European Society of Gynecological Oncology Statement on Fibroid and Uterine Morcellation

Michael J. Halaska, MD, PhD, Dimitrios Haidopoulos, MD, PhD,† Frédéric Guyon, MD,‡ Philippe Morice, MD,§ Ignacio Zapardiel, MD, PhD,|| and Vesna Kesic, MD, PhD¶, ESGO Council*

Abstract: Recently, there has been an intense discussion about the issue of fibroid and uterine morcellation in relation to the risk of unrecognized uterine sarcoma spread. Morcellation can negatively influence the prognosis of patients, and transecting the specimen into pieces prevents the pathologist from performing proper disease staging. Many societies have published their statements regarding this issue. The European Society for Gynecological Oncology has established a working group of clinicians involved in diagnostics and treatment of oncogynecological patients to provide a statement from the oncological point of view. Leiomyosarcomas and undifferentiated endometrial sarcomas have generally dismal prognosis, whereas low-grade endometrial stromal sarcomas and adenosarcomas have variable prognosis based on their stage. A focus on the detection of patients at risk of having a sarcoma should be mandatory before every surgery where morcellation is planned by evaluation of risk factors (African American descent, previous pelvic irradiation, use of tamoxifen, rapid lesion growth particularly in postmenopausal patients) and exclusion of patients with any suspicious ultrasonographic signs. Preoperative endometrial biopsy should be mandatory, although the sensitivity to detect sarcomas is low. An indication for myomectomy should be used only in patients with pregnancy plans; otherwise en bloc hysterectomy is preferred in both symptomatic and postmenopausal patients. Eliminating the technique of morcellation could lead to an increased morbidity in low-risk patients; therefore, after thorough preoperative evaluation and discussion with patients, morcellation still has its place in the armamentarium of gynecologic surgery.

Key Words: Uterine sarcoma, Leiomyosarcoma, European Society of Gynecological Oncology, Statement, Power morcellation, Prognosis

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A recent debate has emerged on the use of fibroid and uterine morcellation. In short, the view argues that power morcellators increase the risk of unrecognized uterine sarcomas spreading.[1] In the United States, it was estimated that the risk of finding an unexpected sarcoma in a patient undergoing surgery for presumed fibroid tumors is approximately 1 in 352 cases.[2]

*Department of Obstetrics and Gynaecology, 3rd Medical Faculty, Charles University, Prague and Faculty Hospital Kralovske Vinohrady, Czech Republic; †First Department of Obstetrics and Gynecology, Alexandra Hospital, Athens, Greece; ‡Chirurgie Gynécologique, Institut Bergonie, Bordeaux; §Department of Surgery, Institute Gustave Roussy, Villejuif, France; ||Gynecologic Oncology Unit, La Paz University Hospital, Madrid, Spain; and ¶Institute of Obstetrics and Gynecology, Clinical Center of Serbia, Belgrade, Serbia.

Address correspondence and reprint requests to Michael J. Halaska, MD, PhD, Department of Obstetrics and Gynaecology, 3rd Medical Faculty, Charles University, Prague and Faculty Hospital Kralovske Vinohrady, Srobarova 1150/50, Praha 10, 100 34, Czech Republic. E-mail: mhalaska@seznam.cz.

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In response to these reports, the US Food and Drug Administration (FDA) issued a warning against power morcellation. The consequences of the FDA statement are profound, leading to a shift from minimally invasive surgery to open surgery as a means to improve oncological safety.

The European Society for Gynecological Oncology has established a working group of clinicians involved in diagnostics and treatment of oncogynecological patients. Core questions about morcellation have been formulated and discussed within the group. A summary and consensus statement has been endorsed by the working group to give relevant figures and arguments for and against morcellation techniques.

The main issue is the risk of an undiagnosed sarcoma while treating a patient with presumed benign uterine fibroid tumors. Some reports have observed a worse prognosis of patients with uterine sarcoma who underwent power morcellation during surgery because such a procedure may cause the spread of cancer cells to the abdominal cavity of women, especially in leiomyosarcomas (LMSs).[3,4] A complete resection and achievement of clear margins are other prognostic factors aggravated by morcellation.[5]

Fibroids are common benign uterine tumors affecting approximately 70% of the female population. Treatment is required in approximately 15% to 30% of female patients,[6] and in 2013, hysterectomy was indicated in approximately 450,000 patients in Europe annually.[7] A misdiagnosis concerns not only radical treatment of fibroid tumors but also other therapeutic options such as uterine artery embolization and magnetic resonance imaging–guided focused ultrasound surgery.[8]

Uterine sarcomas are rare tumors. The incidence rates are retrieved from retrospective data. In European countries, the incidence rates (based on 2011 data) range from 0.35 to 1.53 of 100,000, representing 1332 to 5824 women in the overall female population of 380,686,199.[9] Because most of the sarcomas develop from mesenchymal tissue, it is difficult to diagnose such malignant tumors preoperatively.

Oncogynecological remarks on prognosis and behavior of different histopathological subtypes based on the last World Health Organization classification[10] are listed as follows:

1. Leiomyosarcomas are usually found in postmenopausal women with mean age of 55 years. They can mimic leiomyomas and constitute approximately 60% to 70% of all sarcomas. Their prognosis is poor, even in stage I, with a recurrence rate from 53% to 71%. The 5-year survival rate for LMS is approximately 41%.[11,12]
2. Atypical smooth muscle tumors of uncertain malignant potential have a highly favorable prognosis in that they exhibit only some suspicious histological features.
3. Low-grade endometrial stromal sarcomas (ESSs) have a generally favorable prognosis with stage being the strongest prognostic factor. Endometrial stromal sarcomas make up approximately 20% to 30% of all sarcomas. For stage I, the 5-year survival rate is approximately 90% versus 50% for stage III or IV.[13]
4. Undifferentiated endometrial sarcomas, also referred to as high-grade endometrial stromal neoplasms, present at stages III and IV in approximately 60% of all sarcomas. These undifferentiated endometrial sarcomas exhibit a highly aggressive biology, and the prognosis of these patients is dismal.[14]
5. Adenosarcomas (ASs) are rare tumors that usually arise as polypoid lesions and are thought to have a favorable prognosis. These tumors have a tendency to fill and distend the uterine cavity. Approximately 25% of patients with AS will die from the disease. The incidence rate is approximately 5% of all sarcomas.[15]

How Should We Preoperatively Identify the Patient Group at High Risk for Uterine Sarcomas Requiring an en bloc Resection?

The need for improvements in preoperative work-up is essential because this stage could further decrease the number of unsuspected sarcomas.

Risk factors for uterine sarcoma are ethnic background (women with uterine sarcomas are more likely to be of African American descent), previous pelvic irradiation, use of tamoxifen, history of hereditary retinoblastoma, age older than 50 years, and rapid lesion growth, particularly in postmenopausal patients.

Ultrasonographic examination can reveal indirect signs, including oval lesions, central necrosis, high central vascularization, fast growth, absence of calcifications, and shadowing.[16–18] Measurement of serum lactate dehydrogenase (LDH) has been proposed as a potential marker largely because it may be elevated in LMS. However, its low specificity limits its use because LDH may be elevated in simple leiomyomas.[19] Another imaging method that could help to detect a potential sarcoma is diffusion-weighted magnetic resonance imaging combined with serum levels of LDH, but costs and access may be limiting factors in some countries.[20–22] Nevertheless, the specificity of imaging to accurately predict a sarcoma before a potential surgery is low. Another potential diagnostic procedure, which has already been used successfully in other soft tissue tumors and which is being currently tested, is ultrasound-guided biopsy, a procedure generally performed under local anesthesia.

Hysteroscopy and endometrial biopsy could be helpful to increase the rate of identification of sarcomas before surgery in patients with bleeding, even though LMSs have been diagnosed only in approximately 35% and ESSs in 25% of cases undergoing endometrial biopsy.[23]

In all cases of a growing *uterine* mass or fibroid, especially in postmenopausal women without hormonal replacement therapy, a uterine sarcoma should be suspected and managed surgically.

Methods of Morcellation

Morcellation is conducted using several techniques that should be meticulously discriminated during risk evaluation:

- power morcellation of fibroid
- power morcellation of the uterus
- uterine morcellation during vaginal hysterectomy
- morcellation with minilaparotomy incision

What Is the General Impact of Morcellation Techniques?

- potential dissemination of malignant cells through hematologic spread during manipulation with the specimen,

which is a risk not influenced by morcellation, but rather by an indication for surgery
- potential spread of malignant cells by seeding on the peritoneum during morcellation (sarcomatosis)
- potential local spread/recurrence of the tumor after morcellation of the uterus during the vaginal approach (after a vaginal pure or a laparoscopic-assisted vaginal hysterectomy)
- transecting the specimen into pieces will prevent the pathologist from adequately evaluating the specimen for size, invasion, or resection margin status, and thus, stage cannot be properly determined

What Are the Consequences in the Shift From Minimally Invasive Procedures to Open Procedures?

Consequences additional to oncological outcomes should be mentioned. A Cochrane review of 4495 patients undergoing hysterectomy for benign gynecological pathology provided a comparison between abdominal, laparoscopic, and vaginal hysterectomy for complications, surgical time, length of hospital stay, and out of work stay. Clear advantages were noted for the vaginal and laparoscopic approaches over abdominal hysterectomy.[24] United States data show that omitting the use of morcellation during hysterectomy can lead to a 99,000-day absence from work per year.[17,25] Eight months after the FDA statement, one report showed a decrease in the use of laparoscopic hysterectomies by 4.1%, leading to an increase in major surgical complications from 2.2% to 2.8% and the rate of readmissions from 3.4% to 4.2%.[26]

In Europe, based on Eurostat data, there are approximately 600,000 hysterectomies performed annually, and the rate of laparoscopic hysterectomy relative to the total number of hysterectomies was approximately 20% in 2013.[7] Long-term complications (eg, additional reoperation, absence from work, and scar herniation) requiring surgical repair will need to be included in any further evaluation of the impact in the shift of management.

Are There Surgical Techniques That Could Be Used to Minimize the Risks of Tumor Spread?

Most of the techniques are considered to be preventive based on expert opinion rather than on evidence based data. The following precautions should help in minimizing the risks of tumor spread:

- avoid unnecessary manipulation of the tumor by forceps
- for morcellation, use specifically designed containers or an endobag for morcellation
- take special care of necrotic fibroids, which are more vulnerable during manipulation
- in case of a fibroid or uterus rupture, perform peritoneal washings
- total hysterectomy (laparoscopy-assisted vaginal hysterectomy, total laparoscopic hysterectomy) with en bloc resection is preferred over supracervical hysterectomy

Further Research Should Address the Following Key Areas

- improvements on the sensitivity and specificity of preoperative work-up
- more relevant statistical data on the risks of morcellation using specified registries, differentiating power, and vaginal morcellation
- modification of surgical techniques
- modification of adjuvant therapy when morcellated sarcoma has been diagnosed

CONCLUSIONS

Uterine sarcomas are rare, aggressive tumors, with the majority of patients having a poor prognosis. Their prognosis could be iatrogenically negatively induced by morcellation in approximately 30% of all sarcomas (low-grade ESSs and ASs). Currently, the risk of having an unexpected sarcoma is approximately 1:352, but a proper preoperative examination can help to some extent in decreasing the number of unrecognized uterine sarcomas. An indication for myomectomy should be used only in patients with pregnancy plans; otherwise, en bloc hysterectomy is preferred in both symptomatic and postmenopausal patients, especially in those with a growing mass. Power morcellation has still its place in the armamentarium of gynecologic surgery, particularly for large fibroids undergoing myomectomy, and the use of an endobag could be a safe option to prevent iatrogenic seeding of tumor cells.

Rather than banning morcellation techniques altogether, attempts should be made to increase a proper preoperative work-up, evaluate risk factors, and develop techniques to decrease the risk of spillage. Proper informed consent is mandatory, and patient preference should be a part of indication procedure.

FINAL RECOMMENDATIONS

Examination should be performed by an experienced ultrasonographist in patients for whom myomectomy or hysterectomy with morcellation is considered, even though there are no fixed criteria for establishing sarcoma.

Avoid morcellation if there are suspicious ultrasonographic signs, fast growth within 3 months, and rapid postmenopausal growth.

When planning a power morcellation, a preoperative endometrial biopsy with hysteroscopy should be mandatory.

Morcellation should not be used if there is a suspicion of a sarcoma or if a sarcoma is present after endometrial biopsy/resection for uterine bleeding. A hysterectomy with en bloc resection should be the standard approach (by laparotomy for a bulky uterus).

Use power morcellation only for uterine fibroids rather than for the whole uterus, which could be extracted vaginally or by minilaparotomy.

Surgical removal of uterine fibroids by myomectomy should be morcellated in endobag containers.

In case of morcellation in a patient with unrecognized sarcoma, the patient should be reported to an online database designed to look at the follow-up of such patients.

Informed consent should state the following information:

- risk of dissemination of unknown malignancy by the manipulation of the uterus/fibroid exists in both techniques
- risk of dissemination of unknown malignancy by power morcellation is higher when using laparoscopic techniques,

but the exact relative risk is unclear. The worse estimates state that the risk of unrecognized sarcomas of surgically treated fibroids is 1 case out of 352 procedures, and approximately 30% of these cases could have a prognosis worsened by power morcellation techniques, resulting in a risk of approximately 1 in 1000 that morcellation could exacerbate the patient's prognosis
- risks of higher blood loss, prolonged recovery, infectious complications, and hernias are more often associated with open procedures

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