Review Article

Chirurgia (2025) 120: 519-528
No. 5, September - October
Copyright© Celsius
http://dx.doi.org/10.21614/chirurgia.3216

Lymphadenectomy Indications in Endometrial Cancer. A Surgeon's Dilemma in the Era of Perpetual Changes

Ioana-Maria Ignat[1#], Corina-Elena Minciuna[1,2#], Romina-Marina Sima[1,3], Liana Ples[1,3], Mircea Octavian Poenaru[1,3], Andrei Diaconescu[1,2]*, Catalin Vasilescu[1,2]

[1]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
[2]Department of General Surgery, Fundeni Clinical Institute, Bucharest, Romania
[3]Department of Obstetrics and Gynecology, Bucur Maternity, Saint John Hospital, Bucharest, Romania

***Corresponding author:**
Andrei Diaconescu, MD, PhD,
Department of General Surgery
and Liver Transplantation
Fundeni Clinical Institute
258 Fundeni Street, Bucharest
022328, Romania
E-mail: andrei.diaconescu@umfcd.ro

[#]Ioana Ignat and Corina-Elena Minciuna contributed equally to this work and share first authorship

Rezumat

Indicațiile limfadenectomiei în cancerul endometrial. Dilema chirurgului în era schimbărilor continue

Introducere: Rolul limfadenectomiei în cancerul endometrial a fost mult timp controversat. Considerată inițial utilă atât prognostic, cât şi terapeutic, practica actuală impune echilibrarea beneficiului unei stadializări mai precise cu morbiditatea procedurii. Acest review sintetizează indicațiile actuale ale limfadenectomiei sistematice în carcinomul endometrial, integrând actualizarea FIGO 2023 şi recomandările ESGO–ESTRO–ESP 2025.
Metode: Sunt analizate studiile randomizate esențiale, recomandările ghidurilor şi tranziția către tehnica ganglionului santinelă (SLN), cu accent pe stratificarea riscului în funcție de histologie, grad, invazia limfovasculară (LVSI) şi profilul molecular.
Rezultate: Dovezile actuale au demonstrat că limfadenectomia sistematică nu îmbunătățeşte supraviețuirea globală sau supraviețuirea fără progresie în stadiile precoce ale bolii, în timp ce creşte semnificativ morbiditatea operatorie, incluzând incidența limfocelului, limfedemului şi a leziunilor vasculare sau neurologice. Ghidurile rămân complexe şi uneori ambigue, necesitând o sinteză atentă pentru a defini cu precizie situațiile în care limfadenectomia este indicată. Algoritmii actuali plasează tehnica ganglionului santinelă (SLN) în centrul evaluării ganglionare. Limfadenectomia nu mai este justificată ca procedură de rutină; ea rămâne indicată doar atunci când SLN eşuează la pacienții cu risc intermediar-înalt şi înalt, fiind efectuată ca disecție lato-specifică în zona unde maparea a eşuat. În stadiile avansate, obiectivul chirurgical este citoreducția completă, cu excizia selectivă a ganglionilor voluminoşi sau suspecți, fără disecție sistematică; limfadenectomia sistematică nu trebuie efectuată în stadiile III-IV.
Concluzie: Paradigma s-a schimbat de la aplicarea universală a limfadenectomiei către o abordare personalizată, adaptată riscului. Biopsia ganglionului santinelă reprezintă noul standard terapeutic, reducând morbiditatea fără a compromite rezultatele oncologice. Extinderea accesului la efectuarea profilului molecular, în prezent limitată în România, este esențială pentru o stratificare corectă a riscului şi alinierea la standardele europene.

Received: 03.09.2025
Accepted: 20.10.2025

Cuvinte cheie: cancer endometrial, limfadenectomie, ganglion santinelă, FIGO 2023, ESGO–ESTRO–ESP 2025, clasificare moleculară

Abstract

Background: The role of lymphadenectomy in endometrial cancer has long been debated. Once considered to have prognostic and therapeutic value, it is now evident that balancing accurate staging with procedure-related morbidity remains a challenge. *Objective:* This review aims to clarify the current indications for systematic lymphadenectomy in endometrial carcinoma, integrating the updated FIGO 2023 staging system, the ESGO-ESTRO-ESP 2025 guidelines, and the emerging role of molecular classification.
Methods: We analyzed landmark randomized controlled trials, updated guideline recommendations, and the evolving paradigm of sentinel lymph node (SLN) mapping, with emphasis on risk stratification based on histology, grade, lymphovascular space invasion (LVSI), and molecular features.
Results: High-level evidence demonstrated that systematic lymphadenectomy does not improve survival in early-stage disease, while significantly increasing morbidity. Current guidelines remain complex, but consistently emphasize SLN mapping as the preferred method of nodal assessment. Systematic lymphadenectomy is no longer justified as routine; it is reserved for high-intermediate and high-risk patients when SLN mapping fails, performed as side-specific dissection. In advanced disease, the surgical goal is complete cytoreduction, with selective removal of bulky or suspicious nodes; systematic lymphadenectomy must not be performed in stages III-IV.
Conclusion: The paradigm has shifted from universal lymphadenectomy to a tailored, risk-adapted approach. SLN biopsy represents the new standard, reducing morbidity without compromising oncologic outcomes. Expanding access to molecular profiling, still limited in Romania, is crucial for better oncological results and alignment with European standards.

Keywords: endometrial cancer, lymphadenectomy, sentinel node, FIGO 2023, ESGO–ESTRO–ESP 2025, molecular classification

Introduction

Endometrial cancer arises from abnormal proliferation of endometrial epithelial cells and may extend into the myometrium or beyond the uterus. Prolonged, unopposed estrogen exposure is a major risk factor, while combined estrogen - progesterone therapy is protective. Other risks include advanced age, obesity, diabetes, metabolic syndrome, reproductive factors (nulliparity, early menarche, late menopause, polycystic ovary syndrome), genetic predisposition (e.g., Lynch syndrome), and use of tamoxifen (1).

According to GLOBOCAN 2022, in Romania there were an estimated 3,368 new cases of cervical cancer and 2,282 new cases of endometrial cancer in 2022, highlighting that cervical cancer still remains more frequent nationally, although endometrial cancer is steadily increasing in incidence (2). In the United States, this is currently the most common gynecologic malignancy, surpassing cervical cancer in incidence (3,4). As nationwide HPV vaccination campaigns and cervical cancer screening programs continue to expand and reach broader coverage, endometrial cancer is projected to mirror the situation already observed in the United States and surpass cervical cancer when it comes to incidence in our country as well.

Traditionally, endometrial tumors were classified by Bokhman's dualistic model into type I (estrogen-driven, usually endometrioid, low-grade, with favorable prognosis) and type II (non-endometrioid, estrogen-independent, high-grade, with poorer prognosis) (5). Contemporary guidelines emphasize other types of classifications that will be discussed further on.

The treatment of choice for early-stage endometrial cancer remains surgical, consisting of total hysterectomy with bilateral salpingo-oophorectomy (TH/BSO), while advanced disease is mostly treated with cytoreductive surgery (1). In carefully selected young women with low-risk disease and a desire to maintain fertility, a conservative approach with progestin therapy and strict surveillance may be offered, with definitive surgery recommended after completion of childbearing(1). Pelvic and para-aortic lymphadenectomy can be an option in some carefully selected cases, and has been a topic of interest in the field of oncological surgery for decades (1).

Some support its prognostic and therapeutic role. Others reject it due to risks and questionable benefits. Proponents cite potential prognostic/therapeutic value [e.g., the SEPAL cohort, 2010; registry analyses suggesting improved OS with extensive nodal assessment in selected stage I (6)]. Opponents reference randomized data showing no survival benefit and higher morbidity [e.g., ASTEC RCT - (7,8)]. Guidelines offer recommendations, yet with a certain lack of clarity. Current European guidance generally favors sentinel-node mapping for uterine-confined disease and reserves systematic pelvic/para-aortic lymphadenectomy for well-defined indications(1). Because it may lead to serious complications, a thorough preoperative evaluation and accurate disease classification are essential for determining the indication for surgery (1). Reported complications include lymphocele, lymphedema, and deep venous thrombosis, which negatively affect quality of life (9). These issues, together with other concerns, have been part of the rationale for attempts to remove systematic lymphadenectomy, a topic that has been debated for many years.

The aim of this study is to provide an updated overview of the role and clinical utility of systematic lymphadenectomy in endometrial cancer, with a focus on recent evidence and current international guideline recommendations.

Preoperative Evaluation

The preoperative evaluation of patients with suspected endometrial carcinoma follows a structured, guideline-based approach as outlined in the NCCN 2025 recommendations (10).

The process begins with a thorough history and physical examination, followed by routine laboratory tests, including complete blood count, liver and renal function tests, a chemistry profile, and measurement of CA-125 when clinically indicated (10). CA-125 is not a standard test for all patients but may be useful in those with high-grade histologies or when extrauterine disease is suspected (10). Endometrial biopsies are mandatory, and sampling must be repeated if the initial material is inconclusive (10).

Molecular characterization is now considered a cornerstone of preoperative workup, with assessment of and classification into one of the four following categories: POLE mutated, MMRd, NSMP, and p53 abnormality status (11). The new FIGO classification and the ESGO/ESTRO/ESP guidelines integrate molecular classification to improve identification of distinct prognostic patient populations (11).

Additional biomarkers, such as HER2 in serous and carcinosarcomas, and estrogen or progesterone receptor status in advanced or recurrent disease, provide further guidance for treatment planning (10,11).

Imaging is tailored to the treatment intent, depending on whether fertility-saving is the chosen option or not (10). In non-fertility-sparing settings, imaging includes chest X-ray, pelvic MRI to determine if the origin is endocervical or endometrial and local spread, and pelvic ultrasound for assessing uterine size (10).

For fertility-sparing therapy, pelvic MRI is preferred to exclude myometrial invasion and assess local tumor extent (10). Ultrasound is an option when MRI is contraindicated (10). Ovarian preservation is not recommended in patients with a hereditary cancer risk including tubo-ovarian cancer (e.g. germline BRCA mutation, Lynch syndrome, etc.), however, oocyte cryopreservation might be considered in these patients (1,10). Ovarian preservation should be carefully discussed in patients with ovarian or breast cancer family history without verified hereditary mutations (11).

Regardless of planned therapy, fluorodeoxyglucose (FDG)-PET/CT is reserved for cases with suspected metastatic disease and CT is recommended if abnormalities are found on the chest X-Ray (10). CT of the chest, abdomen, and pelvis is recommended for high-grade histologies or when staging has been incomplete after hysterectomy (10).

Genetic risk evaluation complements tumor profiling, including universal MMR testing and, when indicated, multigene panel testing for Lynch syndrome (11). Approximately 3% of all endometrial carcinomas (ECs) and about 10% of mismatch repair deficient (MMRd)/microsatellite instable ECs are causally related to germline mutations of one of the MMR genes MLH1, PMS2, MSH2, and MSH6 (11).

A schematic overview of the recommended preoperative workup is shown in *Fig. 1.*

Classification

The classification of endometrial carcinoma is currently hybrid, integrating morphological and molecular features to better reflect prognosis and guide therapy. Morphologically, tumors are assessed by histological type, grade, and lymphovascular space invasion (LVSI). LVSI can be of two types: focal (1-2 invaded vessels around the

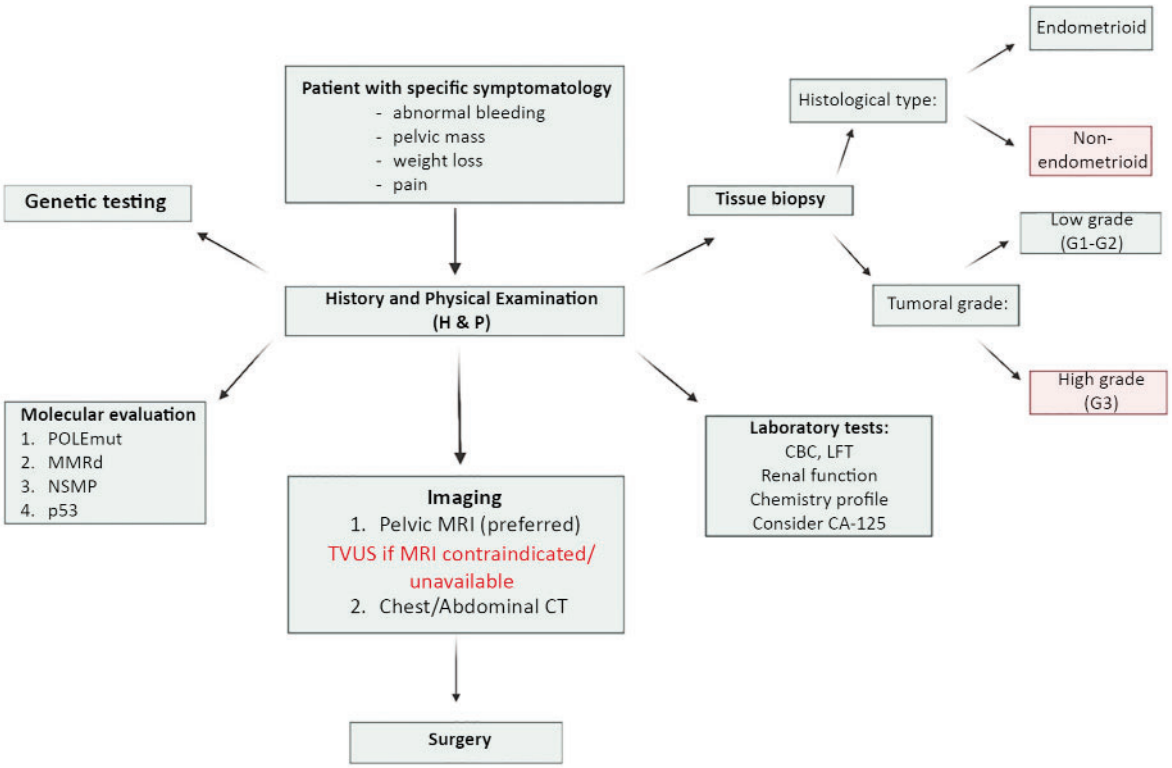

Figure 1. Schematic preoperative evaluation of a patient according to NCCN Uterine Cancer Guidelines 2025: CBC, complete blood count; LFT, liver function tests; CA-125, cancer antigen 125; IHC, immunohistochemistry; MSI, microsatellite instability; MMRd, mismatch repair deficient; NSMP, no specific molecular profile; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; FISH, fluorescence in situ hybridization; TVUS, transvaginal ultrasound; MRI, magnetic resonance imaging; CT, computed tomography; FDG-PET/CT, fluorodeoxyglucose positron emission tomography/computed tomography; TH, total hysterectomy; EC, endometrial carcinoma.

tumor) or substantial (more than 3-5 vessels involved), the latter carrying a high risk of recurrence (12).

A key distinction must be made between aggressive and non-aggressive histologies, given their divergent prognostic implications. Non-aggressive histology includes endometrioid carcinomas grade of differentiation 1–2 (G1-2) without substantial LVSI, whereas aggressive histology comprises serous, clear cell carcinomas, carcinosarcoma, undifferentiated carcinomas, mesonephric-like, and gastrointestinal mucinous type carcinoma (1), and endometrioid grade 3 or any histology with substantial LVSI. It becomes evident that high-grade tumors (G3) and substantial LVSI are risk factors.

According to the proportion of solid non-squamous, non-morular growth, tumors can be classified as follows: G1, ≤5%; G2, 6–50%; G3, >50% (13). Even though molecular classification into the four subgroups previously mentioned remains the main prognostic framework, histological grading still carries clinical relevance and rises some issues. G2 is notoriously subjective and observer-dependent, and represents the highest percentage of cases (14).

The presence or absence of molecular testing directly impacts risk stratification: POLE mutations may downgrade prognosis despite adverse morphology, while p53-aberrant tumors remain high-risk regardless of stage (10). In the absence of molecular profiling, risk grouping relies only on morphology (histotype, grade, LVSI), but this may misclassify patients (10). By combining FIGO stage, histology, grade, LVSI, and molecular profile, patients are grouped into risk categories as defined: low, intermediate, high-intermediate, and high (1).

This stratification is not merely descriptive, but has direct therapeutic consequences,

modifying the technique chosen for LN (lymph node) evaluation (sentinel LN mapping versus systematic lympha-denectomy) as well as the type and intensity of adjuvant therapy. In the last years, there have been significant changes to the indications of the forementioned, as well as to the exact definitions of each category and what they imply, highlighting again the progressive integration of molecular classification into clinical decision-making.

Staging

In discussing staging, particular attention should be given to the 2023 FIGO update. The revised classification expands beyond the purely anatomical framework of 2009 by incorporating histological type, patterns of myoinvasion, and molecular alterations (12). *Table 1* provides a comparative outline of the 2009 and 2023 systems.

This updated FIGO staging now serves as the universal oncological framework, but its true clinical relevance emerges when combined with molecular classification. Rather than replacing one another, these systems complement each other, providing both an anatomical and a biological perspective. For example, early-stage tumors harboring a POLE mutation may be reclassified into the low-risk group despite deep myometrial invasion, while stage I p53-aberrant tumors remain high-risk and often require adjuvant treatment.

Table 1. Comparison of the FIGO staging classifications for endometrial cancer (2009 vs. 2023). The updated 2023 system introduces more detailed subdivisions, incorporates histological aggressiveness, lymphovascular space invasion (LVSI), and ovarian involvement, and refines nodal and metastatic categories to better stratify prognosis and guide treatment.

	FIGO 2009	**FIGO 2023**
I	Tumor confined to uterus	Tumor confined to uterus and ovary
IA	No or <50% myometrial invasion	Disease limited to the endometrium OR non-aggressive histological type, i.e. low-grade endometroid, with invasion of less than half of myometrium with no or focal involvement LVSI OR good prognosis disease
IA1	-	Non-aggressive histological type limited to an endometrial polyp OR confined to the endometrium
IA2	-	Non-aggressive histological types involving <50% of the myometrium with no or focal LVSI
IA3	-	Low-grade endometrioid carcinomas limited to the uterus and ovary
IB	Myometrial invasion equal or >50%	Non-aggressive histological types with invasion of half or >50% of the myometrium, and with no or focal LVSI
IC	-	Aggressive histological types limited to a polyp or confined to the endometrium
II	Tumor invades the cervical stroma but does not extend beyond uterus	Invasion of cervical stroma without extrauterine extension OR with substantial LVSI OR aggressive histological types with myometrial invasion
IIA	-	Invasion of the cervical stroma of non-aggressive histological types
IIB	-	Substantial LVSI of non-aggressive histological types
IIC	-	Aggressive histological types with any myometrial involvement
III	Local/regional spread	Local and/or regional spread of the tumor of any histological subtype
IIIA	Tumor invades serosa of uterus and/or adnexas	IIIA1 Spread to ovary or fallopian tube (except when meeting stage IA3 criteria) IIIA2 Involvement of uterine subserosa or spread through the uterine serosa
IIIB	Vaginal and/or parametrial involvement	IIIB1 Metastasis or direct spread to the vagina and/or the parametria IIIB2 Metastasis to the pelvic peritoneum
IIIC1	Positive pelvic nodes	IIIC1 Metastasis to the pelvic lymph nodes; IIIC1i Micrometastasis; IIIC1ii Macrometastasis
IIIC2	Positive para-aortic LN with/without positive pelvic LN	IIIC2 Metastasis to para-aortic lymph nodes up to the renal vessels, with or without metastasis to the pelvic lymph nodes; IIIC2i Micrometastasis; IIIC2ii Macrometastasis
IV	Invasion into bladder and/or bowel mucosa and/or distant metastases	Spread to the bladder mucosa and/or intestinal mucosa and/or distance metastasis
IVA	Invasion into bladder and/or bowel mucosa	Invasion of the bladder mucosa and/or the intestinal/bowel mucosa
IVB	Distant metastases, including intra-abdominal metastases and/or inguinal LN	Abdominal peritoneal metastasis beyond the pelvis
IVC	-	Distant metastasis, including metastasis to any extra- or intra-abdominal lymph nodes above the renal vessels, lungs, liver, brain, or bone

Source for FIGO 2009: Brincat et al., Eur J Gynaecol Oncol 2017
Source for FIGO 2023: Berek et al., Int J Gynaecol Obstet. 2023

The Breaking Point: Is Lymphadenectomy Indicated in Endometrial Cancer or Not?

Lymphadenectomy refers to the systematic removal of pelvic and/or para-aortic lymph nodes during surgical intervention. This concept was introduced after the FIGO 1988 revision, which replaced clinical staging with a surgical system. This landmark change was largely informed by Gynecologic Oncology Group (GOG) studies, particularly Creasman et al. (1987)(15), which demonstrated the prognostic importance of nodal status and identified reproducible patterns of spread. As a result, pelvic and para-aortic lymph node dissection became part of the comprehensive staging procedure, alongside TH/BSO. The expectation was twofold: to improve the accuracy of staging, and to potentially improve survival through removal of occult metastases.

Traditionally, on the basis of FIGO recommendations, systematic pelvic and para-aortic lymphadenectomy was routinely performed for EC staging (16). Observational studies such as Creasman et al., 1987 (15) and Kilgore LC et al., 1995 (17) suggested possible survival benefits in selected groups, reinforcing the practice. However, these studies were limited by inherent biases and lacked the rigor of randomized evidence. The turning point came with the publication of two major and more recent randomized controlled trials.

The Benedetti Panici trial (8) randomized 514 women with presumed stage I endometrial carcinoma to either standard surgery with systematic pelvic lymphadenectomy (n=264) or surgery without lymphadenectomy (n=250). After a median follow-up of 49 months, there was no significant difference in overall survival (81.0% vs. 81.7%) or progression-free survival (81.3% vs. 82.6%) between the two arms. In contrast, morbidity was significantly higher in the lymphadenectomy arm, with increased rates of intraoperative vascular injury, lymphocyst formation, and lymphedema.

The ASTEC trial (7) was even larger, enrolling 1,408 women with endometrial cancer apparently confined to the uterus. Patients were randomized to standard surgery with (n=704) or without (n=704) pelvic lymphadenectomy. After a median follow-up of 37 months, 5-year overall survival was identical in both arms (81%), with no benefit in recurrence-free survival either. Moreover, it was emphasized again that lymphadenectomy leads to longer operative times, increased blood loss, and higher rates of complications.

Together, these two high-level trials provided evidence that systematic lymphadenectomy in early-stage endometrial cancer does not confer a survival benefit, despite yielding more accurate staging information. This revelation marked the beginning of the decline of routine lymphadenectomy.

Risks and Complications

One of the most frequent and challenging postoperative complications is the development of a lymphocele, which represents an extraperitoneal collection of lymphatic fluid lacking an epithelial lining. Its incidence is influenced by multiple factors, such as: technical and procedural aspects which include the extent of lymphadenectomy, the total number of lymph nodes removed, failure to adequately ligate lymphatic vessels, the administration of pre- or postoperative radiotherapy, and the presence of lymph node metastases. Additional contributors may involve the use of retroperitoneal suction drainage and low-dose heparin for thromboembolic prophylaxis (18). While many lymphoceles are detected incidentally and remain clinically insignificant, some can lead to symptomatic complications. Small collections are typically asymptomatic, whereas large or infected lymphoceles may cause fever, abdominal discomfort, tenesmus, urinary frequency, hydronephrosis, lower limb edema, or deep venous thrombosis (18). Management is generally conservative for small, sterile lymphoceles, whereas larger ones are less likely to resolve spontaneously and may require more invasive treatments such as needle aspiration, sclerotherapy, catheter drainage, or surgical marsupialization (18).

The ureter is a vulnerable structure, crossing the pelvis near the iliac bifurcation. Inattentive clipping or transection may lead to injury, often requiring immediate reimplantation into the bladder with stent placement (19). Similarly, injury to the obturator nerve can leave patients with debilitating motor and sensory deficits. Though rarer, vascular injuries to the iliac or obturator vessels can trigger severe hemorrhage (19).

Late side-effects, especially lymphedema of the lower limbs, affect the patient's quality of life severely. Recent data are sobering: Terada et al. (2023) (20) reported a 21% rate of lymphedema after pelvic lymphadenectomy compared with only 2% after sentinel node biopsy. Added to this is the reality that lymphadenectomy prolongs surgery substantially (20). Thus, in the balance between

oncological benefit and surgical morbidity, the role of lymphadenectomy, even in early-stage disease, continues to be critically reassessed.

Evolving Role and Contemporary Indications for Lymphadenectomy

In the present analysis, the patients assigned to the low- and intermediate-risk categories will be explicitly identified; by exclusion, the remaining cases can thus be classified within the high-intermediate and high-risk groups, which are frequently considered jointly when determining the optimal therapeutic strategy.

It is, however, crucial to emphasize that there are important differences between the traditional clinicopathological classification of risk groups and the more recent integrated molecularly informed approach. When the aim is to deliberately exclude molecular classification and to examine the risk stratification purely on the basis of clinicopathological features, one should refer to the Supplementary appendix of the ESGO–ESTRO–ESP guidelines (11) which provide a clear visual synthesis of the risk categories in this context. In contrast, if we adopt the current standard approach that incorporates molecular features into clinical decision-making, the appropriate reference remains the main guideline publication.

To simplify, we reach the intraoperative decision point, where several options exist depending on the information gathered up to that moment. For patients staged I–II, standard surgery consists of total hysterectomy with bilateral adnexectomy (TH/BSO) and SLN biopsy.

The first step is to perform sentinel lymph node (SLN) mapping and biopsy (1). The decisive question is if the biopsy is performed alone, or it is followed by a systematic, side-specific lymphadenectomy. Indocyanine green (ICG) is injected at the cervical level and intraoperatively identifying the first draining lymph nodes, which are subsequently excised and analyzed histopathologically (11). The standard dose of ICG, as used in clinical studies, is 1.25 mg/ml, obtained by diluting 15 ml of ICG with 20 ml of saline, with a total volume of 4 ml injected into the cervix at the 3 and 9 o'clock positions (11). Typically, 1 ml is injected superficially (2-3 mm) and 1 ml deeply (1-2 cm) on each side (11). Re-injection is indicated only once, in the event of unilateral or bilateral failure of dye uptake (11).

Ultrastaging techniques are also used for the detection of ITCs (isolated tumor cells) or micrometastases (1). Ultrastaging refers to sectioning at much smaller intervals, between 50-200 µm, combined with immunohistochemistry (1). Micrometastases are relevant for the same reason as macrometastases, as their presence directly upstages the patient to stage IIIC (1). ITCs alone do not mandate treatment escalation, but they do influence the therapeutic decision in conjunction with other mentioned risk factors (1).

Regardless of whether the SLNs are positive or negative at final pathology, no additional action is required. The dilemma arises in cases with inconclusive results, where the solution lies hidden within the risk categories. Infracolic (total or partial) omentectomy should be done for clinical stage I and II serous endometrial carcinoma, carcinosarcoma, and undifferentiated carcinoma (1). Omentectomy is not necessary in other histological types (1). Upper vaginal resection is stage-dependent and is encouraged in stage IIA in order to obtain negative margins (1).

For low-risk patients (IA, IC G3), unsuccessful mapping does not require further surgical intervention, as the risk-benefit balance does not justify a time-consuming procedure and the morbidity associated with lymphadenectomy (1,11). For intermediate-risk patients (IB G1-G2 without or with focal LVSI, IIC G3 with <50% myometrial invasion and absent/focal LVSI, IC non-endometrioid, IIA G1-G2 with absent/focal LVSI), systematic lymphadenectomy may be considered, and the decision belongs to the surgeon (1, 11). By exclusion, the remaining patients fall into the high-intermediate and high-risk categories, in which systematic, side-specific lymphadenectomy is mandatory if SLNB does not provide a conclusive result (*Fig. 2*) (1).

For advanced stages (III-IV), the approach depends on tumor resectability. In resectable disease, cytoreductive surgery is indicated, aiming for R0–R1 resection, with excision of suspicious or bulky lymph nodes, but systematic lymphadenectomy is not recommended (1). In unresectable disease, neoadjuvant treatment is followed by an attempt at cytoreduction under the same principles, after which patients receive adjuvant radio-chemotherapy (1). Here as well, systematic lymphadenectomy is not indicated (1).

An important mention is that the absence of sentinel lymph node visualization does not equal to the absence of lymphatic dissemination. Such a result may be explained by: (1) technical failure of tracer injection or intraoperative detection; (2) lymphatic obstruction due to direct tumor invasion

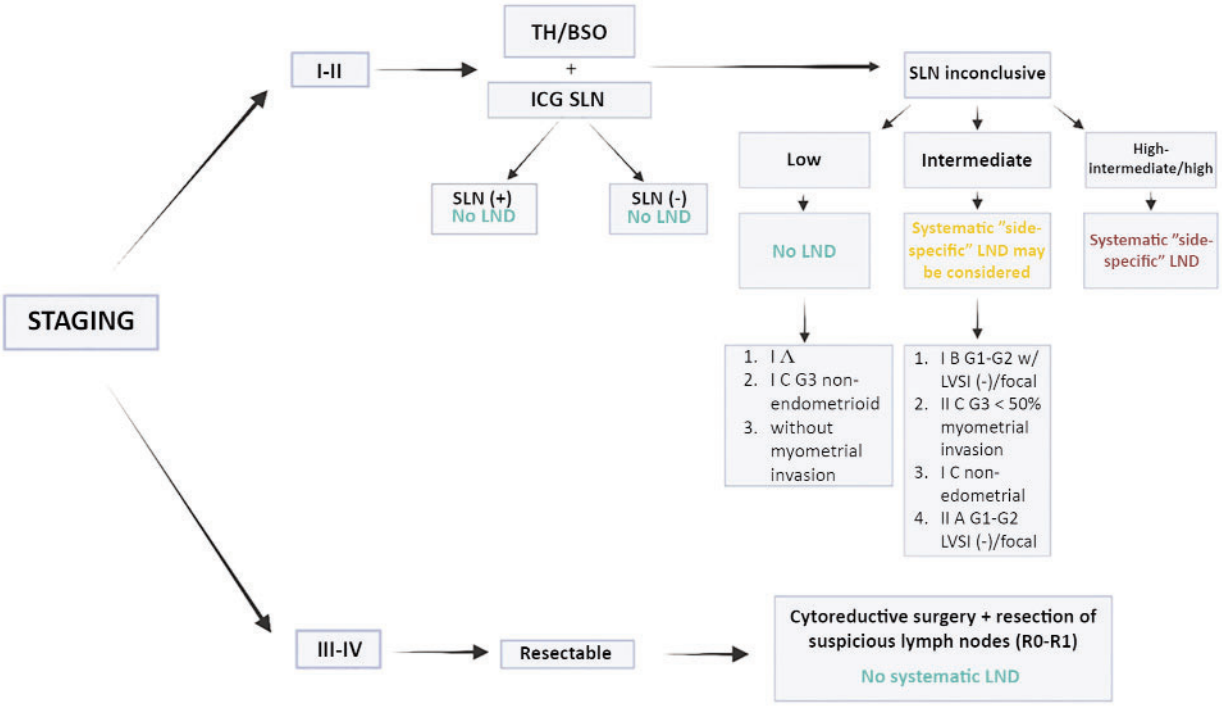

Figure 2. Surgical algorithm for LN assessment in endometrial cancer.
TH/BSO -total hysterectomy with bilateral salpingo-oophorectomy; SLN – Sentinel lymph node; ICG – Indocyanine green; LND – Lymphadenectomy; LVSI – Lymphovascular space invasion; R0–R1 – Complete resection / microscopic residual disease

of the vessels; (3) atypical lymphatic drainage, particularly in tumors located at the uterine fundus, where the flow may bypass the pelvic network and proceed directly through the infundibulo-pelvic ligament to the para-aortic chain; or (4) the true absence of nodal metastases. For these reasons, all inconclusive uses of ICG will be categorized as mapping failure, and actions will be taken as previously explained (22-25).

Future Directions

Despite the paradigm shift toward sentinel lymph node (SLN) mapping, several unanswered questions remain regarding the optimal management of lymph nodes in endometrial cancer. Current research is focusing on refining the accuracy, reproducibility, and prognostic value of SLN biopsy. Ongoing studies are evaluating novel tracers (including near-infrared fluorescent dyes and hybrid radio-fluorescent agents), improved mapping algorithms, and the role of ultrastaging and molecular diagnostics in enhancing the detection of micrometastases. The integration of molecular risk stratification with nodal assessment is also a growing area of investigation, aiming to better define which patients truly benefit from nodal evaluation and which may safely avoid it.

Another important research direction concerns the therapeutic value of lymphadenectomy in advanced or high-risk disease. While systematic dissection has not demonstrated a survival benefit in randomized trials, questions remain regarding its role in specific molecular subgroups, in tailoring adjuvant therapy, or when combined with modern systemic treatments. Prospective registries and multicenter trials are needed to clarify the prognostic versus therapeutic contributions of nodal surgery. Additionally, research in quality-of-life outcomes, cost-effectiveness analyses, and the development of minimally invasive approaches to reduce morbidity will be essential in guiding evidence-based practice.

Finally, as clinicians are increasingly required to integrate vast amounts of clinical, surgical, pathological, and molecular data, artificial intelligence (AI) and machine learning tools represent a promising frontier. AI-driven decision-support systems could help synthesize complex datasets, predict nodal involvement, stratify recurrence risk,

and even personalize surgical planning. Incorporating such technologies into clinical workflows may enhance accuracy, reduce variability in practice, and ultimately support a more individualized, evidence-based approach to lymph node management in endometrial cancer.

In Romania, a key limitation in the modern management of endometrial carcinoma is the restricted access to molecular testing. This significantly reduces the precision of risk stratification and therapeutic decision-making, as clinically relevant subgroups such as POLE-mutated tumors cannot currently be identified.

According to the Official Gazette of Romania, Part I, No. 1092 bis/December 5, 2023 (Order No. 4049/2023) (21), the national guidelines for endometrial cancer recommend immunohistochemical evaluation for dMMR/MSI and molecular testing for MSI, NTRK, TMB, p53, and POLE mutations, all of which carry prognostic and therapeutic significance (21). However, these tests are not yet reimbursed through the national program, which limits their systematic implementation; unfortunately, POLEmut analysis is not available, although it is well-established that any early-stage tumor harboring this mutation – and even some stage III tumors, according to ongoing discussions – would fall into the low-risk group.

Yet, this challenge also highlights a clear opportunity for constructive progress. The establishment of a national endometrial cancer registry would represent a crucial first step, enabling systematic collection of clinical, pathological, and outcome data while facilitating benchmarking against European standards. In parallel, continuous education programs and specialized training for gynecological oncologists, pathologists, and molecular biologists would strengthen technical expertise and prepare the healthcare system for the gradual integration of comprehensive molecular profiling. Active participation in international research networks and multicenter collaborations could further accelerate the adoption of innovative diagnostic and therapeutic approaches.

Conclusion

The role of lymphadenectomy in endometrial cancer has shifted dramatically over the past decades. Once considered a routine component of surgery, systematic pelvic and para-aortic dissection is now recognized as offering no survival benefit while adding significant morbidity. Sentinel lymph node (SLN) biopsy has become the modern standard for patients with presumed stage I-II disease, providing accurate staging with far less harm. Systematic lymphadenectomy is reserved only for well-defined scenarios – namely, failed or inconclusive SLN mapping in high-intermediate and high-risk patients – while in advanced disease the principle is limited cytoreduction with selective removal of suspicious nodes. This evolution reflects a move away from a universal approach toward tailored strategies that prioritize both oncological safety and patient quality of life.

In Romania, however, the full adoption of risk-adapted strategies is hampered by limited access to molecular testing. While p53 immunohistochemistry is performed, POLE mutation analysis and comprehensive molecular profiling remain largely unavailable, leading to potential overtreatment of patients who would otherwise qualify as low-risk. Bridging this gap requires national investment in diagnostic infrastructure, training, and registries to align local practice with European standards. Ultimately, the refinement of lymph node management in endometrial cancer embodies a wider transformation in oncologic surgery – one that must be implemented consistently in clinical practice and supported by advances in molecular diagnostics to ensure equitable care for Romanian patients.

Author's Contributions

Conceptualization, IMI and CEM; Methodology, AD and CV; Writing-review and editing, IMI and CEM; Supervision, AD, RMS, LP, MOP and CV. All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Funding

This work was supported by a grant from the Ministry of European Investments and Projects, project number 324809/2024 (to C.V. and C.E.M.).

Declaration of Generative AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work the author(s) used OpenAI. (2025, February 25). ChatGPT (Version 4) (Large language model). OpenAI.

https://openai.com in order to improve the language and readability. After using this tool/ service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

References

1. Concin N, Matias-Guiu X, Cibula D, Colombo N, Creutzberg CL, Ledermann J, et al. ESGO–ESTRO–ESP guidelines for the management of patients with endometrial carcinoma: update 2025. Lancet Oncol. 2025;26(8):e423-e435.
2. International Agency for Research on, C., GLOBOCAN 2022: Romania Fact Sheet. 2022, IARC: Lyon.
3. American Cancer, S., Key Statistics for Endometrial Cancer. 2025.
4. National Cancer Institute, S.E. and P. End Results, Cancer Stat Facts: Uterine Cancer (Corpus Uteri). 2025.
5. Bokhman JV. Two pathogenetic types of endometrial carcinoma. Gynecol Oncol. 1983;15(1):10-7.
6. Seagle BLL, Alexander AL, Lantsman T, Shahabi S. Prognosis and treatment of positive peritoneal cytology in early endometrial cancer: matched cohort analyses from the National Cancer Database. Am J Obstet Gynecol. 2018;218(3): 329.e1-329.e15.
7. ASTEC study group; Kitchener H, Swart AMC, Qian Q, Amos C, Parmar MKB. Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study. Lancet. 2009;373(9658): 125-36.
8. Benedetti Panici P, Basile S, Maneschi F, Lissoni AA, Signorelli M, Scambia G, et al. Systematic pelvic lymphadenectomy vs. no lymphadenectomy in early-stage endometrial carcinoma: randomized clinical trial. J Natl Cancer Inst. 2008;100(23):1707-16.
9. Torrent A, Amengual J, Ruiz A, Serra A, Fuertes L, Sampol CM, et al. Impact of lymph node staging techniques on lymphedema and quality of life in early-stage endometrial cancer: A prospective cohort study. Gynecol Oncol Rep. 2025;60:101919.
10. National Comprehensive Cancer, N., NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Uterine Neoplasms. Version 3.2025. 2025.
11. Concin N, Matias-Guiu X, Cibula D, Colombo N, Creutzberg CL, Ledermann J, et al. ESGO–ESTRO–ESP guidelines for the management of patients with endometrial carcinoma: update 2025. Supplementary Appendix. Lancet Oncol. 2025; 26(8):e423-e435.
12. Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, et al. FIGO staging of endometrial cancer: 2023. Int J Gynaecol Obstet. 2023;162(2): 383-394.
13. Murali R, Delair DF, Bean SM, Abu-Rustum NR, Soslow RA. Evolving Roles of Histologic Evaluation and Molecular/Genomic Profiling in the Management of Endometrial Cancer. J Natl Compr Canc Netw. 2018;16(2):201-209.
14. Scholten AN, Smit VTHBM, Beerman H, van Putten WLJ, Creutzberg CL. Prognostic significance and interobserver variability of histologic grading systems for endometrial carcinoma. Cancer. 2004;100(4):764-72.
15. Creasman WT, Morrow CP, Bundy BN, Homesley HD, Graham JE, Heller PB. Surgical pathologic spread patterns of endometrial cancer. A Gynecologic Oncology Group Study. Cancer. 1987;60(8 Suppl):2035-41.
16. Pinelli C, Artuso V, Bogani G, Laganà AS, Ghezzi F, Casarin J. Lymph node evaluation in endometrial cancer: how did it change over the last two decades? Transl Cancer Res. 2020;9(12):7778-7784.
17. Kilgore LC, Partridge EE, Alvarez RD, Austin JM, Shingleton HM, Noojin 3rd F, et al. Adenocarcinoma of the endometrium: survival comparisons of patients with and without pelvic node sampling. Gynecol Oncol. 1995;56(1):29-33.
18. Kim HY, Kim JW, Kim SH, Kim YT, Kim JH. An analysis of the risk factors and management of lymphocele after pelvic lymphadenectomy in patients with gynecologic malignancies. Cancer Res Treat. 2004;36(6):377-83.
19. Gülseren V, Özcan A, Çakır İ, Özer M, Özçelik B, Serin İS, et al. Intraoperative complications, treatments and outcomes of lymph node dissection for gynecological malignancies. Eur J Gynaecol Oncol, 2025;46(4):58-63.
20. Terada S, Tanaka T, Murakami H, Tsuchihashi H, Toji A, Daimon A, et al. Lymphatic Complications Following Sentinel Node Biopsy or Pelvic Lymphadenectomy for Endometrial Cancer. J Clin Med. 2023;12(13): 4540.
21. Ministry of Health. Order No. 4049/27.11.2023, in Official Gazette of Romania, Part I. 2023, Monitorul Oficial: Bucharest. p. No. 1092 bis.
22. Wang T, Xu Y, Shao W, Wang C. Sentinel Lymph Node Mapping: Current Applications and Future Perspectives in Gynecology Malignant Tumors. Front Med (Lausanne). 2022;9:922585. 2022.
23. Freytag D, Pape J, Dhanawat J, Günther V, Maass N, Gitas G, et al. Challenges Posed by Embryonic and Anatomical Factors in Systematic Lymphadenectomy for Endometrial Cancer. J Clin Med. 2020; 9(12):4107.
24. Bretová P, Minář L, Ovesná P, Weinberger V, Felsinger M, Koblížková M, Hausnerová J, et al. Predictors for sentinel lymph node mapping failure using indocyanine green injection in apparent early stages of endometrial cancer: a single-center prospective study. Int J Gynaecol Obstet. Epub 2025 Apr 10..
25. Andreika L, Šiaudinytė M, Vankevičienė K, Ramašauskaitė D, Rudaitis V. Analysis of Predictive Factors Associated with Unsuccessful Sentinel Lymph Node Mapping in Endometrial Carcinoma. Cancers (Basel). 2024;16(21):3680.