UTERINE LIOMYOSARCOMA PANEL

Coordinator: Tahereh Ashrafganjoei MD

July 23 2020

Introduction

- Uterine sarcomas comprise 3% of uterine malignancies and leiomyosarcoma (LMS) accounts one-third of all uterine sarcomas .
- LMS is a significant reason for uterine cancer deaths and its five-year overall survival rates range from 30% to42%.
- The patient age is the major risk factor and patients older than 55 are at increased risk.

Risk factors

- Black race (2-3×)
- Increasing age (postmenopausal, average age at diagnosis : 60 years)

a new or growing uterine mass , discontinue HRT

- Tamoxifen: two to five years following the start of tamoxifen therapy ,often at an advanced stage at diagnosis.
- Pelvic radiation: stronger for carcinosarcoma .
- Hereditary conditions :Hereditary leiomyomatosis and renal cell carcinoma (HLRCC) syndrome
- Childhood retinoblastoma (particularly the hereditary type).
- Leiomyomas do **not** appear to be the precursor to leiomyosarcomas, with rare exceptions (atypical or cellular variants).
- Parity and time of menarche and menopause???

Signs and symptoms

- Postmenopausal bleeding (31 to 46 percent)
- Premenopausal abnormal uterine bleeding (27 to 34 percent)
- Abdominal distension (8 to 17 percent)
- Abdominal pain (4 to 13 percent)
- Urinary symptoms (1 to 2 percent)
- Asymptomatic (1 to 2 percent)
- bleeding accompanied by a foul smelling vaginal discharge
- Pelvic pain/pressure, and a pelvic mass
- Hematogenous spread, lungs (benign leiomyoma or sarcoma?)
- Failure to respond to treatment :gonadotropin-releasing hormone agonist treatment , uterine artery embolization

An enlarged uterus –D.DX

- Benign leiomyoma
- Leiomyoma variant
- Uterine adenomyoma or diffuse adenomyosis
- Uterine sarcoma
- Uterine carcinosarcoma
- Endometrial carcinoma
- Metastatic neoplasm
- Endometrial processes that may enlarge the uterus – Endometrial polyp, endometrial hyperplasia, hematometra
- Pregnancy

Leiomyoma vs leiomyosarcoma

- Leiomyoma are common (lifetime risk 70 to 80 percent).
- Most uterine sarcomas occur in women over age 40; however, they have been diagnosed in women as young as 20 years old .The mean age at diagnosis is approximately 60 years old.
- leiomyomas (fibroids) are the most common pelvic neoplasm in women (estimated lifetime risk of 70 percent in white women and 80 percent in black women) .
- Uterine sarcomas are significantly rarer than leiomyomas (3 to 7/100,000 in the United States population) and have a poor prognosis.
- Uterine LMSs are rare uterine malignancies. However, the incidence of sarcoma is 1–2% in postmenopausal women .
- Unfortunately, the clinical features of benign leiomyomas and uterine sarcomas are often indistinguishable.

- Asymptomatic women :Hysterectomy should not be performed in most women with asymptomatic presumed leiomyomas for the sole purpose of excluding a uterine sarcoma.
- likelihood of finding sarcoma: approximately 0.2 percent
- risk of severe complications associated with hysterectomy (3.5 to 11.0 percent) for benign disease
- ACOG : there is insufficient evidence to support hysterectomy for asymptomatic leiomyomas solely to rule out malignancy

Following the detection of presumed uterine fibroids in an asymptomatic woman

- An initial imaging study (usually an ultrasound) to confirm that a pelvic mass is consistent with a fibroid rather than with other etiologies (eg, ovarian mass).
- After this initial evaluation, we perform annual pelvic examinations.
- If the characteristics of the uterus change or symptoms develop, we proceed with further evaluation and patient counseling regarding treatment options.

WHEN TO SUSPECT UTERINE SARCOMA

- in postmenopausal women: presumed uterine leiomyomas with symptoms sufficiently bothersome to consider hysterectomy(0.2%).
- premenopausal women: presumed uterine leiomyomas if bleeding is disproportionate to uterine size and the patient reports significant pain.
- rapidly growing" uterus or leiomyoma (ie, doubling in size over a period of three to six months or increasing by six weeks gestational size within one year???

Findings that do NOT reliably predict sarcoma

- Rapidly growing uterine mass in premenopausal women.
- Large or solitary uterine mass :a sarcoma is often the largest (or the only) mass within a uterus, averaging 7 to 9 cm in diameter .However, leiomyomas may also be singular and may be of any size.
- large uterine size (in excess of 20 gestational weeks) has also **not** been shown to be associated with sarcoma risk

DIAGNOSIS

- The diagnosis of uterine sarcoma is based upon histologic examination of multiple sites in the mass .
- The three most important histologic criteria for the diagnosis of uterine sarcomas are mitotic index, cellular atypia, and geographic areas of coagulative necrosis separated from viable neoplasm.
- There is no reliable way to determine if a leiomyoma might be a leiomyosarcoma prior to surgical removal and review by the pathologist.

Tissue sampling

- **Endometrial biopsy** :sens:38-62%
- Endometrial biopsy may yield an accurate diagnosis in some patients, but a negative biopsy does not rule out the disease.
- An expert pathology review will determine whether a patient has a malignant epithelial tumor or a stromal/malignant mesenchymal tumor.
- Endometrial sampling for women with :abnormal uterine bleeding ,a uterine mass , who have signs, symptoms, risk factors, or other findings that raise suspicion of uterine sarcoma or endometrial carcinoma , for whom with plan of intraperitoneal morcellation.

- **Transvaginal biopsy of a prolapsed mass:** Biopsy before excision is indicated only if the appearance of the mass is not consistent with a common benign lesion. Leiomyomas tend to be white and hard, whereas sarcomas are more fleshy and can be friable. However, assuming a prolapsed mass is benign and removing it vaginally does not worsen the prognosis if it is actually a sarcoma.
- **Transabdominal biopsy:** Limitations of this method are that the accurate diagnosis of sarcoma requires sampling of multiple sites and that the procedure may spill malignant cells within the peritoneal cavity.

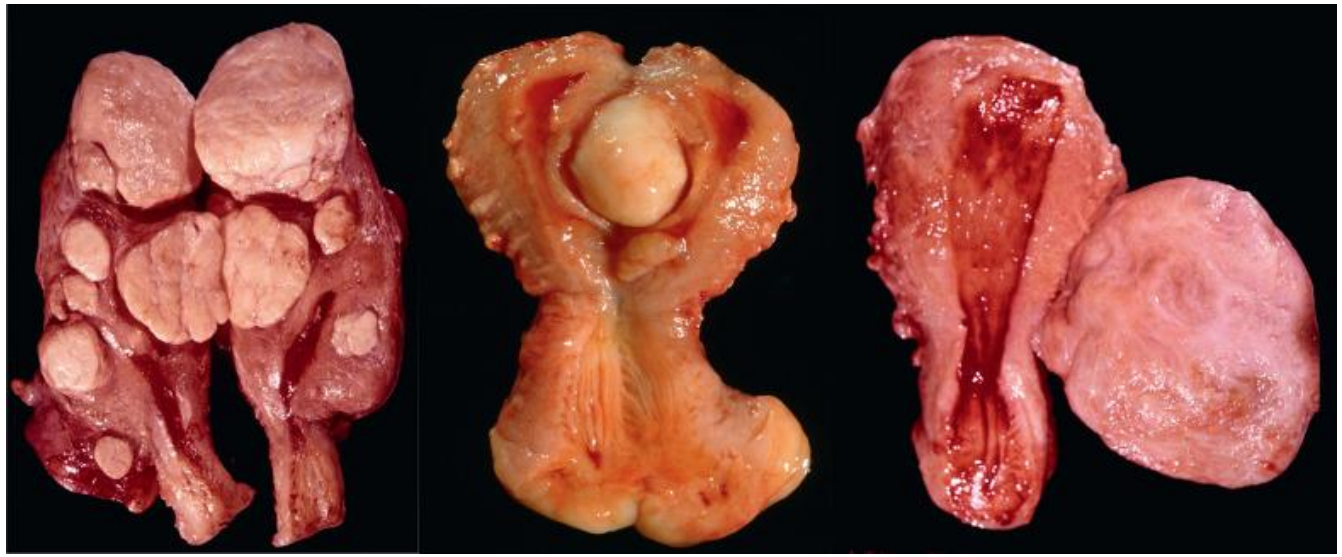
- The use of endometrial biopsy in LMS is limited, with only half of patients ultimately diagnosed with LMS having had pathologically significant endometrial biopsies with cancer or atypical spindle cell proliferations.
- In most cases, the diagnosis of uterine LMS is made following hysterectomy or myomectomy for presumed benign uterine leiomyomas .
- As an example, in one series of 106 women with uterine sarcoma, 65 percent of those with LMS were preoperatively diagnosed with a benign leiomyoma.
- Among women planning surgery for one or more uterine masses that are presumed to be benign leiomyomata, the reported prevalence of uterine sarcoma ranges from 1 in 350 to 1 in 500.

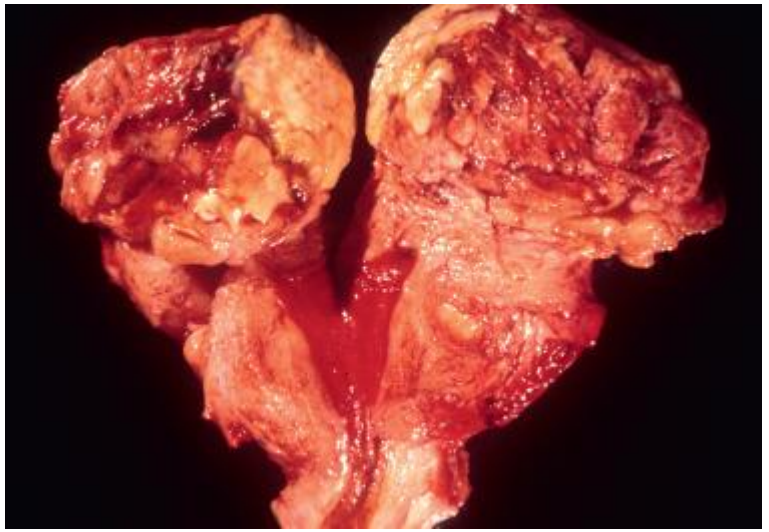
Leiomyosarcoma

- Leiomyosarcomas are typically large (>10 cm), yellow or tan solitary masses with soft, fleshy cut surfaces with areas of hemorrhage and necrosis .
- The mass may bulge into the uterine cavity, but the epicenter is in the myometrium.

Gross characteristics of the mass :

- Loss of the typical whorl pattern.
- Homogeneous texture.
- Yellow color.
- Soft consistency.
- Absence of a bulging surface when the capsule is incised.
- Ill-defined margins





- Most uLMS are found within the uterine wall as single tumors;
- in case of multiple uterine leimyomas the largest tumor should be examined carefully to exclude malignant degeneration.
- The tumor surface often appears grayish yellow or red and has a soft or fleshy consistency. Hemorrhagic and necrotic areas may be seen macroscopically.
- Tumor cell necrosis is the main criterion in malign leiomyogenic tumors, followed by infiltrating growth into the myometrium with blurry margins, extrauterine spread and tumor size > 10 cm.

DIAGNOSTIC METHODS

- Uterine sarcoma is a histologic diagnosis (An expert pathology review).
- Preoperative evaluation:

Pelvic examination : no examination findings that can distinguish a leiomyoma from a uterine sarcoma.

- women should undergo routine screening for cervical neoplasm.
- Choice of imaging modality : Pelvic ultrasound followed by MRI is the most useful imaging strategy

IMAGING

- In newly diagnosed uterine LMS :>33% distant metastasis, most commonly involving the liver, lung, or upper abdomen.
- Uterine LMS most commonly metastasizes to the lungs, liver, abdomen, pelvis, and pelvic or para-aortic lymph nodes.
- Imaging should be taken
- Chest,abdominopelvic CT scan, MRI, PET Scan

Oncology Research and Treatment

Review Article

Oncol Res Treat 2018;41:680–686
DOI: [illegible]

Received: August 23, 2018
Accepted: October 05, 2018
Published online: October 16, 2018

Uterine Leiomyosarcoma

Ingolf Juhasz-Böss[a] Lena Gabriel[a] Rainer M. Bohle[b] Lars C. Horn[c]
Erich-Franz Solomayer[a] Georg-Peter Breitbach[a]

[a]Department of Gynecology, Obstetrics and Reproductive Medicine, Saarland University, Homburg/Saar, Germany;
[b]Department of Pathology, Saarland University, Homburg/Saar, Germany;
[c]Division of Gynecologic Pathology, Department of Pathology, Leipzig University, Leipzig, Germany

Surgery is the basis of therapy, and it should be done in order to remove the uterus intact. As vaginal, abdominal, and endoscopic surgery – possibly including morcellation – are the methods of choice for the treatment of uterine fibroids, pre-operatively undiagnosed leiomyosarcoma detected by pathologic examination will have a worsened prognosis.

Surgical staging

TABLE 6.3 Frequency and Distribution of Disease Spread in Patients With Uterine Malignancies

	Carcinosarcoma (%) ($n = 301$)	Leiomyosarcoma (%) ($n = 59$)	Endometrial Adenocarcinoma (%) ($n = 621$)
Deep myometrial invasion	37	—	22
Positive peritoneal cytology	21	5	12
Adnexal involvement	12	3	5
Nodal metastases	17	3.5	9

BSO?

- TheNCCN panel recommends ER/PR testing to guide decisions regarding management of the ovaries, particularly in young premenopausal patients.
- In general, BSO is favored for low-grade ESS or tumors expressing ER/PR, although management of the ovaries may be individualized in reproductive-age patients. ????

LYMPHADENECTOMY

- incidence of lymph node metastases in clinical stage I or II: < 5%
- Routine lymphadenectomy should not be performed in women with uterine LMS confined to the uterus and normal-appearing lymph nodes.
- If the pelvic nodes are palpably enlarged intraoperatively or there is evidence of extrauterine disease: **LYMPHADENECTOMY**

DX after surgery

- The GOG sarcoma study on patterns of spread found that in 59 surgically staged patients, 5% had positive extrauterine spread to peritoneal cytology, 3% had adnexal involvement, and 3.5% had nodal metastases.
- **After hysterectomy :**BSO???, surgical staging
- **After myomectomy:** hysterectomy with resection of any visible residual disease if possible±BSO
- **After supracervical hysterectomy:** removal of the cervix with resection of any visible residual disease if possible±BSO
- **Tumor morcellation:** surgical exploration and staging(immediately)

Gynecologic Oncology 151 (2018) 562–572

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Review Article

Uterine leiomyosarcoma: A review of the literature and update on management options

Maureen E. Roberts [a,*], Jason T. Aynardi [b], Christina S. Chu [a]

[a] Division of Gynecologic Oncology, Department of Surgical Oncology, Fox Chase Cancer Center/Temple University Hospital, 333 Cottman Avenue, Philadelphia, PA 19111, United States of America
[b] Department of Pathology and Laboratory Medicine, Hospital of the University of Pennsylvania, 3400 Spruce St, 6 Founders, Philadelphia, PA 19104, United States of America

HIGHLIGHTS

- Uterine morcellation should be discouraged due to the risk of intraperitoneal dissemination of malignant tissue.
- Adjuvant therapy for uterine-confined disease remains controversial as no improvement in survival has been demonstrated.
- Adding olaratumab to doxorubicin for the treatment of advanced disease improves survival compared to doxorubicin alone.

Morcellation

- four retrospective single-centre studies found that morcellation was associated with a three- to fourfold increase in overall and intra-abdominal recurrence of uterine LMS, aswell as a 2.5-fold worsening of OS compared with tumours that were removed intact.

- US Food and Drug Administration guideline : power morcellation should not be used in peri- and postmenopausal women with fibroids (November 2014).

Management: stage I or II premenopausal women

- The mainstay of therapy for LMS confined to the uterine corpus or disease limited to the pelvis remains surgical excision with total abdominal Several studies found that ovarian preservation does not appear to worsen outcomes in overall survival (OS) and recurrence rates,despite theoretical concerns that some LMS express ERs that may render the tumours hormonally responsive.
- At least 40 percent of uterine LMS express estrogen and/or progesterone receptors.
- Some may reasonably recommend BSO for patients whose stage I uterine LMS is estrogen and/or progesterone receptor positive. However, there have not been any reports suggesting that such an approach will improve outcomes.
- The correlation of expression of estrogen receptor and/or progesterone receptor and performing BSO is speculative at this time.

Management of advanced or metastatic uterine LMS

- Surgical resection of metastatic sarcoma should be performed at the time of initial diagnosis.

Adjuvant cytotoxic agents

- Patients with advanced or metastatic disease beyond the pelvis are often not surgical candidates, but palliative chemotherapy may be offered to women with good performance status.

Medically inoperable patients

- individualized.
- Given the poor prognosis for patients with uterine LMS regardless of stage, nonsurgical treatment is palliative, not curative.
- Therefore, careful consideration of the benefits (eg, control of pain or bleeding) must be weighed against the toxicities of medical treatment.
- The treatment approach to medically inoperable patients mirrors that of women with metastatic disease

ADJUVANT TREATMENT

- **Early-stage disease** (stage I or II) : observation is the standard management.

  No Chemotherapy

  No Radiation therapy

- **Advanced disease:** high risk of disease progression following surgery alone, adjuvant chemotherapy is offered rather than postoperative surveillance.

POST-TREATMENT SURVEILLANCE

- high risk of relapse, even in stage I
- physical exam every three to four months and chest, abdomen, and pelvic imaging every three to four months for two to three years, then every 6 to 12 months for the next two years.

RECURRENCE

- The relapse rate is approximately 70% for stages I and II.
- The site of metastasis or recurrence is often distant due to the haematogenous spread into the lungs or liver.
- In the GOG study, the most common first site of recurrence was the lung (41%), and only 13% had a pelvic failure.
- All deaths and recurrences are during the 4 years after diagnosis
- In cases of disease recurrence, secondary cytoreduction may be considered, as neither chemotherapy nor radiation improved outcomes in recurrent disease.
- Outcomes were best for patients with a prolonged time to recurrence (>12 months) and an isolated site of recurrence amenable to resection.

LOCAL RECURRENCE OR OLIGOMETASTATIC DISEASE

- Surgical resection may offer a survival advantage and should be offered to appropriately selected patients.
- In one series of 31 patients with pulmonary metastases, for example, metastasectomy resulted in a median overall survival (OS) of 70 months.
- The best candidates for this approach are those who recur after a prolonged progression-free interval (at least 12 to 18 months) and with an isolated site of recurrence that is amenable to complete resection.
- For patients who are not surgical candidates, radiation therapy is an alternative treatment option for locally recurrent disease.
- Another approach to localized metastatic disease is radiofrequency ablation (RFA). small (generally under 4 cm) and accessible (generally not near major blood vessels) .

Staging–Uterine Sarcoma

Table 3
AJCC Tumor-Node-Metastases (TNM) and International Federation of Gynecology and Obstetrics (FIGO) Surgical Staging Systems for Uterine Sarcomas (includes Leiomyosarcoma and Endometrial Stromal Sarcoma)

Leiomyosarcoma and Endometrial Stromal Sarcoma

T	FIGO Stage	Primary Tumor
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	**I**	Tumor limited to the uterus
T1a	**IA**	Tumor 5 cm or less in greatest dimension
T1b	**IB**	Tumor more than 5 cm
T2	**II**	Tumor extends beyond the uterus, within the pelvis
T2a	**IIA**	Tumor involves adnexa
T2b	**IIB**	Tumor involves other pelvic tissues
T3	**III**	Tumor infiltrates abdominal tissues
T3a	**IIIA**	One site
T3b	**IIIB**	More than one site
T4	**IVA**	Tumor invades bladder or rectum

N	FIGO Stage	Regional Lymph Nodes
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N0(i+)		Isolated tumor cells in regional lymph node(s) no greater than 0.2 mm
N1	**IIIC**	Regional lymph node metastasis

M	FIGO Stage	Distant Metastasis
M0		No distant metastasis
M1	**IVB**	Distant metastasis (excluding adnexa, pelvic, and abdominal tissues)

G	Histologic Grade
GX	Grade cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated or undifferentiated

Table 4. **AJCC Prognostic Stage Groups**

	T	N	M
Stage I	T1	N0	M0
Stage IA	T1a	N0	M0
Stage IB	T1b	N0	M0
Stage II	T2	N0	M0
Stage IIIA	T3a	N0	M0
Stage IIIB	T3b	N0	M0
Stage IIIC	T1-3	N1	M0
Stage IVA	T4	Any N	M0
Stage IVB	Any T	Any N	M1

PROGNOSIS

Table 2. Summary of survival in uterine LMS stratified by FIGO stage

FIGO stage	No. patients	5-year DSS (SE), %
I	951	75.8 (1.7)
II	43	60.1 (10.4)
III	99	44.9 (6.8)
IV	303	28.7 (4.4)

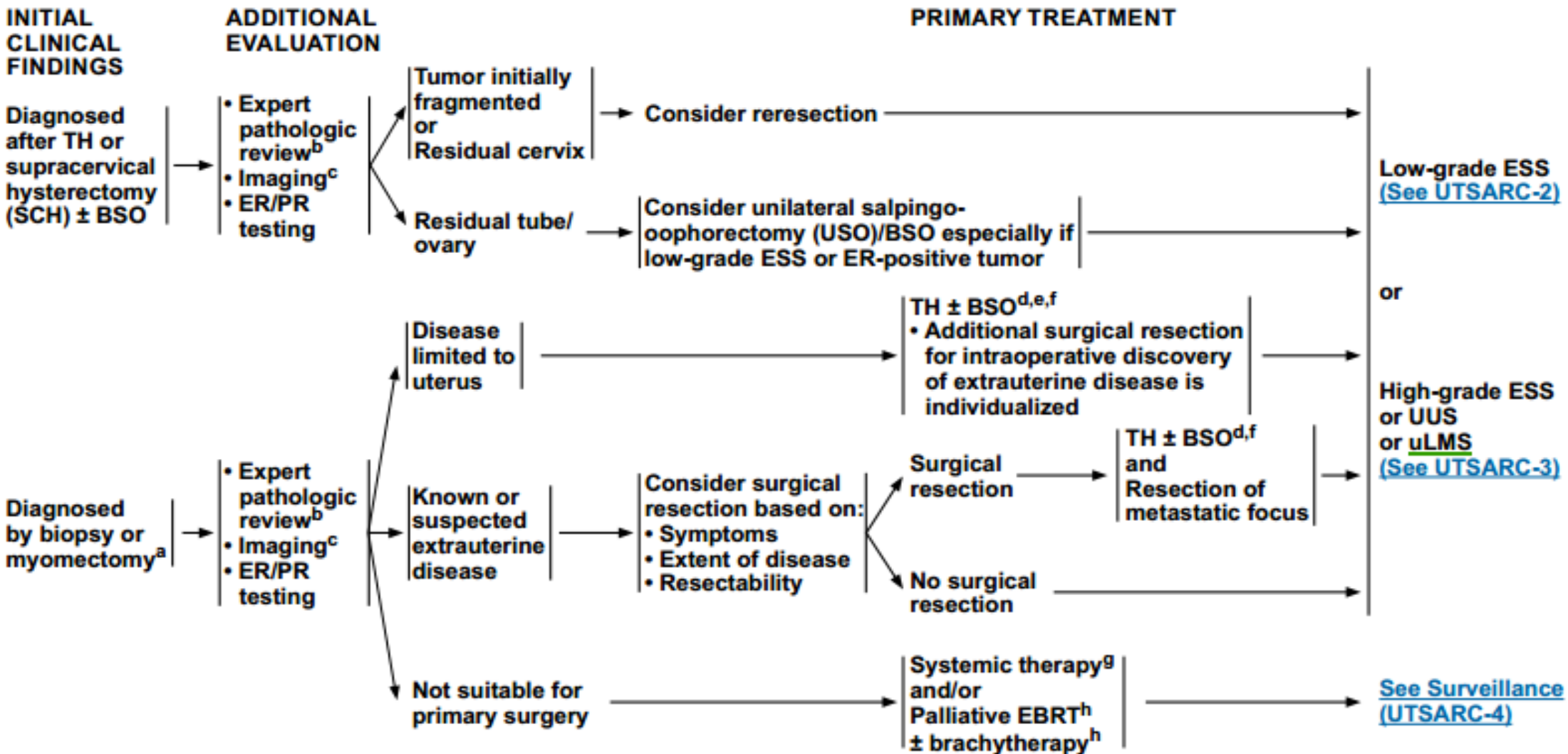
DSS, disease-specific survival.
Adapted from Kapp et al.[31] Data abstracted from SEER database 1988–2003.

Prognostic factors: grade, stage, race, age, tumor size, local extension, distant metastases, and mitotic rate.

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2020
Uterine Sarcoma

NCCN Guidelines Index
Table of Contents
Discussion

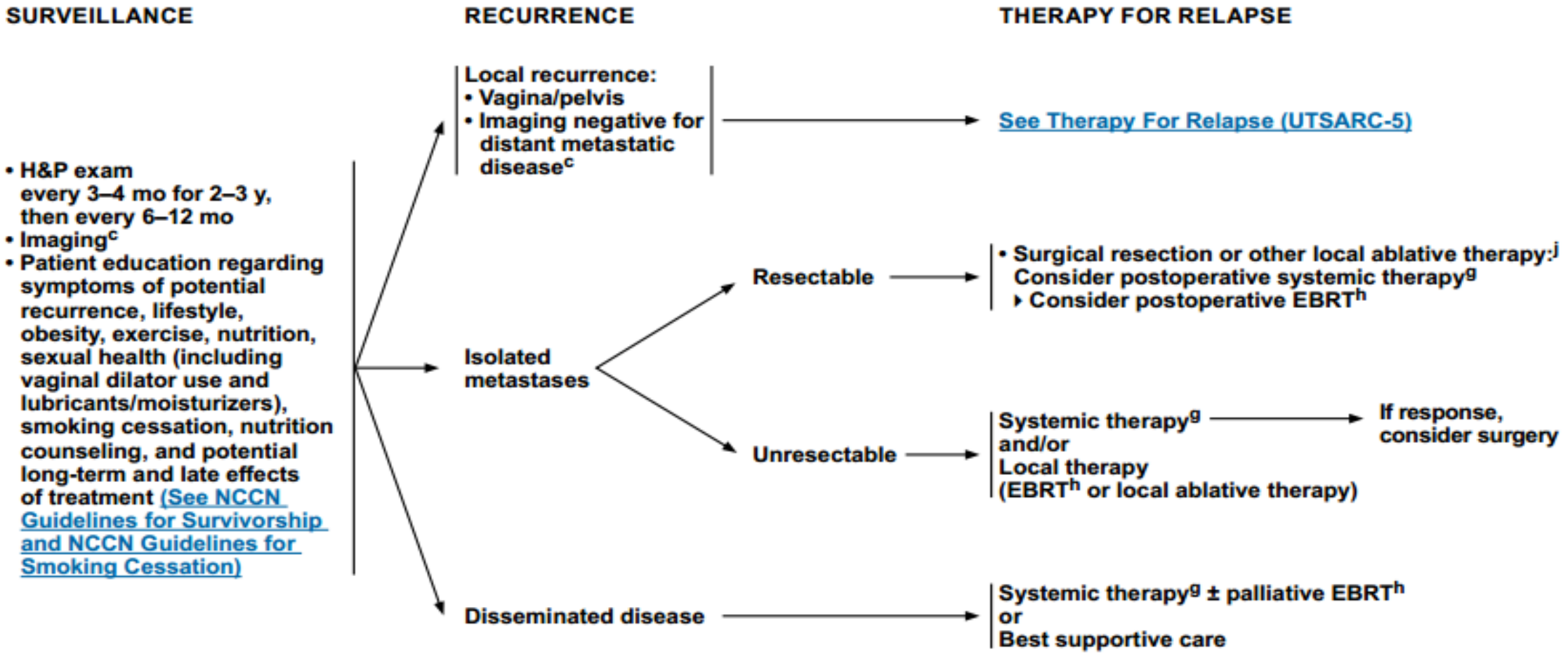


[a]Preoperative imaging and biopsy may help to identify uterine sarcomas, although biopsy sensitivity is less than for endometrial cancer. If there is suspicion of malignant

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2020
Uterine Sarcoma

NCCN Guidelines Index
Table of Contents
Discussion



National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2020
Uterine Sarcoma

NCCN Guidelines Index
Table of Contents
Discussion

PRINCIPLES OF IMAGING[a,1-9]

Initial Workup

- Chest/abdomen/pelvic CT.
- For patients who underwent TH with incidental finding of uterine sarcoma or incompletely resected uterus/adnexa (ie, supracervical hysterectomy (SCH), myomectomy, possible tumor fragmentation, intraperitoneal morcellation) perform chest/abdominal/pelvic CT or abdominal/pelvic MRI and chest CT without contrast to evaluate for metastatic disease.
- Consider pelvic MRI to evaluate local tumor extension or residual abnormality in cases where the uterus or adnexa were not resected or incompletely resected (ie, SCH, myomectomy, possible tumor fragmentation, intraperitoneal morcellation).
- Consider whole body PET/CT to clarify ambiguous findings.
- Additional imaging should be based on symptomatology and clinical concern for metastatic disease.[b]

Follow-up/Surveillance

- Chest/abdominal/pelvic CT every 3–6 months for the first 3 years and then every 6–12 months for the next 2 years. Depending on histology grade and initial stage, consider annual to biannual imaging thereafter up to an additional 5 years.[c]
- Optional abdominal/pelvic MRI and chest CT without contrast every 3–6 months for the first 3 years and then every 6–12 months for the next 2 years. Depending on histology, grade, and initial stage, consider annual to biannual imaging thereafter up to an additional 5 years.[c]
- Consider whole body PET/CT if metastasis is suspected in select patients.
- Additional imaging should be based on symptomatology and clinical concern for metastatic disease.[d]

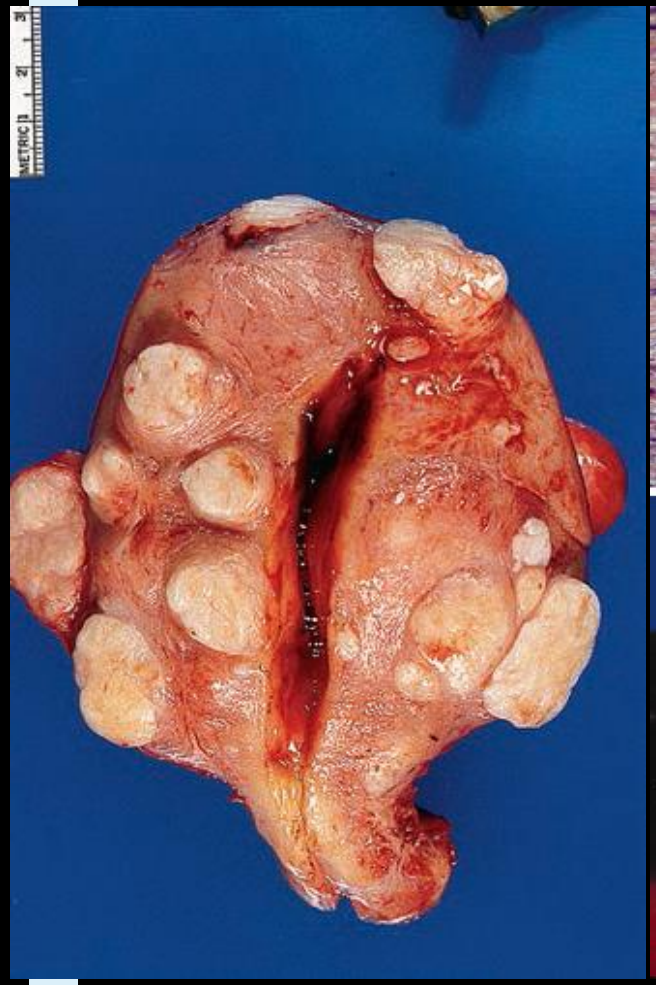
CASE

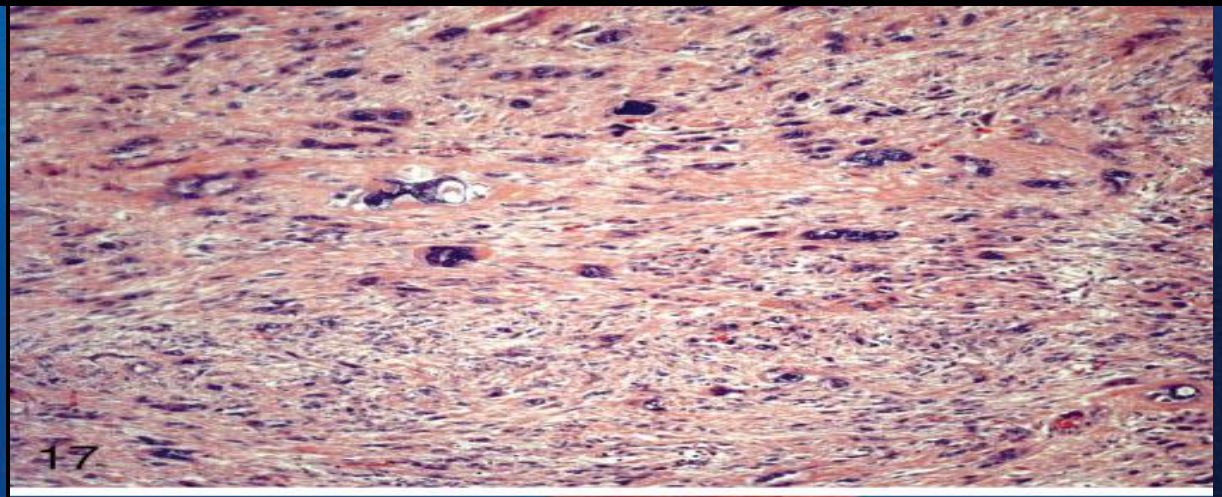
- A 37year-old woman G0 presented to the hospital with a pelvic mass and hypermenorrhea . Ultrasonography revealed a mass consistent with a degenerated myoma measuring 77x82mm, in the posterior wall.
- MRI revealed a mass with a hypovascular appearance following a heterogeneous and hypointense IV contrast material with a diameter of 8 cm, which appeared to displace the posterior cervix.
- Laparoscopic myomectomy was performed.
- A soft mass with bulging cut surface that displayed scattered areas of hemorrhage and necrosis
- It was removed by morcellating in an isolated bag.
- Pathologic report: marked cellularity and pleomorphism, extensive necrosis,mitosis>5/10HPF, KI67 proliferation index>%50.

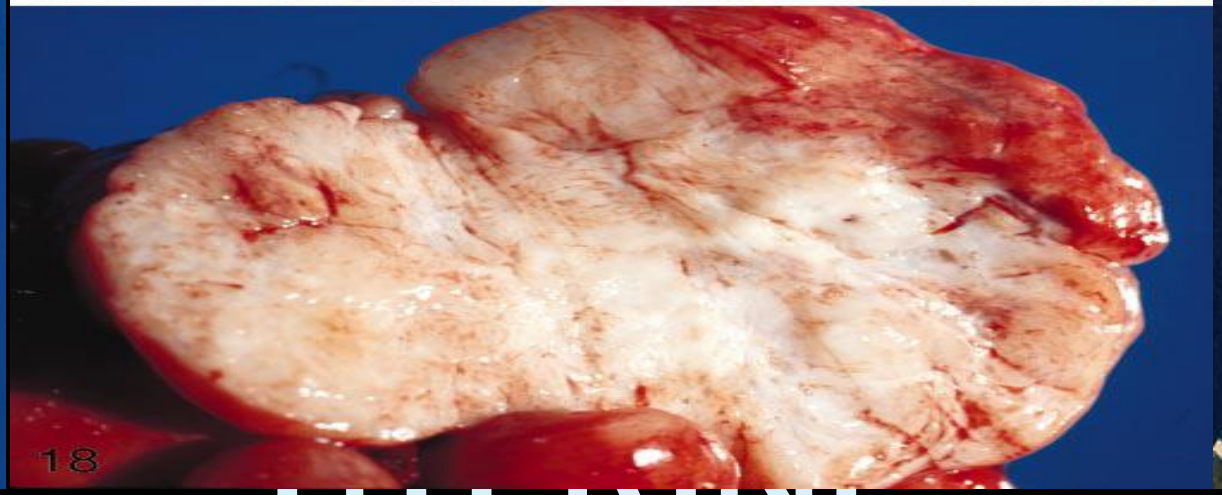
- تشخیص افتراقی های لیومیوسارکوم رحمی؟
- در چه صورت تشخیص STUMP است؟
- وجه تشابه میوم با لیومیوسارکوم در پاتولوژی؟
- علت خطای تشخیص پاتولوژیک؟
- ارزش frozen section در تشخیص لیومیوسارکومای رحمی؟

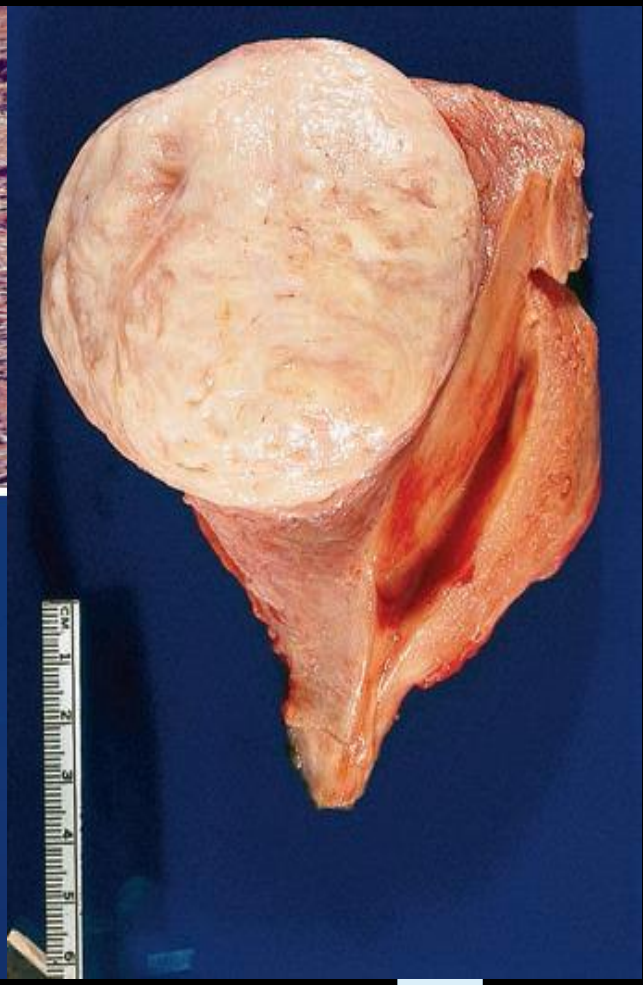
بسم الله الرحمن الرحیم

Narges Izadi Mood,M.D
Professor of pathology
Yas Women Hospital
Tehran university of Medical sciences









UTERINE LEIOMYOSARCOMA

Uterine smooth muscle tumors (SMTs) cause of diagnostic error

Epithelial neoplasms have a clearly defined behavior (invasion) that indicates metastatic potential.

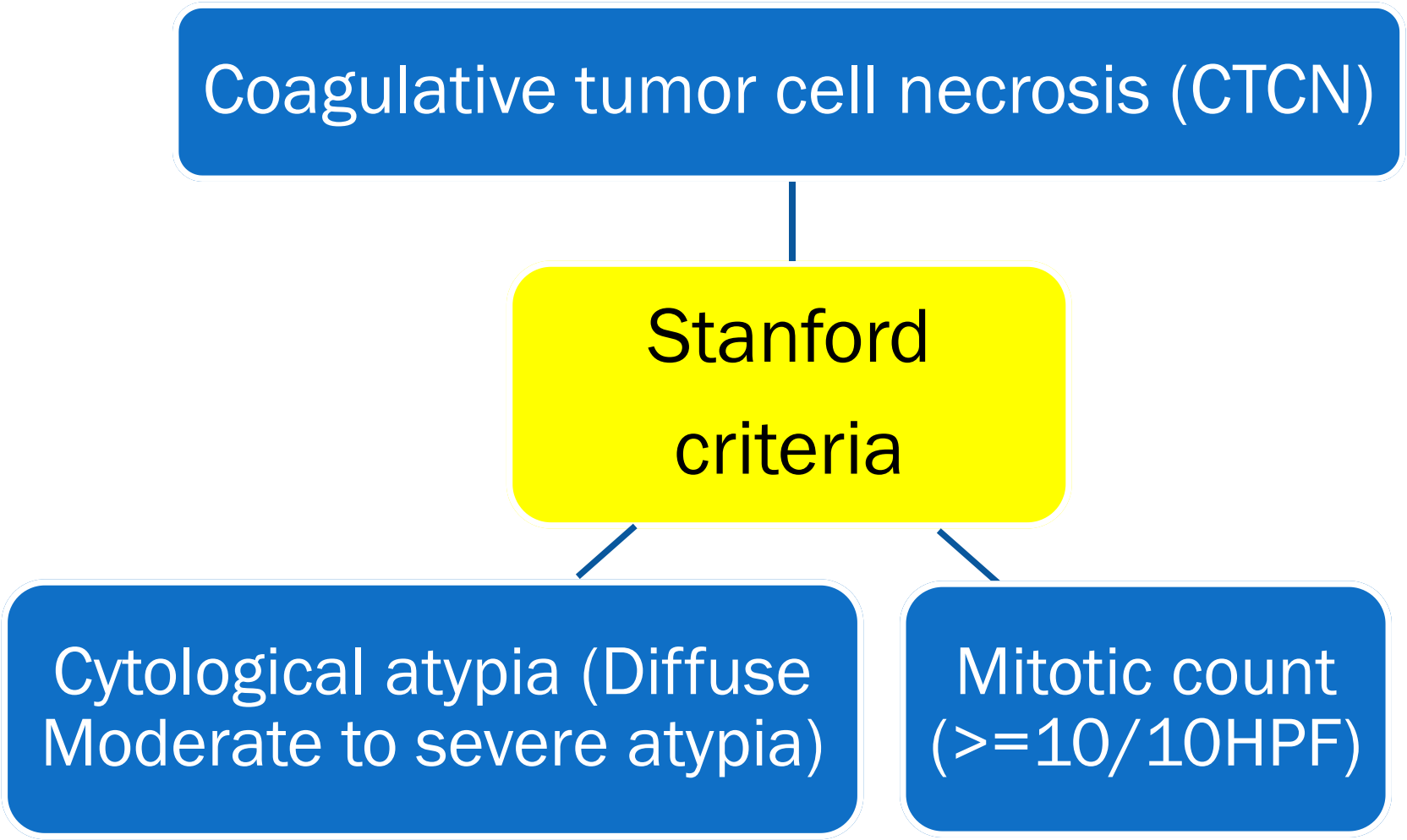
Because smooth muscle neoplasms arise in the stroma (do not live in a compartment), they are more difficult to distinguish as benign (without metastatic potential) or malignant (with metastatic potential).

The proportion of uterine smooth muscle tumors that are malignant ranges from 0.13 to 6%, a 50-fold variation reflecting usage of differing diagnostic criteria.

Historical evolution in the pathologic diagnosis of Leiomyosarcoma

- 1966 : Taylor and Norris → 10 Mitotoses/10HPFs
- 1973: Kempson → Smooth muscle tumors of unknown malignant potential (STUMP)
- 1994: Bell et al → Stanford study

Bell et al, Stanford study LMS



Bell et al, Stanford study LMS

- Suggesting thus that tumors showing:
- ***At least two of the these three features should be interpreted as conventional leiomyosarcomas***.

  (No for Epithelioid LMS and Myxoid LMS)

- ***Leiomyomas*** were defined as tumors with a ***mitotic count =<4/10 HPF, without atypical cells and with no tumor cell necrosis.***

- In this article, the term '***STUMP' was not used***; however, the authors delineated ***four histological categories*** of uterine smooth muscle tumors with an uncertain malignant potential:

- 1) Aatypical leiomyoma with limited experience (AL-LE),

focal or multifocal moderate-severe atypia, no tumor cell necrosis and a mitotic =<10 mitoses /10 HPF

- 2) Smooth muscle tumor with low malignant potential (SMT-LMP) *tumor cell necrosis*, with absent or minimal atypia and <10 mitoses/10 HPF;
- 3) Atypical leiomyoma with low risk of recurrence (AL-LRR), diffuse *moderate-to-severe atypia*, no tumor cell necrosis and a mitotic count <10/10 HPF;
- 4) Mitotically active leiomyoma with limited experience (MAL-LE) *increased mitotic activity, =>20/10 HPF*, but with no evidence of atypia and tumor cell necrosis.

Smooth muscle tumors of unknown malignant potential (STUMP)

- STUMPs represent a group of rare and heterogeneous neoplasms from both a histological and a clinical point of view.
- Due to the rarity of these tumors, existing literature on the topic remains scarse and therefore consensus regarding diagnosis, malignant potential, treatment of choice and follow-up has not yet been reached
- STUMPs are *characterized by the possibility of delayed reccurences*.

Histopathological parameters for the diagnosis of STUMP according to the largest published works.

Reference	Atypia	MF/10 HPF	Necrosis	Other features
Bell [1]	Focal/multifocal moderate-severe	≥10	Absent	–
Ip [3]	Absent or minimal atypia	<10	Present	–
	Diffuse moderate-to-severe atypia	<10	Absent	–
	None	≥20	Absent	–
	None	≥10	Uncertain	–
	Diffuse/multifocal, moderate to severe	Borderline/uncertain	Absent	–
Oliva [2]	Focal/multifocal moderate-severe	<10	Absent	–
	Diffuse	<10	Absent	–
	None	<10	Present	–
	None	>15	Absent	–
Guntupalli [4]	None	<10	Present	–
	Diffuse	<10	Absent	–
	None	>20	Absent	–
	None	>4	Absent	Increased cellularity Irregular margins or vascular invasion
	–	–	–	
D' Angelo and Prat [49]	None	Any	Present	–
	None	≥10	Ambiguous/difficult to classify	–
	Marked-diffuse	<10	Ambiguous/difficult to classify	–
	Marked-diffuse/focal	Borderline (8–9)	Absent	–
Gupta [10]	–	–	Ambiguous/difficult to classify	–
	Diffuse or multifocal	Borderline (range 8–9)	Absent	–
	None	> 15	Absent	–
	–	–	–	Coagulative/ischemic necrosis in multifocal or irregularly-shaped foci
	–	–	–	Epithelioid morphology/myxoid smooth muscle tumors showing atypia
	–	–	–	Epithelioid morphology/myxoid smooth muscle tumors showing increased proliferative activity
	–	–	–	Myometrial invasion
	–	–	–	Atypical mitotic figures

No consensus regarding the histological features able to predict the likelihood and the clinical characteristics of a recurrence, such as:

- *Anatomical site* (pelvis, abdomen, liver, lungs, lymph nodes, ...and uterus-if hysterectomy was not previously performed)
- *Timing* (ranging from 15 months to 9 years)
- *Histological type* (STUMP or leiomyosarcoma)

- Patients with ***STUMPs*** must be ***counselled regarding the potential risk of recurrence as leiomyosarcoma***

- ***A multidisciplinary management*** carried out by a team composed of ***gynaecologist, dedicated pathologist (with expertise in gynaecological pathology) and oncologist*** is mandatory for early detection of this disease and to establish the treatment of choice and follow up program.

Differential diagnosis

- Endometrial stromal sarcoma
  - *Low grade Endometrial stromal sarcoma
  - *High grade Endometrial stromal sarcoma
- Leiomyoma variants
  - *Mitotically active leiomyoma
  - *Cellular leiomyoma
  - *Leiomyoma with Bizarre nuclei
  - *Myxoid leiomyoma
  - *Epithelioid leiomyoma
- Smooth muscle tumor of uncertain malignant potential (STUMP)
- Inflammatory myofibroblastic tumor
- Perivascular epithelioid cell tumor (PEComa)

frozen section

- Myomectomy specimens are sometimes submitted for frozen section evaluation if the clinical manifestations are alarming, such as a rapid increase in the size, and if hysterectomy is to be avoided for clinical considerations such as desire to maintain fertility.
- *Differentiation of leiomyomas from leiomyosarcomas may be difficult*
- Evaluation of cellular smooth muscle neoplasms
- Accurate mitotic counts may be difficult. Unfortunately, artifacts, including apoptosis, can simulate mitotic figures.
- Benign smooth muscle tumors may be mitotically active
- Unless there is significant atypia and/or areas of coagulative necrosis

frozen section

- Evaluation should include any of the grossly suspicious areas that have lost the characteristic whorled pattern of a benign leiomyoma.
- A definitive diagnosis is often deferred until permanent section analysis, in which extensive sampling with accurate mitotic counts and evaluation of other histologic parameters can be performed.
- If there is any unusual pattern or histologic feature, the temporary diagnosis of STUMP is rendered, and the definitive diagnosis awaits permanent section analysis

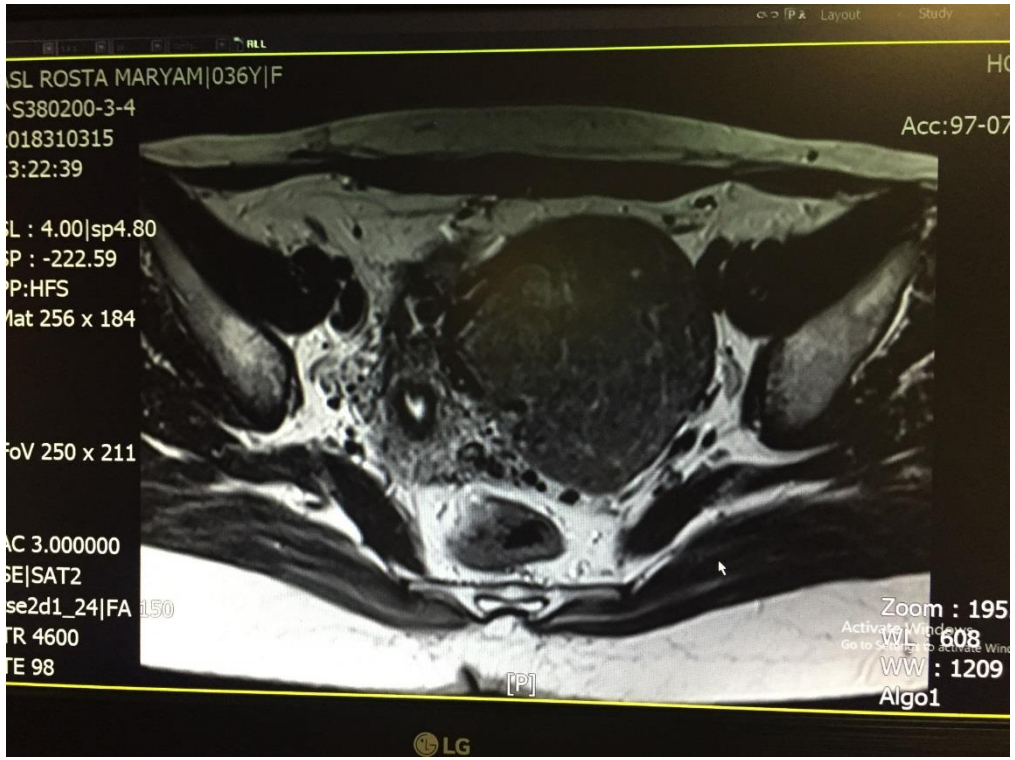
- There is no consensus on how to grade; therefore, it is not advised to grade as low or high grade
- ***Most powerful prognostic factor is tumor stage***
- Other factors such as **tumor size, mitotic count and percentage of necrosis** have been suggested to predict patient's outcome

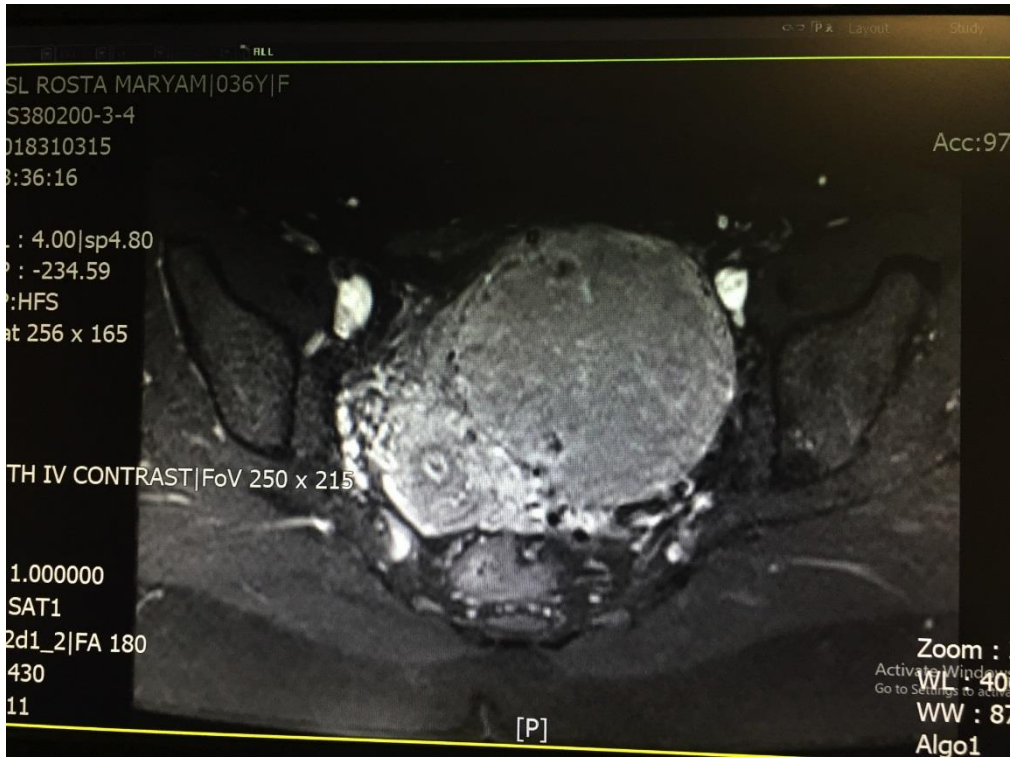
- آیا Imaging در افتراق میوم از لیومیوسارکوم کمک کننده است؟
- ارزش سونوگرافی کالر داپلر ؟
- کدام imaging توصیه میشود؟
- یافته های MRI ؟
- نحوه درخواست MRI ؟

MARYAM RAHMANI MD

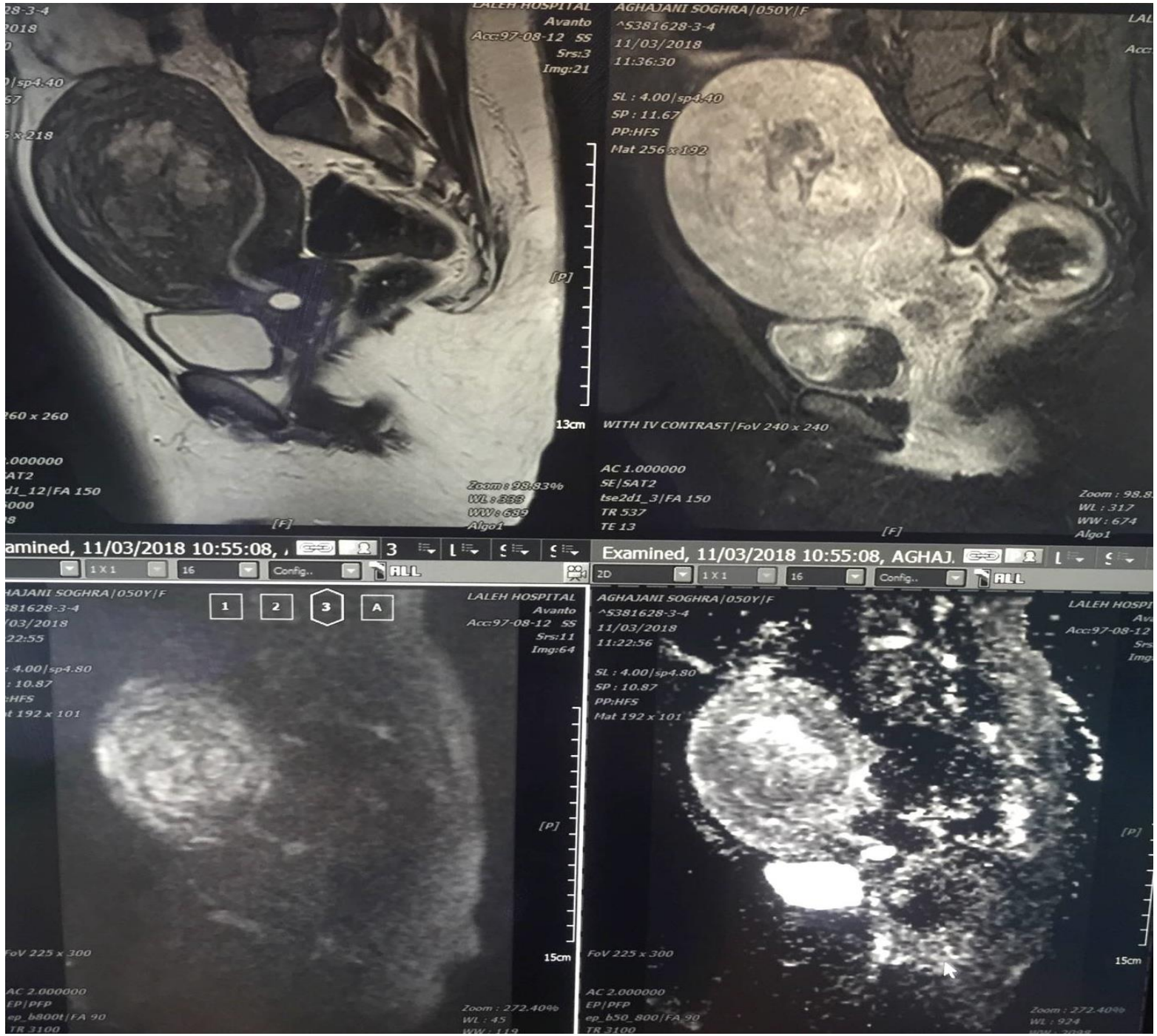
Professor of Radiology

Tehran University of Medical Science
Imam Khomeini Hospital


Layout
Study
SL ROSTA MARYAM|036Y|F
S380200-3-4
018310315
3:22:39
L : 4.00|sp4.80
P : -222.59
P:HFS
lat 256 x 184
oV 250 x 211
C 3.000000
E|SAT2
se2d1_24|FA
R 4600
E 98
Acc:97-07
Zoom : 195
WL : 608
WW : 1209
Algo1
[P]
LG


SL ROSTA MARYAM|036Y|F
S380200-3-4
018310315
:36:16
Acc:97
: 4.00|sp4.80
: -234.59
:HFS
t 256 x 165
TH IV CONTRAST|FoV 250 x 215
1.000000
SAT1
2d1_2|FA 180
430
11
[P]
Zoom :
WW : 87
Algo1

TYPICAL MYOMA


LALEH HOSPITAL
Avanto
Acc:97-08-12 SS
Srs:3
Img:21
AGHAJANI SOGHRA|050Y|F
^S381628-3-4
11/03/2018
11:36:30
SL : 4.00|sp4.40
SP : 11.67
PP:HFS
Mat 256 x 192
WITH IV CONTRAST|FoV 240 x 240
AC 1.000000
SE|SAT2
tse2d1_3|FA 150
TR 537
TE 13
13cm
Zoom : 98.83%
WL : 333
WW : 639
Algo1
Examined, 11/03/2018 10:55:08, AGHAJ.
1 X 1
16
Config..
ALL
2D
LALEH HOSPITAL
Avanto
Acc:97-08-12 SS
Srs:11
Img:64
AGHAJANI SOGHRA|050Y|F
^S381628-3-4
11/03/2018
11:22:56
SL : 4.00|sp4.80
SP : 10.87
PP:HFS
Mat 192 x 101
FoV 225 x 300
15cm
AC 2.000000
EP|PFP
ep_b50_800|FA 90
TR 3100
Zoom : 272.40%
WL : 924

UTERINE MASS , ESS

imaging

- A consistent finding in leiomyosarcomas is the absence of calcifications.
- Two small studies using different techniques of MRI with gadolinium contrast have reported specificities of 93 to 100 percent and positive predictive values of 53 to 100 percent .
- Diffusion weighted MRI also appears to differentiate ordinary and degenerated leiomyomas from sarcomas and cellular leiomyomas .
- Finally, the presence of intralesional hemorrhage appears to be suggestive of sarcoma.

- آیا قبل از عمل جراحی با توجه به signs , symptoms می توان میوم را از لیومیوسارکوم افتراق داد؟
- ارزش بیوپسی آندومتر در تشخیص سارکوم؟
- آیا مورسلیشن توده در اندوبگ خطر انتشار سلولهای تومورال را منتفی میکند؟
- آیا جراحی مجدد این بیمارلازم است؟ وسعت آن در چه حد است؟
- آیا حفظ باروریFertility-Sparing Therapy جایی دارد؟
- BSO ؟ لنفادنکتومی؟

Should unplanned hysterectomy be performed based on intraoperative findings

- The only indications for hysterectomy are a definitive frozen section diagnosis of sarcoma and/or gross evidence of metastases. One note of caution is that women with apparent intra-abdominal metastases may have a primary neoplasm at another site or leiomyomatosis peritonealis disseminata, which is a rare and benign condition. Unplanned hysterectomy should not be performed in women of reproductive age without a pathologic diagnosis of sarcoma and a documented preoperative discussion.
- ovarian preservation may be carried out in the case of unexpected intraoperative findings of sarcoma

- آیا رادیوتراپی در این بیمار اندیکاسیون دارد؟
- طی فالوآپ در چه صورت رادیوتراپی توصیه میشود؟

- نقش کموتراپی در اداره لیومیوسارکوم رحمی در این بیمار؟
- ارزش چک رسپتورهای استروژنی و پروژسترونی چیست؟
- آیا هورمون درمانی در manage لیومیوساکوم نقش دارد؟
- فالوآپ این بیمار چگونه است؟
- پروگنوز این بیمارچگونه است؟
- پروگنوز این بیماران به چه فاکتورهایی بستگی دارد؟

- Leiomyosarcoma are rare, aggressive tumours with heterogeneous genetic make-up. Pre-operative detection remains a clinical challenge as the majority of LMS are diagnosed at the time of surgery.
- Prognosis is poor regardless of initial stage at diagnosis, and surgery and adjuvant therapies have not been effective at improving prognosis.

Take home message

- Missing a sarcoma is a concern with alternatives to hysterectomy for a presumed fibroid(without tissue diagnosis).
- the diagnostic delay was increased with uterine artery embolization, ranging from 6 to 14 months.
- Leiomyomas do not appear to progress to sarcoma, with the exception of rare atypical or cellular variants.
- For most women with presumed uterine leiomyomas, whether asymptomatic or symptomatic, ACOG guidline recommend **NOT** performing hysterectomy for the sole purpose of excluding malignant neoplasm .
- hysterectomy :women with endometrial sampling and/or MRI results that strongly suggest sarcoma, those with thoracic imaging consistent with lung metastases, or those with multiple risk factors for uterine sarcoma.

Take home message

- Factors that may raise a suspicion of sarcoma include symptoms, risk factors, failure of response to prior therapy, and the findings of MRI and endometrial sampling.
- Only a definitive diagnosis of sarcoma on frozen section should influence surgical decisions (eg, whether to perform hysterectomy or staging).
- Whenever possible, women with uterine sarcomas should be referred to specialty centers with expertise in their diagnosis and management.
- All patients with a diagnosis of uterine sarcoma must be presented to an interdisciplinary tumor conference.
- conservative management of symptomatic leiomyomas by myomectomy, after Lupron treatment before myomectomy, and after vascular embolization of presumed leiomyomas speak to the importance of pretreatment counseling of patients who undergo such therapies.

Thank you for your attention