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# Surgical treatment of uterine sarcoma patients. Review

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**Uterine sarcoma is a rare neoplasm, originating from mesenchymal tissue, with aggressive clinical course and poor prognosis. Due to morphological classification there are four main histological subtypes: leiomyosarcoma, carcinosarcoma, endometrial stromal sarcoma and undefined sarcoma. Surgery is regarded as the main treatment method, but usually is required as diagnostic procedure for final morphological submission of the diagnosis. Total abdominal hysterectomy with bilateral salpingo-oophorectomy represents the standard surgery type for uterine sarcoma patients stage I–II. Pelvic lymph node dissection is recommended in patients with carcinosarcoma. Chemoradiation therapy is prescribed for patients with advanced disease. Patients with uterine sarcoma should be referred to specialized oncology center for treatment and follow-up.**
***Key words:*** *uterine sarcoma, classification, surgery.*

Uterine Sarcoma (US) is a very aggressive malignant disease, which comprise from 3 to 9% of all uterine tumors [1, 2] and 1% among genital cancers. The morbidity rate is 1-3 cases per 100,000 of the female population [3]. Aggressive clinical course with frequent local and distant (metastatic) recurrence is a very characteristic for this tumor. Age of patients varies from 20 to 80 years old, the average age is 50.2 years old [3].

The purpose of this study is to provide information about surgical treatment of uterine sarcoma patients.

Little is known regarding etiology of uterine sarcoma. There has been reported association between prior pelvic irradiation and appearance of leiomiosarcoma (LMS) and carcinosarcoma (CS), but included only a few patients with a history of pelvic irradiation. Mark et al. reviewed the literature and estimated the risk of appearance of postirradiated (median dose of 55 Gy) LMS and endometrial stromal sarcoma (ESS) to range from 0.003% to 0.8% following a latency period of 3–30 years [4]. Uterine sarcoma, so as carcinoma are associated with obesity, nulliparity, and use of exogenous estrogen and tamoxifen [5].

**Histopathological classification** proposed by W. Ober separates sarcomas according to the number and type of recognizable sarcomatous and carcinomatous tissues. Further he has divided histological classification into pure and mixed sarcomas [6]. Nowadays, according to the World Health Organization (WHO) 2003 classification, they consist of two main groups: mesenchymal tumors and mixed – epithelial and mesenchymal tumors [7].

The pure mesenchymal tumors can be further classified into endometrial stromal sarcoma, leiomyosarcoma (including the epithelioid and myxoid variants), and undifferentiated endometrial/uterine sarcoma (UUS) according to the cell of origin.

Mixed tumors include carcinosarcoma (so as malignant Mьllerian mixed tumor) and adenosarcoma are composed of a mixture of epithelial and mesenchymal components. However, today it is regarded as a subset of endometrial carcinoma, and as such should be excluded from studies of uterine sarcoma [4]. Despite this, carcinosarcoma is still included in most retrospective studies of uterine sarcoma, as well as in the WHO 2003 classification [7].

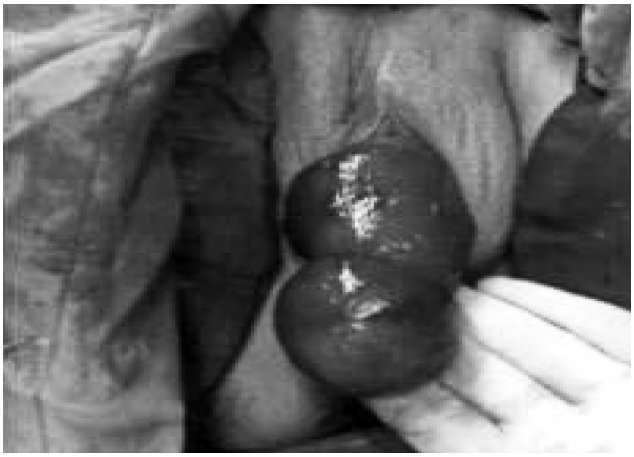
Uterine leiomyosarcomas need to be distinguished from mitotically active or atypical leiomyomas and uterine smooth-muscle neoplasms with low malignant potential [8].

Morphological verification contributes for performing the adequate type of operation. The diagnosis of uterine sarcoma was strongly suspected and proved before the initial operation in 20% of cases and during the operation in 60% of cases, due to data Hassini A. et al [9].

At macroscopic analysis the tumor is presented as a cooked fish of yellow color with separate small necrotic cavities. Its consistency may be sometimes soft, sometimes dense. In some parts of tumor tissue, along with necrobiosis, there can be revealed hemorrhage foci and redness in case of joined infection (Pic. 1).

The typical clinical features are postmenopausal or abnormal vaginal bleeding (15.4%), abdominal pain (23%), which is presented in all types of uterine sarcoma. Uterine enlargement/mass is more characteristic (100%) for LMS and uterine leiomyoma. These tumors growth show an exophytic pattern within the endometrial cavity. Bleeding and uterine cramping are common as the uterus attempts to expel the globular mass (Pic. 2) [10, 11]. In 7.7% the presentation was a com-

**Pic. 1. Macroscopic view of tumor**



**Pic 2. Clinical presentation of uterine sarcoma**

plication of either a pregnancy or an intrauterine contraceptive device (IUCD), respectively [12].

Metastatic spread of uterine sarcoma may be proceed hematogenously, on lymphatic system or in implantation manner, most often to the lungs. Other sites include the liver, bone and brain. Patients with distant metastasis at the time of diagnosis have symptoms that correspond to the location(s) of their disease [10].

**Imaging.** Preoperative imaging is mandatory, because ESS tends to spread to the lungs and peritoneum. Most ESSs (65–86%) will be presented with disease limited to the uterus (stage I–II disease) [13]. Most uterine leiomyosarcomas are described as large oval-shaped tumours with inhomogeneous and bizarre internal echo pattern at ultrasonography. They contain mixed echogenic and poor echogenic parts surrounded by a thinned myometrium. Central necrosis is common [14]. At ultrasonography, ESS can present as a hypoechogenic mass with irregular margins originating from the endometrium and with irregular central or circular vascularisation. A heterogeneous pattern of the endometrium with high-intensity and hypoechoic areas scattered in the myometrium has also been linked to ESS [14].

Findings in uterine leiomyosarcomas on MRI vary and include a lobulated mass of high-signal intensity on T2-weighted images, a sharply marginated mass of low-signal intensity that closely resembles a leiomyoma, or a mass with focally infiltrative margins [15, 16].

Uterine leiomyosarcomas accumulate 18-fluorodeoxyglucose ([18F]FDG), which is detected by PET, and the combined use of PET with CT is promising, because it provides both morphological and anatomical information [17].

Although several features at ultrasonography and MRI can raise suspicion of a uterine sarcoma, there are no pathognomonic features on any imaging technique. Hysterectomy is advocated when imaging modalities cannot exclude a malignancy [14].

Up to date the staging system for uterine sarcomas is almost the same, which was proposed for endometrial cancer by the International Federation of Gynecology and Obstetrics (FIGO). But in year 2009 FIGO has approved renewed surgical staging system for uterine sarcoma and subsequently published [18, 19]. The new one is presented in Table I.

**Surgery.** Uterine sarcomas are very uncommon and the preoperative diagnosis is problematic. Many women have surgery for presumed benign conditions such as uterine leiomyoma [14]. From the other hand, patients with preoperative suspected uterine sarcoma should be referred to specialist centers, where appropriate surgery can be performed in order not to decrease patients' survival.

Adnexal or lymphatic spread is only present in about 3% of early stage uterine leiomyosarcomas. Lymph-node involvement is more frequent in advanced-stage disease [20, 21].

However, the ovaries are frequently removed because of age, probability of ovarian metastasis presence, and low-grade hormonesensitive uterine leiomyosarcoma. A simple hysterectomy with bilateral salpingo-oophorectomy (BSOE), but without lymphadenectomy, is therefore standard treatment for early stage uterine leiomyosarcomas. In premenopausal women, a simple hysterectomy (without oophorectomy) can be considered sufficient [22]. F. Amant with colleagues have proposed treatment algorithm (fig.1) for LMS and ESS [14]. Total hysterectomy is important if uterine sarcoma is suspected, and can be curative if the tumor is confined to the uterus. In the case of the preoperative diagnosis is ESS, radical hysterectomy is also recommended, as this tumor type often involves parametrium, sometimes only intravascular invasion, which is difficult for preoperative diagnostic. Simple hysterectomy has been recommended for women with stage I uterine carcinosarcoma, because no survival differences in stage I patients who underwent simple versus radical hysterectomy were found. Radical hysterectomy can be considered for women whose tumours have spread to the cervix or parametrial tissue [23].

*Table I*

**Staging for uterine sarcomas (leiomyosarcomas, endometrial stromal sarcomas, adenosarcomas, and carcinosarcomas)**

| Stage Definition |
|---|
| (1) Leiomyosarcomas and endometrial stromal sarcomas (ESS) * |
| I Tumor is limited to uterus<br>IA ≤ 5 cm<br>IB > 5 cm<br><br>II Tumor extends beyond the uterus, within the pelvis<br>IIA Adnexal involvement<br>IIB Involvement of other pelvic tissues<br><br>III Tumor invades abdominal tissues (not just protruding into the abdomen)<br>IIIA One site<br>IIIB > one site<br>IIIC Metastasis to pelvic and/or para-aortic lymph nodes<br><br>IV – IVA Tumor invades bladder and/or rectum<br>IVB Distant metastasis |
| *(2) Adenosarcoma* |
| I Tumor limited to uterus<br>I Tumor limited to uterus<br>IA Tumor limited to endometrium/endocervix with no myometrial invasion<br>IB Less than or equal to half myometrial invasion<br>IC More than half myometrial invasion<br><br>II Tumor extends beyond the uterus, within the pelvis<br>IIA Adnexal involvement<br>IIB Involvement of other pelvic tissues<br><br>III Tumor invades abdominal tissues (not just protruding into the abdomen)<br>IIIA One site<br>IIIB >one site<br>IIIC Metastasis to pelvic and/or para-aortic lymph nodes<br><br>IV IVA Tumor invades bladder and/or rectum<br>IVB Distant metastasis |
| *(3) Carcinosarcoma* |
| Carcinosarcomas should be staged as carcinomas of the endometrium |

It is a malpractice to cut through the tumor, because it is very important to prevent spillage. If the tumor invades the uterine wall up to serosa, all tumors must be removed «*en bloc*», without spillage. Laparoscopic removal of known sarcoma by morcellation is not permissible due to the risk of metastatic spread and spillage of tumor cells into the pelvic or abdominal cavity [24]. Additional surgery is important when uterine sarcoma (particularly LMS) is found incidentally after morcellation [25]. About 25% to 75% of patients with early ESS have recurrence in pelvis and abdominal cavity [26, 27]. And one of the causes is a non-ablastic surgery, so as using morcellation [26, 27]. Due to Park JY et al. data the overall survival of these patients was not highly decreased, because most patients with recurrent disease were salvaged successfully through additional surgery [27].

Bilateral salpingo-oophorectomy has traditionally been recommended, even in premenopausal women with ESS stage I, as this tumor is hormone-sensitive, and a much higher recurrence rate was found (50%) among patients after surgery without BSOE, compared to those (4%), whom was also performed this procedure [28]. However, recent larger reports indicate that preserving the ovaries may be possible in premenopausal women with ESS stage I, if the tumor is radically removed [29-31]. Occult ovarian metastases in women with LMS stage I have been found in 3.4–3.9% cases, and in 23% of all CS cases [21, 23]. However, preservation of ovarian tis-

sues does not increase the risk of recurrence [4], indicating that preservation of ovaries in premenopausal women may be possible, unless these tissues show macroscopic involvement [4]. There is one study showing that BSOE has a negative effect on survival of women with LMS [29].

Quality of life should be considered at every stage. Uterine leiomyosarcoma with transperitoneal spread is more difficult to be resected than ovarian cancer. This difficulty is mainly explained by a more infiltrative growth and high probability of metastatic spread. As a result, cytoreductive surgery without residual tumour is less likely to be achieved. Systemic treatment is the best option for advanced cases of uterine sarcoma with the aim to extend patients life [14].

**Lymphatic nodes involvement**. Resection of lymph nodes is controversial. In year 1966, Aaro LA. et al. studied data of 177 patients with uterine sarcomas and concluded that hematogenous spread may occur early and that lymphatic spread was relatively infrequent [32]. In year 1978, Di Saia and colleagues published articles, devoted primarily to lymph node sampling in patients with uterine sarcomas. In 28 uterine sarcomas patients with Stage 1 and 2, they have reported a 35% incidence of pelvic node involvement [33]. This study stimulated several researchers for further investigation.

Peters and associates, in year 1984 reported that 8 of 59 patients (14%) undergoing surgical exploration had nodal metastasis. Five patients had positive pelvic and para-aortic nodes, two patients had only positive pelvic nodes, and one patient had positive para-aortic and negative pelvic lymph nodes. Since year 1970, 13 patients with various uterine sarcomas have had planned nodal sampling, and four of them (31%) had positive nodes [34].

Wheelock and colleagues, in year 1985, studied data of patients with different morphological types of uterine sarcomas. Part of this study included pelvic and para-aortic node biopsies. Only two (20%) of these patients with stage 1 or 2 had nodal involvement [35].

Riopel I. et al. reported about 33% of nodal involvement in uterine sarcoma patients after surgery [36].

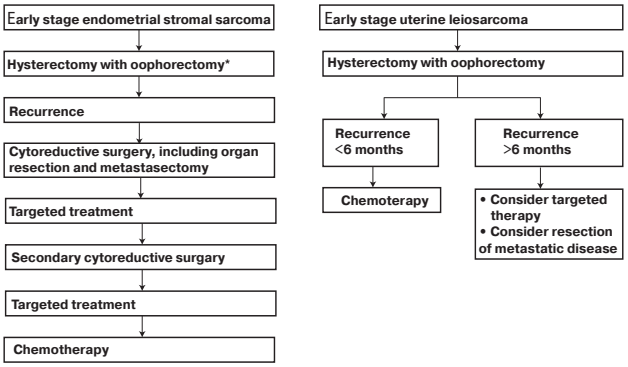
Nam JH et al. reported that incidence of lymph node involvement in patients with early stage LMS, ESS and CS is very low, showing 0 – 3.7%, 0 – 5% and 0 – 6.5%, respectively [23]. The frequency and pattern of lymph-node metastasis of carcinosarcoma is similar to that of high-risk endometrial adenocarcinoma. Therefore, lymph node dissection is not recommended for patients with early-stage LMS and ESS, but may be done in patients with CS [23].

As lymph node metastasis is most commonly associated with extrauterine disease, lymphadenectomy should be reserved for patients with clinically suspicious nodes [4, 30]. Lymph nodes dissection with microscopic disease does not seem to be clinically beneficial [23]. Restaging has been shown to be unnecessary [23, 37].

**Conservative surgery** is applicable for young fertile women who have undergone myomectomy, and there was detected a low-grade LMS. There can be allowed local (focal) excision with sample resection of margins. Conservative surgery must be done only by gynecologic oncologists, and after final morphological report these patients should be followed up very carefully in the oncological clinic. For that uterine sarcoma patients with inoperable disease, there are following options: chemo-radiation therapy or hormone therapy (only for ESS) [23].

**Surgery at relapse.** However, survival of most patients with recurrent disease is poor, surgery can be also proposed for treatment of patients with localized recurrent disease as complete removal of tumor (residual tumor = 0 cm) [23, 37]. In study from Mayo Clinic, comprising 128 patients with recurrent LMS, secondary cytoreductive surgery has prolonged survival in only a select group of patients [38]. Several other studies have also evaluated the feasibility of resection of recurrent LMS [39, 40]. According to Mayo study, there was found a survival benefit only in patients with a disease-free interval of more than six months, with either local, or distant recurrence, and optimal resection. These factors should be considered when making decision about secondary cytoreductive surgery. Recurrence in uterine sarcoma patients can appear long after primary surgery [41, 42], and is often localized (presence of isolated foci) in lungs and/or pelvis, when repeated surgery may be indicated after evaluation of patients' general condition. Palliative surgery may be indicated if the patient has bowel obstructions, bleeding or pain. However, patients with wide-spread or bulky unresectable tumors should not be prescribed high-risk debulking surgery [4].

**Treatment algorithm for LMS and ESS**




**Conclusions and future directions.** Uterine sarcoma is a rare, but sometimes deadly disease. The prognosis for patients with uterine sarcoma has not changed in the last 20 years, with overall five-year survival between 17% and 54%. Patients with ESS have a better prognosis, than those with other histological types, with a five-year survival of about 69%. Currently evidence is still lacking precise preoperative imaging for staging purposes, and so uterine sarcomas are still surgically staged [43]. Ovarian tissue can be preserved in stage I premenopausal women unless the ovaries show macroscopic involvement. Primary surgery without residual disease and spillage of tumor cells, with tumor-free resection margins is the main prognostic factor for the outcome of uterine sarcoma patients.

It is of utmost importance that uterine sarcoma surgery should be centralized to institutions that have the enough expertise in radical abdominal sarcoma surgery.

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## Хирургическое лечение больных саркомой матки. Обзор литературы

***В.С. Сухин***

Саркома матки является редким злокачественным новообразованием, происходящим из мезенхимальной ткани, которое характеризуется агрессивным клиническим течением и неблагоприятным прогнозом. Согласно морфологической классификации существуют четыре основных подтипа: лейомиосаркома, карциносаркома, эндометриальная стромальная саркома и саркома неопределенного происхождения. Хирургическое лечение является основным методом лечения больных саркомой матки, но также требуется в качестве диагностической процедуры для постановки окончательного диагноза. Абдоминальная простая гистерэктомия с двусторонней аднексэктомией является стандартным типом хирургического лечения больных саркомой матки I–II стадией. Тазовую лимфодиссекцию рекомендуется проводить больным карциносаркомой матки. Химиолучевая терапия показана пациентам с рецидивом заболеванием. Больные саркомой матки должны проходить лечение в специализированных онкологических клиниках.

***Ключевые слова:*** *саркома матки, классификация, хирургия.*

## Хірургічне лікування хворих на саркому матки. Огляд літератури

***В.С. Сухін***

Саркома матки є рідкісним злоякісним новоутворенням, що походить з мезенхімальної тканини, яке характеризується агресивним клінічним перебігом та несприятливим прогнозом. Згідно з морфологічною класифікацією існують чотири основних підтипи: лейоміосаркома, карциносаркома, ендометріальна стромальна саркома та саркома невизначеного походження. Хірургічне лікування є основним методом терапії хворих на саркому матки, але воно також потрібне в якості діагностичної процедури для встановлення остаточного діагнозу. Абдомінальна проста гістеректомія з двосторонньою аднексектомією є стандартним типом хірургічного лікування хворих на саркому матки I–II стадій. Тазову лімфодиссекцію рекомендується проводити хворим на карциносаркому матки. Хіміопроменева терапія показана пацієнткам з рецидивом захворювання. Хворі на саркому матки повинні проходити лікування в спеціалізованих онкологічних клініках.

***Ключові слова:*** *саркома матки, класифікація, хірургія.*

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