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Original Research

Reproducibility of sentinel node detection in endometrial cancer by ICG fundic & cervical injection

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Objective: The aim of this study is to study the reproducibility of the dual injection technique of IndoCyanine Green (ICG) in the cervix and fundus in endometrial cancer. *Methods*: Between June 2014, and December 2019, 278 patients underwent laparoscopic surgery for endometrial cancer at our institution. In all cases, under a prospective cohort study, we performed Sentinel Lymph Node (SLN) biopsy with dual cervical and fundal ICG injection. Lymphadenectomy was also performed if intermediate or high-risk criteria were present. All cases were performed independently by three surgeons, with the same protocol and system, and their results were compared. *Results*: Global, aortic, pelvic and bilateral pelvic detection rates (DRs) were 93.45%, 67.27%, 90.18% and 67.64%. There were no significant differences for DRs between the three surgeons. The probability of finding a positive SLN was 8.8% (SD 2.8), 21% (SD 4.1) and 12% (SD 3.3), respectively, with a significant chi-squared difference ($p = 0.041$), which was statistically associated with preoperative risk factors ($p < 0.001$) and not to a surgeon's factor in a multivariate logistic regression. *Conclusions*: The SLN biopsy with both cervical and fundal ICG injection offers good overall detection rates and improved mapping of the aortic area and can be reproduced with similar results among different surgeons.

Keywords

Sentinel node; Endometrial cancer; Indocyanine green; Lymphadenectomy; Reproducibility; Aortic sentinel node

1. Introduction

Sentinel lymph node (SLN) mapping promises to become an alternative to lymphadenectomy for targeted and accurate staging of nodal involvement in endometrial cancer (EC) [1]. Its high sensitivity has been tested prospectively in the FIRES trial, demonstrating a sensitivity of 97.2% and negative predictive value (NPV) of 99.6% [2]. SLN has been included in the National Comprehensive Cancer Network (NCCN) guidelines since 2014. Numerous voices call for its incorporation outside of research protocols in the surgical staging strategy for EC [3], with the power to increase the detection of nodal involvement through better selection of the node most likely to be affected, location of aberrant pathways and ultrastaging [4, 5], and nowadays it is considered the standard of care for early-stage tumors with low risk of nodal metastases according to the ESGO-ESTRO-ESP (European Society of Gynaecological Oncology- European Society for Radiotherapy and Oncology - European Society of Pathology) risk class [6].

The precise sentinel node technique must be performed by dedicated teams, with an established learning curve that avoids errors in detection, follows a specific algorithm and maximizes detection options while decreasing the possibility of false negatives. An improvement in the mapping is well described with the increase in the number of procedures performed, with differences between an earlier and later period of the application of the technique [7]. The incorporation of a well-established algorithm [8] has a remarkable benefit by producing a decrease of false negatives. This improvement in mapping performance requires that this procedure be carried out by well-trained and dedicated teams.

Although there are studies where the learning curve of the SLN technique in EC can be studied [9, 10], with figures ranging from 27 to 40 procedures, there is no study to analyze the reproducibility of the dual cervical and transcervical fundic injection technique [11] or the reproducibility of the active search for the aortic sentinel node [12], which is more complex than the pelvic one, among different surgeons. The aim of this publication is to describe and compare the results we have found in the reproducibility of the technique in our series.

2. Material and methods

In April 2014, the Donostia University Hospital Ethics Committee approved a prospective interventional clinical trial (ref. RRS-ECG-2014) entitled "Evaluation of SLN biopsy for management of endometrial adenocarcinoma". Between June 26, 2014, and December 31, 2019, 278 patients underwent laparoscopic surgery for EC at our hospital. All patients gave written consent for SLN biopsy. Data were obtained prospectively.

The technique of dual transcervical and cervical superficial and deep fundic injection of indocyanine green (ICG) and its subsequent localization at the aortic level by dissection of the para-aortic and precaval space, as well as the pelvic sentinel node, has been previously described by our group [11] (Fig. 1). First, a direct transcervical injection of ICG into the fundus is performed with a follicular puncture needle protected in a cut-out protective sheath under laparoscope, followed by a cervical injection at 3 and 9 o'clock superficial and deep; tracer migration can be observed after a few seconds. The protective sheath of the needle is cut so that a few millimeters of the needle penetrate the myometrium and prevents the possibility of perforating the serosa. In addition, the injection into the fundus can be monitored under laparoscopy. No waiting is necessary to perform the aortic sentinel lymph node search, which is performed first.

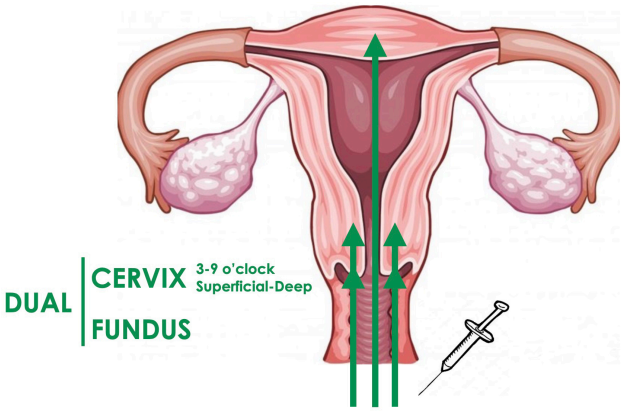

Fig. 1. Tracer injection sites.

Inclusion and exclusion criteria have already been published [11]. Women with low-risk preoperative stratification according to the European Society for Medical Oncology guidelines [13] (<50% myometrial invasion assessed by Magnetic Resonance Imaging (MRI) and histological grade Grade 1-2 endometrioid disease assessed by endometrial biopsy) underwent transperitoneal SLN biopsy of the pelvic and para-aortic areas, followed by hysterectomy and bilateral salpingo-oophorectomy, as well as uterine frozen section with subsequent pelvic and aortic lymphadenectomy if deep myometrial invasion was detected. High risk EC (intermediate, high-intermediate and high ESGO-ESTRO-ESP risk classification) also underwent SLN biopsy of the pelvic and para-aortic areas, but in these cases, an extraperitoneal approach was followed, with full pelvic and para-aortic lymphadenectomy, as well as hysterectomy and bilateral salpingo-oophorectomy, being completed. In cases of serous carcinoma & carcinosarcoma histology, omentectomy and peritoneal biopsies were mandatory. In cases of clear cell carcinoma peritoneal biopsies were also performed.

Our goal is to analyze the differences found in terms of detection rate (DR) and reproducibility between the three surgeons involved in this type of surgery in our department. All surgeries were performed by 3 surgeons: R.R., expert gynecologic oncologist and head of the surgical section of the obstetrics and gynecology department; M.G., gynecologic oncologist and expert in minimally invasive surgery and I.J., fellow in training of the gynecologic oncology section.

The results have been analyzed with Stata 15 statistical software (StataCorp. 2017. *Stata Statistical Software: Release 15.* StataCorp LLC, College Station, TX USA), describing means and standard deviations or medians and interquartile ranges (25–75) for quantitative variables and proportions for categorical variables. Means were compared using Student's *t*-test or ANOVA test for more than two predictor categories, and proportions were compared using chi-squared or Fisher's exact two-tailed test as required. The significance level has been set at a $p < 0.05$. A diagnostic test was also performed using lymphadenectomy as the gold standard.

3. Results

A total of 278 patients were studied; three patients were excluded who were operated on by doctors in training, assisted by a surgical oncologist from the team, leaving 275 patients for the final analysis, who were divided into 147 low-risk and 128 high-risk patients. The demographic characteristics of the population and the distribution of the different variables studied are summarized in Table 1.

Global, aortic, pelvic and bilateral pelvic DRs were 93.45%, 67.27%, 90.18% and 67.64% respectively, with no significant differences in any of the locations between the three studied surgeons using a two-tailed chi-squared test (Table 2).

The aortic DR was influenced by BMI, and the difference was significant. A simple logistic regression was applied for BMI (p = 0.001), with a coefficient of –0.07338 (95% CI –0.11772 to –0.02904). However, it was not significant in the bilateral pelvic DR (p = 0.0716), pelvic DR (p = 0.2864) and global DR (p = 0.4232). When the multivariate logistic regression was performed, adjusted for the rest of the variables of interest, the BMI is a factor that remained statistically significant associated with aortic DR (p = 0.005).

There were no significant differences in the mean BMI per surgeon using the ANOVA test (p = 0.3505), with the mean being 28.4 (SD 6), 28.8 (SD 5.8) and 27.3 (SD 5.5), respectively. There were also no significant differences in BMI by category operated by each surgeon, with a non-significant chi-squared test (p = 0.669) (Table 3). Grouping the patients of surgeons 1 and 2 vs. surgeon 3 (fellow), there were also no significant differences by two-tailed Student's *t*-test (p = 0.1644) or one-tailed Student's *t*-test (p = 0.0822).

A median of one aortic node (Interquartile range (IQR) 25–75: 0–2) and two pelvic nodes (IQR 25–75: 2–3) were removed, with this detection being pelvic and aortic in 64.4%, isolated pelvic in 25.8% and isolated aortic in 2.9% of the cases (Table 4). There were no statistically significant differences with respect to either the number of sentinel nodes obtained

Table 1. Characteristics of the population.

	Surgeon 1	Surgeon 2	Surgeon 3	Total	*p*
n	80	153	42	275	
Age (years)	61.8 (10.6)	64.7 (10.2)	60.5 (10.5)	63.2 (10.5)	***p* = 0.0269****
BMI (kg/m^2)	28.43 (6.0)	28.8 (5.8)	27.3 (5.5)	28.4 (5.8)	*p* = 0.3505
Hospital stay (days)	2.3 (1.4)	2.4 (1.8)	2.1 (1.1)	2.3 (1.6)	*p* = 0.6465
Uterus weight (g)	121.5 (65)	127.8 (77)	150.5 (122)	129 (81)	*p* = 0.3304
Tumor size (mm)	30.2 (14)	33.8 (17)	33 (13)	32.6 (16)	*p* = 0.2524
Tumor grade					*p* = 0.169
• G1	42 (55.5%)	67 (43.8%)	27 (64.3%)	136 (49.5%)	
• G2	22 (27.5%)	44 (28.8%)	8 (19.1%)	74 (26.9%)	
• G3	16 (20%)	42 (27.5%)	7 (16.7%)	65 (23.6%)	
LVSI	21 (26.3%)	33 (21.6%)	10 (23.8%)	21 (23.3%)	*p* = 0.722
Myometrial invasion					*p* = 0.178
• No invasion	9 (11.4%)	13 (8.5%)	2 (4.8%)	24 (8.8%)	
• <50%	54 (68.4%)	89 (58.2%)	30 (71.4%)	173 (63.1%)	
• ≥50%	16 (20.3%)	51 (33.3%)	10 (23.8%)	77 (28.1%)	
Preop risk					***p* = 0.001****
• Low-risk	51 (63.8%)	64 (41.8%)	32 (76.2%)	147 (63.8%)	
• High-risk	29 (36.3%)	89 (58.2%)	10 (23.8%)	128 (36.3%)	
• Number of lymphadenectomies	27	88	10	125	***p* < 0.001****
• Number of lymph nodes:					*p* = 0.0534
• Pelvic	11.3 (3.9)	16.5 (6.8)	13.3 (5.9)	15.1 (6.6)	
• Aortic	13.9 (4.6)	14.1 (6.6)	19 (6.2)	14.4 (6.3)	
FIGO stage					*p* = 0.231
• IA	74 (92.5%)	130 (85%)	40 (95.2%)	244 (88.7%)	
• IB	2 (2.5%)	5 (3.3%)	0 (0%)	7 (2.5%)	
• II	4 (5%)	18 (11.8%)	2 (4.8%)	24 (8.7%)	
Histology					*p* = 0.617
• Endometrial cancer	72 (90%)	126 (82.4%)	37 (88.1%)	235 (85.5%)	
• Serous carcinoma	5 (6.25%)	15 (9.8%)	4 (9.5%)	24 (8.7%)	
• Carcinosarcoma	1 (1.25%)	3 (1.96%)	1 (2.4%)	5 (1.8%)	
• Clear-cell carcinoma	0 (0%)	5 (3.3)	0 (0%)	5 (1.8%)	
• Mixed	2 (2.5%)	4 (2.6)	0 (0%)	6 (2.2%)	

Data presented as mean (+/–SD: Standard Deviation) or percentage in case of categories. Statistics: ANOVA for quantitative outcomes; Pearson chi-squared for categoric outcomes. In bold if there is statistical significance.
BMI, Body Mass Index; G, Grade; LVSI, Lymph Vascular Space Invasion; FIGO, International Federation of Gynaecology and Obstetrics. **, Statistically significant.

Table 2. Global, aortic, pelvic and bilateral pelvic DRs by surgeon.

Detection rate	Global	Surgeon 1	Surgeon 2	Surgeon 3	Two-tailed chi-squared
Global	93.45%	93.75%	93.46%	92.86%	*p* = 0.99
Aortic	67.27%	67.50%	65.36%	73.81%	*p* = 0.499
Pelvic	90.18%	91.25%	89.54%	92.86%	*p* = 0.927
Bilateral pelvic	67.64%	67.50%	67.67%	71.43%	*p* = 0.778

per surgeon (ANOVA test) or the proportion of isolated sentinel node detection obtained per area (Table 4).

The probability of finding a positive SN was 8.8% (SD 2.8), 21% (SD 4.1) and 12% (SD 3.3), respectively, with a significant chi-squared difference ($p = 0.041$), but by means of multivariate logistic regression, the surgeon factor was cancelled out, with preoperative risk stratification being the variable significantly associated with this difference ($p < 0.001$).

The sentinel node was detected in isolation in the aortic area in 11 patients, representing 4% of the sample and 25% of the total number of patients with positive nodes. The high-

Table 3. Weight distribution by BMI categories among the different surgeons.

BMI	Surgeon			
	Surgeon 1	Surgeon 2	Surgeon 3	Total
Underweight (BMI <20)	4 (5%)	4 (2.61%)	1 (2.38%)	9 (3.23%)
Normal (BMI 20– <25)	17 (21.25%)	32 (20.91%)	14 (33.33%)	63 (22.9%)
Overweight (BMI 25– <30)	28 (35%)	55 (35.95%)	15 (35.71%)	98 (35.64%)
Obese type 1 (BMI 30– <35)	14 (17.5%)	38 (24.84%)	7 (16.67%)	59 (21.22%)
Obese type 2 (BMI 35– <40)	15 (18.75%)	19 (12.42%)	4 (9.52%)	38 (13.67%)
Morbid obese (BMI >40)	2 (2.5%)	5 (3.27%)	1 (2.38%)	8 (2.88%)
Total	80	153	42	275

Total number and percentage. chi-squared test $p = 0.669$.

Table 4. Distribution of number of sentinel nodes detected and sentinel node detection rates by area among the different surgeons.

	Surgeon 1	Surgeon 2	Surgeon 3	Total	p
Sentinel node count					
Aortic	1 (0–2.5)	1 (0–2)	1 (0–3)	1 (0–2)	
• Inframesenteric	1 (0–2)	1 (0–1)	1 (0–2)	1 (0–2)	
• Supramesenteric	0 (0–1)	0 (0–1)	0 (0–1)	0 (0–1)	
Pelvic	2 (1–3)	3 (2–3)	3 (2–3)	2 (2–3)	
Total	4 (2–5)	4 (2–6)	4 (2–6)	4 (2–6)	
Isolated detection rate (DR)					
Isolated aortic DR	3 (3.8%)	5 (3.3%)	0 (0%)	8 (2.9%)	$p = 0.466$
Isolated pelvic DR	21 (26.3%)	42 (27.5%)	8 (19.1%)	71 (25.8%)	$p = 0.542$
Pelvic & aortic DR	51 (63.8%)	95 (62.1%)	31 (73.8%)	177 (64.4%)	$p = 0.369$

Isolated aortic detection rate represent cases in which sentinel lymph node is detected at the aortic level and not at the pelvic level, and viceversa. Median sentinel node count and IQR 25–75%. Number of cases and percentage for DR. Pearson chi-squared statistic.

IQR, Interquartile range; DR, Detection Rate.

est percentage of these isolated aortic metastases occurred in high-risk tumors (eight cases, 6.3% of the sample and 23.5% of the patients with positive nodes), although there were also cases in low-risk tumors (three cases, 2% of isolated aortic metastases and 30% of the positive cases) (Table 5). Again, in a multivariate logistic regression, everything is conditioned by the high-risk cases ($p < 0.001$, Coef 1.63, 95% CI 0.87–2.39).

The NPV of the technique was 98.6% (95% CI 92.6–99.8), 100% (95% CI 96.9–100) and 100% (95% CI 91.6–100), respectively.

4. Discussion

In this prospective study of dual ICG injection in the uterine fundus and cervix, we have demonstrated similar results among different surgeons of the oncological gynecology staff, without finding significant differences. Using the same systematic and injection protocols, we reproduced the DRs, even in territories of higher SLN detection complexity, such as the aortic territory [14]. According to our protocol, in all cases, we performed a dissection of the aortocaval territory up to the renal vein actively searching for areas of the aortic SLN, and we did not limit ourselves to a simple transillumination.

Other authors have also performed active search in the aortic territory by injecting the tracer in the uterine body; and when it is performed, a very significant improvement in the detection of a sentinel lymph node in the aortic territory has been demonstrated. But unlike our simple transcervical injection system, it requires prior hysteroscopy [15, 16], which adds complexity of the procedure to be used systematically, or it is performed via subserosal laparoscopy [17–19], which causes dispersion of the tracer and possible risk of contamination. Our system is very simple and easily performed by a surgeon with no hysteroscopic expertise.

The population operated on by the three surgeons was similar, although surgeon 2 performed a greater number of high-risk preoperative stratification cases and therefore a greater number of lymphadenectomies.

The only factor that we found statistically significant by means of multivariate logistic regression associated with the aortic DR was the BMI, proving that detection worsened by 7.3% for each increase of one unit in the BMI. This factor justifies a slightly higher DR by surgeon 3, a fellow in oncological gynecology in training, where the proportion of non-obese patients was higher, although it did not reach significant differences for lower weight compared to the other two

Table 5. Isolated metastases separated by pelvic and aortic areas in EC and divided by low-risk and high-risk EC.

Sentinel node	Surgeon 1	Surgeon 2	Surgeon 3	Total	Fisher
Total					
Isolated aortic metastasis	1 (1.3%)	8 (5.2%)	2 (4.76%)	11 (4%)	$p = 0.326$
Isolated pelvic metastasis	4 (5%)	20 (13.1%)	1 (2.4%)	25 (9.1%)	$\mathbf{p = 0.041}$**
Pelvic & aortic metastases	2 (2.5%)	4 (2.6%)	2 (4.8%)	8 (2.9%)	$p = 0.778$
Total nodal metastasis	7 (8.8%)	32 (20.9%)	5 (11.9%)	44 (16%)	$\mathbf{p = 0.045}$**
Low-risk					
Isolated aortic metastasis	0 (0%)	2 (3.1%)	1 (3.1%)	3 (2%)	$p = 0.443$
Isolated pelvic metastasis	2 (3.9%)	2 (3.1%)	1 (3.1%)	5 (3.4%)	$p = 1$
Pelvic & aortic metastases	2 (3.9%)	0 (0%)	0 (0%)	2 (1.4%)	$p = 0.165$
Total nodal metastasis	4 (7.8%)	4 (6.3%)	2 (6.3%)	10 (6.8%)	$p = 1$
High-risk					
Isolated aortic metastasis	1 (3.5%)	6 (6.7%)	1 (10%)	8 (6.3%)	$p = 0.695$
Isolated pelvic metastasis	2 (6.9%)	18 (20.2%)	0 (0%)	20 (15.6%)	$p = 0.127$
Pelvic & aortic metastases	0 (0%)	4 (4.5%)	2 (20%)	6 (4.7%)	$p = 0.066$
Total nodal metastasis	3 (10.3%)	28 (31.5%)	3 (30%)	34 (26.6%)	$p = 0.065$

Isolated aortic metastases represent cases in which nodal disease is detected at the aortic level and not at the pelvic level, and viceversa. **, Statistically significant.

senior surgeons (one-tailed Student's *t*-test, $p = 0.0822$). BMI has been known to make the DR of other tracers difficult. But, although it has been proven that it does not affect the DR at the pelvic level [20], it has not been studied in the aortic territory.

Pelvic sentinel node detection is easy and can be performed with minimal lengthening of surgical time by most gynecologic oncologists. But it is true that aortic sentinel lymph node detection adds complexity to the procedure and requires surgical skills to perform the laparoscopic aortic lymph node approach, and this may be the major difficulty in extending its use in other centers. Nevertheless, with this study we demonstrate that a fellow in training can perform a correct aortic sentinel node detection and that our system is reproducible.

The number of sentinel nodes obtained in each area was also very similar and without significant differences, which is of maximum importance in the technique of the SLN where it is of vital importance to extract the primary station and not the secondary ones and knowing that the use of the ICG tracer has the peculiarity of not remaining in the first node to which it drains and spreads early to the rest of the node chain.

Data that is reflected little in the publications of the sentinel node is the percentage of cases where detection has been positive and has occurred. But it has been exclusively in the aortic area and not in the pelvis, and these percentages were similar and without significant differences ($p = 0.466$), despite the fact that the proportion of cases where this happens is low (8 cases, 2.9%). But it would undoubtedly have had a negative impact on DRs if our technique had been limited to the pelvic territory.

Surgeon 2 found more positive sentinel nodes in his population but justified and nullified this difference by adjusting for high-risk EC cases through multivariate logistic regression. This same situation was repeated when comparing cases of isolated pelvic metastases, where significant differences were found that once again were associated with risk stratification.

The finding of isolated aortic metastases is striking and is reproduced by the three surgeons, which are located with the active search for the aortic sentinel node, finding an overall 4% of the cases of EC, which corresponds to 25% of the total patients with lymph node involvement, being 23.5% in high-risk cases and 30% in low-risk cases. In other words, one out of every four patients with lymph node involvement is found exclusively in the aortic area.

Bilateral detection rates have been similar ($p = 0.778$). If no detection is found in one hemipelvis, the procedure is performed in the other hemipelvis to allow more time for the tracer to migrate. If it persists without detection, a reinjection of the tracer in the cervix is performed [21].

The main limitation of our study lies in its post-hoc character, not being a study designed to establish differences between three surgeons. However, its strength lies in the broad collection of data prospectively over 5 years, with active and systematic searches for the aortic sentinel node, following the same protocol and demonstrating internal validity of our data.

The main contribution of our study is that it is the only study that compares the reproducibility of the technique in the aortic territory, demonstrating that it is a feasible and reproducible technique among different surgeons with adequate training.

5. Conclusions

The SLN biopsy with both cervical and fundal ICG injection offers good overall DRs and improved mapping of the aortic area and can be reproduced with similar results among different surgeons.

Despite the greater complexity of detection of the SLN in the aortic territory, we obtained similar DRs among the three surgeons involved in the study. The search for the aortic sentinel node in EC is a feasible and reproducible procedure.

Author contributions

MG—conceptualization, methodology, formal analysis, data curation, writing—original draft, writing—review and editing, visualization. RR—conceptualization, data curation, and writing—review and editing. IJ—methodology, data curation, writing—review and editing, and visualization. PC—supervision, visualization. AL: resources, supervision, and project administration. ID—supervision, visualization. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Donostia University Hospital (approval number: RRS-ECG-2014).

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Conflict of interest

The authors declare no conflict of interest. MG is our Reviewer Board, given his role as Reviewer Board, had no involvement in the peer-review of this article and has no access to information regarding its peer-review.

References

[1] Khoury-Collado F, St Clair C, Abu-Rustum NR. Sentinel Lymph Node Mapping in Endometrial Cancer: an Update. The Oncologist. 2016; 21: 461–466.

[2] 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. The Lancet Oncology. 2017; 18: 384–392.

[3] Amant F, Trum H. Sentinel-lymph-node mapping in endometrial cancer: routine practice? The Lancet Oncology. 2017; 18: 281–282.

[4] Abu-Rustum NR. The increasing credibility of sentinel lymph node mapping in endometrial cancer. Annals of Surgical Oncology. 2013; 20: 353–354.

[5] Kim CH, Soslow RA, Park KJ, Barber EL, Khoury-Collado F, Barlin JN, *et al.* Pathologic ultrastaging improves micrometastasis detection in sentinel lymph nodes during endometrial cancer staging. International Journal of Gynecological Cancer. 2013; 23: 964–970.

[6] 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. International Journal of Gynecologic Cancer. 2020; 31: 12–39.

[7] Khoury-Collado F, Glaser GE, Zivanovic O, Sonoda Y, Levine DA, Chi DS, *et al.* Improving sentinel lymph node detection rates in endometrial cancer: how many cases are needed? Gynecologic Oncology. 2009; 115: 453–455.

[8] Barlin JN, Khoury-Collado F, Kim CH, Leitao 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. Gynecologic Oncology. 2012; 125: 531–535.

[9] Kim S, Ryu KJ, Min KJ, Lee S, Jung US, Hong JH, *et al.* Learning curve for sentinel lymph node mapping in gynecologic malignancies. Journal of Surgical Oncology. 2020; 121: 599–604.

[10] Tucker K, Staley S, Gehrig PA, Soper JT, Boggess JF, Ivanova A, *et al.* Defining the learning curve for successful staging with sentinel lymph node biopsy for endometrial cancer among surgeons at an academic institution. International Journal of Gynecologic Cancer. 2020; 30: 346–351.

[11] Ruiz R, Gorostidi M, Jaunarena I, Goiri C, Aguerre J, Lekuona A. Sentinel Node Biopsy in Endometrial Cancer with Dual Cervical and Fundal Indocyanine Green Injection. International Journal of Gynecologic Cancer. 2018; 28: 139–144.

[12] Eoh KJ, Lee YJ, Kim H, Lee J, Nam EJ, Kim S, *et al.* Two-step sentinel lymph node mapping strategy in endometrial cancer staging using fluorescent imaging: a novel sentinel lymph node tracer injection procedure. Surgical Oncology. 2018; 27: 514–519.

[13] Colombo N, Creutzberg C, Amant F, Bosse T, González-Martín A, Ledermann J, *et al.* ESMO-ESGO-ESTRO Consensus Conference on Endometrial Cancer: Diagnosis, Treatment and Follow-up. International Journal of Gynecological Cancer. 2016; 26: 2–30.

[14] 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. Gynecologic Oncology. 2017; 147: 120–125.

[15] Martinelli F, Ditto A, Signorelli M, Bogani G, Chiappa V, Lorusso D, *et al.* Sentinel node mapping in endometrial cancer following Hysteroscopic injection of tracers: a single center evaluation over 200 cases. Gynecologic Oncology. 2017; 146: 525–530.

[16] Ditto A, Casarin J, 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. European Journal of Cancer. 2020; 140: 1–10.

[17] Kataoka F, Susumu N, Yamagami W, Kuwahata M, Takigawa A, Nomura H, *et al.* The importance of para-aortic lymph nodes in sentinel lymph node mapping for endometrial cancer by using hysteroscopic radio-isotope tracer injection combined with subserosal dye injection: Prospective study. Gynecologic Oncology. 2016; 140: 400–404.

[18] Holub Z, Jabor A, Kliment L. Comparison of two procedures for sentinel lymph node detection in patients with endometrial cancer: a pilot study. European Journal of Gynaecological Oncology. 2002; 23: 53–57.

[19] Kang S, Yoo HJ, Hwang JH, Lim M, Seo S, Park S. Sentinel lymph node biopsy in endometrial cancer: meta-analysis of 26 studies. Gynecologic Oncology. 2011; 123: 522–527.

[20] How JA, O'Farrell P, Amajoud Z, Lau S, Salvador S, How E, *et al.* Sentinel lymph node mapping in endometrial cancer: a systematic review and meta-analysis. Minerva Obstetrics and Gynecology. 2018; 70: 194–214.

[21] 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. Taiwanese Journal of Obstetrics and Gynecology. 2021; 60: 31–35.