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Advancements in uterine sarcoma management: A review

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ABSTRACT

Uterine sarcomas are rare, accounting for 3–7% of uterine malignancies. This review aims to summarize advancements in diagnostics and treatment over the last decade, focusing on innovative imaging techniques, molecular diagnostics, and treatment modalities.

Recent diagnostic advancements include enhanced imaging techniques such as MRI and AI-driven algorithms, improving accuracy in differentiating between benign and malignant uterine tumors. Biomarkers like lactate dehydrogenase (LDH) and microRNAs have shown potential in preoperative identification. Treatment strategies continue to evolve, with surgical resection being the cornerstone. The role of lymphadenectomy and adnexectomy varies by histopathological subtype, emphasizing personalized approaches. Adjuvant therapies remain controversial, tailored to patient risk factors and tumor characteristics. Fertility-sparing options are viable for selected patients, though not recommended for high-grade tumors.

Significant progress in diagnostic techniques and personalized treatment approaches has improved the management of uterine sarcomas. Future guidelines from major oncology groups are expected to standardize care. Continued research is essential for refining treatment protocols and enhancing patient outcomes.

1. Introduction

Uterine sarcomas (US) are rare mesenchymal malignant tumors, accounting for about 3–7% of all uterine malignancies and less than 1 % of all malignancies of the female genital tract [1].

According to the updated World Health Organization (WHO, fifth edition) classification, uterine sarcomas are categorized histologically into uterine leiomyosarcoma (uLMS), low-grade endometrial stromal sarcoma (LGESS), high-grade endometrial stromal sarcoma (HGESS), undifferentiated uterine sarcoma (UUS), adenosarcoma, rhabdomyosarcoma, and perivascular epithelioid cell tumor (PEComa). Uterine leiomyosarcoma (uLMS) is the most prevalent subtype, while adenosarcoma, rhabdomyosarcoma, and PEComa are exceedingly rare. Carcinosarcomas (malignant mixed Müllerian tumors, MMMTs), previously classified as sarcomas, are now recognized as dedifferentiated carcinomas comprising both epithelial and stromal components. Consequently, they are staged and treated as high-grade endometrial cancers [2].

The clinical presentation of uterine sarcomas (US) is non-specific, often manifesting as abnormal vaginal bleeding, uterine enlargement, palpable pelvic mass, and pelvic pain. Occasionally, initial symptoms may include signs of tumor rupture (hemoperitoneum), extrauterine extension, or metastases. Distant metastases can occur at an early stage, and distant relapse is common following radical surgery.

The 2009 FIGO staging system for uterine sarcomas (Table 1) includes more detailed subcategories to better define the extent of the disease. This includes differentiating stages based on tumor size, location, and metastasis. For instance, Stage I is now divided into IA (tumor $\leq$5 cm) and IB (tumor >5 cm) based on tumor size. Other stages detail the extent of spread within and beyond the pelvis, including lymph node involvement and distant metastases (Stages III and IV) [3].

The findings and innovations of the last 10 years in the field of

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Table 1
FIGO Surgical staging of uterine sarcoma: Leiomyosarcoma and endometrial stromal sarcoma.

Stage	Description
I	Limited to the uterus
a. IA	Tumor ≤5 cm in largest dimension
a. IB	Tumor >5 cm
II	Extending beyond the uterus but within the pelvis
a. IIA	Involving the adnexa
a. IIB	Involving other pelvic tissues
III	Infiltrating abdominal tissues
a. IIIA	In one site
a. IIIB	>1 site
a. IIIC	Pelvic and/or para-aortic lymph node metastasis
IVA	Invading bladder or rectum
IVB	Distant metastases

diagnostics and treatment of uterine sarcomas are presented in the article.

2. Initial diagnostic techniques

Most of the times, the first imaging technique used is the ultrasound. It can be challenging to differentiate between benign and malign tumors of the uterus, for example between fibroids and uLMS. Some key features are gathered in Table 2 [4].

Uterine leiomyomas and sarcomas often show an overlap of clinical and imaging features. This overlap makes differentiation challenging. The application of a diagnostic algorithm can help radiologists to standardize their approach to a complex myometrial mass and to easily identify suspicious MRI features favoring malignancy.

An MRI diagnostic algorithm has been proposed by Rosa et al. [5]. The proposed algorithm predicts the malignancy of uterine lesions by assigning a Likert score ranging from 1 (benign lesion) to 5 (high suspicious malignant lesion (very high risk of uterine sarcoma)), or M (malignant lesion but not specific for Uterine sarcoma). It primarily relies on Diffusion-weighted imaging (DWI), T2, T1 signals, and contrast enhancement, while additional features like lesion margins and growth patterns help clarify uncertain scores. Independent evaluation of malignancy indicators such as ascites, implants, and lymphadenomegalies is also incorporated. This algorithm enhances diagnostic accuracy, especially benefiting less experienced radiologists.

In 2020 Abdel Wahab et al. reported of an algorithm that had been generated to differentiate benign atypical leiomyoma from malignant uterine sarcoma using MRI with four criteria [6]: enlarged lymph node or peritoneal implants, region of low T2 signal, intensity diffusion weighted imaging signal, apparent diffusion coefficient value. The algorithm classifies uterine mass in three categories: highly suspicious, probably benign, and certainly benign.

Inclusion of AI (artificial intelligence)-driven diagnostic algorithms has also been studied in the last years and has shown some potential. In a study by Toyohara et al., AI-driven diagnostic algorithms significantly enhanced the accuracy of identifying uterine sarcomas. Deep neural network (DNN) models showed 90.3 % accuracy, outperforming radiologists without AI support (88.3 %) and demonstrating higher sensitivity (89.8 % vs. 71.0 %). These findings suggest AI's potential to surpass human interpretation in diagnosing rare uterine tumors, improving diagnostic reliability [7,8]. The ADMIRAL study explored the use of radiomics and machine learning with ultrasonography to differentiate between benign and malignant uterine myometrial tumors, such as myomas and sarcomas. Conducted retrospectively with 70 patients, the study extracted features from ultrasound images and trained machine learning classifiers to predict malignancy. The best-performing model achieved an accuracy of 85 %, sensitivity of 80 %, and specificity of 87 %. This approach demonstrated the potential of radiomics as a decision-support tool, particularly in improving diagnostic confidence for conditions where traditional imaging often fails to provide clear differentiation [9]. Although AI-driven diagnostic algorithms show potential, they also face some challenges. AI models often rely on datasets that may not be representative of diverse populations, leading to biases in outcomes and reduced applicability to underrepresented groups. There is also concern about "black box" decision-making, where the inner workings of AI models are opaque, making it difficult for clinicians to understand how or why specific predictions are made. This lack of transparency can undermine trust and complicate accountability when errors occur. Additionally, the use of sensitive medical data raises serious concerns about privacy and security, as health records are highly vulnerable to breaches and misuse. These challenges necessitate cautious implementation and stringent safeguards to ensure AI enhances healthcare responsibly [10,11].

With advances in molecular biology, some differentiating techniques are being developed to separate malignant and benign tumors.

Table 2
Features of fibroids and leiomyosarcomas.

Feature	Fibroid	Leiomyosarcoma
Number	Multiple	Solitary
Shape	Round	Oval/lobulated
Echogenicity	Calcifications	Inhomogenous
Fan-shaped shadowing	Frequent	Rare
Irregular cystic areas central necrosis	Rare	Frequent
Vasculature	Circumferential flow	Irregular vessels Score 3–4[a]
Size	Variable	≥8 cm Fast-growing

[a] According to MUSA (Morphological Uterus Sonographic Assessment) criteria.

2.1. Lactate dehydrogenase (LDH)

Lactate dehydrogenase is an enzyme that is present in almost all body tissues. Many conditions that have an elevated cell turnover (including cancer) can cause increased LDH levels in the blood [12].

Protein expression levels of LDHA (a subunit of LDHL gene) and gene LDHD were determined in tissue samples with immunohistochemistry in a study by Song et al. Immunohistochemistry on postoperative pathology revealed significantly higher positive rates of LDHA and LDHD in uterine sarcomas compared to uterine leiomyomas [13]. A Chinese study identified serum LDH levels ≥185 U/L as an independent predictor of uLMS [14]. There are different isozymes of LDH: LDH1 through LDH5, each having differential expression in different tissues. LDH1 is predominantly present in the myocardium, LDH3 is the major isozyme in the lungs, LDH5 can be found in muscle tissue. One can measure overall LDH in the serum or different isozymes [12]. Goto et al. demonstrated that elevated LDH and LDH3 levels, combined with contrast-enhanced magnetic resonance imaging (CE-MRI), provided high sensitivity and specificity for LMS diagnosis [15]. Mollo et al. reported a strong association between a high LDH5/LDH1 ratio and the development of uterine sarcomas [16]. In 2019, an Italian research team introduced the Uterine Mass Magna Graecia (U.M.G.) risk index, which integrates LDH3 and LDH1 isoenzymes in an inverse algebraic relationship, showing that uterine sarcomas are likely when the U.M.G. index is ≥ 29 [17]. Lauren et al. validated the U.M.G. risk index in 179 patients with uterine fibroids, achieving 91.1 % specificity and noting a higher false-positivity rate among obese women [18]. Furthermore, combining LDH with MRI [15] and positron-emission tomography--computed tomography (PET-CT) [19,20] can enhance the sensitivity and specificity of preoperative uterine sarcoma diagnosis.

2.2. Neutrophil/lymphocyte ratio (NLR)

The inflammatory response characterized by an elevated neutrophil count and reduced lymphocyte count within the tumor

microenvironment can aid in differentiating uterine sarcomas, with threshold values of 2.12, 2.1, and 2.8 suggested by multiple studies [14,21,22].

2.3. Growth differentiation Factor-15 (GDF-15)

GDF-15 has emerged as a potential biomarker for preoperative identification of malignant pelvic diseases [23]. Japanese researchers identified three biomarkers—GDF15, granulocyte precursor protein, and bone bridge protein—that could differentiate uterine sarcomas from uterine fibroids using data from the Gene Expression Omnibus and The Cancer Genome Atlas databases [24].

2.4. CRP and D-dimer

Elevated levels of C-reactive protein (CRP) and D-dimer were observed in patients with LMS compared to those with uterine leiomyomas [25]. Combining preoperative serum LDH, D-dimer, and CRP levels can aid in distinguishing LMS from uterine leiomyomas, particularly in cases of degenerative or atypical fibroids [26].

2.5. MicroRNA

Seven microRNAs (miRNAs) have been identified as potential markers for the preoperative identification of uterine sarcomas [24]. When miR-1246 and miR-191-5p were combined, the area under the curve (AUC) for distinguishing uterine sarcomas from fibroids reached 0.83, and for LMS and uterine leiomyomas, the AUC was 0.97. Yokoi et al. utilized a microarray to sequence serum miRNAs from patients with benign and malignant tumors, identifying seven miRNAs with significantly lower expression levels in uterine LMS. They developed an optimal diagnostic model using miR-191-5p and miR-1246, which exhibited superior predictive performance for uterine LMS compared to the conventional biomarker LDH, with AUCs of 0.83 and 0.62, respectively [24]. This miRNA model represents a promising preoperative biomarker for differentiating between uterine LMS and leiomyomas.

All these results will need future studies with a larger sample size and also prospective analyses before we can use them in routine practice.

3. Treatment approaches

3.1. Surgical treatment of uterine sarcoma

Uterine sarcomas, including leiomyosarcoma (uLMS), endometrial stromal sarcoma (ESS), and undifferentiated uterine sarcoma (UUS), require individualized surgical approaches depending on the tumor type and stage. Surgical management remains the cornerstone of treatment for localized disease, with the goal of complete tumor resection. Treatment approaches for different uterine sarcoma subtypes are summarised in Table 3.

3.1.1. Leiomyosarcoma (LMS)

Surgical treatment for early-stage LMS typically involves total hysterectomy with bilateral salpingo-oophorectomy (TH-BSO) in postmenopausal women. This approach aims to remove the primary tumor and prevent potential ovarian metastasis. Ovarian preservation (OP) is not associated with worse overall survival or a high recurrence rate. It may be considered for pre-menopause women with early-stage disease (I–II) [27] Lymphadenectomy is generally not indicated unless lymph nodes are clinically suspicious, as LMS has a low propensity for lymphatic spread.

In advanced stages, surgical debulking is pursued to achieve maximum tumor reduction. Complete cytoreduction, when feasible, can improve survival outcomes. However, the extensive spread often limits the possibility of achieving clear margins. Multidisciplinary evaluation (gynaecologic oncology surgeons, general and vascular surgeons, medical oncologists, radiation oncologists, pathologists, radiologists and care managers) is crucial for optimal management.

3.1.2. Endometrial stromal sarcoma (ESS)

Low-Grade ESS (LG-ESS): For LG-ESS, surgical treatment involves TH-BSO, due to the tumor's hormone-sensitive nature. Complete surgical excision is vital, as residual disease can lead to recurrence. Lymphadenectomy is not routinely performed unless there is evidence of lymph node involvement.

High-Grade ESS (HG-ESS): Currently, the rarity of the disease leads to many controversies regarding the most preferable treatment options. Consequently, treatment options should be presented as recommendations rather than definitive guidelines. Total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAHBSO) is considered the standard surgical procedure. For advanced stages, optimal cytoreduction is advised. Given the higher metastatic potential, thorough exploration for extra-uterine disease is essential. Adjuvant therapy, including radiotherapy or chemotherapy, is often considered postoperatively.

3.1.3. Undifferentiated uterine sarcoma (UUS)

Early-Stage UUS (Stage I-II): Surgical management for early-stage UUS involves TH-BSO with the goal of achieving negative margins. Due to its aggressive nature, even early-stage disease is approached with caution, considering adjuvant therapy.

Advanced-Stage UUS (Stage III-IV): For advanced UUS, aggressive surgical debulking is indicated, though achieving complete resection is challenging. Multimodal treatment involving surgery, chemotherapy, and radiotherapy is often necessary due to the high recurrence rates and poor prognosis associated with UUS.

3.1.4. Is adnexectomy mandatory at the time of hysterectomy for uterine sarcomas?

Most studies indicate that adnexectomy does not significantly affect the recurrence rate, disease-free survival or overall survival in treating FIGO stage I uterine sarcomas. Thus, while bilateral adnexectomy is

Table 3
Treatment approaches for different uterine sarcoma subtypes.

Subtype	Early-Stage Treatment	Advanced-Stage Treatment	Adjuvant Therapy	Special Considerations
Leiomyosarcoma (LMS)	Total hysterectomy (TH) ± ovarian preservation	Surgical debulking for tumor reduction	Chemotherapy for high-risk cases	Ovarian preservation possible in premenopausal women; lymphadenectomy generally not indicated.
Low-Grade Endometrial Stromal Sarcoma (LG-ESS)	Total hysterectomy with bilateral salpingo-oophorectomy (TH-BSO)	Complete surgical excision	Hormonal therapy may reduce recurrence	Hormone-sensitive tumor; lymphadenectomy not routinely required.
High-Grade Endometrial Stromal Sarcoma (HG-ESS)	Total hysterectomy with bilateral salpingo-oophorectomy (TH-BSO)	Aggressive surgical cytoreduction	Chemotherapy ± radiotherapy	High metastatic potential; some studies report that lymphadenectomy may improve survival.
Undifferentiated Uterine Sarcoma (UUS)	Total hysterectomy with bilateral salpingo-oophorectomy (TH-BSO)	Aggressive surgical cytoreduction	Chemotherapy ± radiotherapy	Very poor prognosis; multimodal treatment often required.
Adenosarcoma	Fertility-preserving surgery possible in select cases	Total hysterectomy ± salpingo-oophorectomy	Rarely used	Minimal metastatic potential; requires close follow-up if fertility preservation is attempted.

universally recommended for menopausal patients, ovarian tissue preservation may be considered for premenopausal women. Nonetheless, there are not enough cases in the literature to draw definitive conclusions and recommendations for this procedure [28].

Nasioudis et al. analyzed 800 women with uLMS, of whom 29.6 % underwent TAH with OP, and concluded that women with stage I uLMS and OP had better 5-year OS and cancer-specific survival compared to those who underwent oophorectomy [27].

3.1.5. Place of lymphadenectomy in uterine sarcomas

Li et al. conducted a systematic review and meta analysis with thirty-two retrospective cohort studies that included 26,693 patients in total. They found that patients with uLMS or LG-ESS had no survival benefits from lymphadenectomy. However, patients with HG-ESS did show survival benefits from lymphadenectomy [29].

Nasioudis et al. analyzed data from patients affected by each histotype individually and found that lymphadenectomy did not improve survival for patients with LMS or LG-ESS but improved survival for those with HG-ESS [30]. Of the 3517 patients with LMS, 1250 (35.5 %) underwent lymphadenectomy and only 3.4 % had positive lymph nodes. Contrary to expectations, patients without lymphadenectomy had a higher survival rate than the other group [death 37.1 % (842/2267) vs 46 % (575/1250), respectively; $p < 0.001$]. Of the 1168 patients with LG-ESS, 464 (39.7 %) underwent lymphadenectomy and 4.5 % had lymph node metastases. For this histotype, there was no significant difference in survival between women who underwent lymphadenectomy and women who did not undergo lymphadenectomy [death 5.8 % (41/704) vs 8.1 % (38/464), respectively; $p = 0.19$]. Four hundred and six patients had HG-ESS and 280 (68.9 %) underwent lymphadenectomy. Prognosis was better in the lymphadenectomy group, although 7.9 % of these patients had nodal metastases [death 54.7 % (69/126) vs 46.4 % (130/280), respectively; $p = 0.018$]. Finally, of the 1321 patients with UAS, 495 (37.4 %) underwent lymphadenectomy and 2.3 % had positive lymph nodes. Overall survival did not differ between the groups [death 24.6 % (122/495) vs 24.9 % (206/826), respectively; $p = 0.99$].

Seagle et al. found that, compared with women with negative lymphadenectomy, women with HG-ESS and no surgical node evaluation had significantly decreased survival ($p = 0.001$); 5-year survival was 43.3 % in women with negative lymph nodes, 19.6 % in women with positive lymph nodes, and 27 % if the lymph nodes were not evaluated [31].

The meta-analyses referenced, including those by Li et al. and Nasioudis et al., exhibit significant heterogeneity due to differences in patient populations, staging definitions, and surgical practices. For instance, the studies included varied in the proportion of high-grade endometrial stromal sarcoma (HG-ESS) cases, the definition of lymph node involvement, and follow-up durations, which may have influenced survival outcomes. Due to this heterogeneity, the findings must be interpreted with caution. While lymphadenectomy appears to improve survival in HG-ESS patients in some studies, others report conflicting results [32,33]. These variations underline the need for individualized treatment approaches.artifici In conclusion, systematic lymphadenectomy is not recommended unless there is a clinical or radiological suspicion of nodal involvement [29].

3.2. Adjuvant therapy

The role of adjuvant chemotherapy or local radiotherapy is still controversial. The rarity of uterine sarcomas poses a challenge for conducting large-scale, long-term prospective studies. Many recommendations are based on retrospective data or small cohort studies, which limit their generalizability. Adjuvant therapy should be offered on the basis of histopathological subtype and stage. In patients with uLMS, adjuvant chemotherapy can be suggested in selected cases with high-risk factors (such as morcellation, tumour size greater than 5 cm, high mitotic index), after accurate discussion with the patient; on the other hand, in patients with early LGESS, observation is the recommended management after surgery; however, it should be noted that some retrospective studies [34] reported that adjuvant hormonal therapy with progestins may determine recurrence risk reduction in these latter patients. Adjuvant treatment for stage I patients is not recommended for the less common histologies HGESS and UUS, while patients with FIGO stage II and III should be offered systemic adjuvant chemotherapy [35].

In patients with metastatic or recurrent disease, systemic chemotherapy represents the standard approach for the treatment of uLMS, HGESS, UUS; first-line treatment is based on anthracyclines either administered as single agents or in combination with ifosfamide or dacarbazine. Another effective combination is represented by gemcitabine-docetaxel, while trabectedin, pazopanib, dacarbazine and eribulin might also be active. Particularly in uLMS, the ER/PR expression rate in LMS is lower than LGESS, but even uLMS with a positive receptor expression (ER+/PR+) may be sensitive to hormonal therapy [35].

The ESGO/EURACAN/GCIG guidelines also recommend a nuanced approach to adjuvant therapies for uterine sarcomas, given the rarity and heterogeneity of these tumors. Radiotherapy is generally not standard practice but may be considered to reduce local recurrence in patients with HG-ESS or UUS, particularly when there are high-risk features, such as positive surgical margins or cervical involvement. Adjuvant chemotherapy is also not routinely advised but can be considered in selected high-risk cases, such as those involving advanced-stage disease or morcellation, after shared decision-making. The lack of robust evidence supporting these therapies highlights the importance of tailoring treatment to individual patient profiles and enrolling patients in clinical trials to refine management strategies. Radiotherapy may also play a role in symptom control for recurrent or metastatic disease when quality of life is impacted [36].

3.3. Fertility sparing – does it have a place in uterine sarcoma treatment?

Surgery remains the standard of care for uterine sarcomas, emphasizing complete resection of the disease without fragmentation and achieving negative surgical margins. Fertility-sparing management, while theoretically possible, is associated with significant risks and should only be considered in highly selected cases under stringent follow-up protocols. This approach is generally not recommended for high-grade endometrial stromal sarcoma (HG-ESS) or other aggressive subtypes due to their high recurrence rates and poor prognoses. Patients with adenocarcinoma may also have a low chance of childbearing [37]. For young nulliparous women with low-grade tumors, conservative management may be an option; however, this decision must be made after thorough counseling about the risks of recurrence and potential compromises in oncologic outcomes. Even in these cases, definitive surgical management is often advised upon the completion of childbearing. Further research is needed to determine the long-term safety and efficacy of fertility-sparing approaches in uterine sarcomas, particularly in light of their aggressive nature and limited evidence base [38].

3.4. Unexpected malignant diseases

If an undiagnosed uterine malignancy is intra-abdominally morcellated, there is a risk of intraperitoneal dissemination of the disease [39]. Therefore, the European Society of Gynecological Oncology recommended in 2016 to avoid morcellation if there is any suspicion of sarcoma and to use endobag containers for morcellation of surgically removed uterine myomas [40]. In the United States, the FDA recommends performing laparoscopic power morcellation for myomectomy or hysterectomy only with a tissue containment system legally marketed in the country [41].

Devassy et al. conducted a retrospective analysis of 239 cases of laparoscopic in-bag morcellation procedures, finding that the majority

of histological examinations showed fibroids, but some also revealed adenomyosis, endometriosis, endometrial hyperplasia, or severe dysplasia of the cervix. Malignancy was diagnosed in three cases (two endometrial carcinomas and one sarcoma). In these cases, due to suspicious intraoperative findings, a frozen section was performed, leading to laparoscopic radical hysterectomy during the same session. Disease-free survival was documented in all cases over three years [42].

A review of 11 studies, including 1160 patients, used various endobag containment systems for morcellation, finding that using endobags did not significantly increase operative time or complications Only half of the studies comparing uncontained and contained morcellation found a significant increase of total operative time. Finally, the number of complications was not increased when endobag was used [43].

Uncontained morcellation of unexpected uterine sarcomas can modify the natural history of the disease causing disseminated sarcomatosis, thus leading to worse oncologic survival outcomes compared to women whose lesions are extracted intact [44]. Pedra Nobre et al. reported of significantly higher risk of recurrence and a nearly 4-fold increase in peritoneal recurrence [45]. In addition to disseminated peritoneal metastases, the literature has documented cases of port-site metastases not only from overt malignancies like leiomyosarcoma but also from smooth muscle tumors of uncertain malignant potential (STUMP) [46,47]. These reports underscore the need for extreme caution when considering morcellation, even in cases initially presumed benign. The unpredictable behavior of STUMP, which can occasionally manifest with late recurrence or metastatic spread, further complicates the risk assessment. There is no clear evidence or guideline about the proper management of an uncontained morcellated unexpected malignancy after an endoscopic procedure. Surgical reexploration after morcellation is an option to ascertain the potential spread of the disease in the abdominal cavity; however, no definitive data are available to support this procedure, and no conclusive recommendation can be suggested [48].

4. New guidelines

In 2023, the European Society of Gynaecological Oncology (ESGO), EURACAN, and the Gynecologic Cancer InterGroup (GCIG) initiated a joint project to develop comprehensive management guidelines for patients with uterine sarcomas, covering low-grade endometrial stromal sarcoma, uterine leiomyosarcoma, high-grade endometrial undifferentiated stromal sarcoma, adenosarcoma of the uterus, and other rare types of uterine sarcomas. The 2024 ESGO-EURACAN-GCIG guidelines for uterine sarcoma management reflect significant advancements in diagnostic and therapeutic approaches over the past decade. They emphasize the integration of molecular diagnostics, such as genetic testing and RNA sequencing, to refine tumor classification and guide personalized therapies. New chemotherapy regimens, including doxorubicin with trabectedin, and the incorporation of targeted and endocrine therapies are highlighted for their role in specific subtypes. The guidelines advocate against morcellation due to its association with worse prognoses and outline conditions under which fertility-preserving surgeries may be considered for low-grade sarcomas. Enhanced imaging protocols, including MRI and PET/CT, provide precise diagnostic and staging tools, while tailored management pathways are delineated for histological subtypes like leiomyosarcomas, high- and low-grade endometrial stromal sarcomas, and rare entities such as PEComa and NTRK-rearranged sarcomas. The guidelines stress the importance of multidisciplinary care in specialized centers, enrolling patients in clinical trials and fostering international collaboration to address research gaps in this rare but aggressive cancer [36].

5. Conclusion

Uterine sarcomas, though rare, present significant diagnostic and therapeutic challenges. Recent advancements in diagnostic techniques, including imaging algorithms and molecular biology have potential in the differentiation between benign and malignant uterine tumors. The integration of AI-driven algorithms shows promise in enhancing diagnostic accuracy. Surgical management remains the cornerstone of treatment, with strategies tailored to the tumor type and stage. The role of lymphadenectomy and adnexectomy varies, emphasizing the need for individualized approaches. Adjuvant therapies, while controversial, are considered based on specific histopathological subtypes and patient risk factors. Fertility-sparing options may be viable for selected patients, though caution is warranted. Continued research and clinical trials are essential to further refine treatment protocols and improve patient outcomes.

CRediT authorship contribution statement

Vojka Lebar: Investigation, Writing – original draft, Writing – review & editing. **Aleksandar Čelebić:** Writing – review & editing. **Jean Calleja-Agius:** Writing – review & editing. **Marina Jakimovska Stefanovska:** Writing – review & editing. **Kristina Drusany Staric:** Conceptualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

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