leiomyoma and uterine leiomyosarcoma. Eur J Obstet Gynecol Reprod Biol 2006;12:354-61.

32. Seidman MA, Oduyebo T, Muto MG, Crum CP, Nucci MR, Quade BJ, et al. Peritoneal dissemination complicating morcellation of uterine leiomyosarcoma. J Minim Invasive Gynecol 2006;13:370-4.

33. Cusidó M, Fargas F, Baulies S, Plana A, Rodríguez I, Tresserra F, et al. Impact of surgery on the evolution of uterine sarcomas. J Minim Invasive Gynecol 2015;22:1068-74.

34. Nappi L, Di Spiezio Sardo A, Indraccolo U, Bettocchi S. Hysteroscopic resection of uterine leiomyosarcoma: A case report and literature review. J Minim Invasive Gynecol 2008;15:380-3.

35. Oduyebo T, Rauh-Hain AJ, Meserve EE, Seidman MA, Hinchcliff E, George S, et al. The value of re-exploration in patients with inadvertent morcellated uterine sarcoma. Gynecol Oncol 2014;132:360-5.

36. Einstein MH, Barakat RR, Chi DS, Sonoda Y, Alektiar KM, Hensley ML, et al. Management of uterine malignancy found incidentally after supracervical hysterectomy or uterine morcellation for presumed benign disease. Int J Gynecol Cancer 2008;18:1065-70.

37. Perri T, Korach J, Sadetzki S, Oberman B, Fridman E, Ben-Baruch G, et al. Uterine leiomyosarcoma: Does the primary surgical procedure matter? Int J Gynecol Cancer 2009;19:257-60.

38. Park JY, Park SK, Kim DY, Kim JH, Kim YM, Kim YT, et al. The impact of tumor morcellation during surgery on the prognosis of patients with apparently early uterine leiomyosarcoma. Gynecol Oncol 2011;122:255-9.

39. George S, Barysaukas C, Serrano C, Oduyebo T, Rauh-Hain JA, Del Carmen MG, et al. Retrospective cohort study evaluating the impact of intraperitoneal morcellation on outcomes of localized uterine leiomyosarcoma. Cancer 2014;120:3154-8.

40. Bogani G, Ciby WA, Aletti GD. Impact of morcellation on survival outcomes of patients with unexpected uterine leiomyosarcoma: A systematic review and meta-analysis. Gynecol Oncol 2015;137:167-72.

41. Lin KH, Ho-Jun S, Chen CL, Torng PL. Effect of tumor morcellation during surgery in patients with early uterine leiomyosarcoma. Gynecology and Minimally Invasive Therapy 2015;4:81-6.

42. Balgobin S, Maldonado PA, Chin K, Schaffer JI, Hamid CA. Safety of manual morcellation after vaginal or laparoscopic-assisted vaginal hysterectomy. J Minim Invasive Gynecol 2016;23:542-7.

43. Cohen SL, Greenberg JA, Wang KC, Srouji SS, Gargiulo AR, Pozner CN, et al. Risk of leakage and tissue dissemination with various contained tissue extraction (CTE) techniques: An in vitro pilot study. J Minim Invasive Gynecol 2014;21:935-9.

44. Cohen SL, Morris SN, Brown DN, Greenberg JA, Walsh BW, Gargiulo AR, et al. Contained tissue extraction using power morcellation: Prospective evaluation of leakage parameters. Am J Obstet Gynecol 2016;214:257.e1-257.e6.

45. Solima E, Scagnellli G, Austoni V, Natale A, Bertualesi C, Busacca M, et al. Vaginal uterine morcellation within a specimen containment system: A study of bag integrity. J Minim Invasive Gynecol 2015;22:886.

46. Toubia T, Moulder JK, Schiff LD, Clarke-Pearson D, O’Connor SM, Siedhoff MT, et al. Peritoneal washings after power morcellation in laparoscopic myomectomy: A pilot study. J Minim Invasive Gynecol 2016;23:578-81.

47. Lissoni A, Cormio G, Bonazzi C, Perego P, Lomonico S, Gabriele A, et al. Distinctive value of re-exploration in patients with non-tumor-related complications after power morcellation of uterine sarcoma. Gynecol Oncol 2008;110:43-8.

48. Mansuria SM, et al. Characterization and preoperative risk analysis of leiomyosarcomas at a high-volume tertiary care center. Int J Gynecol Cancer 2017;27:1183-90.

49. Perri T, Korach J, Sadetzki S, Oberman B, Fridman E, Ben-Baruch G, et al. Uterine leiomyosarcoma: Does the primary surgical procedure matter? Int J Gynecol Cancer 2009;19:257-60.

50. Park JY, Park SK, Kim DY, Kim JH, Kim YM, Kim YT, et al. The impact of tumor morcellation during surgery on the prognosis of patients with apparently early uterine leiomyosarcoma. Gynecol Oncol 2011;122:255-9.

51. George S, Barysaukas C, Serrano C, Oduyebo T, Rauh-Hain JA, Del Carmen MG, et al. Retrospective cohort study evaluating the impact of intraperitoneal morcellation on outcomes of localized uterine leiomyosarcoma. Cancer 2014;120:3154-8.

52. Bogani G, Ciby WA, Aletti GD. Impact of morcellation on survival outcomes of patients with unexpected uterine leiomyosarcoma: A systematic review and meta-analysis. Gynecol Oncol 2015;137:167-72.

53. Lin KH, Ho-Jun S, Chen CL, Torng PL. Effect of tumor morcellation during surgery in patients with early uterine leiomyosarcoma. Gynecology and Minimally Invasive Therapy 2015;4:81-6.

54. Balgobin S, Maldonado PA, Chin K, Schaffer JI, Hamid CA. Safety of manual morcellation after vaginal or laparoscopic-assisted vaginal hysterectomy. J Minim Invasive Gynecol 2016;23:542-7.

55. Cohen SL, Greenberg JA, Wang KC, Srouji SS, Gargiulo AR, Pozner CN, et al. Risk of leakage and tissue dissemination with various contained tissue extraction (CTE) techniques: An in vitro pilot study. J Minim Invasive Gynecol 2014;21:935-9.