European Journal of Surgical Oncology xxx (xxxx) xxx

Contents lists available at ScienceDirect

European Journal of Surgical Oncology

journal homepage: www.ejso.com

Hysteroscopic endometrial tumor localization and sentinel lymph node mapping. An upgrade of the hysteroscopic role in endometrial cancer patients

Vito Andrea Capozzi [a, *], Giulia Armano [a], Giuseppe Maglietta [b], Andrea Rosati [c], Virginia Vargiu [c, d], Elisa Scarpelli [a], Giulio Sozzi [e], Vito Chiantera [e], Francesco Cosentino [d, g], Alessandro Gioè [c], Ursula Catena [c], Giovanni Scambia [c], Francesco Fanfani [c], Attilio Di Spiezio Sardo [f], Tullio Ghi [a], Roberto Berretta [a]

[a] Department of Medicine and Surgery, University Hospital of Parma, Parma, Italy
[b] Clinical and Epidemiological Research Unit, University Hospital of Parma, University of Parma, Parma, Italy
[c] Division of Gynecologic Oncology, Department of Woman and Child Health and Public Health, Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy
[d] Department of Oncology, Gemelli Molise Spa, Campobasso, Italy
[e] Department of Gynecologic Oncology, University of Palermo, Palermo, Italy
[f] Department of Public Health, School of Medicine, University of Naples Federico II, Naples, Italy
[g] Dipartimento di Medicina e Scienze della Salute "Vincenzo Tiberio", Università del Molise, Campobasso, Italy

ARTICLE INFO

Article history:
Received 9 March 2023
Received in revised form
4 June 2023
Accepted 5 June 2023
Available online xxx

Keywords:
Endometrial cancer
Hysteroscopy
Sentinel lymph node biopsy

ABSTRACT

Introduction: Given the growing interest in sentinel node mapping (SLN) biopsy in Endometrial Cancer (EC) patients, many efforts have been made to maximize the SLN bilateral detection rate. However, at present, no previous research assessed the potential correlation between primary EC location in the uterine cavity and SLN mapping. In this context, this study aims to investigate the possible role of intrauterine EC hysteroscopic localization in predicting SLN nodal placement.

Materials and methods: EC patients surgically treated from January 2017 to December 2021 were retrospectively analyzed. All patients underwent hysterectomy, bilateral salpingo-oophorectomy, and SLN mapping. During hysteroscopy, the location of the neoplastic lesion was described as follows: uterine fundus (comprising the most cranial portion of the uterine cavity up to the tubal ostium including the cornual areas), corpus uteri (from the tubal ostium to the inner uterine orifice), and diffuse (when the tumor invades more than 50% of the uterine cavity).

Results: Three hundred ninety patients met the inclusion criteria. The tumor pattern diffused to the whole uterine cavity was statistically associated with SLN uptake on common iliac lymph nodes (OR 2.4, 95%CI 1–5.8, $p = 0.05$). Patients'age is an independent factor associated with SLN failure (OR: 0.95, 95%CI 0.93–0.98, $p < 0.001$).

Conclusions: The study showed a statistically significant association between EC hysteroscopically spread throughout the whole uterine cavity and SLN uptake at the common iliac lymph nodes. Furthermore, patient age negatively affected the SLN detection rate.

© 2023 Elsevier Ltd, BASO ~ The Association for Cancer Surgery, and the European Society of Surgical Oncology. All rights reserved.

1. Introduction

Endometrial cancer (EC) is the most common gynecological neoplasm with almost 417.000 new cases diagnosed worldwide in 2020 [1]. EC incidence increased by 132% in the last 30 years due to a higher prevalence of EC risk factors [2]. The aging population and

* Corresponding author. Department of Medicine and Surgery, University Hospital of Parma, Parma, via Gramsci, 43125, Italy.
E-mail address: vitoandrea.capozzi@studenti.unipr.it (V.A. Capozzi).

https://doi.org/10.1016/j.ejso.2023.06.004
0748-7983/© 2023 Elsevier Ltd, BASO ~ The Association for Cancer Surgery, and the European Society of Surgical Oncology. All rights reserved.

Please cite this article as: V.A. Capozzi, G. Armano, G. Maglietta *et al.*, Hysteroscopic endometrial tumor localization and sentinel lymph node mapping. An upgrade of the hysteroscopic role in endometrial cancer patients, European Journal of Surgical Oncology, https://doi.org/10.1016/j.ejso.2023.06.004

the growing obesity prevalence are reported as the main causes of this phenomenon [3]. EC is often diagnosed at an early stage due to the presence of onset symptoms [4]. In case of abnormal uterine bleeding, current international guidelines recommend hysteroscopy as the preferred approach for endometrial biopsy [5]. Compared with foregoing blind biopsies, Hysteroscopy allows direct visualization with high magnification of the uterine cavity and enables a guided biopsy performance also in an outpatient setting [6]. Furthermore, hysteroscopy-guided biopsy showed higher accuracy in endometrial cancer histological type and grade diagnosis, allowing proper planning of the subsequent surgical treatment [7,8]. Conversely, Dilatation and Curettage require an operating room and a 10% false negative in EC detection has been reported caused by scraping of less than 50% of the endometrial cavity [9,10]. Besides, the Pipelle biopsy reliability can be affected by an inadequate sample for histologic examination and the risk of missing focal anomalies [11]. Thereby, some authors suggest that blind endometrial biopsy techniques should be abandoned [12].

Currently, EC surgical treatment consists of total hysterectomy, bilateral salpingo-oophorectomy, and nodal staging through sentinel node mapping (SLN). Minimally invasive surgery (MIS) is the recommended approach in early-stage EC [5]. Robotic surgery, compared to traditional laparoscopy, extended MIS boundaries also in the context of extremely obese and very elderly patients [13,14].

Since lymphadenectomy has been proven not to improve survival, and SLN accuracy in detecting nodal metastasis reaches 96%, SLN became the gold standard for nodal staging in EC patients [15,16]. Furthermore, SLN biopsy feasibility and oncological safety are currently being prospectively evaluated also in the context of high-risk EC [17]. Given the growing interest in SLN biopsy in EC patients, many efforts have been made to maximize the SLN bilateral detection rate through an optimized injection technique and accurate lymphatic pathways identification [18,19].

In 2018 the FILM trial, a randomized clinical trial including 180 patients with endometrial or cervical cancer, reported the non-inferiority of indocyanine green (ICG) compared to blue dye with a bilateral detection rate of 82% vs 32% respectively. Consequently, ICG is currently the preferred tracer.

In addition, growing expertise about the best infiltration technique, the widespread adoption of sentinel node biopsy, and a deeper knowledge of unfavorable factors for SLN detection led over the years to a progressive improvement in the overall and bilateral SLN detection rate. Starting from the 52% bilateral detection rate reported in the FIRES trial [20], today most authors describe a bilateral detection rate of more than 75% [21–23]. Advanced age, obesity, lymphovascular space invasion, presence of nodal metastasis, non-endometrioid histology, and previous surgery has been described as risk factors for SLN failure [24–26].

Previous studies described different pathways of uterine lymphatic drainage for specific uterine regions [27–29]. Furthermore, several studies evidenced improved bilateral SLN detection rate through reinjection in failed mapping cases, use of Indocyanine Green dye, and cervical infiltration performed by experienced surgeons [23,25,30].

However, at present, no previous research assessed the potential correlation between primary EC location in the uterine cavity and SLN detection in or outside the pelvis. In this context, to further improve SLN intraoperative detection rate, this study aims to investigate the possible role of intrauterine EC hysteroscopic localization in predicting SLN pelvic or extrapelvic nodal placement.

2. Material and methods

EC patients treated consecutively at the University Hospital of Parma, Department of Women's, Children's and Public Health Sciences Agostino Gemelli University Polyclinic Foundation IRCCS of Rome, Gynecologic Oncology Unit A. R.N.A.S. Ospedali Civico Di Cristina Benfratelli of Palermo, University Hospital Federico II Integrated Maternal and Child Care Department of Naples, and Department of Gynecologic Oncology Gemelli Molise SpA of Campobasso from January 2017 to December 2021 were retrospectively analyzed.

All medical history, clinical, instrumental investigation, anatomopathological, and surgical treatment details were collected for each patient. All patients underwent a laparoscopic or robotic surgical treatment for apparent early-stage EC including hysterectomy, bilateral salpingo-oophorectomy, and SLN mapping. Four ml of ICG were injected into the cervical stroma at 3 and 9 o'clock. SLN pathologic assessment included ultrastaging and cytokeratin immunohistochemistry. Inclusion criteria required that all patients had performed diagnostic hysteroscopy at the tertiary cancer centers where they were then treated. Hysteroscopies were performed in an ambulatory outpatient setting or operating room with a fluid-distending medium delivered by pressure bag or a peristaltic pump. Normal saline or hypotonic solutions were used as a distension medium depending on the type of instrumentation adopted. Through direct identification of endometrial lesions suggestive of EC, targeted endometrial biopsies were collected by using one of the following instruments: continuous flow hysteroscopes with an oblique view and an operating 5 Fr channel; 15 Fr, 26 Fr, and 27 Fr resectoscopes armed with either monopolar or bipolar loops; Hysteroscopic Tissue Removal Devices. During hysteroscopy, the location of the neoplastic lesion was described as follows: uterine fundus (comprising the most cranial portion of the uterine cavity up to the tubal ostium including the cornual areas), corpus uteri (from the tubal ostium to the inner uterine orifice), and diffuse (when the tumor invades more than 50% of the uterine cavity) [31,32]. Once the malignant nature of the endometrial lesion was histologically confirmed, international guidelines were followed for preoperative workup [5,33]. The Memorial Sloan Kettering Cancer Center Algorithm was applied for SLN mapping [34]. During surgery, surgeons described the SLN location for each hemipelvis as follows: parametrial, internal iliac, external iliac, common iliac, para-aortic, paracaval, interaortocaval, sacral, and obturator. In case of SLN failed mapping, a side-specific lymphadenectomy of the non-capturing hemipelvis was performed.

Patients <18 years old, with missing pathological data, who performed EC diagnosis not by hysteroscopy, or women not consenting to the publication of their data for scientific purposes were excluded from the analysis.

The primary objective was to determine whether a correlation is present between endometrial tumor location within the uterine cavity and the SLN site within or outside the pelvis. In case of SLN failed mapping, the secondary aim was to identify factors correlated with failed tracer uptake in the lymph node stations.

The authors ensure that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki). All patients gave informed consent for the publication of their anonymized data for scientific purposes.

This retrospective multicenter study was approved by the Parma Ethics Committee under code 181/2021/OSS/AOUPR [19].

2.1. Statistical analysis

The baseline characteristics of patients were summarized by absolute numbers and relative frequencies (percentages) for categorical variables and mean values ± standard deviation (SD) for continuous variables. Comparisons are respectively performed by using the chi-squared test using a *t*-test for independent samples.

To describe the explorative hypothesis aimed to identify if at least one tumor site could be frequently intercepted by a tracer, a contingency table was developed with a chord diagram to graphically represent every single connection and its relative frequencies. Multinomial models were implemented to measure the simultaneous associations among SLN locations and tumor sites. Overall and stratified right and left tracer models were performed, and the degree of the association was summarized with Odds Ratio (OR), 95% Confidence Interval (CI), and p-values. Finally, the multivariable ordinal logistic regression model was developed to test the main factor associated with the three levels of SLN detection outcome (0 = none, 1 = unilateral, 2 = bilateral). The R Statistical software version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analyses.

3. Results

Three hundred ninety patients met the inclusion criteria during the study period. Patient characteristics are summarized in Table 1. Median age was 65 years (range 37–88) and median BMI was 29 kg/m^2 (range 18–51). Table 2 shows that the corpus uteri is the most frequent location among the three uterine tumor sites (258 cases, 66.9%) followed by 81 (20.8%) patients with EC located on the uterine fundus, and 51 (13.1%) women with cancer spread to the whole uterine cavity. On the other hand, SLN mapping on external iliac lymph nodes was reported in 420 (53.8%) patients, followed by obturators (141; 18.1%), common iliac (56; 7.2%), and internal iliac (33; 4.2%) lymph nodes. Regarding the primary outcome, only the tumor pattern diffused to the whole uterine cavity was statistically associated with SLN uptake on common iliac lymph nodes (OR 2.4, 95%CI 1–5.8, p = 0.05). Conversely, EC arising from the uterine corpus and fundus did not show significant correlations with SLN localizations (see chord diagram representation in Fig. 1).

Of the entire series, 298 (76.4%) patients showed bilateral SLN uptake, 62 (15.9%) unilateral uptake, and in 30 (7.7%) cases SLN failed. Table 3 shows the results of the multivariable ordinal logistic regression analysis in which only age is an independent factor negatively associated with the SLN detection (OR: 0.95, 95%CI

Table 1
Patients' characteristics.

Variable		n; %
Age median (years, range)		65 (37–88)
BMI median (Kg/m^2)		29 (18–51)
Histology	Endometrioid	325; 83.3
	Not Endometrioid	65; 16.7
FIGO Stage	IA	182; 46.9
	IB	105; 26.9
	II	36; 9.2
	IIIA	9; 2.3
	IIIB	2; 0.5
	IIIC1	46; 11.8
	IIIC2	7; 1.8
	IVB	3; 0.6
Tumor Grade	G1	135; 34.5
	G2	160; 41.1
	G3	95; 24.4
LVSI	Substantial	70; 18
	Focal	121; 31
	Negative	199; 51
Surgical approach	Laparoscopy	344; 87.2
	Robotic-assisted laparoscopy	46; 11.8
Mapping	Bilateral	298; 76.4
	Monolateral	62; 15.9
	Absent	30; 7.7
Nodal staging		
SLN biopsy only		280; 71.8
Lymphadenectomy		
	Monolateral pelvic lymphadenectomy	55; 14.1
	Bilateral pelvic lymphadenectomy	55; 14.1
	Lomboaortic lymphadenectomy	16; 4.1
FIGO stage IIIC		53
	SLN positive	35; 66
	lymphadenectomy	18; 34
SLN status		280
	N0	237; 84.6
	Ni	8; 2.9
	Nmi	11; 3.9
	N1	24; 8.6
Adjuvant treatment	Brachytherapy	75; 19.2
	External-beam radiotherapy	56; 14.4
	Chemotherapy + Radiotherapy	63; 16.2
	Chemotherapy	16; 4.1

BMI: Body Mass Index; SLN: sentinel lymph node; N0: negative node; Ni: isolated tumor cells; Nmi: micrometastasis; N1: macrometastasis.

Table 2
Uterine tumor site and SLN locations.

	Total Patients n; %	Total Emipelvis n; %	External Iliac n; % (p-value)	Obturator n; % (p-value)	Common Iliac n; % (p-value)	Internal Iliac/Parametrial n; % (p-value)	Failed Mapping n; %
Total	**390; 100**	**780; 100**	**420; 53.8**	**141; 18.1**	**56; 7.2**	**33; 4.2**	**130; 16.7**
Corpus	258; 66.9	516; 66.2	276; 53.5 (0.56)	94; 18.2 (0.96)	35; 6.8 (0.52)	24; 4.7 (0.52)	87; 16.9
Fundus	81; 20.8	162; 20.8	84; 51.9 (0.35)	31; 19.1 (0.72)	10; 6.2 (0.37)	6; 3.7 (0.49)	31; 19.1
Diffuse	51; 13.1	102; 13.1	60; 58.8 (0.14)	16; 15.7 (0.57)	11; 10.8 (**0.05**)	3; 2.9 (0.98)	12; 11.8

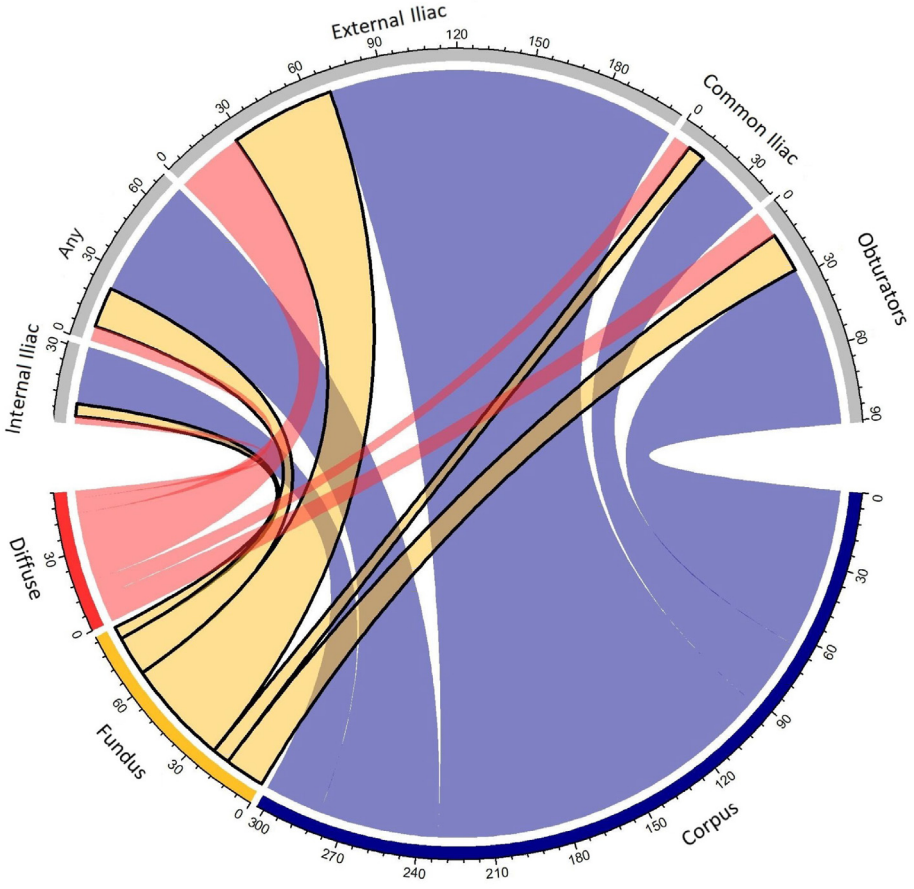

Fig. 1. Chord diagram representation of uterine tumor site with sentinel lymph node localization.

Table 3
Multivariable ordinal logistic regression analysis for SLN failure risk factors.

	Odds Ratio	95% Confidence Interval	p value
Age	0.95	0.92–0.98	<0.001
BMI	0.96	0.92–1.00	0.06
Endometrioid histology	1.45	0.65–3.13	0.35
Figo Stage IIIC1	0.78	0.65–1.62	0.49
Uterine tumor location			
Fundus	0.61	0.34–1.13	0.11
Corpus	1.06	0.61–1.81	0.83
Diffuse	2.24	0.92–6.38	0.10

SLN: sentinel lymph node; BMI: Body Mass Index. FIGO: International Federation of Gynecology and Obstetrics.

0.93–0.98, $p < 0.001$). On the contrary, the uterine tumor site (diffuse vs corpus/fundus) showed no statistically significant correlation with SLN mapping failure (OR: 2.24, 95%CI 0.92–6.38 $p = 0.097$). Finally, BMI showed a bordering statistical association with SLN failure (OR: 0.96, 95%CI 0.92–1.00; $p = 0.058$).

4. Discussion

4.1. Study finding

The present study found that EC hysteroscopically spread over the entire uterine cavity was statistically associated with SLN mapping at the level of common iliac lymph nodes. In addition, the patient's age negatively affected the bilateral SLN detection rate.

4.2. Interpretation

From the previous experience of various authors, we can state that uterine lymphatic drainage pathways are extremely complex, suffer from enormous interindividual variability, and are anastomosed to each other [15,35,36]. These aspects make the interpretation of our results particularly arduous. Anyway, although there are no studies with objectives overlapping with ours, interpretations of our results could be multiple even if speculative. First, diffuse tumors within the uterine cavity could cause huge

neoplastic lymphangitis occluding the smaller lymphatic pathways thus promoting drainage into the larger lymphatic channels draining to the common iliac lymph nodes. Then, In diffuse tumor forms increased lymph load could be produced by the neoplastic cells with the development of new lymphatic drainage pathways draining into the common iliac lymph nodes. Finally, the increased lymph load could create a greater pressure gradient within the lymphatic vessels favoring the skipping of lymph node stations more proximal to the uterus with dye collection at the most distal nodal stations.

Moreover, as previously reported by Cianci et al. [24], patient age would cause physiologic deterioration of lymphatic channels and increased permeability of lymphatic ducts resulting in reduced SLN dye uptake.

4.3. Previous literature and clinical implication

Over the years, several authors attempted to improve SLN detection by studying different types of tracers, infiltration sites, and dye infiltration techniques. In a recent meta-analysis comparing ICG, Blue dye, and (99)Tc, Ruscito et al. [37] reported that ICG showed higher overall (95% CI 0.15–0.50; $p < 0.001$) and bilateral SLN detection rates (95% CI 0.19–0.40; $p < 0.001$) than the other tracers. In 2021, Ditto et al. [38] demonstrated with a multicenter prospective randomized controlled trial of the MITO group that cervical infiltration was superior in SLN detection compared with hysteroscopic ICG injection. Finally, Persson et al. [39] first showed the superiority of re-injection in SLN mapping failure over the single dye injection.

As mentioned above, all these efforts lead to a bilateral detection rate of more than 75% in the literature [21–23]. Nevertheless, the SLN detection rate is still highly variable among various cancer centers and side-specific lymphadenectomy is burdened with severe morbidities negatively impacting patient quality of life [40].

In this scenario, the present study would help the surgeon in SLN identification. In patients with EC spread to the entire uterine cavity, the gynecologist should pay major attention to the exploration of common iliac lymph nodes. Finally, as this data is preoperative, the results of our study allow better planning of the patient's surgery. Surgical exploration of level 2 pelvic lymph nodes (common and presacral iliac) is certainly more complex than level 1 (external and obturator iliac), therefore, in selected cases, an experienced surgeon should be available to maximize SLN detection.

4.4. Strengths and limitations

The merit of this study lies in the large case series collected in referral cancer centers with strict adherence to the most updated international guidelines. Besides, to our best knowledge, no study investigated the correlation between hysteroscopic tumor localization and SLN identification before the present study. On the other hand, the retrospective nature is the major limitation of the study. Data about survival, tumor location, and prognosis are missing.

Furthermore, the arbitrary partition of the uterine cavity into three slices was due to statistical issues. A finer description of the hysteroscopic tumor localizations would not have allowed an adequate number of cases to achieve the objective of the study. In addition, atypical SLN locations were not considered, as well as SLN mapping in the presence of node metastasis, and this may have influenced our results. Therefore, further prospective studies with more cases are needed to better explore this topic.

5. Conclusions

The study showed a statistically significant association between EC hysteroscopically spread throughout the whole uterine cavity and SLN uptake at the common iliac lymph nodes. Furthermore, patient age negatively affected the SLN detection rate.

CRediT authorship contribution statement

Vito Andrea Capozzi: Study concepts, Formal analysis, interpretation, Formal analysis, Manuscript preparation. **Giulia Armano:** Study concepts, Manuscript preparation. **Giuseppe Maglietta:** Study design, Formal analysis, interpretation, Formal analysis, Manuscript preparation. **Andrea Rosati:** Study design. **Virginia Vargiu:** Study design. **Elisa Scarpelli:** Data acquisition. **Giulio Sozzi:** Data acquisition. **Vito Chiantera:** Quality control of data, algorithms, Manuscript review. **Francesco Cosentino:** Quality control of data , algorithms. **Alessandro Gioè:** Data acquisition. **Ursula Catena:** Manuscript editing. **Giovanni Scambia:** Manuscript review. **Francesco Fanfani:** Quality control of data and algorithms, Manuscript editing, Manuscript review. **Attilio Di Spiezio Sardo:** Manuscript editing, Manuscript review. **Tullio Ghi:** Formal analysis, interpretation, Manuscript editing. **Roberto Berretta:** Study concepts, Formal analysis, interpretation, Manuscript preparation.

Declaration of competing interest

None of the authors has a conflict of interest to declare.

References

[1] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA A Cancer J Clin 2021;71(3):209–49. https://doi.org/10.3322/caac.21660.

[2] Gu B, Shang X, Yan M, Li X, Wang W, Wang Q, et al. Variations in incidence and mortality rates of endometrial cancer at the global, regional, and national levels, 1990-2019.,". Gynecol Oncol 2021;161(2):573–80. https://doi.org/10.1016/j.ygyno.2021.01.036.

[3] Crosbie EJ, Kitson SJ, McAlpine JN, Mukhopadhyay A, Powell ME, Singh N. Endometrial cancer. Lancet (London, England) 2022;399(10333):1412–28. https://doi.org/10.1016/S0140-6736(22)00323-3.

[4] Trojano G, Olivieri C, Tinelli R, Damiani GR, Pellegrino A, Cicinelli E. Conservative treatment in early stage endometrial cancer: a review. Acta Biomed : Atenei Parmensis 2019;90(4):405–10. https://doi.org/10.23750/abm.v90i4.7800".

[5] Concin N, Matias-Guiu X, Vergote I, Cibula D, Mirza MR, Marnitz, et al. ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma.,". Int J Gynecol Cancer : Off J Int Gynecol Cancer Soc 2021;31(1):12–39. https://doi.org/10.1136/ijgc-2020-002230.

[6] Bourdel N, Chauvet P, Tognazza E, Pereira B, Botchorishvili R, Canis M. Sampling in atypical endometrial hyperplasia: which method results in the lowest underestimation of endometrial cancer? A systematic review and meta-analysis.,". J Minim Invasive Gynecol 2016;23(5):692–701. https://doi.org/10.1016/j.jmig.2016.03.017.

[7] Di Spiezio Sardo A, De Angelis MC, Della Corte L, Carugno J, Zizolfi B, Guadagno E, et al. Should endometrial biopsy under direct hysteroscopic visualization using the grasp technique become the new gold standard for the preoperative evaluation of the patient with endometrial cancer? Gynecol Oncol 2020;158(2):347–53. https://doi.org/10.1016/j.ygyno.2020.05.012.

[8] Lago V, Martín B, Ballesteros E, Cárdenas-Rebollo JM, Minig L. Tumor grade correlation between preoperative biopsy and final surgical specimen in endometrial cancer:," The use of different diagnostic methods and analysis of associated factors. Int J Gynecol Cancer 2018;28(7):1258–63. https://doi.org/10.1097/IGC.0000000000001304.

[9] Bettocchi S, Ceci O, Vicino M, Marello F, Impedovo L, Selvaggi L. Diagnostic inadequacy of dilatation and curettage. Fertil Steril 2001;75(4):803–5. https://doi.org/10.1016/s0015-0282(00)01792-1.

[10] Rosenblatt P, Barcia S, DiSciullo A, Warda H. Improved adequacy of endometrial tissue sampled from postmenopausal women using the MyoSure Lite hysteroscopic tissue removal system versus conventional curettage,". Int J Wom Health 2017;9:789–94. https://doi.org/10.2147/IJWH.S147338.

[11] Terzic MM, Aimagambetova G, Terzic S, Norton M, Bapayeva G, Garzon S. Current role of Pipelle endometrial sampling in early diagnosis of endometrial cancer. Transl Cancer Res 2020 Dec;9(12):7716–24. https://doi.org/10.21037/

tcr.2020.04.20.
[12] Kotdawala P, Kotdawala S, Nagar N. Evaluation of endometrium in perimenopausal abnormal uterine bleeding. J Midlife Health 2013 Jan;4(1):16–21. https://doi.org/10.4103/0976-7800.109628. 23833528.
[13] Gallotta V, Conte C, D'Indinosante M, et al. Robotic surgery in elderly and very elderly gynecologic cancer patients. J Minim Invasive Gynecol 2018;25(5):872–7. https://doi.org/10.1016/j.jmig.2018.01.007.
[14] Cusimano MC, Simpson AN, Dossa F, et al. Laparoscopic and robotic hysterectomy in endometrial cancer patients with obesity: a systematic review and meta-analysis of conversions and complications. Am J Obstet Gynecol 2019;221(5):410–28. https://doi.org/10.1016/j.ajog.2019.05.004. *e19*.
[15] Benedetti-Panici P, Maneschi F, Scambia G, Greggi S, Mancuso S. Anatomic abnormalities of the retroperitoneum encountered during aortic and pelvic lymphadenectomy. Am J Obstet Gynecol 1994 Jan;170(1 Pt 1):111–6. https://doi.org/10.1016/s0002-9378(94)70394-9.
[16] ASTEC study group, Kitchener H, Swart AM, Qian Q, Amos C, Parmar MK. Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study [published correction appears in Lancet. Lancet 2009;373(9658):125–36. https://doi.org/10.1016/S0140-6736(08)61766-3. 2009 May 23;373(9677):1764.
[17] Baiocchi G, Andrade CEMC, Ribeiro R, et al. Sentinel lymph node mapping versus sentinel lymph node mapping with systematic lymphadenectomy in endometrial cancer: an open-label, non-inferiority, randomized trial (ALICE trial). Int J Gynecol Cancer 2022;32(5):676–9. https://doi.org/10.1136/ijgc-2022-003378. Published 2022 May 3.
[18] Body N, Grégoire J, Renaud MC, Sebastianelli A, Grondin K, Plante M. Tips and tricks to improve sentinel lymph node mapping with Indocyanin green in endometrial cancer. Gynecol Oncol 2018;150(2):267–73. https://doi.org/10.1016/j.ygyno.2018.06.001.
[19] Bollino M, Geppert B, Lönnerfors C, Falconer H, Salehi S, Persson J. Pelvic sentinel lymph node biopsy in endometrial cancer-a simplified algorithm based on histology and lymphatic anatomy. Int J Gynecol Cancer : Off J Int Gynecol Cancer Soc 2020;30(3):339–45. https://doi.org/10.1136/ijgc-2019-000935.
[20] 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;18(3):384–92. https://doi.org/10.1016/S1470-2045(17)30068-2.
[21] Lin H, Ding Z, Kota VG, Zhang X, Zhou J. Sentinel lymph node mapping in endometrial cancer: a systematic review and meta-analysis. Oncotarget 2017 Jul 11;8(28):46601–10. https://doi.org/10.18632/oncotarget.16662.
[22] Capozzi VA, Valentina C, Giulio S, Alessandra C, Giulia G, Giulia A, et al. Sentinel node mapping in endometrial cancer: tips and tricks to improve bilateral detection rate. The sentitricks study, a monocentric experience. Taiwan J Obstet Gynecol 2021 Jan;60(1):31–5. https://doi.org/10.1016/j.tjog.2020.11.006.
[23] Persson J, Salehi S, Bollino M, Lönnerfors C, Falconer H, Geppert B. Pelvic Sentinel lymph node detection in High-Risk Endometrial Cancer (SHREC-trial)-the final step towards a paradigm shift in surgical staging. Eur J Cancer 2019 Jul;116:77–85. https://doi.org/10.1016/j.ejca.2019.04.025.
[24] Cianci S, Rosati A, Vargiu V, Capozzi VA, Sozzi G, Gioè A, et al. Sentinel lymph node in aged endometrial cancer patients "the SAGE study": a multicenter experience. Front Oncol 2021 Oct 19;11:737096. https://doi.org/10.3389/fonc.2021.737096.
[25] Sozzi G, Fanfani F, Berretta R, Capozzi VA, Uccella S, Buono N, et al. Laparoscopic sentinel node mapping with intracervical indocyanine green injection for endometrial cancer: the SENTIFAIL study - a multicentric analysis of predictors of failed mapping. Int J Gynecol Cancer 2020 Nov;30(11):1713–8. https://doi.org/10.1136/ijgc-2020-001724.
[26] Vargiu V, Rosati A, Capozzi VA, et al. Impact of obesity on sentinel lymph node mapping in patients with apparent early-stage endometrial cancer: the ObeLyX study. Gynecol Oncol 2022;165(2):215–22. https://doi.org/10.1016/j.ygyno.2022.03.003.
[27] Morice P, Leary A, Creutzberg C, Abu-Rustum N, Darai E. Endometrial cancer. Lancet (London, England) 2016;387(10023):1094–108. https://doi.org/10.1016/S0140-6736(15)00130-0.
[28] Clarke MA, Long BJ, Del Mar Morillo A, Arbyn M, Bakkum-Gamez JN, Wentzensen N. Association of endometrial cancer risk with postmenopausal bleeding in women: a systematic review and meta-analysis. JAMA Intern Med 2018;178(9):1210–22. https://doi.org/10.1001/jamainternmed.2018.2820.
[29] Pennant ME, Mehta R, Moody P, Hackett G, Prentice A, Sharp SJ, et al. Premenopausal abnormal uterine bleeding and risk of endometrial cancer. BJOG An Int J Obstet Gynaecol 2017;124(3):404–11. https://doi.org/10.1111/1471-0528.14385.
[30] Plante M, Touhami O, Trinh XB, Renaud MC, Sebastianelli A, Grondin K, et al. Sentinel node mapping with indocyanine green and endoscopic near-infrared fluorescence imaging in endometrial cancer. A pilot study and review of the literature. Gynecol Oncol 2015 Jun;137(3):443–7. https://doi.org/10.1016/j.ygyno.2015.03.004.
[31] Carugno J, Grimbizis G, Franchini M, Alonso L, Bradley L, Campo R, et al. International Consensus Statement for recommended terminology describing hysteroscopic procedures. Facts, views & vision in ObGyn 2021;13(4):287–94. https://doi.org/10.52054/FVVO.13.4.037.
[32] Carugno J, Grimbizis G, Franchini M, Alonso L, Bradley L, Campo R, et al. International Consensus Statement for Recommended Terminology Describing Hysteroscopic Procedures. J Minimally Invasive Gynecol 2022;29(3):385–91. https://doi.org/10.1016/j.jmig.2021.10.004.
[33] National Comprehensive Cancer Network. Title of Guidelines (Version 1.2023). https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed Jenuary 31".
[34] Barlin JN, Khoury-Collado F, Kim CH, Leitao Jr MM, Chi DS, Sonoda Y, et al. The importance of applying a sentinel lymph node mapping algorithm in endometrial cancer staging: beyond removal of blue nodes. Gynecol Oncol 2012 Jun;125(3):531–5. https://doi.org/10.1016/j.ygyno.2012.02.021.
[35] Ercoli A, Delmas V, Iannone V, Fagotti A, Fanfani F, Corrado G, et al. The lymphatic drainage of the uterine cervix in adult fresh cadavers: anatomy and surgical implications,". Eur J Surg Oncol 2010 Mar;36(3):298–303. https://doi.org/10.1016/j.ejso.2009.06.009.
[36] Geppert B, Lönnerfors C, Bollino M, Arechvo A, Persson J. A study on uterine lymphatic anatomy for standardization of pelvic sentinel lymph node detection in endometrial cancer. Gynecol Oncol 2017 May;145(2):256–61. https://doi.org/10.1016/j.ygyno.2017.02.018.
[37] Ruscito I, Gasparri ML, Braicu EI, Bellati F, Raio L, Sehouli J, et al. Sentinel node mapping in cervical and endometrial cancer: indocyanine green versus other conventional dyes-A meta-analysis. Ann Surg Oncol 2016 Oct;23(11):3749–56. https://doi.org/10.1245/s10434-016-5236-x.
[38] Ditto A, Casarin I, Pinelli C, Perrone AM, Scollo P, Martinelli F, et al. Hysteroscopic versus cervical injection for sentinel node detection in endometrial cancer: a multicenter prospective randomised controlled trial from the Multicenter Italian Trials in Ovarian cancer (MITO) study group. Eur J Cancer 2020 Nov;140:1–10. https://doi.org/10.1016/j.ejca.2020.08.030.
[39] Persson J, Geppert B, Lönnerfors C, Bollino M, Måsbäck A. Description of a reproducible anatomically based surgical algorithm for detection of pelvic sentinel lymph nodes in endometrial cancer. Gynecol Oncol 2017 Oct;147(1):120–5. https://doi.org/10.1016/j.ygyno.2017.07.131.
[40] Diniz TP, Drizlionoks E, Faloppa CC, et al. Impact of sentinel node mapping in decreasing the risk of lymphocele in endometrial cancer. Ann Surg Oncol 2021;28(6):3293–9. https://doi.org/10.1245/s10434-020-09282-z.