Performance of Sentinel Lymph Node Mapping in Early-Stage Endometrial Cancer: A Single-Centre Analysis

Precisão Diagnóstica da Pesquisa do Gânglio Sentinela no Cancro do Endométrio em Estadios Iniciais – Um Estudo Unicêntrico

Kristina Hundarova[1], Cristina Frutuoso[1], Fernanda Águas[1], Cláudia Andrade[1]
Centro Hospitalar e Universitário de Coimbra EPE

Abstract

Introduction: The lymph node status is of utmost importance in endometrial cancer staging. However, the therapeutic importance of systematic lymphadenectomy was not proven, thus the sentinel lymph node biopsy (SLNB) is emerging as an alternative to classic surgical staging procedure. We aimed to evaluate the feasibility of SLNB in clinical early-stage endometrial cancer, at a university-affiliated teaching hospital.

Material and Methods: Retrospective, single-centre, observational analysis, including patients with clinical stage I or II endometrial cancer, submitted to minimally invasive primary surgery. Patients underwent sentinel lymph node mapping with indocyanine green dye, after cervical injection, from September 2019 to September 2022. The ultra-staging protocol was followed. The map rate, sensitivity, negative predictive value, and false negatives were calculated.

Results: Fifty-six patients met the inclusion criteria. The overall and bilateral detection rate was o 96.4% and 80.3%, respectively. After SLNB, complete pelvic lymphadenectomy was performed in 33.9% of patients. Lymphatic metastases were found in 6 (10.7%) cases, all of them in sentinel lymph node sampling. Four patients, with pre-operative low-risk of recurrence, had bilateral SLNB and the histopathological evaluation revealed micrometastases. Two patients, who underwent pelvic lymphadenectomy, had macrometastases. The sensitivity and negative predictive value of SLNB were 100%, with a false negative rate of 0%. Comparative analysis between the groups with a low-risk of recurrence, that underwent SLNB alone, and intermediate/high-risk groups, that performed systematic lymphadenectomy, showed a significant difference in surgery duration, hospital stay, and complication rate (higher in the systematic lymphadenectomy group). There were no adverse effects related to the indocyanine green injection.

Conclusion: SLNB is a safe procedure, with a high detection rate and sensitivity, avoiding the morbidities related to systematic lymphadenectomy. The implementation of the ultra-staging protocol is crucial to allow the diagnosis of the low-volume metastatic involvement, influencing the definitive staging of apparently low-risk patients.

Keywords: Endometrial cancer; Sentinel lymph node biopsy; Indocyanine green; Minimally invasive surgery; Lymphadenectomy.

Resumo

Introdução: No cancro do endométrio (CE), o estadiamento cirúrgico é fundamental para estabelecer o prognóstico. Contudo, o valor terapêutico da linfadenectomia sistemática não foi demonstrado. A biópsia do gânglio sentinela (BGS) tem-se revelado como alternativa ao estadiamento cirúrgico clássico. O objetivo deste estudo foi avaliar a precisão diagnóstica da BGS em doentes com CE em estádios iniciais, num centro terciário.

1. Centro Hospitalar e Universitário de Coimbra EPE, Coimbra, Portugal.

Materiais e Métodos: Estudo retrospetivo observacional, unicêntrico, de doentes com CE no estádio I ou II da FIGO, submetidas a cirurgia primária por laparoscopia com BGS, após injeção cervical de verde de indocianina. Realizou-se protocolo de ultraestadiamento em todos os gânglios sentinela identificados. Calcularam-se a taxa de deteção, sensibilidade, valor preditivo negativo e taxa de falsos negativos.
Resultados: Incluíram-se 56 doentes. A taxa de deteção total e bilateral foi de 96,4% e 80,3%, respetivamente. Após a BGS, a linfadenectomia sistemática foi realizada em 19 (33,9%) doentes. A metastização ganglionar foi detetada em 6 (10,7%) casos, todos em gânglios sentinela. Nas quatro doentes, do grupo de baixo risco de recorrência, submetidas apenas a BGS, a invasão ganglionar foi sob a forma de micrometástases, nos 2 casos que realizaram linfadenectomia pélvica foram encontradas macrometástases. A sensibilidade e o valor preditivo negativo da BGS foi de 100%, com taxa de falsos negativos de 0%. A análise comparativa entre o grupo submetido apenas a BGS e o submetido ao estadiamento ganglionar clássico, demonstrou diferenças significativas na duração da cirurgia, dias de internamento e complicações, que foram superiores neste último. Não houve efeitos adversos associados à utilização do verde de indocianina.
Conclusão: A BGS é um procedimento seguro com elevada taxa de deteção e sensibilidade, permitindo reduzir a morbilidade associada ao estadiamento clássico. O protocolo de ultrastaging é essencial para diagnosticar envolvimento metastático de baixo volume, influenciando o estadiamento definitivo de doentes com aparente baixo-risco de recorrência.

Palavras-Chave: Cancro do endométrio; Biópsia do gânglio sentinela; Verde de indocianina; Cirurgia minimamente invasiva; Linfadenectomia.

INTRODUCTION

Endometrial cancer (EC) is the most common gynecologic malignancy in developed countries, with a growing prevalence due to high rates of obesity combined with extended life expectancy[1]. Its estimated incidence and standardized mortality rate in Portugal are 9.9/100000 and 2.0/100000, respectively, according to Globocan 2020[2].

Although the majority of cases are detected early, with a low risk of lymph node invasion[3], lymph node metastases are an important factor, not only to provide information about staging and prognosis, but also to select adjuvant treatment[4]. Thus, according to the International Federation of Gynaecology and Obstetrics (FIGO) 2009, the standard staging for endometrial cancer is surgical, through total hysterectomy with bilateral salpingo-oophorectomy and pelvic and para-aortic lymphadenectomy (LDN)[5].

Since nodal metastasis in early-stage EC are rare, systematic lymph node removal changes preoperative staging in less than 10% of cases[6]. Furthermore, a Cochrane review from 2017, as well as two recently published studies, revealed that LDN did not improve overall and disease-free survival of patients with presumed stage I disease[6-8]. On the contrary, it was associated with a higher incidence of serious short and long-term adverse events, such as surgery-related systemic morbidity and lymphoedema formation[6,9].

Sentinel lymph node biopsy (SLNB) has therefore been proposed as a less invasive strategy for nodal status assessment. Multiple recent studies demonstrated the advantages of this technique when applied in early-stage endometrial cancer, reporting a high sensitivity, ranging from 91 to 100%, and a negative predictive value of 98--100%[10-12]. Additionally, the ultrastaging technique allows an increase in the detection of malignant cells in sentinel lymph nodes (SLN) compared to the standard histologic examination of non-sentinel lymph nodes (LN)[13-15].

According to multiple research projects and guidelines, indocyanine green (ICG) dye, injected in the cervix, with detection of the SLN under near-infrared (NIR) light, is the recommended tracer in minimally invasive surgery[13,14,16-18], providing the highest detection rate, with a low incidence of adverse effects[13,19,20].

Recent international guidelines updated their recommendations regarding lymph node assessment in endometrial cancer: the guideline from the European Society of Gynaecological Oncology (ESGO), European Society for Radiotherapy and Oncology (ESTRO), and the European Society of Pathology (ESP) recommends SLNB for patients with low-risk/intermediate-risk disease,

advising against systematic LDN in this group[21]. For patients with high-intermediate/high-risk disease lymph node biopsy is considered an acceptable alternative to systematic lymphadenectomy for lymph node staging in stage I/II[21]. The *National Comprehensive Cancer Network* (NCCN) 2021 suggests performing SLNB for the uterine-confined tumour, with a level of evidence 2A[14].

The purpose of this study was to analyse the performance of SLNB using assisted fluorescence imaging of the ICG in patients with early EC, concerning detection rate, sensitivity and negative predictive value (NPV).

METHODS

Patients

From September 2019 to September 2022, a retrospective observational analysis of prospectively collected data in a university-affiliated teaching hospital was performed. Patients with clinical stage I or II histologically confirmed endometrial cancer, who underwent SLN mapping, were included. Patients with synchronous cancer were excluded.

All patients with histologically confirmed EC underwent preoperative evaluation with Magnetic Resonance imaging (MRI) of the pelvis to assess myometrial and cervical invasion. Based on MRI and histopathological results, patients were preoperatively stratified into three risk groups for recurrence (low, intermediate, and high), as defined by the European Consensus (2016)[22] and the Portuguese Guidelines on Gynaecological Cancer (2020)[23]. High-risk group patients also underwent positron emission tomography scan preoperatively to exclude extrauterine disease.

The study was approved by the local institutional Clinical Research and Ethics Committee, with the number 033-2022.

Surgery

Surgery consisted of laparoscopic SLN mapping followed by total laparoscopic hysterectomy with bilateral salpingo-oophorectomy in all patients. Preoperative intermediate and high-risk patients were also submitted to pelvic ± para-aortic lymphadenectomy up to the level of the renal veins and omentectomy in serous EC and carcinosarcoma, by laparotomy or laparoscopy. Systematic LND was skipped in low-risk patients, based on pre-operative evaluation by MRI, or due to low performance status or high surgical risk.

For the SLNB, ICG was used as the tracer, which is provided as 25mg of sterile powder. The powder was diluted in 10 mL of sterile water. Then, prior to the insertion of the manipulator and the beginning of the laparoscopy, ICG solution was slowly injected into the cervix, with a 22-gauge needle, at the 3 and 9 o'clock positions, superficially (3 mm) under the mucosa and deeply (1 cm) in the cervical stroma. At each moment, 0,25 mL of solution was injected, for a total of 1 mL in a concentration of 2,5 mg/mL.

Intraoperatively, fluorescence detection was performed using the *EleVision*™ infrared Platform, *Medtronic*®. After peritoneal evaluation, NIR was activated to identify the tracer in the lymphatic channels, leading to one or more lymph nodes. The identified SLNs were dissected, removed into an endobag and fluorescence confirmed.

Histopathologic Evaluation

All SLNs underwent pathological examination using the ultrastaging technique. Each SLN was sliced at 2 mm intervals and embedded in a paraffin block. Four paraffin-embedded slides were created from each section, 250 µm apart. The slides were stained with Hematoxylin and Eosin, and when negative, analyzed through immunohistochemistry for pan-cytokeratin AE1/AE3 (Dako).

Metastatic disease was classified according to American Joint Committee on Cancer definitions in: isolated tumour cells (single cells or clusters measuring ≤ 0.2 mm), micrometastasis (focus of disease measuring 0.2-2 mm) and macromestastasis (tumour burden > 2 mm)[24].

Statistical analysis

The primary outcome was the SLN detection rate (DR), defined as the detection of SLNs in at least one hemipelvis. The secondary outcomes included bilateral DR, the evaluation of sensitivity, false negative rate, and NPV.

Patients who had mapping of at least one sentinel lymph node were included in the sensitivity and NPV analysis (per protocol). The sensitivity was defined as the proportion of patients with node-positive disease who had metastatic disease correctly identified in SLN. The NPV resulted of the proportion of negative SLN

TABLE I. CLINICOPATHOLOGIC PATIENT CHARACTERISTICS.

Clinicopathologic patient characteristics	n (%)
Age, mean ± SD, years	67.1±10.4
BMI, mean ± SD, Kg/m^2	30.3±5.7
Prior abdominal surgery	22 (39.3)
Postmenopausal	54 (96.4)
Histologic subtype	
Endometrioid carcinoma	49 (87.5)
Serous	3 (5.3)
Clear cell carcinoma	1 (1.8)
Carcinossarcoma	1 (1.8)
Mixed (2)	
– Endometrioid + Serous	1 (1.8)
– Endometrioid + Clear Cell	1 (1.8)
Tumor FIGO Grade (endometrioid carcinoma)[a]	
Low-grade (G1 and G2)	45 (91.8)
High-grade (G3)	4 (8.2)

Abbreviations: BMI, Body mass index; EBL, Estimated blood loss; FIGO, International Federation of Gynecology and Obstetrics; SD, Standard deviation. [a]The denominator was 49.

for metastatic disease associated with negative non-sentinel lymph node specimens.

Regarding the comparative analysis of lymph node involvement, each patient served as her own control regarding SLNB and lymphadenectomy results.

All statistical analyses were performed using IBM SPSS Statistics V.26. The comparative analysis was performed using Fisher's exact test for categorical variables and by Student's T-Test, Mann Whitney and Kruskal-Wallis tests for continuous variables, according to the normality test results. Statistical significance was defined as $p<0.05$.

Descriptive data, including demographics, comorbidities, operative, postoperative, and pathologic findings, are presented as mean ± standard deviation (SD) and as median, [interquartile range (IQR), minimum – maximum], according to normality test results, for continuous variables and as frequency (percentage) for categorical variables, respectively.

RESULTS

During the study period, 59 patients with a diagnosis of endometrial cancer apparently confined to the uterus were evaluated for SLN mapping. Three patients with synchronous cancer (renal, ovarian, and lymphoma) were excluded, leaving 56 cases that met the inclusion criteria.

The mean patient age was 67.1±10.4 years and the mean body mass index (BMI) 30.3±5.7 kg/m^2. Two patients (3.5%) were premenopausal and 22 (39.3%) had at least one previous abdominal surgery. The clinical and histopathological characteristics of the patients are described in Table I.

Among the included patients, pre-operative risk of recurrence was defined as low in 34 cases (60.7%), intermediate in 14 patients (25.0%), and high-risk in 8 cases (14.2%).

The mean operative time was 233±65 minutes and the mean estimated blood loss (EBL) 122±93mL. (Table II) Forty-five patients (91.8%) had low-grade endometrioid EC and eleven (19.6%) had high-grade cancer. (Table I) Most patients (n=47, 83.9%) were diagnosed as stage IA or IB on the final pathology report. (Table III).

After SLN mapping, systematic pelvic LND was performed in 19 (33.9%) patients and para-aortic LND in 9 (16.1%) (Table III). Omentectomy was additionally performed in five patients.

Mapping identified at least one SLN in 54 (96.4%) patients. Bilateral mapping was achieved in 45 (80.3%) cases and unilateral in 9 (16.1%). Of the 9 cases with unilateral mapping, 2 patients had pelvic LND, ano-ther 2 had pelvic and para-aortic LDN, and 5 had only uni-

TABLE II. SURGICAL DATA.

Surgical data	n (%)
Operative time, mean ± SD, minutes	233.7 ± 65.9
EBL, mean ± SD, mL	122.8 ± 93.7
Hospital stay after surgery, mean ± SD, days	3.1 ± 2.4
Surgical complications	
Absent	51 (91.1)
Present	5 (8.9)
– Bowel injury	1 (1.8)
– Nerve injury	3 (5.3)
– Surgical wound infection	1 (1.8)

Abbreviations: EBL, Estimated blood loss; SD, Standard deviation;

TABLE III. POST-OPERATIVE CHARACTERISTICS.

Post-operative characteristics	n (%)
Surgical	
SLN detection	
Any	54 (96.4)
Bilateral	45 (80.3)
Pelvic lymphadenectomy	19 (33.9)
Para-aortic lymphadenectomy	9 (16.1)
Lymph nodes removed	
SLN, mean ± SD	2.5 (±1.7)
Pelvic, mean ± SD	11.1 (±3.8)
Para-aortic, mean ± SD	8.7 (±3.8)
Pathology	
Lymph node metastases	
Yes	6 (10.7)
No	50 (89.3)
Lymphovascular invasion	
Yes	14 (25.0)
No	42 (75.0)
Depth of myometrial invasion	
< 50%	35 (62.5)
> 50%	21 (37.5)
FIGO stage	
IA	32 (57.1)
IB	15 (26.8)
IIIA	3 (5.4)
IIIC1	6 (10.7)

Abbreviations: FIGO, International Federation of Gynecology and Obstetrics; SD, Standard deviation; SLN, Sentinel Lymph node.

lateral SLN sampling without contralateral lymph node evaluation. The latter 5 cases belong to the low-risk recurrence group according to pre-operative evaluation. Two cases with negative bilateral mapping were submitted to pelvic LDN. None of them had LN metastasis.

Overall, 161 SLN were detected and retrieved, with a mean (±SD) number per patient of 2.8 (±1.7). The most frequent location (Table IV) was the obturator fossa (32.9%), followed by the external iliac (32.3%).

Metastatic lymph node involvement was identified in 6 cases (10.7%). Low-grade endometrioid EC was the histologic subtype in 5 cases. One patient had high-grade disease. Four of them were in the low-risk preoperative group and had only bilateral SLN mapping. Two patients had bilateral SLN mapping followed by pelvic and paraaortic LDN in one case. The lymph node histopathological evaluation revealed micrometastases in 4 patients and macrometastases in 2.

Seventeen patients underwent both SLNB and systematic pelvic and/or para-aortic lymphadenectomy. Two of them had LN metastasis. In one case, the SLN was the only positive node, and in the other one, metastases were identified both in SLN and in pelvic LDN. This leads to a sensitivity and NPV of 100%, with a 0% of false negative rate (Table V).

We performed a comparative analysis between the group of 34 patients at low-risk of recurrence who underwent SLN mapping alone (group 1), and the 19 patients from the intermediate and high-risk groups that underwent systematic lymphadenectomy after SLN mapping (group 2) (Table VI). The demographic and clinical characteristics (including age, prior abdominal surgeries and comorbidities) were similar between groups, except for BMI, which was higher in group 1 (median of 32.0 *vs.* 27.5 kg/m^2, p=0.016). We found a significant difference in operative time (median of 190 *vs.* 315 min, p<0.001) and hospital stay after surgery (median of 2 *vs.* 3 days, p=0.001), with both being higher in group 2. However, there was no significant statistical difference in EBL between groups. We noted a higher incidence of adverse events in group 2 (21.1% *vs.* 2.9%, p=0.010). The only surgical complication in group 1 was bowel injury, and there were no adverse effects related to the ICG injection (Table II).

DISCUSSION

This retrospective single-center study aimed to evaluate the accuracy and performance of SLNB using the

TABLE IV. ANATOMICAL LOCATION OF SENTINEL LYMPH NODES.

Anatomical location of Sentinel Lymph Nodes	n (%)
External Iliac	52 (32.3)
Obturator	53 (32.9)
Common Iliac	11 (6.8)
Internal iliac	10 (6.2)
Not described	35 (21.7)

TABLE V. SENSITIVITY AND NPV ANALYSIS.

	LN +	LN –	Total
SLN +	2	0	2
SLN –	0	15	15
Total	2	15	17

Abbreviations: LN, Lymph node; NPV, Negative predictive value; SLN, sentinel lymph node.

cervical injection of ICG dye in endometrial cancer patients.

Our results confirmed the high accuracy of this technique, with a high overall and bilateral DR, 96.4% and 80.3%, respectively. Our favorable results are consistent with several other series reported in the literature, with overall and bilateral DR ranging from 86-100%, and 71-90%, respectively[12,25,26].

In fact, SLN mapping using the cervical injection of ICG was associated with a higher bilateral DR and similar anatomic lymph node distribution as the hysteroscopic dye injection[27] but is easier to perform, making it the recommended alternative to systematic LND by European and NCCN guidelines[14,21].

In our study, lymph node metastases were found in 10.7% of the patients, which is consistent with what is reported in the literature[6], and all were identified by SLN mapping. No paraaortic SLN were detected in our study, which could be explained by the small sample size. The presence of macrometatic SLN was concomitant with non-SLN metastatic involvement.

Contrary to expected, most of the metastatic lymph nodes were found in a low-risk group (4 of 6 cases), and all of them were classified as micrometastases. These metastases would have been missed if the classic protocol had been followed[22]. On the other hand, the incorporation of ultrastaging protocol was of great value for identifying the low-volume metastatic disease, considering that 67% of lymph node metastases in our study were micrometastases. All of them were identified through SLNB in presumed low-risk patients, accounting for a prevalence of 11,7% (4/34) of metastasis in this group. In fact, in a study from 2013, Ballester, et al, also identified positive lymph nodes through SLNB in 12,5% of presumed low-risk patients, with detection by ultrastaging of SLN metastases in 42,8% of patients, which would otherwise have gone undiagnosed by conventional histology[28].

In our centre, for the purpose of staging and adjuvant therapy selection, micrometastases were considered as lymphatic metastases, resulting in the upstaging of patients and prescription of adjuvant chemotherapy to improve survival rates, as recommended by several studies[29,30] and by ESGO, ESTRO and ESP guidelines 2020[21].

In our study, we achieved a sensitivity and NPV of 100%, with a false negative rate of 0% in a total of 17 cases. This was consistent with multiple previous retrospective and prospective studies, which reported

TABLE VI. COMPARATIVE ANALYSIS BETWEEN GROUP 1 AND 2.

	Group 1 (n=34)	Group 2 (n=19)	p
Age, median (IQR; Min – Max)	65.0 (43; 49 – 92)	70 (39; 43 – 82)	0.121
BMI median (IQR; Min – Max)	32.0 (25; 20.1 – 45.4)	27.5 (16.6; 21.0 – 37.6)	**0.016**
Prior abdominal surgery, n (%)	15 (44.1%)	6 (31.6)	0.371
Comorbidities[a], n (%)	21 (61.8%)	9 (47.4%)	0.311
Operative time, median (IQR; Min – Max), minutes	190 (170; 110 – 280)	315 (170; 185 – 355)	**<0.001**
EBL, median (IQR; Min – Max)	80 (395; 5 – 400)	150 (350; 50 – 400)	0.059
Hospital stay after surgery, median (IQR; Min – Max), days	2 (13; 2 – 15)	3 (11; 2 – 13)	**0.001**
Adverse events, n (%)	1 (2.9%)	4 (21.1%)	**0.010**
Metastatic LN involvement, n (%)	4 (11.8%)	2 (10.5%)	0.891

[a] The comorbidities included diabetes mellitus, hypertension, metabolic syndrome, pulmonary obstructive chronic disease, coronary heart disease and/or cardiac insufficiency.

Abbreviations BMI, Body Mass Index; EBL, Estimated Blood Loss; IQR, Interquartile range; LN, Lymphatic nodes.

sensitivities of 92.7- 100% and NPV of 99.0 - 100%[11,12,25]. These results are also in agreement with European Society of Gynaecological Oncology quality indicators for the surgical treatment of endometrial carcinoma[31]. These findings support the high diagnostic accuracy of the SLNB algorithm for EC in detecting lymph node metastases, sparing unnecessary systematic lymphadenectomies.

The comparative analysis between the low-risk and intermediate/high-risk group showed results similar to those described by Cela V. *et al,*[32] for SLN mapping with ICG in robotic-assisted laparoscopic surgery and suggest that SLN mapping with ICG is a safe procedure that allows quicker surgery with fewer complications and faster recovery for EC patients. Moreover, multiple other studies have suggested a high incidence of intra- and post-operative complications when lymphadenectomy is performed (*vs.* SLNB)[6,33]. The ENDO-3 trial (Phase III Randomised Clinical Trial Comparing Sentinel Node Biopsy With No Retroperitoneal Node Dissection in Apparent Early-Stage Endometrial Cancer – ClinicalTrials.gov NCT04073706) will be the first trial to define the incidence of adverse events, healthcare system costs and health-related quality of life of SLN in the surgical treatment of early endometrial cancer[34].

To the best of our knowledge, this is the first study to evaluate the performance of SLNB using ICG in Portugal. We must recognize some limitations of our study, including its small sample size and retrospective single-institution analysis. The strengths rely on the fact that all the surgeries were performed by the same surgical team, minimizing possible discrepancies between different surgeons, and the centralization of all histology samples in the same pathology laboratory, reducing the interobserver bias.

In conclusion, our study provides further evidence to support the clinical application of SLN mapping with ICG cervical injection, as previously demonstrated by other studies. This method appears to be safe and effective in diagnosing lymph node metastases, with a high detection rate and sensitivity. The incorporation of an ultrastaging protocol is crucial for identifying low--volume metastatic disease, which is important for determining definitive staging and adjuvant treatment. In our study, this was especially important for the preoperative low-risk patients' group.

REFERENCES

1. Amant F, Mirza MR, Koskas M, Creutzberg CL. Cancer of the corpus uteri. International Journal of Gynecology and Obstetrics. 2018 Oct 1;143:37-50.

2. IARC new global Cancer Data: GLOBOCAN 2020 | UICC. Int. Agency Res. Cancer (2021)

3. Creasman WT, Morrow CP, Bundy BN, Homesley HD, Graham JE, Heller PB. Surgical Pathologic Spread Patterns of Endometrial Cancer: A Gynecologic Oncology Group Study. 1987 Oct 15;60(8 Suppl):2035-41

4. Sharma C, Deutsch I, Lewin SN, Burke WM, Qiao Y, Sun X, et al. Lymphadenectomy influences the utilization of adjuvant radiation treatment for endometrial cancer. Am J Obstet Gynecol. 2011;205(6):562.e1-562.e9.

5. Pecorelli S. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. Vol. 105, International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2009. p. 103-4.

6. Frost JA, Webster KE, Bryant A, Morrison J. Lymphadenectomy for the management of endometrial cancer. Vol. 2017, Cochrane Database of Systematic Reviews. John Wiley and Sons Ltd; 2017.

7. Bougherara L, Azaïs H, Béhal H, Canlorbe G, Ballester M, Bendifallah S, et al. Does lymphadenectomy improve survival in patients with intermediate risk endometrial cancer? A multicentric study from the FRANCOGYN Research Group. International Journal of Gynecological Cancer. 2019 Feb 1;29(2):282-9.

8. Zheng Y, Yang X, Liang Y, Zhang T, Chen J, Li Y, et al. Effects of lymphadenectomy among women with stage IA endometrial cancer: A SEER database analysis. Future Oncology. 2019 Jul 1;15(19):2251-66.

9. Dowdy SC, Borah BJ, Bakkum-Gamez JN, Weaver AL, McGree ME, Haas LR, et al. Prospective assessment of survival, morbidity, and cost associated with lymphadenectomy in low-risk endometrial cancer. Gynecol Oncol. 2012 Oct;127(1):5-10.

10. Ye L, Li S, Lu W, He Q, Li Y, Li B, et al. A Prospective Study of Sentinel Lymph Node Mapping for Endometrial Cancer: Is It Effective in High-Risk Subtypes? Oncologist. 2019 Dec 1;24(12):e1381-7.

11. Cusimano MC, Vicus D, Pulman K, Maganti M, Bernardini MQ, Bouchard-Fortier G, et al. Assessment of Sentinel Lymph Node Biopsy vs Lymphadenectomy for Intermediate- And High-Grade Endometrial Cancer Staging. JAMA Surg. 2021 Feb 1;156(2):157-64.

12. Rossi EC, Kowalski LD, Scalici J, Cantrell L, Schuler K, Hanna RK, et al. A comparison of sentinel lymph node biopsy to lymphadenectomy for endometrial cancer staging (FIRES trial): a multicentre, prospective, cohort study. Lancet Oncol. 2017 Mar 1;18(3):384-92.

13. Holloway RW, Abu-Rustum NR, Backes FJ, Boggess JF, Gotlieb WH, Jeffrey Lowery W, et al. Sentinel lymph node mapping and staging in endometrial cancer: A Society of Gynecologic Oncology literature review with consensus recommendations. Vol. 146, Gynecologic Oncology. Academic Press Inc.; 2017. p. 405-15.

14. Nicole McMillian N, Angela Motter M, Frederick P, Gaffney DK, George S, Giuntoli RI, et al. NCCN Clinical Practice Guidelines in Oncology – Uterine Neoplasms. Version 1.2022

15. Delpech Y, Cortez A, Coutant C, Callard P, Uzan S, Darai E, et al. The sentinel node concept in endometrial cancer: Histopathologic validation by serial section and immunohistochemistry. Annals of Oncology. 2007;18(11):1799-803.

16. Bodurtha Smith AJ, Fader AN, Tanner EJ. Sentinel lymph node assessment in endometrial cancer: a systematic review and meta-analysis. Vol. 216, American Journal of Obstetrics and Gynecology. Mosby Inc.; 2017. p. 459-476.e10.

17. Khoury-Collado F, st. Clair C, Abu-Rustum NR. Sentinel Lymph Node Mapping in Endometrial Cancer: An Update. Oncologist. 2016 Apr 1;21(4):461-6.

18. Nagar H, Wietek N, Goodall RJ, Hughes W, Schmidt-Hansen M, Morrison J. Sentinel node biopsy for diagnosis of lymph node involvement in endometrial cancer. Vol. 2021, Cochrane Database of Systematic Reviews. John Wiley and Sons Ltd; 2021.

19. Reneé Franklin C, Tanner EJ. Where Are We Going with Sentinel Lymph Node Mapping in Gynecologic Cancers? Vol. 20, Current Oncology Reports. Current Medicine Group LLC 1; 2018.

20. Zhai L, Zhang X, Cui M, Wang J. Sentinel Lymph Node Mapping in Endometrial Cancer: A Comprehensive Review. Vol. 11, Frontiers in Oncology. Frontiers Media S.A.; 2021.

21. Concin N, Matias-Guiu X, Vergote I, Cibula D, Mirza MR, Marnitz S, et al. ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. Vol. 31, International Journal of Gynecological Cancer. BMJ Publishing Group; 2021. p. 12-39.

22. Colombo N, Creutzberg C, Amant F, Bosse T, González-Martón A, Ledermann J, et al. ESMO-ESGO-ESTRO consensus conference on endometrial cancer: Diagnosis, treatment and follow-up. Annals of Oncology. 2016 Jan 1;27(1):16-41.

23. Cancro Ginecológico, Consensos Nacionais 2020 [Internet]. [cited 2022 Nov 1]. Available from: https://spginecologia.pt/wp-content/uploads/2021/07/spg-consenso-nacional-cancro-ginecologico-2020.pdf

24. AJCC Cancer Staging Atlas. AJCC Cancer Staging Atlas. Springer New York; 2012.

25. Lee GW, Park JY, Kim DY, Suh DS, Kim JH, Kim YM, et al. Usefulness of sentinel lymph node mapping using indocyanine green and fluorescent imaging in the diagnosis of lymph node metastasis in endometrial cancer. J Obstet Gynaecol (Lahore). 2021;41(4):605-11.

26. Bellaminutti S, Bonollo M, Gasparri ML, Clivio L, Migliora P, Mazzucchelli L, et al. Sentinel lymph node intraoperative analysis in endometrial cancer. J Cancer Res Clin Oncol. 2020 Dec 1; 146(12):3199-205.

27. Leitao MM. Sentinel Lymph Node Mapping in Patients with Endometrial Carcinoma: Less Can Be More. Vol. 5, Current Obstetrics and Gynecology Reports. Current Medicine Group LLC 1; 2016. p. 279-85.

28. Ballester M, Naoura I, Chéreau E, Seror J, Bats AS, Bricou A, et al. Sentinel node biopsy upstages patients with presumed low- and intermediate-risk endometrial cancer: Results of a multicenter study. Ann Surg Oncol. 2013 Feb;20(2):407-12.

29. Ignatov A, Lebius C, Ignatov T, Ivros S, Knueppel R, Papathemelis T, et al. Lymph node micrometastases and outcome of endometrial cancer. Gynecol Oncol. 2019 Sep 1;154(3):475-9.

30. st. Clair CM, Eriksson AGZ, Ducie JA, Jewell EL, Alektiar KM, Hensley ML, et al. Low-Volume Lymph Node Metastasis Discovered During Sentinel Lymph Node Mapping for Endometrial Carcinoma. Ann Surg Oncol. 2016 May 1;23(5):1653-9.

31. Concin N, Planchamp F, Abu-Rustum NR, Ataseven B, Cibula D, Fagotti A, et al. European Society of Gynaecological Oncology quality indicators for the surgical treatment of endometrial carcinoma. Int J Gynecol Cancer. 2021 Dec 1;31(12):1508-29.

32. Cela V, Sergiampietri C, Rosa Obino ME, Bifulco G, Giovanni Artini P, Papini F. Sentinel-lymph-node mapping with indocyanine green in robotic-assisted laparoscopic surgery for early endometrial cancer: a retrospective analysis. Facts Views Vis Obgyn 2020 Mar 27;11(4):323-328

33. Dowdy SC, Borah BJ, Bakkum-Gamez JN, Weaver AL, McGree ME, Haas LR, et al. Prospective assessment of survival, morbidity, and cost associated with lymphadenectomy in low-risk endometrial cancer. Gynecol Oncol. 2012 Oct 1;127(1):5-10.

34. Obermair A, Nicklin J, Gebski V, Hayes SC, Graves N, Mileshkin L, et al. A phase III randomized clinical trial comparing sentinel node biopsy with no retroperitoneal node dissection in apparent early-stage endometrial cancer - ENDO-3: ANZGOG trial 1911/2020. Int J Gynecol Cancer. 2021 Dec;31(12):1595-1601.

AUTHORS' CONTRIBUTION STATEMENT

Kristina Hundarova and Cláudia Andrade contributed to the concept and study design. Cláudia Andrade was responsible for the collection of data. Kristina Hundarova was responsible for the analysis and interpretation of data and the article draft. Cristina Frutuoso, Fernanda Águas and Cláudia Andrade supervised the team research and revised the article critically. All authors approved the final article as submitted and agreed to be accountable for all aspects of the work.

CONFLICTS OF INTEREST

The authors declare that there were no conflicts of interest in writing this manuscript.

FINANCIAL SUPPORT

The authors declare that there was no public or private financial support in writing this manuscript.

CORRESPONDENCE TO:

Kristina Hundarova
E-mail: Kristina.hundarova@gmail.com
https://orcid.org/0000-0003-1756-4219

RECEIVED: 12/02/2023
ACCEPTED: 03/09/2023