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«Χειρουργική αντιμετώπιση ινομυωμάτων. Ο ρόλος της λαπαροσκοπικής χειρουργικής.»

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INTRODUCTION

Uterine leiomyomas (also reported as myomas or fibroids) are the most common pelvic tumor in women. Their incidence among women is generally cited as 20 to 25 per cent but is as high as 70 to 80 per cent in studies using histologic or sonographic examination, in women from 25 to 55 years old **2**. Uterine myomas are benign tumors composed of disordered monoclonal cells of the myometrium. They are thought to proliferate under the hormonal control of estrogen and progesterone, although the exact pathogenesis is not yet known **1,2,3**. The majority of myomas remains asymptomatic. When symptomatic, women experience symptoms that can be classified in three categories: 1) abnormal uterine bleeding, 2) bulk-related symptoms, such as pelvic pressure to adjacent organs such as the bowel and the bladder and pain and 3) reproductive dysfunction (i.e. infertility, , pregnancy loss or obstetric complications). Occasionally, the impact of symptomatic fibroids on women's daily life is so severe that they often report lower scores on quality-of-life assessments when compared to women who have hypertension, heart disease, chronic lung disease or arthritis. Additionally, the annual excess cost per woman with symptomatic fibroids is estimated at more than $4600, $771of which are related to missed working days. **4,5,6**.

Traditionally surgical treatment for uterine leiomyomas involved two options: hysterectomy, for those who do not wish to retain their uterus, and myomectomy for those who wish to maintain uterine structure and function, often for reproductive reasons. In most cases these procedures in the past were performed through large abdominal incisions (laparotomy) mainly directed by the large size of the fibroid uterus.

Less invasive surgical approaches such as laparoscopic, hysteroscopic and vaginal hysterectomy or myomectomy are offering patients many advantages comparing to laparotomy such as shortened hospital stays, faster recovery, and rapid return to daily activities. **7,8,9,10**.

The removal of large fibroid tumors through small laparoscopic incision has always been a challenge. Manual morcellation, of large tumors via scalpel was initially performed in order to reduce the size of the specimen and complete the procedure either vaginally or laparoscopically. Recently the development of new instruments such as the electric power morcellator, greatly facilitated this laborious task. Electromechanically assisted (power) morcellation was approved by the Food and Drug Administration in 1995 and greatly improved the capacity to morcellate large benign tumors, making minimally invasive surgical procedures more widespread and available to significantly more women. **11**

Recently however, following a legal case of a patient with unsuspected sarcoma who underwent mechanical morcellation the use of power morcellators has been subject to inspection and scrutiny. **12**. On October 14, 2014, FDA issued a statement discouraging the use of power morcellators, citing safety concerns, chief among these being the inadvertent dissemination of occult uterine cancer in patients undergoing hysterectomy and myomectomy for presumed benign leiomyomas. The FDA estimated prevalence of unsuspected sarcoma after primary analysis of 9 out of 18 identified studies in the literature, was one case of unsuspected uterine sarcoma in 352 women and on case of unsuspected leiomyosarcoma in 458 women undergoing hysterectomy or myomectomy for presumed benign leiomyoma. **13,14,15,16**

Undoubtedly, the dissemination of the tumor and the ensuing increased rate of recurrence and poorer survival, are matters to be addressed with great concern. So we felt it was important to review the existing medical literature on the subject in order to try to elucidate the risk might be.

MYOMAS

EPIDEMIOLOGY FOR MYOMAS

Uterine leiomyomas are the most common benign tumor of the female genital tract. By the age of 50, more than 70% of white and 84% of African women will have been diagnosed either by ultrasound findings or by surgical records. **1.** They are monoclonal smooth muscle cell tumors derived from the myometrium. They contain extracellular matrix including collagen, proteoglycan and fibronectin) and they are surrounded by a thin pseudo capsule. **17-18.** They also have less than 5 mitotic divisions per high powered field (HPF) with minimal cytological atypia.

Despite their high prevalence, their etiology and pathogenesis are far from being well understood. A variety of factors including, age, age at menarche, race/ethnicity, parity, hormonal factors, endocrine disruptors, obesity, and lifestyle, have been associated and examined. **19.**

Symptomatology of uterine leiomyomas is very variant. Most of women are asymptomatic. Symptoms derive from the myoma's location, size and number. The most common fibroid symptom is abnormal uterine bleeding. **20-21.** Following symptoms in

prevalence is pelvic pressure and/or pain, urinary frequency, abnormal bowel function, pain with during intercourse (dyspareunia), as well as effects on fertility and pregnancy outcomes. **22-24.**

CLASSIFICATION

Uterine fibroids are described according to their location in the uterus. A fibroid though, might have more than one location designation. The International Federation of Gynecology and Obstetrics (FIGO) classification system for fibroid location is as follows **25**:

- Submucosal myomas (FIGO type 0, 1, 2): These leiomyomas derive from myometrial cells just below the endometrium. They protrude into the endometrial cavity. The extent of the protrusion is described by the FIGO/European Society of Hysteroscopy classification system and is clinical relevant for predicting outcomes of hysteroscopic myomectomy:

  Type 0: Completely within the endometrial cavity

  Type 1: Extend less than 50% into the myometrium

  Type 2: Extend more than 50% into the myometrium

- Intramural myomas (FIGO type 3, 4, 5): These leiomyomas are located within the uterine wall. They may enlarge sufficiently to distort the uterine cavity or serosal surface. Some leiomyomas may be transmural and extend from the serosal to the mucosal surface.
- Sub serosal myomas (FIGO type 6, 7): These leiomyomas originate from the myometrium at the serosal surface of the uterus. They may have a broad or pedunculated base and may be intraligamentary (i.e. extending between the folds of the broad ligament)
- Cervical myomas (FIGO type 8): These leiomyomas are located in the cervix rather than the corpus of the uterus.

INDICATIONS FOR SURGERY FOR MYOMAS

Surgery is the mainstay treatment for leiomyomas. There are many surgical options provided such as hysterectomy, a myomectomy through an abdominal incision and less invasive techniques like laparoscopically and vaginally assisted hysterectomy and myomectomy. Whichever the following procedure will be determined to be, indications for surgical therapy are the following **25-26**:

- Abnormal uterine bleeding or bulk-related symptoms
- Rapidly enlarging tumors
- Infertility or recurrent pregnancy loss

SARCOMAS

Uterine sarcomas are rare tumors that account for approximately 1% of female genital tract malignancies and 3% to 7% of uterine cancers. Uterine sarcomas are aggressive, but many presents at an early stage. In one series of over 1000 cases, the stage distribution was as follows: stage I (60 %), stage II and III (16 %), and IV (22 %)**. 27-28.** Uterine sarcomas arise from dividing cell populations in the myometrium or connective tissue elements within the endometrium. Compared with the more common endometrial carcinomas (epithelial neoplasms), uterine sarcomas, particularly leiomyosarcomas (connective tissue neoplasms), behave aggressively and are associated with a poorer prognosis **28.**

Histologically, uterine sarcomas were classified initially into carcinosarcomas (malignant mesodermal mixed tumors), accounting for 50% of cases, leiomyosarcomas (30%), endometrial stromal sarcomas (15%), and undifferentiated sarcomas (5%). Subsequently, carcinosarcoma has been reclassified, largely based on its spreading pattern, as a dedifferentiated or metaplastic form of endometrial carcinoma. However, as it behaves more aggressively than the usual type of endometrial carcinoma, carcinosarcoma is still included in most retrospective studies of uterine sarcomas, as well as in the separate section of "mixed epithelial and mesenchymal tumors" of the 2014 WHO classification. **29.**

Recently, however, a new FIGO classification and staging system has been specifically designed for uterine sarcomas in an attempt to reflect their different biologic behavior. Briefly, three new classifications have been developed: (1) staging for leiomyosarcomas and endometrial stromal sarcomas; (2) staging for adenosarcomas; and (3) staging for carcinosarcomas (MMMT). Whereas in the first classification stage I sarcomas are subdivided according to size, subdivision of stage I adenosarcomas takes into account myometrial invasion. On the other hand, carcinosarcomas will continue to be staged as endometrial carcinomas. **30.**

LEIOMYOSARCOMA

Leiomyosarcoma represents about 1.3% of uterine malignancies and about one-third of uterine sarcomas. Approximately 1 of *every* 800 smooth muscle tumors of the uterus is a leiomyosarcoma, but less than 1 % of women thought clinically to have leiomyoma prove to have leiomyosarcoma. Most occur in women over 40 years of age who usually present with abnormal vaginal bleeding (56%), palpable pelvic mass (54%), and pelvic pain (22%). Signs and symptoms resemble those of the far more common leiomyoma and preoperative distinction between the two tumors may be difficult. **31-32.** Malignancy should be suspected by the presence of tumor growth in postmenopausal women who are not using hormonal replacement therapy, although it is rare for a leiomyosarcoma to present as a rapidly growing tumor. Occasionally, the presenting manifestations are

related to tumor rupture (hemoperitoneum), extrauterine extension (one-third to one-half of cases), or metastases. Only very rarely does a leiomyosarcoma originate from a leiomyoma.

Most leiomyosarcomas are intramural and 50--75% are solitary masses in a uterus that does not also contain benign leiomyomas. A higher proportion involve the cervix than isn the case with leiomyoma. **33.** Leiomyosarcomas are typically voluminous tumors with a mean diameter of 10 cm (only 25% of cases measure less than 5 cm). The cut surface is gray-yellow or pink with areas of necrosis and hemorrhage. Leiomyosarcoma tends to be larger and softer than leiomyoma, it has a more irregular margin, and it is more likely to be hemorrhagic and necrotic. There are three main criteria for the diagnosis of leiomyosarcoma; hypercellularity, significant nuclear atypia, and frequent mitotic figures generally exceeding 15 mitotic figures per 10 high-power-fields (MF/10 HPF). **34-36.** However, epithelioid and myxoid leiomyosarcomas are two rare variants that may be difficult to recognize microscopically as their pathologic features differ from those of ordinary spindle cell leiomyosarcomas. In both tumor types nuclear atypia is usually mild and the mitotic rate often less than 3 MF/10 HPF **29.** Necrosis may be absent in epithelioid leiomyosarcomas and myxoid leiomyosarcomas are often hypocellular. In the absence of severe cytologic atypia and high mitotic activity, both tumors are diagnosed as sarcomas based on their infiltrative borders.

Leiomyosarcoma differs from leiomyoma in that the nuclei are more pleomorphic and the cytoplasmic features are incompletely developed and often disorganized. **37.** Bundles of thin myofilaments usually are limited to zones along the plasma membranes or parallel to the nuclei. The myofilament bundles contain dense bodies and occasionally they terminate in marginal plaques. Pinocytotic vesicles are present at the plasma membrane. The intermediate filament system of malignant smooth muscle cells is poorly described. A basal lamina surrounds the cells.

The minimal pathological criteria for the diagnosis of leiomyosarcoma are more problematic and, in such cases, the differential diagnosis includes, not only benign smooth muscle tumors that exhibit variant histologic features and unusual growth patterns, but also atypical smooth muscle tumors (so-called smooth muscle tumors of uncertain malignant potential [STUMPs]). Application of the WHO diagnostic criteria has allowed distinguishing these unusual histologic variants of leiomyoma frequently misdiagnosed as "well-differentiated" or "low-grade" leiomyosarcomas in the past. In a population-based study of uterine sarcomas from Norway, of 356 tumors classified initially as leiomyosarcomas, the diagnosis was confirmed in only 259 (73%) cases, whereas 97 (27%) were excluded on review and reclassified, according to WHO criteria, as leiomyomas or leiomyoma variants **38.**

Leiomyosarcomas diagnosed according to the WHO criteria **29** are associated with poor prognosis even when confined to the uterus at the time of diagnosis **38-39**. Recurrence

rate ranges from 53% to 71% **40-41**. First recurrences occur in the lungs in 40% of patients and in the pelvis in only 13% **42**. Overall five-year survival rate ranges from 15% to 25% with a median survival of only 10 months in one study **43**. In the Norwegian series, 148 patients with leiomyosarcomas limited to the uterus had a five-year survival of 51% at Stage I and 25% at Stage II (by the 1988 FIGO staging classification). All patients with tumor spread outside the pelvis died within 5 years **38**.

There has been no consistency among various studies regarding correlation between survival and patient age, clinical stage, tumor size, type of border (pushing versus infiltrative), presence or absence of necrosis, mitotic rate, degree of nuclear pleomorphism, and vascular invasion **31, 39-47.** One study, however, found tumor size to be a major prognostic parameter **31**: 5 of 8 patients with tumors <5 cm in diameter survived, whereas all patients with tumors >5 cm in diameter died of tumor. In this study of 208 uterine leiomyosarcomas, the only other parameters predictive of prognosis were tumor grade and stage. Histologic grade, however, has not been consistently identified as a significant prognostic parameter. In the report from Norway **38**, including 245 leiomyosarcomas confined to the uterus, tumor size and mitotic index were significant prognostic factors and allowed for separation of patients into 3 risk groups with marked differences in prognosis. Ancillary parameters including p53, p16, Ki 67, and Bcl-2 have been used in leiomyosarcomas trying to predict outcome **39**. However, it is not clear whether they act independently of stage which still is the most significant prognostic factor for uterine sarcomas.

Treatment of leiomyosarcomas includes total abdominal hysterectomy and debulking of the tumor if present outside the uterus. Removal of the ovaries and lymph node dissection remain controversial as metastases to these organs occur in only a small percentage of cases and are frequently associated with intra-abdominal disease **31**. Ovarian preservation may be considered in premenopausal patients with early stage leiomyosarcomas **31**. Lymph node metastases have been identified in 6.6% and 11% in two series of patients with leiomyosarcoma who underwent lymphadenectomy **31, 75**. In the first series, the five-year disease-specific survival rate was 26% in patients who had positive lymph nodes compared with 64.2% in patients who had negative lymph nodes ($P<0.001$) **75**. The influence of adjuvant therapy on survival is uncertain. Radiotherapy may be useful in controlling local recurrences and chemotherapy with doxorubicin or docetaxel/gemcitabine is now used for advanced or recurrent disease with response rates ranging from 27% to 36% **76**. Some tumors may respond to hormonal treatment **77**. Targeted therapies such as trabectedin have been investigated as treatment in advanced stage or metastatic leiomyosarcoma with some appreciable disease control **51**.

SMOOTH MUSCLE CELL TUMORS OF UNCERTAIN MALIGNANT POTENTIAL (STUMP)

Uterine smooth muscle tumors that show some worrisome histological features (i.e. necrosis, nuclear atypia, or mitoses), but do not meet all diagnostic criteria for leiomyosarcoma, fall into the category of atypical smooth muscle tumors (STUMP) **31**. This diagnosis, however, should be used sparingly and every effort should be made to classify a smooth muscle tumor into a specific category when possible. Most tumors classified as atypical smooth muscle tumors (STUMP) have been associated with favorable prognosis and, in these cases, only follow-up of the patients is recommended.

ENDOMETRIAL STROMAL TUMORS

Endometrial stromal tumors occur in two basic forms. The first is the ***benign endometrial stromal nodule,*** which is a circumscribed, expansile neoplasm that does not infiltrate the myometrium. The second is ***endometrial stromal sarcoma,*** which infiltrates the myometrium and has metastatic potential. Endometrial sarcomas are further classified by the latest WHO classification, based on resemblance to (or lack of) proliferative type endometrial stroma, into the following three main categories: (1) low-grade endometrial stromal sarcoma (LGSS); (2) high-grade endometrial stromal sarcoma (HGSS); and (3) undifferentiated endometrial sarcoma **29.**

1. ENDOMETRIAL STROMAL NODULE

Women with endometrial stromal nodules range from 23 to 75 years of age. The median age is 47 years and three-quarters of the neoplasms occur in premenopausal women. There is no unusual racial predisposition. The main symptoms are abnormal bleeding and menorrhagia. The bleeding occasionally is severe enough to cause anemia. Pelvic or abdominal discomfort is a frequent complaint. The duration of symptoms averages 2.2 months. About 10% of patients are asymptomatic, their tumors being found incidentally in hysterectomy specimens.

Endometrial stromal nodules are fleshy and yellow or tan. They have a rounded contour and bulge above the surrounding myometrium. Their size ranges from 0.8 to 15 cm, with a median diameter of 4 cm. Cysts 0.5-5 cm in diameter occasionally are present, but necrosis and hemorrhage are infrequent. Nodules often are polypoid and protrude into the uterine cavity. About 5% of them are multiple. About 50% of endometrial stromal nodules are located entirely within the myometrium in an intramural or subserosal location, with no apparent connection to the endometrium. Subserosal stromal nodules rarely become pedunculated, but their external surface may adhere to the round ligament or omentum. Endometrial stromal nodules seldom involve the cervix.

Endometrial stromal nodules are composed of cells identical to or closely resembling normal proliferative phase endometrial stromal cells. Stromal nodules have an expansile,

non-infiltrative margin that compresses the adjacent endometrium and myometrium. The neoplastic cells are uniform in size, shape, and staining qualities, and there is minimal cytologic atypia. Decidual change is rare. Mitotic activity ranges from none to 15 MF/1O HPF in the most active areas of the nodule. It usually is very low (fewer than 3 MF/1O HPF), and in about one-half of cases, mitotic figures are not seen in 50 consecutive HPF. Only 5--10% of stromal nodules have more than 5 MF/1O HPF. The behavior of nodules with high mitotic activity appears similar to that of nodules in which few mitotic figures are identified.

The main distinguishing feature of endometrial stromal nodules is their expansile, non-infiltrating, smooth margin that contrasts with the infiltrating irregular margin of stromal sarcomas **48**. Focal irregularities in the form of lobulated or finger-like projections into the adjacent myometrium not exceeding 3mm and not exceeding 3 in number may be seen **49**. Vascular invasion should not be present. Endometrial stromal nodules have an excellent prognosis and patients are cured by hysterectomy **50**.

2. LOW-GRADE ENDOMETRIAL STROMAL SARCOMA (LGSS)

Endometrial stromal sarcomas account for approximately 0.2% of all malignant uterine tumors and 10-15% of uterine malignancies with a mesenchymal component. They occur in women between 40 and 55 years of age. Some cases have been reported in patients with ovarian

polycystic disease, after estrogen use, or tamoxifen therapy. Patients commonly present with abnormal uterine bleeding, pelvic pain, and dysmenorrhea but as many as 25% of them are asymptomatic **51**. At presentation, extrauterine pelvic extension, most commonly involving the ovary, is found in up to 1/3 of patients. Thus, when evaluating an ovarian tumor microscopically consistent with an endometrial stromal tumor, it is important to exclude a prior history of uterine endometrial stromal tumor and to suggest inspection of the uterus, as the latter are far more common.

The endometrial component of LGSS usually is soft, tan, smooth-surfaced, and polypoid. Intramural growth predominates and exhibits three main patterns. In the first, the myometrium is diffusely thickened but a clearly defined tumor is not evident. In the second, there is a nodular tumor that differs from a leiomyoma in that the cut surfaces are tan or yellow-orange and soft, unlike the white, whorled, firm surface of a leiomyoma. The third, and most familiar, appearance of LGSS is that of a poorly demarcated mass in which pink, tan, or yellow cords and nodules of tumor permeate the myometrium. LGSS tends to be smaller than HGSS, and its margins are ill defined and difficult to measure.

Microscopically, LGSS is composed of cells that resemble the stromal cells of proliferative phase endometrium. There is little variation of the cells in LGSS. They have round or ovoid nuclei with dispersed chromatin and small, inconspicuous nucleoli. The cytoplasm is amphophilic, and the cell border is ill-defined. The uniformity of the cells imparts a monotonous appearance to LGSS. There are typically fewer than 3 MF/10 HPF **51-52,**

but there is more mitotic activity in occasional neoplasms that are otherwise typical of LGSS. **52-54.**

The tumor cells are strongly immunoreactive for CD10, usually positive for smooth-muscle actin and less frequently for desmin (30%), but they are negative for h-caldesmon and HDAC8. Estrogen receptors (only alpha isoform), progesterone receptors, androgen receptors, and WT-1 are typically positive. Nuclear beta-catenin expression has been shown in up to 40% of low-grade endometrial stromal sarcomas. The most common cytogenetic abnormality of low-grade endometrial stromal sarcomas is a recurrent translocation involving chromosomes 7 and 17 t(7;17)(p15;q21)], which results in a fusion between JAZF1 and SUZ12 (formerly designated as JJAZ1) **56**. The fusion can be detected by fluorescence in situ hybridization as well as by reverse transcriptase–polymerase chain reaction.

Arterioles that resemble the endometrial spiral arterioles are uniformly distributed throughout most LGSS, and capillaries and veins often are conspicuous as well. The prominent vascularity is the reason that LGSS can be mistaken for a hemangiopericytoma. Reticulin fibers surround individual cells or small groups of cells, resulting in a basket-weave pattern.**52** Hyalinized zones or plaques are common in LGSS and aggregates of foam cells or foci of necrosis occur in some neoplasms.**55** Decidual change is seen occasionally in a stromal tumor as a response to pregnancy or exogenous progesterone.

LGSS invades the myometrium and may extensively permeate it. Invasion of lymphatic and vascular channels is a characteristic of LGSS **52, 55.**

Areas of epithelial-like differentiation are present in about one quarter of LGSS.**52, 55.** Highly varied in appearance, epithelial-like differentiation can be manifested as trabecular cords of epithelioid cells, mesothelial-like structures, endometrial-type glands, or as glands lined by clear cells.

Low-grade endometrial stromal sarcomas are indolent tumors with a favorable prognosis **51**. Tumor behavior is characterized by later recurrences even in patients with Stage I disease; thus, long-term follow-up is required. About one-third of patients develop recurrences, most commonly in the pelvis and abdomen, and less frequently in the lungs and vagina **51**. Stage of the tumor is the most significant prognostic factor. Surgical stage higher than Stage I is a univariate predictor of unfavorable outcome. Five-year survival for patients with Stages I and II tumors is 90% compared with 50% for Stages III and IV **57**.

Treatment of low-grade endometrial stromal sarcomas is largely surgical in the form of hysterectomy and bilateral salpingo-oophorectomy. The tumors are often sensitive to hormones and it has been shown that patients retaining their ovaries have a much higher risk of recurrence (up to 100%) **74**. Lymph node dissection does not seem to have a role in the treatment of these tumors. Patients may also receive adjuvant radiation or

hormonal treatment with progestational agents or aromatase inhibitors. Hormone replacement therapy is discouraged.

3. HIGH-GRADE STROMAL SARCOMAS (HGSS)

These rare tumors have features that are intermediate between low-grade endometrial stromal sarcomas and undifferentiated sarcomas **58**. Patients range in age from 28–67 years (mean 50 years) and usually present with abnormal vaginal bleeding, an enlarged uterus, or a pelvic mass **59**.

The tumors may appear as intracavitary polypoid or mural masses. They range in size up to 9 cm (median 7.5 cm) and often show extrauterine extension at the time of diagnosis. The cut surface is fleshy with extensive areas of necrosis and hemorrhage. Microscopically, they consist predominantly of high-grade round-cells that are sometimes associated with a low-grade spindle cell component that is most commonly fibromyxoid **59**.

Compared with the cells in LGSS, those in HGSS have larger, more vesicular nuclei with more prominent chromatin clumps and nucleoli. The cytoplasm is eosinophilic or amphophilic, and the cell borders are indistinct. Mitotic figures are frequent in HGSS. There are almost always 10 or more MF/10 HPF and typically there are 20 or more MF/10 HPF in the most active areas.

HGSS infiltrates the myometrium destructively, with areas of hemorrhage and necrosis, in contrast to the myometrial and vascular permeation that typifies LGSS. The vascular pattern and reticulin meshwork are irregular in HGSS. **51-57** High-grade endometrial stromal sarcomas are CD10, estrogen receptor, and progesterone receptor negative but show strong diffuse cyclin D1 immunoreactivity (N70% nuclei). They are also typically c-Kit positive but DOG1 negative. High-grade endometrial stromal sarcoma typically harbors the YWHAE-FAM22 genetic fusion as a result of t(10;17) (q22;p13).**59.**

These tumors appear to have a prognosis that is intermediate, between low-grade endometrial stromal sarcomas and undifferentiated uterine sarcomas **59**. Compared with low-grade endometrial stromal sarcomas, patients with high-grade endometrial stromal sarcomas have earlier and more frequent recurrences (often b1 year) and are more likely to die of disease.

Advanced or recurrent tumors should be treated aggressively with a combination of radiation and chemotherapy as they do not respond to conventional treatment for low-grade endometrial stromal sarcomas **59.**

4. UNDIFFERIENTIATED STROMAL SARCOMAS

This tumor is rare. Patients are typically postmenopausal (mean age is 60 years) and have postmenopausal bleeding or signs/symptoms secondary to extra-uterine spread **60**. Approximately 60% of patients present with high-stage disease (Stage III/IV).

The diagnosis of undifferentiated endometrial sarcoma is applied to tumors that exhibit myometrial invasion, severe nuclear pleomorphism, high mitotic activity, and/or tumor cell necrosis, and lack smooth muscle or endometrial stromal differentiation **29.** Grossly, they are often polypoid and show a fleshy, gray to white cut surface and prominent areas of hemorrhage and necrosis. On microscopic examination, there is destructive myometrial invasion while the intravascular worm-like plugs characteristic of low-grade endometrial stromal sarcomas are typically absent. They have marked cellular pleomorphism and brisk mitotic activity, almost always exceeding 10 MF/10HPF and sometimes approaching 50 MF/10HPF. Extensive necrosis is frequently present. These tumors should be diagnosed only after extensive sampling has excluded smooth or skeletal muscle differentiation or even small foci of carcinoma, as this finding would result in a diagnosis of carcinosarcoma.

Undifferentiated endometrial sarcomas lack immunoreaction for ER and PR, but a high proportion is EGFR immunoreactive **29**. CD10 expression is not helpful in the differential diagnosis with other uterine sarcomas because undifferentiated endometrial sarcoma as

well as leiomyosarcoma, rhabdomyosarcoma, and carcinosarcoma may express this marker **60**. Smooth muscle markers and myogenin or myoD1 may be used to rule out leiomyosarcoma or rhabdomyosarcoma respectively, or to identify a rhabdomyosarcomatous component of a carcinosarcoma.

Undifferentiated endometrial sarcomas have very poor prognosis and most patients die of disease within two years of the diagnosis. In a recent study **38**, vascular invasion was the only statistically significant prognostic factor, with a 5-year crude survival of 83% and 17% when vascular invasion was absent or present, respectively (P=0.02). Local recurrences and distant metastases are associated with a high mortality. Patients should be treated by hysterectomy and bilateral salpingo-oophorectomy and adjuvant radiation and/or chemotherapy **72-73.**

ADENOSARCOMA

The rare mullerian adenosarcoma is a mixed tumor of low malignant potential with distinctive clinicopathologic features **61**. It occurs mainly in the uterus of postmenopausal women but also in adolescents and young adults and in extrauterine locations such as the fallopian tube, ovary, paraovarian tissues and the intestinal serosa. Extrauterine adenosarcoma occurs in younger women and is more aggressive than its uterine counterpart **62**. There is no association with obesity or hypertension, nor is there any association with prior pelvic radiation. Some patients have taken tamoxifen therapy. A

minority of patients are diabetic. Some have a history of prior removal of cervical or endometrial polyps.

The most common presenting symptom is abnormal vaginal bleeding but some patients present with pelvic pain, an abdominal mass or vaginal discharge. Most commonly, adenosarcomas arise from the endometrium, including the lower uterine segment, but rare tumors arise in the endocervix and within the myometrium, probably from adenomyosis.

The uterine cavity is typically filled and distended by a soft polypoid and sometimes large mass (range, 1–20 cm) which may project through the cervical os. The cut surface may show variably sized cysts or clefts. There is often focal hemorrhage and necrosis. The margin of the tumor is usually well defined. Microscopically, it shows an intimate admixture of benign but sometimes atypical glandular epithelium and low-grade sarcoma, usually of endometrial stromal type. Typically, the glands are cystic and the stroma concentrates around them forming peri glandular cuffs. The histologic picture is reminiscent of a phyllodes tumor of the breast. Although the mean mitotic rate is 9 MF/10 HPF **61**, in the presence of hypercellular peri glandular cuffs, only 2 MF/10 HPF are enough for the diagnosis **61**. Most adenosarcomas show only mild to moderate nuclear atypia in the stromal component. Heterologous mesenchymal elements (usually rhabdomyosarcoma, but also cartilage, fat, and other elements) are found in 10–15% of cases. Vaginal or pelvic recurrence occurs in approximately 25%−30% of cases at 5 years

and is associated almost exclusively with myometrial invasion and sarcomatous overgrowth **61-62**. Myometrial invasion is found in approximately 15% of cases, but deep invasion in only 5% **61-62.** Sarcomatous overgrowth, defined as the presence of pure sarcoma, usually of high-grade and without a glandular component, occupying at least 25% of the tumor, has been reported in 8% to 54% of uterine adenosarcomas **61-62.**

Whereas immunoreactions for cell proliferation markers (Ki-67 and P53) are stronger in adenosarcomas with sarcomatous overgrowth than in typical adenosarcomas, the expression of markers of cell differentiation (CD10 and PR) is higher in typical adenosarcomas than in adenosarcomas with sarcomatous overgrowth **62.**

Except when associated with myometrial invasion or sarcomatous overgrowth, the prognosis of adenosarcoma is far more favorable than that of carcinosarcoma; however, about 25% of patients with adenosarcoma ultimately die of their disease **64**. Recurrences usually occur in the vagina, pelvis, or abdomen. They may be late, for which reason long-term follow-up is needed. Local recurrences and distant metastases, which occur in 5% of cases, are almost always composed of pure sarcoma (70%).

Treatment of choice is total abdominal hysterectomy with bilateral salpingo-oophorectomy. In the series from Norway **38**, which included 23 adenosarcomas, tumor cell necrosis was the strongest prognostic factor (P=0.006).

CARCINOSARCOMA

Carcinosarcoma, also referred to as "malignant mixed Mullerian tumor," is a biphasic neoplasm composed of distinctive and separate, but admixed, malignant-appearing epithelial and mesenchymal elements. It accounts for almost half of all uterine sarcomas **63-64.** Although they occur typically in post-menopausal women, a small number has been reported in patients less than 40 years of age. Most women present with abnormal vaginal bleeding and uterine enlargement. Another typical presentation of carcinosarcoma is in the form of a polypoid mass that protrudes through the cervical os. The serum level of CA125 is elevated in most cases. At presentation, extrauterine spread (stages III–IV) is found in up to 1/3 of cases. Up to 37% of patients with carcinosarcomas have a history of pelvic irradiation. These tumors tend to occur in younger women, often contain heterologous elements, and are found at advanced stage **63**.

Carcinosarcomas are typically large, bulky polypoid masses, filling the uterine cavity and prolapsing through the cervical os. The cut surface is usually fleshy and often shows areas of hemorrhage, necrosis, and cystic change. Myometrial invasion is frequently seen. Rare tumors may arise in the uterine cervix. The epithelial component is serous, or high-grade carcinoma not otherwise specified, in about two-thirds of cases, and endometrioid carcinoma in approximately one-third **64.** In a recent study, 10% of the carcinomatous components were FIGO grade 1, 10% grade 2, and 80% grade 3 **64**. The homologous

components of carcinosarcoma are usually spindle cell sarcoma without obvious differentiation; many resemble fibrosarcomas or pleomorphic sarcomas. Almost all are high-grade sarcomas. The most common heterologous elements are malignant cartilage or skeletal muscle constituting something that resembles either pleomorphic rhabdomyosarcoma or embryonal rhabdomyosarcoma **27.**

The immunophenotype parallels that of the individual elements; i.e., the serous component should express cytokeratins, epithelial membrane antigen (EMA), and p53, while the rhabdomyoblastic elements should express desmin, myogenin, or MyoD1. However, it is well known that the sarcomatous component can express cytokeratins (as in leiomyosarcomas) and the epithelial component is often immunoreactive for vimentin (as in endometrial carcinomas). Such findings reflect the common mesodermal origin of these tumors. The homologous component can also express CD10, a marker used initially for the diagnosis of endometrial stromal tumors. In most cases, immunohistochemistry is not needed for diagnosis and should only be used to confirm the presence of rhabdomyoblasts **63**.

Carcinosarcomas are overly aggressive tumors—far more aggressive than usual endometrial carcinomas. The overall five-year survival for patients with carcinosarcoma is around 30% and for those with Stage I disease (confined to the uterus) it is approximately 50% **27, 65-67.** This is in contrast with other high-grade endometrial cancers for which five-year survival in Stage I disease is approximately 80% or higher

68-70. This has led to toxic treatment protocols that usually include ifosfamide and cisplatin along with whole pelvic irradiation.

In carcinosarcomas, there is general agreement that surgical stage is the most important prognostic indicator regardless of how the patient was staged. A recent study found that the presence of heterologous elements is a poor prognostic factor in patients with FIGO Stage I tumors **74**. Other factors proposed include the histologic grade of the carcinomatous and sarcomatous elements, the percentage of tumor with sarcomatous differentiation, depth of myometrial invasion, and presence of lymphovascular invasion **27, 65-67.**

Appropriate treatment includes total abdominal hysterectomy with bilateral salpingo-oophorectomy, removal of pelvic and aortic lymph nodes, omentectomy, and peritoneal cytology. The role of adjuvant radiotherapy and chemotherapy is uncertain but some studies have demonstrated the advantage of radiotherapy for disease specific survival in early-stage tumors as well as local control in advanced-stage tumors. Taxanes and cisplatin-based chemotherapy as well as ifosphamide, along with whole pelvic irradiation, may lead to increased survival in patients with metastatic carcinosarcomas **70, 72**.

WHAT IS THE APPROPRIATE EVALUATION PRIOR TO LAPAROSCOPIC MANAGEMENT OF A MYOMA

A thorough medical history is important to determine which fibroid-related symptoms are present (eg, heavy uterine bleeding, bulk symptoms) and whether these symptoms affect the patient's quality of life. The medical history should include questions regarding a personal or family history of bleeding disorders, as well as other medical comorbidities that may impact the ability to tolerate surgery.

A thorough pelvic examination should be performed. On bimanual examination, the size, contour, and mobility of the uterus should be noted, along with any other findings (eg, adnexal mass, cervical mass). These findings impact the choice of preoperative imaging and aid surgical planning.

Women who are planning myomectomy should undergo imaging to confirm the presence of uterine leiomyomas rather than other pelvic pathology. In addition, incidental findings of other lesions (eg, ovarian cyst) may impact surgical planning.

Pelvic sonography is typically the initial imaging study. Ultrasound can confirm the presence of leiomyomas and their approximate number and location **78**. Magnetic

resonance imaging (MRI) provides more accurate information regarding myoma size, number, and location than other imaging modalities **78**. For women who are being evaluated for possible laparoscopic myomectomy, this information may help the surgeon determine whether laparoscopic surgery is feasible and may help avoid missing myomas not palpable during laparoscopic surgery. MRI is also the best modality to diagnose adenomyosis, which can mimic leiomyomas and/or make myomectomy more difficult. MRI is also indicated if uterine sarcoma is suspected.

Abnormal bleeding is a symptom of uterine fibroids, but also of uterine cancer. Prior to myomectomy, endometrial sampling should be performed in all women with bleeding symptoms, particularly intermenstrual bleeding, who are older than 35 years or who have risk factors for endometrial cancer.

WHICH ARE THE DIAGNOSTIC METHODS THAT HELP US SEPARATE MYOMAS FORM SURCOMAS

There is no pelvic imaging modality that can reliably differentiate between benign leiomyomas and uterine sarcomas. Leiomyomas and uterine sarcomas appear similar; both are focal masses within the uterus and both can have central necrosis. Pelvic ultrasound followed by MRI is the most useful imaging strategy.

Pelvic ultrasound is typically the first-line study to evaluate women for potential uterine pathology. Sonographic evaluation of a uterine mass may identify features suggestive of sarcoma (mixed echogenic and poor echogenic parts; central necrosis; and color Doppler findings of irregular vessel distribution, low impedance to flow, and high peak systolic velocity); however, many of these characteristics may also be found in benign leiomyomas **79-80.** Transvaginal spectral Doppler sonography is used for differentiating abnormal blood vessels in malignant tumors from those in benign lesions. It is reported that RI values below a cutoff point of 0.4 had a sensitivity of 90.9% and a specificity of 99.8% in the diagnosis of sarcomas without differentiating between sarcoma subtypes **79-80.**

Distinguishing between LMS, and benign leiomyomas using MRI remains a challenge, especially due to overlapping of variable atypical imaging features **81-82**. Four qualitative MR features most strongly associated with LMS were nodular borders, haemorrhage, "T2 dark" area(s), and central unenhanced areas. **83-87**. MRI achieved the highest sensitivity [1.00 (95%CI:0.82-1.00)/0.95 (95%CI: 0.74-1.00)] and specificity [0.95 (95%CI:0.77-1.00)/1.00 (95%CI:0.85-1.00)], when a lesion had ≥3 of these four features. **84**

Contrast-enhanced MRI has been proven to have superior performance than T2WI in detecting tumor necrosis **83**, due to the shared feature of intratumoral T2 hyperintensity in benign leiomyomas with degeneration. Despite limited available data, central nonenhancement (CNE) and well-demarcated pocket-like non- enhanced areas are reported to have significantly higher diagnostic accuracy than DWI, T2WI, and T1-weighted images (T1WI), in the differentiation between LMS and benign leiomyoma. CE-MRI yielded a significantly superior diagnostic accuracy (0.94 vs. 0.52) and a significantly higher specificity (0.96 vs. 0.36) than DWI ($P < 0.05$ for both) and remained a comparably high sensitivity as DWI (0.88 vs. 1.00) **88**. CNE correlates with areas of coagulative necrosis, a characteristic feature of LMS on histopathology, due to the lack of interposed granulation or hyalinized tissue to support the LMS tumor architecture resulting in areas of coagulative necrosis deviated by the adjacent viable cells. However, this phenomenon should not be confused with the scattered non-enhancing areas throughout the tumor mass as seen in leiomyomas with hyaline degeneration. False positivity of contrast-enhanced (CE)-MRI is reported in patients with infarcted leiomyomas and requires

cautious interpretation **81, 88**. Hyperintensity on DWI is reported to have high sensitivity but limited specificity in differentiation between LMS and benign leiomyoma **85-86, 89-90.**

TUMOR MARKERS

Serum biomarkers are easy to measure and are objective. Serum LDH might be elevated in LMS but identifying LMS by measurement of LDH alone is difficult 6. Two LDH isoenzymes, LDH-A and LDH-D are expressed in uterine sarcomas and may thus be used to aid in the pathological diagnosis of this tumor type **91**.

D-dimer is a fibrin- degenerating product that suggests the existence of thrombosis. In malignant tumor tissue, thrombosis often induces infarction and results to necrosis. In LMS, areas of tumor cell necrosis and hemorrhage are common. Tumor necrosis is highly characteristic of LMS. Moreover, tissue factors, fibrinolytic molecules and proinflammatory or proangiogenic cytokines might be involved in malignant tumors, including sarcomas.**92** Hence, D-dimer could be elevated in uterine LMS.

CRP is induced in the acute phase of inflammatory response, and it reacts to infection and tissue injury **93**. CRP might reflect not only inflammation in cancer tissue

but also, prognosis of various cancers. In LMS tissue, tumor cell necrosis is a common feature; hence, various degrees of inflammation could occur. CRP was highly positive in LMS cases compared with typical or atypical leiomyoma. It is interesting that CRP is frequently positive in LMS cases with poor prognosis **94**.

HOW MORCELLATION MAY AFFECT PROGNOSIS IN CASES OF UNSUSPECTED SARCOMA

Preoperative diagnosis of uterine sarcoma is challenging; therefore, patients should be counselled that there is a small chance that apparent leiomyomas may be LMSs. There is evidence that the prognosis is worse for patients initially treated with myomectomy regardless of route or use of morcellation, instead of hysterectomy when the final pathologic diagnosis is LMS **95-97**.

Several studies have attempted to ascertain whether morcellation of a malignant uterine specimen affects patient prognosis. Seidman et al. reviewed 1091 cases of uterine morcellation from 2005 to 2010 **115**. They found unexpected leiomyoma variants or atypical and malignant smooth muscle tumors in 1.2% of cases using power morcellation, including 1 ESS and 1 LMS. They also examined follow-up laparoscopies, both from in-house and consultation cases, and found that disseminated disease was present in 64.3%

of all tumors. Only disseminated LMS, however, was associated with subsequent death (75%; 95% CI 30.1% –98.7%), with an average postdiagnosis survival of 24.3 months (95% CI 8.4–40.3 months). The dissemination and viability of noncancerous leiomyoma variants in this series also highlighted the potential alteration of their natural history with the use of electromechanical morcellation.

Park et al. also assessed 56 consecutive patients with stage I and II uterine LMS, 25 with and 31 without tumor morcellation **99**. They found that tumor morcellation was significantly associated with worse overall 5-year survival (46% vs. 73%, P = 0.04). The percentage of patients with abdominopelvic dissemination (sarcomatosis or vaginal apex recurrence) was significantly greater in patients with tumor morcellation than in those without morcellation (44% vs. 12.9%, P=0.032). Within the study period, 22.6% and 52% (P = 0.022), respectively, of patients in the non-morcellated group and the morcellated group had a recurrence.

George et al. also published data evaluating intraperitoneal morcellation on outcomes of localized uterine LMS **100**. In this retrospective cohort study, a multivariate adjusted model demonstrated a risk of recurrence associated with morcellation of greater than 3 times that of total abdominal hysterectomy. The median recurrence free survival was 10.8 months for those who underwent a morcellation procedure and 39.6 months for those who did not. There was a trend towards lower overall survival in the morcellation group at 36 months (64% vs. 73%); however, this did not reach statistical significance.

Re-exploration after morcellation of cancer has revealed a significant rate of dissemination of viable tissue. Oduyebo et al. reported that 28.5% of patients with LMS who had undergone tumor morcellation had disseminated peritoneal disease at a median of 33 days after original surgery **101**.

Morice et al. similarly examined 123 patients diagnosed with uterine sarcomas **95**. In this series, 38 patients underwent surgery with some degree of tumor disruption—vaginal or laparoscopic morcellation (with morcellation described in the surgical procedure), myomectomy, tumor biopsy, or hysteroscopic myomectomy. They reported a trend of increased tumor recurrence at 3 months in the group that did not have total hysterectomy, but this trend was not statistically significant. Recurrence rate at 6 months and overall survival did not differ between the 2 groups. If morcellation of an undiagnosed endometrial cancer occurs, pathologic assessment of the tumor can be limited, resulting in difficulty assigning patients to the appropriate adjuvant treatment, thereby affecting prognosis.

MATERIALS AND METHODS

A literature search was initially performed using the PubMed/MEDLINE database and the Cochrane Library. The search was performed for all manuscripts published after 1960 and all languages using the search terms "myomas", "leiomyomas", "fibroids", "hysterectomy", "myomectomy", "leiomyosarcoma", "sarcomas", "malignancy", "neoplasm", "cancer", "incidence", "occurrent", "pathology", "histopathology", "morcellation", "complication", "inadvertent" and "upstaging". The terms were used alone and in combination. All references found were evaluated for inclusion according to the exclusion criteria listed below and their references were then searched for other potentially relevant publications.

One author conducted preliminary review. All papers deemed to meet inclusion and exclusion criteria were then reviewed by another author.

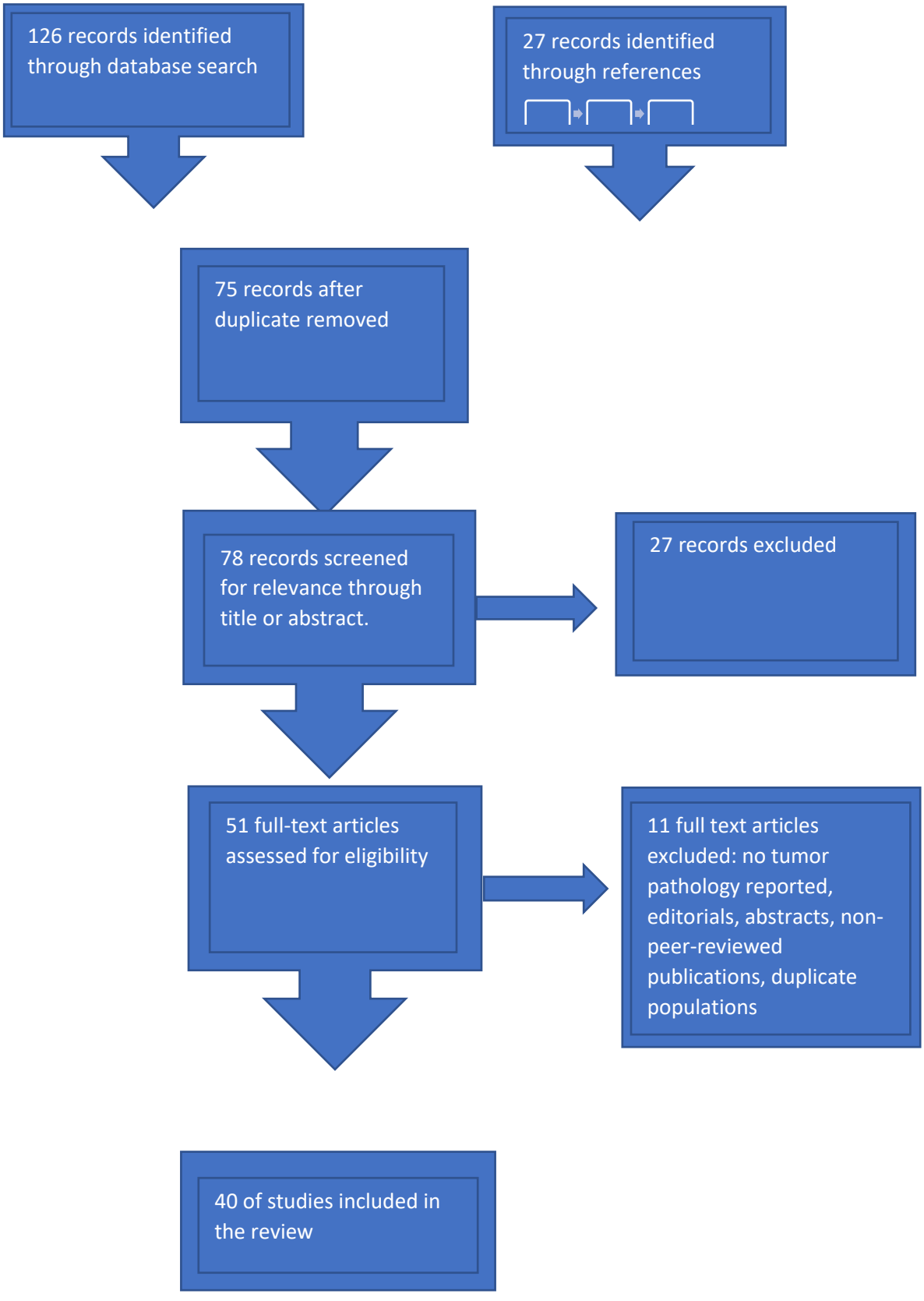
Inclusion criteria included publications involving humans that were peer-reviewed. All publications were required to contain original data. Papers were only included if they contained cases for surgery (hysterectomies or myomectomies) in which fibroid-related indications were the primary indication for surgery. To avoid case reports, a minimum of ten subjects from an individual study was necessary for inclusion in this review.

Only the manuscripts that provided postoperative histopathological findings for all the patients extracted were included in the review. Papers stating "all specimens were sent to pathology" without final reports were considered inadequate for inclusion.

If any manuscript classified a presumed fibroid as a leiomyosarcoma or as any other type of uterine malignancy without any additional information, then the tumor was classified as such in our review. The criteria used for classification are those described by the World Health Organisation **102**.

Studies that initially searched their databases for pathological findings of fibroids, then worked backwards to uncover the primary indication for surgery, were excluded. Additionally, all prospective analyses that a priori excluded any patient with malignancy were excluded as well. All letters to the editor, abstracts and all other non-peer-reviewed publications of data were considered inadequate for the review. The first study adequate for inclusion was published in 2013 and the final was published in 2019.

We identified 153 papers initially and excluded 78 through evaluation of the title or abstract. The remaining 51 were evaluated in full and 12 were excluded after not meeting the inclusion and exclusion criteria reported above. 39 manuscripts were finally included in the review.


126 records identified through database search
27 records identified through references
75 records after duplicate removed
78 records screened for relevance through title or abstract.
27 records excluded
51 full-text articles assessed for eligibility
11 full text articles excluded: no tumor pathology reported, editorials, abstracts, non-peer-reviewed publications, duplicate populations
40 of studies included in the review

REVIEW OF THE PUBLISHED LITERATURE REGARDING THE RISK OR INCIDENTAL FINDING OF SARCOMA OR OCCULT MALIGNANCY AFTER LAPAROSCOPIC SURGERY.

There was substantial heterogeneity in outcomes reporting among the studies. Some included patients that underwent hysterectomy for a solution to symptomatology caused by uterine fibroids **103, 106-108, 110-111, 113-114, 117-120, 123, 127, 131, 133,** some included patients that underwent myomectomy **116, 121, 139-140,** and some included patients that underwent any of either type of surgery **104-105, 109, 112, 115, 122, 124-126, 128-130, 132, 134-138, 141-142.** Twenty-two studies examined the risk of any occult malignancy **103-107, 111-112, 113-114, 117, 119-122, 124, 127-128, 132, 136, 138, 140-141,** eleven studies examined the risk of sarcoma **112, 115-116, 118, 126, 129, 131, 133-135, 142,** whereas the remaining examined the risk of leiomyosarcoma only **108-109, 123, 125, 130, 137, 139.** Overall, the incidence of any unexpected malignancy, including endometrial cancers as well as sarcomas, in presumed leiomyomas after hysterectomy or myomectomy with or without morcellation ranged from 0 – 2.7%. The highest risk (2.7%), including any type of malignancy, was reported by Mahnert et al. **110.** The data was collected from a large sample of Michigan hospitals and included 6,360 hysterectomies were performed for benign indications. The major limitation in this analysis is the lack of available preoperative testing information such as cervical cancer screening, ultrasonography, and

endometrial biopsy, which should all be performed before hysterectomy as clinically indicated. In the largest single-centre study of over 4500 patients, Lieng et al **130** found a 0.0054% risk of unexpected uterine malignancy in presumed fibroids, although reporting was only performed for leiomyosarcoma. A population-based analysis of 41,777 patients undergoing myomectomy found 76 uterine malignancies (0.18%); however, the breakdown of uterine histology was not available **121.**

The prevalence of uterine sarcoma in presumed uterine fibroids, in the studies that evaluated the risk of any type of sarcoma, ranged from 0.00% to 0.49%. **108-109, 112, 115-116, 118, 123, 125-126, 129-131, 134-135, 137, 139, 142.** The most common type of sarcoma was leiomyosarcoma which of the highest risk was reported by Leibsohn S et al. **108** at a value of 0.49%. It is followed by Endometrial Stromal Sarcoma and Carcinosarcoma. The largest single institution series found leiomyosarcoma in 20 of 4785 patients referred for fibroids (0.42%) **109.**

LAPAROSCOPIC MORCELATION AND THE RISK OF SARCOMA REPORTED SERIES

All studies evaluated the use of power morcellation in hysterectomy and/or myomectomy for patients with benign uterine disease. Out of 20 studies that evaluated the risk of any occult malignancy during power morcellation, only 8 studies were focused on the risk of occult finding of sarcoma **109, 115-116,118, 129, 131, 133, 137.** The reported prevalence of sarcoma ranged from 0.00 to 0.6% **118, 137.** In these studies as well the first in frequency sarcoma was leiomyosarcoma, followed by other subtypes of sarcomas. Pados et al **137** reported prevalence of 0.00%, though in this study the population was women of reproductive age and no postmenopausal women participated.

DISCUSSION

Endoscopic techniques have successfully reduced the invasiveness of hysterectomy and myomectomy, when compared to open procedures **143**. In order to retrieve surgical specimens from the abdominal cavity, the minimal invasive concept routinely implied tissue morcellation **144**. While power driven morcellation belonged to operative standards since its introduction in the year 1993 **145**, the technique has become under scrutiny after US Federal Drug Administration (FDA) strong warnings against the use of

power morcellators in April and November 2014, due to intrabdominal dissemination of malignant tissue **14-15**. Potential harm from morcellated tissue spread was also reported in benign conditions, resulting in so called parasitic leiomyoma or iatrogenic peritoneal adenomyosis **146-148**.

To abandon tissue morcellation, however, would essentially question the minimal invasive concept for hysterectomy and myomectomy. The risk of performing a laparotomy on all women who underwent a hysterectomy through an incision in the abdomen could result in a significant increase in postoperative mortality (estimated at 17 women per year in the United States) **149**. A Cochrane review of 4495 patients who underwent a hysterectomy for a benign gynaecological disease compared the complications, operating time, length of hospital stay, and the time away from work between the abdominal, laparoscopic, and vaginal hysterectomies. Obvious benefits were observed for the vaginal and laparoscopic approaches compared to abdominal hysterectomy **150**. The risk-benefit ratio of changing practices could therefore have disastrous consequences for maternal mortality in terms of postoperative complications, with a higher risk of mortality in the case of laparoscopic hysterectomy to prevent the sarcoma compared to the risk of the sarcoma itself.

PREVENTING THE RISK OF SPREADING AN UNDIAGNOSED SARCOMA

Acknowledging that there is currently not enough evidence to estimate accurately the individual risk **151**, a way to increase safety for an individual patient may particularly consist in developing novel operative techniques. Therefore, the idea of morcellating within an intra-abdominally placed, closed containment system has emerged as a potential method to prevent cell spilling **152-154**. The use of an endoscopic bag is the only solution offered by several associations and learned societies (AAGL, ACOG, SOGC, ESGE, FDA, CNGOF, SCGP, ANSM, and SFOG) and seems promising **7**, **14**, **120-121, 156-158**.

Contained power morcellation was performed using MoreCell-Safe system (A.M.I. Austria). The system consists of a polyurethane bag (More-Cell Bag), a 12 mm sheath for its introduction into the peritoneal cavity (MCS Port), and an 11 mm optic sleeve (Visi-Shield). The bag material prevents molecule migration above 2–5 A ° (2–5 9 10-10 m). Feed sizes of 340 9 250 mm correspond to a capacity of 2.5 l. The bag has two openings. The large mouth measures 16 cm in diameter. It serves for specimen placement and morcellator access. The second, tubular opening measures 16 mm in diameter and 190 mm in length. Its outer part is everted to protect it from contamination by spread cells during use, providing an uncontaminated surface distal to the occluding knots during

removal (Fig. 5). The optic sleeve serves to protect the optic against cell contamination during in-bag use and is disposed at the end of it. **159-160**.

Nevertheless, the AAGL (Elevating Gynecologic Surgery, formerly the American Association of Gynecologic Laparoscopists) and the ACOG (American Congress of Obstetricians and Gynecologists) highlight several challenges. The first is that the use of an endoscopic bag requires advanced laparoscopic skills to prevent complications. They also add that visualisation of the mass inside the bag and adjacent organs is often less than optimal. Moreover, they insist that, despite the variations in shape, size, or weight of uterine tissues, placing the sample in the bag can be difficult, in addition to the considerable risk of puncturing the bag if it is not very resistant **160, 161**?. Despite this, in January and February 2015 the SOGC (Society of Obstetricians and Gynaecologists of Canada) insisted that, where possible, the surgeon should use the technique of confined morcellation, either in a bag through a mini-laparotomy using a self-retaining retractor, or through endoscopy or the vaginal route. **161**

CONCLUSION

Patient safety remains a priority and needs to balance maximizing benefits while minimizing harm. Gynecologic surgeons should actively discuss the risks of intracorporeal morcellation with their patients. If the surgeon decides to proceed with morcellation, he or she must consider the contraindications after completing a preoperative assessment. Most learned societies recommend obtaining informed consent prior to the surgery. If the surgeon decides to use an endoscopic bag, as recommended by several associations, it is important to make the patient aware of its limitations (size, tearing, possible injury to adjacent organs, etc.). Lastly, the patient should be informed of alternatives to power morcellation and their risks and benefits.

Finally, the ESGO recommends not prohibiting morcellation techniques but rather improving preoperative screening, risk factor assessment, and technique development to reduce the risk of spreading the disease **150**. Further studies are necessary, however, before making official recommendations on morcellation and the real risks of spreading any type uterine malignancy.

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MYOMAS

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SARCOMAS

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