

(REVIEW ARTICLE)



The impact and correlation of lymphadenectomy with outcomes in patients with uterine sarcoma: A systematic review

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Abstract

Background: Sarcomas are an uncommon type of smooth muscle tumors in the uterus. The most popular form of treatment for uterine sarcomas is surgery. There is disagreement, nonetheless, over the best course of action for initial surgery. The aim of this systematic review was to examine the potential association between patient outcomes and the effects of LAD in individuals diagnosed with uterine sarcoma.

Method: We conducted a comprehensive search of the PubMed database to identify publications assessing the impact of LAD on patients with uterine sarcoma that were published between 2009 and 2024. Based on the references in the studies that we included, we also conducted a search of the PubMed database. To find more relevant studies, the bibliographies of each pertinent paper were thoroughly reviewed. This review only includes studies that were published in English.

Results: We included 7 papers in this systematic review, totaling 7896 patients. Four publications examined ESS, four studies examined LMS, two articles examined adenosarcoma, one study examined carcinosarcoma, and one study examined rhabdomyosarcoma. For individuals with low-grade ESS or adenosarcoma, LAD was not linked to a better prognosis. The survival rate was lower for patients with leiomyosarcoma who had LAD. Those who had LAD and had high-grade undifferentiated ESS fared better. LAD did not significantly correlate with RFS or OS in uterine sarcoma patients.

Conclusion: Resection of lymph nodes or LAD has minimal potential benefit in terms of prognosis and clinical value.

Keywords: Lymphadenectomy; Uterine sarcoma; Outcome; Survival

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1. Introduction

Mesenchymal tumors known as uterine sarcomas make up about 3% of all uterine cancers (D'Angelo et al., 2010). According to D'Angelo et al. (2010) and Amant et al. (2009), leiomyosarcoma (LMS) is the most prevalent histotype, followed by adenocarcinoma, low-grade endometrial stromal sarcoma (ESS), and high-grade undifferentiated ESS. The nature of carcinosarcomas has been the subject of intense research in recent years. Despite being extremely aggressive tumors with a dismal prognosis, carcinosarcomas have lately been classified as high-grade endometrial cancer (Kanthan et al., 2011). The general characteristics of ESSs include a good prognosis and slow behavior. According to reports, 80 to 100% of ESS patients reached 5 years overall survival (OS) (Gadducci et al., 2008). Furthermore, the majority of patients receive an early diagnosis of the disease, and at that time, the majority of the disease was limited to the uterus (Ashraf et al., 2006; Beck et al., 2012), which is the reason behind its poor prognosis and high survival rate. More than one-third of patients experience recurrent disease, despite the fact that late recurrence is common even in individuals with early stage disease (Malouf et al., 2010; Beck et al., 2012).

The excision of the uterus and cervix, bilateral salpingo-oophorectomy, and lymph node assessment are standard procedures for staging uterine cancers. By accurately staging cases and customizing adjuvant therapy for patients with advanced stages of illness, lymph node evaluation may be able to give both prognostic and therapeutic value. However, lymphadenectomy (LAD) may be linked to more blood loss, a lengthier surgical procedure, a higher risk of lymphedema, and an increased risk of intraoperative damage (Tse et al., 2011). There is no clear consensus on the role of LAD in this patient population, as most of the evidence regarding LAD and uterine sarcoma comes from small retrospective studies (Leitao et al., 2003; Tasci et al., 2015). There was no survival advantage for LAD, according to a recent meta-analysis involving 14 studies and 4867 patients (Si et al., 2017). While the behavior of uterine sarcomas differs according to the histologic subtype, in the current study we have chosen to include all histotypes because it is rarely possible to obtain a precise diagnosis during surgery. The aim of this systematic analysis was to examine the potential association between patient outcomes and the effects of LAD in individuals diagnosed with uterine sarcoma.

2. Methods

We conducted a comprehensive search of the PubMed database to identify publications assessing the impact of LAD on patients with uterine sarcoma that were published between 2009 and 2024. Based on the references in the studies that we included in our survey, we also conducted a search of the PubMed database. The subsequent search phrases were employed: 'uterine sarcoma, uterine leiomyosarcoma, LMS, endometrial stromal sarcoma, ESS, high-grade endometrial sarcoma, undifferentiated endometrial sarcoma, undifferentiated uterine sarcomas, Lymphadenectomy, lymph node excision, lymph node resection, lymph node dissection, LAD. To find more relevant studies, the bibliographies of each pertinent paper were thoroughly reviewed. Only information from the most recent study or the largest published report was used where sources of study population recruitment overlapped across multiple studies. This review only includes studies that were published in English.

All of the following requirements had to be met by the studies that we included in our meta-analysis: to examine the relationship between LAD and the prognosis of uterine sarcomas; to involve at least 50 cases; to use either prospective or retrospective data; and to be published in English. The following studies met the main exclusion criteria: those that were not published as complete reports; and those that overlapped or were reprinted.

Following our first database search, which yielded 121 publications, 12 duplicates were eliminated, 109 full text articles had their titles and abstracts evaluated, 31 full text articles had their eligibility evaluated, and 7 of these were included in the review (Fig 1).

Reviewers separately retrieved the following data characteristics for each eligible study based on the inclusion criteria: citation, country, year of publication, tumor type, total number of patients studied, and key conclusions of the study. The investigators discussed and resolved any differences until they came to a consensus. In the event that they couldn't agree, the supervisor was consulted to settle the conflict.

3. Results and discussion

In this systematic review we included 7 articles, with a total of 7896 patients, Yoon et al, (2014) study had the longest duration (22 years), while Nasioudis et al., (2021) study had the shortest duration (11 years). ESS was studied in 4 articles (Zhou et al, 2015; Yoon et al, 2014; Barney et al, 2009; Nasioudis et al., 2021), LMS in 4 studies (Nasioudis et al., 2021; Hoellen et al., 2014; Nesrine et al., 2019; Tasci et al., 2015), adenocarcinoma in 2 articles (Nasioudis et al., 2021;

Hoellen et al., 2014), carcinosarcoma in one study (Hoellen et al., 2014), and Rhabdomyosarcoma in one study (Hoellen et al., 2014) (Table 1).

In a research published in 2021, Nasioudis et al. found no evidence linking LAD to improved survival in patients with low-grade ESS or adenosarcoma. The survival rate was lower for LMS patients who had LAD. After undergoing LAD, patients with high-grade undifferentiated ESS fared well. In their study, Nesrine et al. (2019) sought to examine the prognostic factors and the effect of LAD in OS and disease-free survival (DFS). They concluded that LAD had a statistically significant impact on DFS but not OS, and they recommended against using LAD on a regular basis. In contrast to prior studies that frequently included a heterogeneous collection of all sarcoma subtypes, their analysis only includes LMS uterine, despite certain constraints including the limited population size and retrospective analyses.

There was no significant correlation between LAD and either OS (Barney et al., 2009; Tasci et al., 2015) or recurrence-free survival (RFS) (Yoon et al., 2014) (Table 2). Due to its high rate of lymph node metastases, Tasci et al. (2015) suggested LAD for LMS. According to a research by Nasioudis et al. (2021), patients with high-grade undifferentiated ESS who received LAD had a better prognosis.

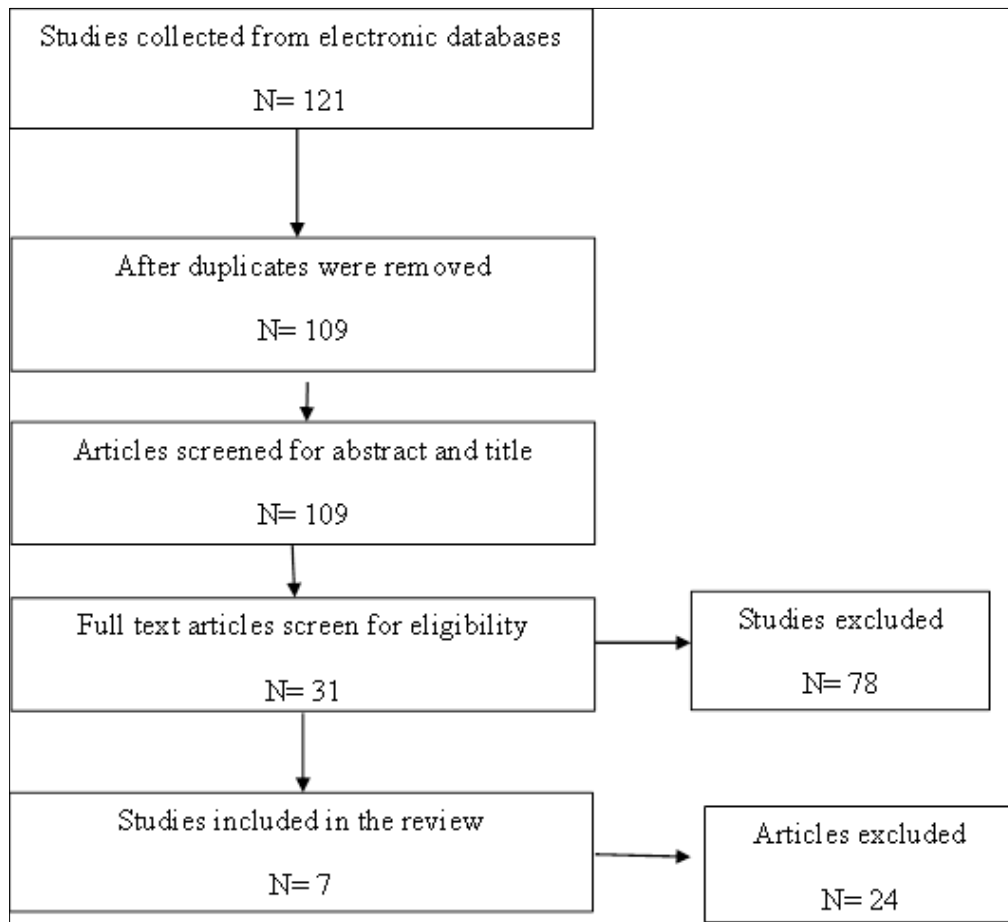


Figure 1 PRISMA consort chart of selection process

Table 1 Characteristics of included studies

Citation	Study duration	Country	Number of patients	Type of cancer	Patients had No LAD	Patients had LAD
Nasioudis et al., 2021	11 years	USA	6412	Adenosarcoma, LMS, ESS	2820	3592
Zhou et al, 2015	22 years	-	114	ESS	43	71
Yoon et al, 2014	22 years	Korea	114	ESS	69	45
Barney et al, 2009	19 years	SEER	1010	ESS	833	177
Hoellen et al., 2014	12 years	Luebeck	52	Rhabdomyosarcoma, adenocarcinoma, carcinosarcoma, LMS	24	28
Nesrine et al., 2019	14 years	Tunisia	99	LMS	50	49
Tasci et al., 2015	16 years	Turkey	95	LMS	59	36

Table 2 Main findings of included studies

Citation	Main findings
Nasioudis et al., 2021	Patients with LMS had a lymph node metastasis rate of 3.4%; patients with adenocarcinoma had a rate of 2.3%; patients with low-grade undifferentiated ESS had a rate of 4.5%; and patients with high-grade undifferentiated ESS had a rate of 7.9%. There was no correlation between LAD and improved survival for patients with low-grade ESS or adenocarcinoma. The survival rate was lower for LMS patients who had LAD. Those who had LAD and had high-grade undifferentiated ESS fared better.
Zhou et al, 2015	The primary course of treatment for all patients was hysterectomy; 17.5% of patients underwent ovarian preservation; and 62.3% of patients underwent laparoscopic aspiration. Eleven patients underwent endocrine therapy, 36 patients underwent radiotherapy, and 56 patients underwent chemotherapy. The follow-up period was 40 months on average. Nine of the 71 individuals who had LAD showed positive lymph nodes. DFS was not significantly affected by LAD, lymph node status, ovarian preservation, chemotherapy, radiation, or endocrine therapy.
Yoon et al, 2014	Forty-five patients had a LAD with para-aortic or pelvic lymph nodes included. Three patients were found to have lymphadenopathy and nodal metastases, but they did not exhibit any other extra-uterine illness symptoms. There were 33 relapses and ten deaths from the illness. For the overall group, the 5-year OS rates were 92.6%, and the 5-year RFS rates were 71.8%. It was discovered that ovarian preservation was a reliable indicator of lower RFS.
Barney et al., 2009	There was no increase in survival rate when LAD was added to a total abdominal hysterectomy and bilateral salpingo-oophorectomy.
Hoellen et al., 2014	Of the 52 cases, 48 were treated surgically. Of those, 58% underwent LAD procedures. Regardless of the existence or lack of swollen lymph nodes, surgeons typically performed pelvic-alone or paraaortic plus pelvic LAD. Patients who had LAD had higher survival rates. This finding could point to a possible application of systematic LAD in uterine sarcoma surgical treatment.
Nesrine et al., 2019	Eighteen of the thirty-one patients treated for uterine LMSs underwent pelvic LAD. Two of the eighteen patients with clinical stages IA and IIIB had lymphatic metastases. There was no discernible variation in the distribution of several characteristics between the patient group who underwent LAD surgery and the non-surgical group. The DFS was 50% and the 5 years OS was 61%. On univariate analysis, it was discovered that the clinical stage, the existence of lymphovascular space invasion, and LAD were significant factors for DFS. The only variables that were found to be predictive of OS were age and menopausal status. This investigation shows that, in contrast to OS, DFS is statistically significantly impacted by LAD.
Tasci et al., 2015	For the patient groups with and without LAD, the median DFS was 19 months for both, and the median OS was 29 and 26 months, respectively. The groups' 5-year OS was 45.4% vs 43.8% and 5-year DFS was

35.9% vs 26.8%. Regarding DFS or OS, multivariate analysis failed to identify a single independent prognostic factor. Patients with extrauterine disease had a higher rate of lymph node metastases, which suggested the significance of LND in LMS. The benefit of LAD for survival, however, could not be demonstrated.

4. Discussion

Three percent of uterine neoplasms are uterine sarcomas, which are uncommon malignant gynecological tumors with an aggressive potency and a terrible prognosis (D'Angelo et al., 2010; Koh et al., 2015). According to Koivisto et al. (2008), women over 40 are usually affected with uterine sarcoma, with a median age of 52 at diagnosis. According to El Husseiny et al. (2002), patients commonly arrive with atypical stomach pain, uterine hemorrhage, and pelvic mass. Surgery, involving a total abdominal hysterectomy with or without bilateral salpingo-oophorectomy, is the best course of treatment for uterine sarcomas. The use of LAD in the staging and treatment of uterine sarcomas is still debatable. Without offering specific guidelines, the Comprehensive National Cancer Network also discusses customized surgical resection, which includes LAD, based on clinical circumstances and intraoperative findings. However, a group study in oncology and gynecology suggested LAD in cases of carcinosarcoma (Major et al., 1993). Lymph node dissection also demonstrated a therapeutic benefit for ESSs (Riipel et al., 2005; Reich et al., 2005). Although several writers examined the advantages and effects of LAD of LMS, their conclusions were debatable.

Three publications in our review (Zhou et al., 2015; Yoon et al., 2014; Barney et al., 2009) indicate that there was no discernible increase in the survival rate of patients with ESS as a result of LAD. Patients with low grade ESS have a low risk of lymph node metastasis; earlier research revealed that patients undergoing lymph node excision had an overall rate of lymph node metastasis ranging from 10% to 30% (Signorelli et al., 2010; Riipel et al., 2005). Lymph node metastases in ESS patients is classified as stage IIIC by the 2009 FIGO classification, suggesting a strong negative impact of lymph node status on patient prognosis. The current debate centers on whether lymph node removal in low grade ESS is beneficial. Three earlier research (Amant et al., 2007; Riipel et al., 2005) suggested that LAD be prescribed for these patients, but other studies (Feng et al., 2013; Dos et al., 2001) suggested that systematic LAD had little therapeutic benefit. Of the 71 patients who got LAD in the Zhou et al., 2015 research, only 9 had lymph node metastases. The 2015 study by Zhou et al. similarly showed that DFS was unrelated to the condition of the lymph nodes or LAD. On the other hand, in certain patients, the lack of LAD may affect FIGO staging and result in stage migration. A research conducted in 2005 by Riipel et al. found that 33% of ESS patients had lymph node metastases at the time of their initial hysterectomy, at a later staging surgery, or when they experienced a recurrence. Accordingly, resection-based assessment of lymph node status may yield prognostic data and inform subsequent adjuvant therapy decisions (Rauh et al., 2013).

The largest study in our review (Nasioudis et al., 2021) found that there was little lymph node metastases and that patients with LMS, low grade ESS, or adenocarcinoma did not benefit from the performance of LAD in terms of survival. The findings from the smaller retrospective studies that we included in our review (Tasci et al., 2015; Barney et al., 2009) are supported by these results.

According to Hoellen et al. (2014), patients without lymph node or distant metastases had a median survival of 32 months, while those with lymph node metastases had a worse median survival of 13.5 months. Patients who underwent LAD had a superior 70-month survival rate than those who did not have lymph nodes or distant metastases.

5. Conclusion

Similar to earlier studies, the results of our systematic review show that LAD had no statistically significant impact on OS. Resection of lymph nodes or LAD has minimal potential benefit in terms of prognosis and clinical value. Patients with clinically worrisome swollen nodes, advanced sarcomas, and evident extra-uterine involvement may be candidates for selective LAD. Large-scale population-based research is ideally needed to obtain more reliable data to support our conclusions.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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