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Review article

Assessing the risk of laparoscopic morcellation of occult uterine sarcomas during hysterectomy and myomectomy: Literature review and the ISGE recommendations

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ABSTRACT

Objective: This project of the International Society for Gynecologic Endoscopy (ISGE) had the objective to review the literature and provide recommendations on the occult sarcoma risk assessment in patients who are candidates for minimally invasive gynecological surgery involving intra-abdominal electromechanical tissue morcellation.

Study design: The ISGE Task Force for Estimation of the Risk in Endoscopic Morcellation initially defined key topics and clinical questions which may guide a comprehensive preoperative patient assessment. A literature search within the Medline/PubMed and Cochrane Database was carried out using keywords "morcellation", "uterine fibroids", "uterine sarcoma", "myomectomy" and "hysterectomy". Relevant publications (original studies, meta-analyses and previous reviews), written in English and published until May 30th, 2017, were selected and analyzed. Previously emitted statements of 12 recognized professional societies or government institutions and their supporting literature were also studied. For each topic/clinical question, the available information was graded by the level of evidence. The ISGE recommendations were established in accordance with the evidence quality.

Results: In the light of available information, 9 recommendations on preoperative clinical, laboratorial and imaging evaluation of the candidates for intracorporeal uterus/leiomyoma morcellation were formulated, mainly based on consensus and expert opinions. There is a lack of high-quality evidence, which does not allow the establishment of strong recommendations.

Conclusion: Electromechanical tissue morcellation may be used in gynecological patients who are considered "low risk" upon appropriate preoperative evaluation; however, further studies and prospective data collection are greatly needed to improve sarcoma risk assessment in women with presumed uterine leiomyomas.

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Introduction

Uterine leiomyoma (LM), also referred to as myoma, fibromyoma or uterine fibroid, is the most common benign gynecologic neoplasm that affects women of reproductive age [1]. Surgical procedures, including myomectomy and total or sub-total hysterectomy, are commonly employed to treat symptomatic uterine LM. When performed using minimally invasive approaches, decreased postoperative hospital stay and/or reduced risks of intraoperative and postoperative morbidity and mortality have been documented [2–12]. In order to remove uterus or LM from the abdominal cavity through laparoscopic ports, laparoscopic power morcellator has been regarded as the instrument of choice. The device's rapidly spinning blades cut the tissues into fragments allowing their removal through a small incision [13], but LM/uterus morcellation does increase the risk of both benign and malignant cell dispersion within the peritoneal cavity [14–26].

The US Food and Drug Administration (FDA) issued a safety communication on April 17th, 2014 urging surgeons not to use laparoscopic power morcellation for hysterectomies or removal of uterine fibroids over concerns that the technique may spread occult uterine sarcomas beyond the uterus [27]. The morcellation-disseminated disease may greatly reduce the woman's chances of survival [14–19,21–23]. In addition, samples obtained via morcellation may be more difficult to evaluate by the pathologists due to the disorientation of the tissues, complicating diagnosis and staging [27]. Other government agencies and professional societies, including Health Canada [28], the Society of Gynecologic Oncology (SGO) [29], the American College of Obstetricians and Gynecologists (ACOG) [30], the American Association of Gynecologic Laparoscopists (AAGL) [31], the European Society for Gynaecological Endoscopy (ESGE) [32], the European Society of Gynecological Oncology (ESGO) [33], the Asia-Pacific Association for Gynecologic Endoscopy and Minimally Invasive Therapy (APAGE) [34], the Australian Gynaecological Endoscopy and Surgery Society/The Royal Australian College of Obstetricians and Gynecologists (AGES/RANZCOG) [35], the British Society for Gynaecological Endoscopy (BSGE) [36], the French College of Obstetrics and Gynecology [37], and the German Society for Gynecology and Obstetrics (DGGG) [38], also issued statements discouraging, but not prohibiting the use of laparoscopic power morcellation in hysterectomy or myomectomy.

As estimated by a FDA analysis, about 1 in 350 women submitted to a myomectomy or hysterectomy for fibroids has an undetected uterine sarcoma, although the American Cancer Society estimates that only about 1600 of the 52,000 cases of uterine cancer newly diagnosed each year turn out to be uterine sarcomas [39]. Seidman et al. observed that unexpected diagnoses of leiomyoma variants or atypical and malignant smooth muscle tumors had occurred in 1.2% of cases using power morcellation for uterine masses clinically presumed to be “fibroids” [40]. In a prospective study assessing the risk of morcellation of a sarcoma in case of laparoscopic myomectomy, Sizzi and collaborators have found 1 case out of 2050 procedures (0.04%) [41].

Although the overall risk of occult uterine malignancy appears to be low, there is a wide consensus that patients being considered for minimally invasive surgery, performed by laparoscopic or robotic techniques, who might require intracorporeal morcellation, should be appropriately evaluated for the possibility of coexisting uterine malignancy. Based on the analysis of pertinent original works, meta-analyses, available reviews, previously published guidelines and consensus expert opinions, we present in this paper practical recommendations regarding preoperative assessment of the risk of sarcoma morcellation in women planed to be submitted to laparoscopic myomectomy or hysterectomy.

Methods

The working group defined morcellation as any surgical procedure resulting in the fragmentation of a surgical specimen into smaller pieces. Different morcellation types may have different risk profiles [42,43]. We have been focused on the electromechanical morcellation, also known as electronic or power morcellation, which is achieved by the use of electrosurgical morcellator devices.

Initially, relevant topics and key clinical questions were defined which may guide a comprehensive preoperative sarcoma risk assessment in the patients with presumed LM who are considered for minimally invasive surgery with intracorporeal electromechanical morcellation (Table 1). A search from Medline/PubMed and the Cochrane Database, written in English and published until May 30th, 2017 was carried out using keywords: morcellation, uterine fibroids, uterine sarcoma, myomectomy and hysterectomy. Relevant publications, including original studies, meta-analyses and previous reviews, were selected. Their bibliographies were also checked and analyzed. In parallel, the working group studied previously emitted statements, supporting literature and recommendations of the US Food and Drug Administration (FDA), Health

Table 1
Relevant topics and key clinical questions regarding preoperative sarcoma risk assessment.

Clinical topics	Key clinical questions
Clinical features relevant for sarcoma risk assessment	How should an appropriate clinical evaluation be performed in preoperative phase to discriminate low- vs. high-risk patients?
Biochemical tests	Are there useful biochemical markers to discriminate LMS from LM?
Imaging-based evaluation	How effective are available imaging techniques to identify mesenchymal malignancies in patients with presumed LM?
Hysteroscopy and biopsy	Should endometrial sampling be considered in all patients?

Canada, the American Association of Gynecologic Laparoscopists (AAGL), the American College of Obstetricians and Gynecologists (ACOG), the Asia-Pacific Association for Gynecologic Endoscopy and Minimally Invasive Therapy (APAGE), the Australian Gynaecological Endoscopy and Surgery Society/The Royal Australian College of Obstetricians and Gynecologists (AGES/RANZCOG), the British Society for Gynaecological Endoscopy (BSGE), the European Society for Gynaecological Endoscopy (ESGE), the European Society of Gynecological Oncology (ESGO), the French College of Obstetrics and Gynecology, the German Society for Gynecology and Obstetrics (DGGG) and the Society of Gynecologic Oncology (SG0). For each topic/clinical question, the available information was graded by the level of evidence (Table 2). In accordance with the evidence quality, our recommendations were established, being subsequently validated through multiple cycles of literature consultation. No Ethical Committee approval was required for this work.

Literature review

Uterine sarcomas account for 2–7% of all uterine malignant lesions [32,44]. In accordance with the last World Health Organization classification (2014), mesenchyme tumors of pure myometrial origin (leiomyoma [LM], smooth muscle tumor of unknown potential [STUMP] and leiomyosarcoma [LMS]) are to be distinguished from the endometrial stromal tumors (endometrial stromal nodule, low-grade endometrial stromal sarcoma [LG-ESS], high-grade endometrial stromal sarcoma [HG-ESS], and undifferentiated endometrial sarcoma), while mixed Müllerian tumor (i.e. carcinosarcoma) is currently classified as carcinoma [45]. LMS represents nearly 70% and ESS nearly 30% of all uterine sarcomas [32,44].

Differentiating LM from LMS is a particular challenge. Since there is not any clinical sign or symptom, biochemical or imaging marker that may lead to an unambiguous and precise preoperative distinction between these lesions [27,31,32,38,29], postoperative histological analysis is the only reliable method to achieve definitive diagnosis. Although clinical evaluation could improve the detection of cancer, it has many limitations in the case of sarcomas, confirming the need for further research to develop reliable tools for preoperative diagnosis of an occult malignancy. To date, there is no single correct approach to evaluate the potential malignancy of uterine LM in pre-surgical phase. Various options are available and differ considerably in cost and inconvenience to the woman [46]. Anyway, meticulous patient evaluation should be performed before choosing the type and route of operation, and every effort should be made to estimate the malignancy likelihood before surgery [27,31,40].

Clinical features

Initial evaluation of any woman planned for gynecologic surgery should be based on a well-structured medical history, resulting in an appropriate characterization of presenting symptoms and identification of uterine cancer risk factors. The initial approach also includes physical examination and cervical cancer screening performed by the use of an adequate test, in agreement with the guidelines [31,32].

The known uterine sarcoma risk factors are summarized in Table 3. Black race is common risk factor for both LM and LMS. In black vs. white women, the LM incidence is 2- to 3-fold greater and the LMS incidence as well as the incidence of carcinosarcoma is 2-fold higher [47–49]. In contrast, increasing age, particularly postmenopausal status, is an important risk factor for uterine sarcomas, while LM typically shrinks following menopause. The mean patient age at sarcoma diagnosis is 60 years [50]. Below the age of 40, sarcoma in a presumed LM is extremely rare [32]. Other risk factors for uterine sarcoma, which do not present statistically significant association with LM, include long-term use of tamoxifen (5 years or more), pelvic irradiation, hereditary leiomyomatosis and renal cell carcinoma (HLRCC) syndrome due to germline mutations of *fumarate hydratase*, and a history of childhood retinoblastoma [31].

The clinical manifestations of LM and LMS are often indistinguishable [30,31]. Abnormal uterine hemorrhage (most frequently, in the form of heavy menstrual bleeding), dysmenorrhea, lower abdominal pain, lumbago, pressure symptoms (e.g. pollakisuria, dysuria, bowel symptoms) and palpable mass on the site of lower abdomen are the principal presenting symptoms and signs for both pathological entities [30,51–54]. Similarly, uterus and lesion size, uterine contour, mobility and any other examination finding cannot accurately distinguish a LM from a LMS [51,52,55–57]. Rapid lesion growth has been traditionally valorized as a sign of a potential malignancy [58]; however, neither large tumors [51,56] nor rapidly enlarging uterine masses [55,57,59–62] have been demonstrated as useful malignancy indicators in premenopausal women. On the other hand, in postmenopausal patients, particularly in women who are not on hormone replacement therapy, new or growing lesions require evaluation and malignant process exclusion. Furthermore, the lesion failure to respond to medical or non-excisional treatment, such as uterine artery embolization or myolysis performed by magnetic resonance-guided focused ultrasound (MRgFUS), is clinically highly important, despite the fact that it does not provide an absolute evidence of the tumor malignant nature [63–69].

The metastatic disease manifestations can be found in women with LMS, while spontaneous benign LM dissemination is very

Table 2
Quality of Evidence and Strength of Recommendations (in accordance with the US Preventive Services Task Force [31,116]).

Quality of evidence	
I	Evidence obtained from at least one properly designed randomized controlled trial
II	Evidence obtained from non-randomized clinical evaluation
II-1	Evidence obtained from well-designed, controlled trials without randomization.
II-2	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research center.
II-3	Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
III	Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.
Strength of recommendations	
A	Recommendations are based on good and consistent scientific evidence.
B	Recommendations are based on limited or inconsistent scientific evidence.
C	Recommendations are based primarily on consensus and expert opinion.

Table 3
Uterine sarcoma clinical risk criteria (adapted from ACOG and AAGL statements [30,31]).

Symptoms	
Abnormal uterine bleeding (including irregular, heavy and/or prolonged menstrual bleeding)	
Dysmenorrhea	
Palpable abdominal mass	
Lower abdominal pain	
Lumbago	
Pressure symptoms (pollakisuria, dysuria, bowel symptoms)	
Risk factors	**Comment**
Black race	Two-fold higher LMS incidence rate comparing to the white race
Increasing age	Mean patient age at diagnosis: 60 years Lowest risk in women <35 years; highest risk in women >65 years
Tamoxifen	Prolonged use (≥5 years)
Pelvic irradiation	Association especially strong for carcinosarcoma
HLRCC syndrome	AD syndrome; sarcomas often found in younger women
Survivors of childhood RB	Higher risk for uterine sarcomas and sarcomas in general

Note: Increased uterine size, large LM and rapid uterine/LM growth increase concern for the presence of an occult sarcoma, but have not been shown to be predictive of LMS [30,59,60].
Abbreviation: AD, autosomal dominant; HLRCC, hereditary leiomyomatosis and renal cell carcinoma; RB, retinoblastoma.

rare, but it may occur giving origin to disseminated peritoneal leiomyomatosis, intravascular leiomyomatosis and benign LM metastasizing to distant tissues [70]. In these clinical settings, procedures requiring morcellation are never considered to be performed.

Routine screening for cervical cancer and endometrial sampling

As already mention, prior to treatment of presumed LM, routine screening for cervical cancer should not be omitted. Uterus morcellation should be avoided in women with cervical dysplasia [31].

Unlike cervical cancer, currently, there is no effective procedure for other uterine cancer screening. For example, routine endometrial screening was not found to be cost-effective in asymptomatic postmenopausal women with pelvic organ prolapse who had undergone uterine morcellation during prolapse repairing surgery [71]. To rule out endometrial atypical hyperplasia or endometrial cancer in women with abnormal uterine bleeding, most guidelines suggest that patients should be selected for endometrial sampling based on a combination of the factors indicating an increased risk (e.g. patient's age, genetic and personal risk factors, endometrial echo-features) [72]. However, the risk of morcellation in the setting of LMS is apparently different in comparison to that of endometrial cancer, since low-risk patients may also hold occult LMS with certain frequency [31,73]. In a recent retrospective study of a prospectively collected database (Canadian Task Force III database), 51.5% of patients with LMS had preoperative endometrial biopsies indicating LMS or atypical spindle cell proliferation, whereas 35.5% of the pre-operative biopsies specifically diagnosed LMS [74]. There was no statistically significant difference in the efficacy between dilation and curettage and office endometrial biopsy. Although these data, as well as the results of previous smaller studies [75,76], show that the sensitivity of endometrial biopsy to detect LMS is low, positive or suspicious result has a decisive impact on the choice of patient management [74].

Performing transcervical LM needle biopsies to rule out sarcoma has also been considered. However, such manipulation may have harmful effect of tumor spread [113].

Biochemical markers

The utility of tumor markers to aid in the diagnosis of LMS has been presupposed. Some studies focused on the correlation between lactate dehydrogenase (LDH) levels, especially its isoenzyme 3 (LDH3), and the pathological diagnosis of LMS [77], revealing that patients with LMS often have somewhat increased serum LDH levels [78]. For instance, Goto et al. observed an abnormally increased level of total LDH and LDH3 in all patients with LMS (LDH3, sensitivity and specificity 90% and 92.3%) [77]. However, these studies have not been reproduced, nor can the presence of LDH definitively predict the possibility of LMS as it is such a nonspecific marker.

Elevated serum cancer antigen 125 (CA125) has been occasionally observed in LMS patients, particularly in advanced-stage disease [79,80]. Interestingly, Menczer et al. did not evidenced CA125 expression in any of 17 immunohistochemically examined LMS tumors, concluding that the origin of increased serum CA125 is not in neoplastic tissue and remains unknown [81]. Inconsistent increase and significant overlapping of CA125 levels between the LM and early-stage LMS patients impede the marker clinical use [79].

Imaging

Ultrasonography: The vast majority of fibroids are discovered and evaluated via sonography, using the trans-abdominal and transvaginal routes, due to its accessibility, relatively low costs and reliability [1]. The Morphological Uterus Sonographic Assessment (MUSA) consensus paper, published in 2015, provides the terms, definitions and measurements for standardized evaluation and reporting of sonographic features of myometrium and myometrial lesions [82].

Sonographically, a typical uterine LM is a well-defined round formation within or attached to myometrium, whose echogenicity varies, often showing some internal hyperechogenicity, internal fan-shaped shadows and/or shadows at the edge of the lesion [82]. Circumferential flow around the formation can be visualized by color or power Doppler, while MUSA group suggests that LM should be labeled as sonographically atypical if the lesion does not exhibit this vascular pattern. When a LM undergoes degeneration, it may show low echogenicity, hyperechogenic rim and no internal vascularity, or mixed echogenicity, or hypoechogenic cystic areas [82–85]. LM with little or no recurrent and/or metastatic potential as well as uterine smooth-muscle tumors of uncertain malignant potential (STUMP) have the same ultrasound characteristics as does an ordinary LM [82,86–91].

Several studies focused their attention on the detection of sonographic parameters that could be used in distinguishing between a benign and a malignant uterine smooth muscle tumor

[92–95]. Uterine sarcomas are typically solitary, large lesions [82,96], often exhibiting ultrasound features that are indistinct from those of LM [97]. Although they may also appear as irregularly and highly vascularized masses, with or without irregular anechogenic areas reflecting tumor central necrosis [1,92,95,98,99], there is no ultrasound characteristic that can reliably differentiate between LM and LMS. Exacoustos et al. proposed a subjective semi-quantitative assessment of the blood flow (vascular score), examined with directional power Doppler imaging, which was similar to that proposed for adnexal masses by the International Ovarian Tumor Analysis (IOTA) Consensus Group, revealing that the increased central and peripheral vascularity had a sensitivity, specificity, and positive predictive value (PPV) of 100%, 86%, and 19% in the diagnosis of LMS [98]. Nevertheless, a 19% PPV is not clinically relevant. Additionally, despite the fact that a large myometrial tumor and/or its rapid growth may increase concern for the presence of an occult sarcoma, such observations have not been evidenced in few other studies as unequivocal, malignancy-specific findings [30,59,60]. Because of the overlapping clinical features and ultrasound morphologies, physicians could decide to further investigate the suspected lesion before surgical intervention or more conservative treatment (e.g. uterine artery embolization, MRgFUS and radiofrequency ablation) [1].

Magnetic resonance imaging (MRI): MRI provides a better image in delineating the exact location and characteristic of the fibroids; however, it is far more expensive and less accessible than ultrasound [1,93]. Therefore, MRI should be considered only for women in whom the nature of the pelvic mass is uncertain after clinical and level II pelvic ultrasound assessment (Table 4). The differentiation of LM from LMS may be suggested by assessing tumor total necrosis and the presence of a peripheral rim, which corresponds to the obstructed veins showing low signal intensity on T2 and high signal intensity on T1WI [100]. Tanaka et al. reported that the highest accuracy in diagnosing non benign smooth muscle lesions is expected when more than 50% of the tumor shows high signal on T2WI, any small area of high signal is seen within the tumor on T1WI, and there are some unenhanced pocket-like areas after administration of contrast materials [101].

Goto et al. compared conventional MRI findings along with post-enhancement behavior (*dynamic MRI*) of degenerated LM and LMS, revealing a specificity, accuracy and positive predictive value (PPV) of 96.9%, 97.1%, and 71.4% for MRI, and 87.5%, 90.5% and 71.4% for dynamic MRI [77]. Both sensitivity and negative predictive value (NPV) were 100%. In particular, they highlighted the importance of obtaining the dynamic images at 40–80s after gadolinium administration because no enhancement was observed in the early phase at nearly 60s in degenerated LM whereas LMS rapidly enhanced at 20–90s [77]. However, other studies did not confirm these results [102].

Table 4
Ultrasound criteria to evaluate uterine sarcoma risk.

Level II: Ultrasound criteria
Echo pattern (homogeneous or inhomogeneous, with mixed echogenic and poor echogenic parts)
Necrotic, cystic, hemorrhagic changes
Single lesion
Presence or absence of central vascularization[a]
Distribution of tumoral vascularization: a high vascularity score[b]
Size (maximal diameter >8 cm)
Presence or absence of calcifications

[a] Subjective color score: 1 – no color, 2 – minimal color, 3 – moderate color, 4 – abundant color.
[b] The score for both central and peripheral region are combined (maximum vascular score: 8).

Sato et al. proposed the use of *diffusion-weighted imaging* (DWI) and corresponding *apparent diffusion coefficient* (ADC) values in the evaluation of myometrial tumors [103]. Decreased ADC values of malignant tumors, compared with normal tissues or benign lesions, had been previously reported for various organs [104–106]. Sato et al. affirmed that cases with low signal intensity on DWI may be regarded as uterine LM, while intermediate to high signal intensity may indicate uterine LMS. For this reason, in patients with parenchymal areas of intermediate to high signal intensity, ADC values were evaluated, revealing that the mean ADC value for the LMS lesions was significantly lower than that of the LM nodules [103]. Another study observed that the combination of ADC and tumor–myometrium contrast ratio is significantly better compared to the apparent diffusion coefficient value or tumor-myometrium contrast ratio alone in differentiating uterine LMS and LM, with no overlap (sensitivity 100%, specificity 100%) [106].

To optimize the treatment of patients with myometrial tumors, *MRI spectroscopy (MRS) imaging* and *dynamic contrast-enhanced MRI (DCE-MRI) with pharmacokinetic analysis* have also been considered. MRS provides tissue-specific metabolic information along a 2D or 3D spectrum based on the fact that the choline metabolite profile in cancer is characterized by an elevation of phosphocholine and total choline (tCho) containing compounds [107]. Takeuchi et al. showed in 14 malignant cases of 32 myometrial lesions that the tCho concentration in malignant tumors was significantly higher than that in benign lesions, although these tumors were mixed endometrial and myometrial lesions. They suggest that a combined diagnosis using T2-WI and tCho concentration may help for differentiation [108]. On the other hand, DCE-MRI with pharmacokinetic analysis assesses tumor microvascular response to direct and indirect antiangiogenic drugs. Using pharmacokinetic models, DCE-MRI allows extraction and mapping of quantitative parameters of tumor biology in vivo [109]. The major problem of both intra-abdominal MRS and DCE-MRI is motion, which is largely due to respiration and intestinal peristalsis [110].

Computed tomography (CT) and positron emission tomography (PET)/CT with fluorodeoxyglucose (FDG): As far as the available data indicate, neither CT nor PET/CT with FDG is useful to distinguish between uterine LM and LMS [111,112]. Although the average FDG uptake is high in sarcomas than in LM nodules, it significantly varies between individual tumors [112].

To sum up, the discriminating capability of pelvic imaging is limited since there is no pathognomonic LMS feature detectable by any of available imaging modalities. Upon clinical assessment, pelvic ultrasonography should be the initial imaging approach in all women with LM. When clinical characteristics of the patient or tumor and/or ultrasound findings give rise to concerns about the lesion nature and sarcoma is suspected, MRI with gadolinium contrast represent an appropriate next step for assessing the likelihood of myometrial malignancy. The definitive diagnosis can only be reached through the lesion histological evaluation. Thus, proper informed consent has to be given to the patients while minimal invasive surgery involving an intra-abdominal morcellation should never be performed in women who are not considered as “low-risk patients” after comprehensive preoperative evaluation.

Similar to the clinical presentation and imaging of LM and LMS, the intraoperative findings are also often indistinguishable [31]. To further reduce the risk, techniques for single or multiport laparoscopic morcellation in contained, new designed sturdy bags have been described [114], but the safety of this technique will have to be studied. The principal unanswered concern in any discussion of myomectomy, whether accomplished laparoscopically or by open laparotomy, is the impact of any disruption of the intact uterus necessary to the performance of myomectomy on

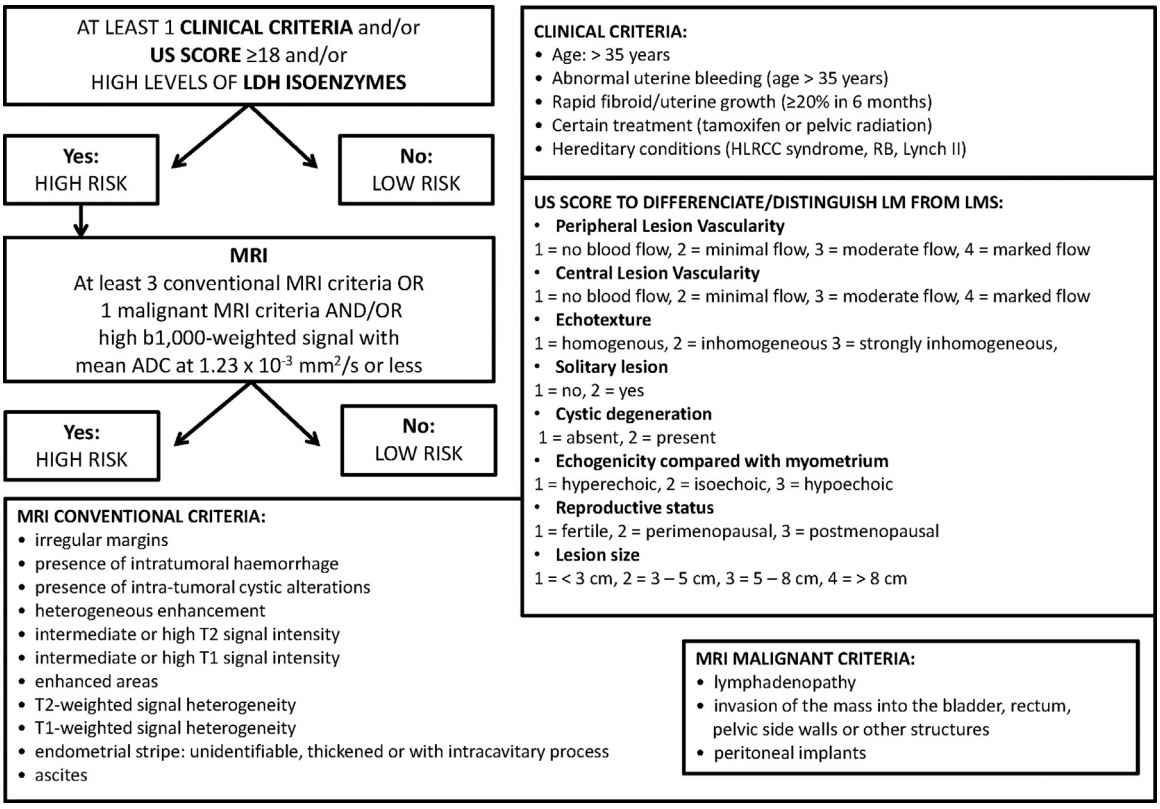

Fig. 1. Preoperative diagnostic flowchart.

tumor spread. Incision in the uterine serosa and myometrium necessary to extract LM by definition opens vascular and lymphatic channels, facilitating the spread of tumor cells. Any blood or tissue fragments spilled into the abdominal cavity as well as contact of any resected tissue with the peritoneum can potentially spread cancerous cells. By the time the tissue has been placed in a bag for morcellation, it may be already too late to prevent the spread of tumor.

On the other hand, it could be considered to perform total laparoscopic hysterectomies instead of supra-cervical hysterectomies, with morcellation of the specimen through the vagina, possibly in a bag. There are no evidence-based medicine data showing that supra-cervical hysterectomy is better for the patient on the long run compared to total laparoscopic hysterectomy (Cochrane Mata-analysis, 2010) [115]. Preference to supra-cervical hysterectomy can be justified only in case of pelvic organ prolapse repair after appropriate preoperative evaluation.

Currently, there is not a single tissue-extracting procedure that offers absolute patient protection. Thus, all methods should remain available [31]. In all circumstances when preoperative evaluation of cervix, endometrium and/or myometrium results in an increased suspicion for malignancy, the surgeons should employ alternatives to morcellation, including laparotomy [30–32,39]. Inversely, low-risk patients may undergo and experience benefits from minimally invasive surgery, but these women, surgeons and hospitals should always be aware that sarcomas are diagnosed, although very rarely, even in patients appropriately evaluated and selected for morcellation-involving interventions. Further epidemiological research, clinical studies and technical innovations are required to enable safe morcellation in a wide range of patients.

Conclusions and recommendations

From the data we have at our disposal, it appears that the risk of unexpected sarcomas found after a laparoscopic intra-abdominal morcellation is probably over estimated by some articles cited by the FDA, but it is generally agreed that the odds of a woman with uterine fibroids having an unsuspected cancer are likely higher than had been assumed in the past (Level III). We, therefore, need to have more data that show how safe and reliable the diagnostic pre-surgical tools are, as to differentiate between low- and high-risk patients. Although newly developed techniques are by now readily available, an effort should be made to focus on how they are applicable.

Recommendation 1: A comprehensive preoperative algorithm should be proposed in order to avoid the morcellation of unexpected LMS (Level C).

Recommendation 2: The preoperative evaluation should start with clinical evaluation of all patients with presumed LM nodules. Detailed history and physical examination, with special attention paid to the clinical risk criteria (Table 3), should guide the clinician regarding the malignancy likelihood assessment and choice of surgical approach (Level A).

Recommendation 3: Ultrasonographic examination should be offered to all patients with fibroids (Level A). MUSA methodology and terminology are recommended to be used for scanning and observation reporting (Level C). Level II ultrasound criteria should orientate the risk evaluation (Table 4).

Recommendation 4: Cervical cancer screening should be performed in all patients following the guidelines of recognized institutions or societies (Level A).

Recommendation 5: To detect unrecognized malignancy and ascertain a woman's eligibility for morcellation, it is also recommended that all patients undergo: total LDH and LDH3 assay and hysteroscopy with biopsy in any case of abnormal uterine bleeding plus a CA-125 assay (Level C).

Recommendation 6: Although MRI provides a better image then ultrasonography to delineate the exact location and characteristics of the fibroids (Level II-2), it should be considered only for women in whom the nature of the pelvic mass is uncertain after clinical assessment followed by blood test assays and pelvic ultrasound examination (Fig. 1). Patients considered "low-risk" can undergo surgery without further investigations while it is recommended to send the other patients to MRI evaluation (Level C).

Recommendation 7: Conventional MRI examinations should be performed while the correlation between conventional MRI findings (T1 and T2-weighted images), diffusion weighted imaging (DWI) intensity and corresponding apparent diffusion coefficient (ADC) values and dynamic contrast-enhanced MRI (DCE-MRI) with pharmacokinetic analysis study may also be evaluated in order to exclude or suspect the presence of a LMS (Level C). Only the patients who are considered "low risk" after MRI imaging may undergo minimal invasive surgery involving an intra-abdominal morcellation, unless the morcellation can be carried out in a contained bag (Level C).

Recommendation 8: Proper informed consent has to be given to the patient explaining the potential risk of sarcoma morcellation and consequent upstaging, taking into account the difficulties encountered in providing a patient-specific risk (Level A).

Recommendation 9: Histological evaluation after myomectomy or hysterectomy should be recorded and computed for statistics analysis.

;1;

Considering the fact that no one is challenging the benefits of minimal invasive surgery for the patients (Level I) and that the recent audit of the FDA on July 11, 2014 has stated that the data in the literature are at best "very weak", it is obvious that new prospective trials will have to be designed to obtain more reliable answers. At the same time, there are no significant data suggesting that surgeons should stop offering minimally invasive interventions to "low-risk" patients.

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Conflict of interest

The authors declare that no conflicts of interest do exist.

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