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A critical assessment of morcellation and its impact on gynecologic surgery and the limitations of the existing literature

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Abstract

Uterine sarcomas are rare uterine malignancies that are difficult to diagnose preoperatively. Because of cases of disseminated sarcoma after laparoscopic hysterectomy, the role of power morcellators in gynecologic surgery has been questioned. Morcellation is an integral part of making laparoscopic surgery possible for the removal of large uterine leiomyomata, and the development of power morcellation has increased efficiency during these procedures. Minimally invasive surgery has demonstrated benefits that include improved pain control, decreased infection risk, and faster surgical recovery and return to work. In this review, we examine the risk of incidental sarcoma at the time of surgery, the quality of the data, the accuracy of clinical and radiologic predictors of uterine sarcoma, and the impact of morcellation on the prognosis of uterine sarcoma.

Keywords

minimally invasive surgery; morcellation; uterine sarcoma

The role of power morcellation in gynecologic surgery recently has come under intense scrutiny after a highly publicized case of dissemination of unexpected uterine leiomyosarcoma. Morcellators were introduced initially in 1973 as a hand-activated device for laparoscopic tissue removal. The first electromechanical morcellator was made available by Steiner in 1993.¹ As minimally invasive surgical techniques evolved, morcellation became a mainstay of gynecologic surgery. However, the risk of spreading malignant tissues must be balanced deliberately with the benefits of minimally invasive surgery. The purpose of this review was to provide an overview of the current literature in incidental uterine sarcomas, the accuracy of clinical and radiologic predictors of uterine malignancy, and a brief review of the impact of morcellation and future guidelines on the use of mechanical morcellators in gynecologic surgery.

Incidence of sarcoma unsuspected at hysterectomy

Uterine sarcomas are rare, comprising <1% of all gynecologic malignancies.² This subgroup of uterine malignancies carries a poor prognosis for those affected, even in early-stage disease (Table 1).^{3–7} In the United States, of the estimated 52,630 new cases of uterine cancer diagnosed annually, approximately 1600 will be uterine sarcomas.⁸ The major challenge with triaging patients to the appropriate surgery is differentiating uterine sarcomas from benign uterine fibroid tumors. Using various imaging techniques, endometrial sampling, obtaining a detailed patient history, and performing a thorough physical examination have been the mainstay of preoperative evaluation for patients with uterine masses. Although these techniques provide adequate evaluation for uterine epithelial cancers, each has limitations and none can exclude the possibility of nonepithelial malignancies.

There are varying reports in the literature on the incidence of unsuspected uterine sarcoma diagnosed on final pathologic evaluation after hysterectomy. Additionally, these studies are retrospective, which further limits the quality of the data. In the special report on power morcellation and occult malignancy in gynecologic surgery issued by the American Congress of Obstetrics and Gynecology (ACOG), it is estimated that 1 in 500 women will have a postoperative diagnosis of stromal sarcoma and leiomyosarcoma.⁹ As part of the safety warning issued by the US Food and Drug Administration (FDA) on power morcellation, a comprehensive literature review of studies that reported unsuspected uterine sarcomas and leiomyosarcomas in patients who underwent hysterectomy or myomectomy for presumed benign fibroid tumors was performed. Among this population, the risks of occult sarcoma and leiomyosarcoma were reported to be 1 in 352 and 1 in 458, respectively.¹⁰

Quality of the data

Further review of the studies used for the FDA's report confirms low-quality evidence from retrospective reviews. Moreover, many of the studies were done at large referral centers on high-risk patients, possibly falsely elevating the risk of uterine sarcomas in these study groups. Of the 9 studies that were included in the FDA quantitative assessment, 5 studies were conducted in the United States (Table 2).^{11–15} All the studies were qualitative in nature, providing level 3 evidence¹⁶ on the risk of uterine sarcoma at the time of hysterectomy. The largest study included 1429 patients who were 36–62 years old with abnormal uterine bleeding or abdominal pain with a pelvic mass of sufficient size or character to warrant surgical exploration. In that study, they reported 7 cases of leiomyosarcoma (0.5%).¹¹ Review of the study criteria shows that there was no standard preoperative evaluation among these patients who were treated between 1983 and 1988. The study was based out of a tertiary care center with a self-referred indigent population. Two additional US studies that were reviewed by the FDA report rates of uterine sarcoma of 0.18–0.23% and leiomyosarcoma of 0.08–0.09% in high-risk patients with inconsistent preoperative work-up.^{12,14} Notably, of the studies that were reviewed by the FDA, multiple surgical and morcellation techniques were used to treat these patients.

Variable preoperative evaluation and lack of age and risk factor stratification among these retrospective studies ultimately lend uncertain relevance to these published data. With an annual reported incidence of 0.64 per 100,000 women, the applicability is further complicated by the rarity of these malignancies.¹⁷ There are limited data on the prevalence of sarcoma in morcellated specimens and even fewer cases and studies on the incidence of disseminated disease in patients who underwent minimally invasive surgical techniques with the use of power morcellation.^{14,18–22} To fully evaluate the effect of power morcellation on disease-free and overall survival in these cases, prospective studies or randomized studies are necessary; however, no such study is possible due to obvious ethical conflicts. Furthermore, the rarity of these cancers requires that data be collected over a long period of time to accrue the necessary numbers to provide sufficient statistical power to detect differences in outcome. Use of epidemiologic modeling systems may be needed to better understand the impact of morcellation in these cases. Without reliable data, any recommendation on the safety of power morcellation is premature, given the known benefits of minimally invasive surgery on patient recovery and quality of life.

Accuracy of clinical and radiographic predictors of malignancy

Historically, clinicians have been challenged by the difficult task of identifying sarcomas before surgery. The accuracy of clinical and radiographic predictors of malignancy varies widely depending on the type of uterine cancer, endometrial vs mesenchymal. The diagnosis of endometrial cancer is made reliably based on histologic and radiologic evaluation. Endometrial biopsy has high sensitivity for a diagnosis of endometrial carcinoma^{23,24}; however, very few studies have reported its sensitivity in diagnosis of mesenchymal tumors and are limited to small single-institution reports.^{11,25} Because of the distribution of sarcomas within the myometrium, the reported sensitivities of 33–67% are not surprising.

No clear clinical features have distinguished benign uterine neoplasms reliably from malignant growths. Rapidly enlarging uterine size traditionally has been taught as a characteristic of malignant tumors²⁶; however, this has not been supported in the contemporary literature.^{12,27–29} Parker et al¹² reported on a cohort of 1332 women who underwent hysterectomy or myomectomy; 371 women had rapid tumor growth as their surgical indication, with only 1 case of leiomyosarcoma among this group. A literature review of 26 studies found that a history of rapid uterine enlargement was documented in only 15 of 580 patients (2.6%) with uterine sarcoma. In a more recent review, Leung et al³⁰ reported only 2 cases of leiomyosarcoma among 155 patients (1.3%) with a “rapidly growing uterus” at the time of hysterectomy. Furthermore, rapid tumor growth of up to 138% of fibroid tumor volume has been demonstrated by benign leiomyomata.²⁹

Black race has been associated with a 2-fold increased risk of carcinosarcoma and leiomyosarcoma³¹; however, black women have a 2- to 3-fold increased baseline risk of uterine leiomyomas.^{32,33} Increasing age and postmenopausal status are also nonspecific risk factors for uterine sarcomas. Because fibroid tumors are hormone responsive, any growing uterine mass in a postmenopausal patient should be treated as malignancy until proved otherwise. Tamoxifen use for >5 years has also been associated with an increased risk for uterine sarcoma.^{34,35} No genetic mutations or polymorphisms have been connected to

uterine sarcomas; however, childhood retinoblastoma and hereditary leiomyomatosis and renal cell carcinoma syndrome have been associated with sarcomas of the uterus.^{36–38}

Imaging modalities have emerged as crucial methods in the evaluation, surveillance, and surgical planning of many gynecologic malignancies and neoplasms. Radiologic studies, however, have limited utility in the diagnosis of uterine malignancy. Imaging cannot reliably differentiate malignant from benign causes, and the low sensitivity and specificity of radiologic studies has made triage of uterine masses to the appropriate surgical procedure difficult. Table 3 provides a summary of the utility of imaging modalities in the diagnosis of uterine sarcomas and their respective measurements of interest. All the studies are based on limited case series.

Ultrasound scanning is often the first-line imaging modality for evaluating patients with pelvic disease because of its sensitivity, accessibility, and relative low cost of services. In cases of suspected endometrial malignancy, an endometrial thickness of >5 mm in postmenopausal women warrants further evaluation.³⁹ In cases of suspected mesenchymal tumors, ultrasound scanning is much less reliable in predicting malignancy. Sarcomas have been associated with certain features (mixed echogenic parts, central necrosis, and irregular vasculature on Doppler evaluation)⁴⁰; none of these characteristics are specific to malignant tumors.⁴¹ Resistance index and peak systolic velocity have emerged as sonographic measurements that could be used to distinguish between benign and malignant uterine mesenchymal tumors; however, the evidence is conflicting and limited to small case series.^{42,43}

Magnetic resonance imaging (MRI) may be helpful in women in whom there is a suspicion of sarcoma. However, there are no definitive MRI characteristics that reliably have predicted the diagnosis of mesenchymal tumors. High signal intensity and ill-defined margins have been associated with leiomyosarcomas, but neither is a reliable indicator.^{41,44–46} Small retrospective studies have demonstrated some promise in the use of both lactate dehydrogenase levels and diffusion-weighted MRI to distinguish uterine leiomyoma from leiomyosarcoma.⁴⁷ In a retrospective analysis of 51 cases, Thomassin-Naggara et al⁴⁸ reported on a model that incorporates signal intensity, mean apparent diffusion coefficient, and patient age to predict benign and malignant masses with 92% accuracy.

Because of the expense of positron emission tomography (PET) imaging and low incidence of uterine sarcomas, there are no large scale studies that have demonstrated efficacy of PET imaging in the diagnosis of these tumors. In a recent review of the PET imaging in the diagnosis and staging of uterine sarcoma, only 2 studies were found in the recent literature on the accuracy of diagnosis.^{49–51} Fluorodeoxyglucose uptake varies between individual tumors, and standardized uptake value activity cannot distinguish reliably between benign and malignant masses. Although more studies are needed to clarify its use in the diagnosis of uterine sarcomas, the high cost of MRI will likely preclude its widespread use in the triage of uterine neoplasms.

Impact of morcellation

The concerns over morcellation include inadvertent trauma to surrounding structure, disruption of the pathologic specimen, and dispersion of tissue. Injuries have been reported to small and large bowel, vasculature, kidney, ureter, bladder, and diaphragm.⁵² Disruption and dispersion of benign tissue has been associated with acute complications, such as peritonitis, intraabdominal abscesses, intestinal obstruction,⁵³ and chronic symptoms from disseminated fibroid tumors, endometriosis, or adenomyosis, which have the potential to transform into malignancy.⁵⁴

One of the major concerns over morcellation of an occult cancer is delayed diagnosis because of misinterpretation of the initial pathologic specimen. Rivard et al⁵⁵ obtained 10 intact uterine specimens, 5 with endometrial adenocarcinoma and 5 without. After the intact specimens were processed, fixed, and analyzed, they were morcellated and re-reviewed. One of 5 specimens with known cancer was interpreted as benign, and none of the morcellated specimens could be staged. It is important to note that this study included only the interpretation of a single pathologist and that a similar study has not been conducted with uterine sarcomas. A recent case report of disseminated leiomyosarcoma shortly after receiving a diagnosis of benign leiomyomas raises concern for similar diagnostic challenges in the pathologic examination of morcellated leiomyosarcomas.²⁰ In this case, malignancy was diagnosed on re-review of the patient's original pathologic specimen. Unfortunately, what role hindsight played cannot be determined.

Another major concern over morcellation of an occult malignancy is the possibility of the seeding of cancer throughout the peritoneal cavity. To examine the frequency of this occurrence, 3 retrospective cohort studies have been conducted that included patients who underwent reexploratory surgery shortly after receiving a presumed diagnosis of stage I uterine sarcoma (Table 4).^{14,18,19} In total, 9 of 31 patients who were presumed to have stage I leiomyosarcoma were found to have disseminated peritoneal disease at the time of reexploratory surgery. Five of 9 patients with smooth-muscle tumors of uncertain malignant potential also had evidence of abdominopelvic tumor nodules. In addition to these retrospective cohort studies, case reports have also described up-staging of sarcoma secondary to peritoneal spread after morcellation.²⁰⁻²²

Although these studies suggest that dispersed particles of malignant uterine tissue have biologic potential for neovascularization and growth, they cannot rule out the possibility that disseminated peritoneal disease may be due to incorrect initial staging, natural disease progression, or incorrect follow-up diagnosis. There was no uniformity in the method for assigning the initial stage, the interval between the first and second surgery, and the procedures used to differentiate peritoneal metastases from reactive fibroblastic proliferation. Furthermore, although all 3 studies commented on worse outcomes for patients with disseminated disease, they were not designed to demonstrate a causal relationship between morcellation and death. This is important to keep in mind, given that leiomyosarcoma, in particular, is an aggressive tumor at baseline. Of 3 studies to calculate higher recurrence rates and lower survival rates for patients with morcellated vs unmorcellated stage I leiomyosarcomas,⁵⁶⁻⁵⁸ the only study to adjust for primary tumor

mitotic rate found no statistically significant difference in overall survival after making the adjustment.⁵⁸ Table 5 summarizes these studies and their outcome measures.

At this time, the finding of disseminated peritoneal disease after morcellation of an occult leiomyosarcoma can be used most appropriately as a prognostic indicator. Other uses of this finding, such as to guide adjuvant therapies, are not supported by a critical review of the existing studies, which “suffer” from retrospective designs at single-institution referral centers, small numbers, and limited patient follow-up evaluation.

In contrast, the benefits of minimally invasive surgery are well-supported by level 1 data. A Cochrane systematic review, which included 27 randomized clinical trials that compared laparoscopic or vaginal hysterectomy to abdominal hysterectomy, found that women who underwent a minimally invasive surgery had significantly less blood loss, fewer incisional infections or febrile episodes, shorter hospital stays, and speedier return to normal activities.⁵⁹ In a Canadian study, patients with laparoscopic-assisted vaginal hysterectomy returned to normal activity and work 14 days sooner than their abdominal and vaginal hysterectomy counterparts.⁶⁰

Epstein et al⁶¹ recently reported on the financial impact of minimally invasive surgery on medical spending and employee absenteeism for 6 common minimally invasive procedures. Using insurance claims data with matched employer-provided absenteeism data, among the 7402 women who underwent “uterine fibroid resection,” 4137 women underwent the traditional approach, and 3259 women had minimally invasive excisions. On average, those women who underwent the minimally invasive procedure had 11.5 fewer days absent from work and \$1500 less in health plan spending per procedure. Based on estimates from ACOG, approximately 600,000 hysterectomies are done per year; in 2008, 10% of these were performed with a laparoscope.⁶² In a hospital database analysis done by Wright et al⁶³ among women who underwent minimally invasive hysterectomy, >15% were performed with morcellation. With the use of these rough estimates and the assumption that the cases that involved morcellation were not possible laparoscopically otherwise, 9000 women ($600,000 \times 0.10 \times 0.15$) would have undergone laparotomy, yielding 99,000 more days absent from work per year and \$13,500,000 more in health plan spending per year. The rapid adoption of robotic-assisted laparoscopic surgery in recent years likely makes this an underestimate in current surgical practice.

Other studies have demonstrated a significant decrease in postoperative narcotic use⁶⁴ and incisional hernias formation⁶⁵ and higher long-term quality-of-life scores on self-reported questionnaires⁶⁶ with a minimally invasive approach compared with an open approach. Given the abundance of high-quality data that compare the different approaches to hysterectomy, both the ACOG and the American Association of Gynecologic Laparoscopists have issued position papers supporting minimally invasive surgery for presumed benign disease in patients at low risk for malignancy.^{9,67}

Surgical alternatives

Strategies to continue to allow surgeons to provide minimally invasive surgery to patients while minimizing the risk of the spread of occult malignancy involve refinement of

contained morcellation techniques. There are reports of power morcellation within an endoscopic bag^{68,69}; however, current endoscopic bags were neither designed for this purpose nor sufficiently studied for this purpose. Notably, there are also mechanical morcellators without the rotational mechanism, which likely would reduce the intraperitoneal dissemination of tumor.

For specimens that are enlarged mildly but do not deliver easily because of nulliparity or obesity, transvaginal insertion of the anchor tissue retrieval system has been described for intact removal of specimens that were not delivered easily vaginally without the retrieval bag.⁷⁰ Specimens too large to be removed intact, even with the use of a retrieval bag may be candidates for extracorporeal morcellation.

Two extracorporeal morcellation techniques have been described to prevent spillage of specimen into the abdomen and to reduce vascular and bowel injuries that are associated with open power morcellation. In a study of 8 women, Favero et al⁷¹ describe a vaginal morcellation approach in which they inserted a nylon with polyurethane Lapsac (Cook Medical, Bloomington, IN) into the pelvis transvaginally and used the Lapsac to retract the vaginal sidewalls and allow bisection of the contained tissue specimen for removal. They were able to remove all specimens successfully, but because the data only reached 3 months of follow up, time for disease-free recurrence is unknown. In a subsequent study, 12 women with endometrial cancer and uterine size >12 weeks underwent total laparoscopic hysterectomy with transvaginal uterine bisection within a sterile plastic wrapping bag that was inserted through a 12-mm port.⁷² All patients had no evidence of local or distant recurrence at median follow up of 18 months. Serur and Lakhi⁷³ describe the transabdominal insertion of an endoscopic bag through a 20- to 30-mm incision, elevating the specimen above the abdominal incision and hand-morcellating the specimen for removal. This involves extension of one of the port site incisions but avoids a larger laparotomy. Both of these techniques keep the specimen contained within a laparoscopic bag, thus eliminating specimen spillage, as long as the integrity of the bag is not damaged inadvertently while hand-morcellating or bisecting the uterus. All port sites should be irrigated to avoid seeding and implantation of neoplastic tissue after extraction from laparoscopy or laparotomy incisions.

Advances in contained power morcellation techniques may provide improved speed of specimen removal while achieving equivalent safety to hand morcellation techniques. In a hospital simulation laboratory, contained tissue extraction of beef tongue specimens that were stained with indigo carmine dye did not result in any leakage or tissue dissemination when a 1-piece clear plastic 50 × 50-cm isolation bag was used.⁷⁴ Another recent report describes an enclosed, motor-actuated mesh that applies inward-directed cutting force to tissue that has been loaded into mesh within a protective bag.⁷⁵ This approach could be applied to a larger range in tissue size and density as compared with current power morcellators, while decreasing the risks of seeding and injury to other organs and structures. As contained power morcellation techniques gain approval for in vivo use, they likely will become the predominant approach with the advantages of decreased operative time while avoiding dissemination of endometriosis or malignancy and decreasing intraoperative injury as compared with current open morcellation techniques.

Summary and conclusion

Specific guidelines for the use of power morcellation may be of benefit while awaiting advances in preoperative diagnosis of sarcomas. Preoperative evaluation before hysterectomy includes cervical cytologic evidence and may include endometrial biopsy and pelvic imaging. If preoperative evaluation raises suspicion for malignancy, morcellation clearly should be avoided. Morcellation should be avoided in patients with a history of tamoxifen use, pelvic radiation, or increased genetic risk for malignancy. Surgeons should review surgical alternatives that include laparotomy, mini-laparotomy, and colpotomy with possible manual morcellation vaginally or within an endoscopic bag.

The impact of minimally invasive surgery on patient quality of life and the economic benefits of shorter recovery time and improved pain management should not be overlooked in gynecologic surgery. New surgical methods are being developed so that women with large uterine leiomyomata can still be offered laparoscopic surgery.

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TABLE 1

Early-stage survival of uterine sarcomas

Variable	Year published	Stage	n	Survival outcome
Leiomyosarcoma				
Kapp et al ³	2008	I	951	5-yr DSS = 75.8%
		II	43	5-yr DSS = 60.1%
Abeler et al ⁴	2009	I	193	5-yr OS = 51%
		II	36	5-yr OS = 25%
Endometrial stromal sarcoma				
Chan et al ⁵	2008	I–II	540	6-yr DSS = 89%
Abeler et al ⁴	2009	I	56	5-yr OS = 84%
		II	21	5-yr OS = 62%
Adenosarcoma				
Arend et al ⁶	2010	I	327	5-yr OS = 79%
Undifferentiated uterine sarcoma				
Abeler et al ⁴	2009	I	14	5-yr OS = 57%
		II	5	5-yr OS = 0%
Tanner et al ⁷	2012	I	7	Median OS = 26.8 mo

DSS, disease specific survival; OS, overall survival.

Liu. Critical assessment of morcellation. *Am J Obstet Gynecol* 2015.

Risk of unsuspected uterine sarcomas at the time of surgical excision, United States, 1980–2014

TABLE 2

Author	Year published	Procedure	n	Cases of sarcomas, n	Risk of uterine sarcoma, % (95% confidence interval)	Level of evidence
Leibsohn et al ¹¹	1990	Hysterectomy	1429	7	0.5 (0.1–0.9)	3
Parker et al ¹²	1994	Hysterectomy or myomectomy	1332	4	0.2 (0.0–0.5)	3
Rowland et al ¹³	2011	Hysterectomy	1115	8	0.5 (0.1–0.8)	3
Seidman et al ¹⁴	2012	Myomectomy	1091	2	0.2 (0.0–0.4)	3
Ehdaivand et al ¹⁵	2014	Hysterectomy	352	3	0.8 (0.2–2.5)	3
TOTAL			5319	24	0.5 (0.1–0.7)	

Liu. Critical assessment of morcellation. Am J Obstet Gynecol 2015.

TABLE 3

Utility of imaging modalities in the diagnosis of uterine sarcomas

Variable	Year published	n	Cases of sarcoma, n	Measurement of interest	Sensitivity, %	Specificity, %	Level of evidence
Ultrasound scan							
Hata et al ²	1997	46	5	Intratumoral PSV 41.0 cm/sec	80	97	3
Szabo et al ³	2002	129	12	Intratumoral RI <0.5	67	87	3
Exacoustos et al ⁴⁰	2007	257	8	Increased central and peripheral vascularity	100	86	3
Magnetic resonance imaging							
Schwartz et al ⁴⁴	1998	45	4	Ill-defined margins	100	100	3
Tanaka et al ⁴⁵	2004	24	12	High signal intensity of T2 and T1WI	73	100	3
Sato et al ⁴⁶	2014	81	5	Signal intensity on diffusion weighted imaging + ADC	100	99	3
Positron emission tomography/computerized tomography							
Nagamatsu et al ⁵¹	2009	53	10	SUV >3.0	100	73	3
Yamane et al ⁵⁰	2012	15	3	SUV >4.32	100	63	3

ADC, apparent diffusion coefficient; PSV, peak systolic velocity; RI, resistance index; SUV, standardized uptake value.

Liu. Critical assessment of morcellation. Am J Obstet Gynecol 2015.

TABLE 4

Disseminated disease after morcellation of uterine sarcomas

Author	Year published	Study years	n	Cases of sarcoma, n	Cases of documented dissemination on reexploration
Einstein et al ¹⁸	2008	2000–2006	—	17 ^a	2
Seidman et al ¹⁴	2012	2005–2010	1091	7	4
Oduyebo et al ¹⁹	2014	2005–2012	—	15 ^b	3

^a Of 17 cases, 13 women underwent reexploratory surgery;^b Of 15 cases, 11 women underwent reexploratory surgery.

Liu. Critical assessment of morcellation. Am J Obstet Gynecol 2015.

TABLE 5

Cases of uterine sarcoma and outcomes after morcellation

Author	Year published	Study years	n	Nonmorcellated cases, n	Morcellated cases, n	Outcome measure	Level of evidence
Perri et al ⁵⁶	2009	1965–2005	37	21	16	Hazard ratio, 2.8 (95% CI, 1.02–7.67) ^a	II-3
Park et al ⁵⁷	2011	1989–2010	56	31	25	Odds ratio, 3.11 (95% CI, 1.07–9.06) ^b	II-3
George et al ⁵⁸	2014	2007–2012	58	39	19	Hazard ratio, 3.18 (95% CI, 1.5–6.8) ^c	II-3

CI, confidence interval.

^a Overall survival, multivariate adjusted model, $P = .04$;

^b Overall survival, multivariate adjusted model, $P = .038$;

^c Recurrence-free survival, multivariate adjusted model, $P = .003$.

Liu. Critical assessment of morcellation. Am J Obstet Gynecol 2015.