Effect of lymph node sampling type on oncologic outcomes in endometrial cancers: comprehensive pelvic and paraaortic lymphadenectomy *vs.* sentinel lymph node mapping with indocyanine green

M. KULHAN[1], A. BILGI[1], F. AVCI[1], N.G. KULHAN[2], C. CELIK[1], M.G. UCAR[1]

[1]Gynaecology and Obstetrics Department, Medical Faculty, Selcuk University, Konya, Turkey
[2]Gynaecology and Obstetrics Department, Konya City Hospital, Konya, Turkey

Abstract. – OBJECTIVE: Sentinel lymph node biopsy refers to an innovative and minimalist surgical approach that has been introduced to reduce both complications and morbidity. A definitive answer to the question of whether lymphadenectomy is performed for staging or curative purposes in endometrial cancer has not yet been found. The aim of this study is to compare patients who underwent sentinel lymph node biopsy with indocyanine green and those who underwent laparoscopic complete surgical staging in terms of survival.

PATIENTS AND METHODS: A total of 182 patients was included in the study. The patients were divided into two groups according to the lymph node sample type. The two groups were compared in terms of oncological outcomes.

RESULTS: 92 patients underwent sentinel lymph node mapping (SLNM cohort) and 90 patients underwent extensive pelvic and paraaortic lymphadenectomy (SCL cohort). Considering only patients with negative lymph nodes, the Sentinel cohort was associated with a reduced DFS and OS ($p=0.008$ and $p=0.005$, respectively). This difference may be due to the longer follow-up times of patients with comprehensive lymph node sampling. On the other hand, There was no difference in survival in lymph node positive cases.

CONCLUSIONS: Sentinel lymph node dissection has no negative effect on survival in lymph node positive patients.

Key Words:
Endometrium cancer, Indocyanine green, Lymphadenectomy, Sentinel lymph node, Survey, Stage.

Introduction

Endometrial cancer is the most common cancer in the female genital tract. The majority of patients are diagnosed at an early stage, and the survival rate for stage 1 cancer is predicted to range from 85% to 91%[1]. However, survival rates are low in cases with advanced stages and in cases with poor prognostic features in pathological examination[2]. The most important prognostic factors are; histological type, grade, depth of myometrial invasion, lymphovascular area involvement and lymph node involvement[3,4]. Sentinel node biopsy is a new alternative to lymph node dissection for lymph node staging and highly confirms lymph node negativity if this method is performed according to the latest principles[5]. Multiple studies have confirmed the high sensitivity of sentinel lymph node status for lymph node staging in patients with early-stage endometrial carcinoma[6-9]. Sentinel lymph node biopsy may be used for staging in patients with low risk/intermediate risk disease. Systematic lymphadenectomy is not recommended in this group[10]. The European Society of Gynaecological Oncology (ESGO), The European Society for Radiotherapy and Oncology (ESTRO), and The European Society of Pathology (ESP) guidelines state that Sentinel lymph node biopsy can be performed as an acceptable alternative to systemic lymphadenectomy in stage I/II[11,12]. Complete surgical staging including pelvic and para-aortic lymph node sampling is recommended even in cases thought to be stage 1[2,3]. However, aggressive surgery; It both prolongs the operation time and increases morbidity by causing operative and postoperative complications. Although the inclusion of pelvic and especially para-aortic lymphadenectomy in surgery is an integral part of staging; It has been shown to be associated with undesirable results such as bleeding during surgery, infection in the early postoperative period and lymphedema in the late

period (especially in patients receiving adjuvant radiotherapy)[13-15]. In addition, obesity is a common comorbidity in endometrial cancer and it is an important obstacle that makes lymphadenectomy technically difficult[16]. Finally, it is claimed that lymph nodes are immune organs and their removal impairs the defense against proliferation of cancer cells through anti-tumor immunity and negatively affects the efficacy of immunotherapy, which is one of the promising targeted therapy options[17]. In this context, the concept of sentinel lymph node mapping (SLNM) refers to an innovative and minimalist surgical approach that has been introduced to reduce both complications and morbidity. A definitive answer to the question of whether lymphadenectomy is performed for staging or curative purposes in endometrial cancer has not yet been found. In other words, it is clear that lymphadenectomy clarifies the stage and thus shapes adjuvant therapy, but its contribution to survival has not been demonstrated[18-21]. However, when the endometrial cancer is evaluated according to risk groups, the effectiveness of lymphadenectomy and lymphadenectomy type on survival becomes more understandable. The aim of this study is to compare patients who underwent sentinel lymph node biopsy with indocyanine green and those who underwent laparoscopic complete surgical staging in terms of survival.

Patients and Methods

From March 2010 to December 2021, we reviewed the records of all patients who underwent laparoscopic surgical staging for endometrial cancer in the gynecological oncology unit of our university hospital. The cases were staged according to the FIGO 2009 staging system. Clinical characteristics, demographic profiles, pathological data, lymph node sample type, adjuvant treatments, complications, recurrences, progression-free survival (DFS) and overall survival (OS) were analyzed retrospectively from the patient files. DFS was determined from the date of diagnosis to the date of first recurrence or last follow-up, and OS from the date of diagnosis to the date of death or last follow-up.

Surgical staging included that laparoscopic total hysterectomy, removal of adnexa; and lymph node evaluation by standard complete lymphadenectomy or SLNM and biopsy. The decision to proceed with systematic lymphadenectomy or SLNM is made at the discretion of the surge-

on. The study was approved by the local ethics committee (21.02.2022-E.238500/2022/82). All surgical procedures were performed laparoscopically by the same surgical team. A total of 182 patients were included in the study. The patients were divided into two groups according to the lymph node sample type. 1.Group consisted of patients who underwent systematic complete lymphadenectomy (SCL) (90 patients: Non-Sentinel), 2.Group consisted of patients who underwent sentinel lymph node mapping with indocyanine green + biopsy (SLNM) (92 patients: Sentinel). All patients underwent a laparoscopic staging surgical procedure using the PINPOINT® endoscopic fluorescent imaging method (Novadaq, Mississauga, Ontario, Canada). Laparoscopic systematic completed lymphadenectomy was performed on all patients in group 1. Sentinel lymph node mapping and biopsy were performed according to previously published standard protocols for the patients in the second group[22]. On examination under anesthesia, patients typically had 4 cc of indocyanine green (ICG, Dongindang, Korea) injected into the cervix at the 3 and 9 o'clock positions 20 minutes before the operation. Then, trocars were placed and the operation was started. After observing the pelvic cavity and removing the intra-abdominal washing fluid, fluorescent imaging was started. Fluorescent luminous lymph nodes in the pelvic region were dissected and sent to the pathology department for frozen section examination. After retroperitoneal evaluation with excision of all mapped Sentinel lymph nodes, suspected diseased lymph nodes were removed in addition to routine peritoneal and serosal evaluations and washings. Complete lymphadenectomy was not performed in the cases in group 2. In our institution, chemotherapy (CT) and radiotherapy (RT) are usually given as adjuvant treatment to patients with advanced disease. CT is applied by medical oncologists and RT is applied by radiation oncologists. All patients are followed up by the treating medical or radiation oncologist as well as the surgeon. Patients are usually seen by a gynecological oncologist every 3 months for the first 2-3 years, and every 6 months for the next 2-3 years. Patients were screened for cancer antigen 125 (CA125) and with computed tomography every 6-12 months for the first 3-5 years of surveillance. Follow-up for disease recurrence was conducted and documented through routine outpatient visits, imaging studies, and monitoring of tumor markers. Recurrence patterns were divided into pure vaginal, pelvic, isolated nodal, and distant/

multifocal spread. Patients in both groups; Age, gravida, parity, menapouse status, complications, tumor size, grade and stage of endometrial tumor, myometrial invasion degree, cervical stromal invasion, lymph node involvement, lymphovascular space invasion, mayo risk scores, peritoneal washing cytology, mean progression-free survival and mean overall survival were compared. In this study, mayo risk score system model was used to assess the lymph node metastases risk. Mayo risk score system model describes low risk group for lymphatic metastasis including patients with grade 1 or 2, endometrioid type endometrial cancer, tumor size ≤20 mm, and ≤ %50 myometrial invazion and lymph node dissection, other parameters were describes high risk group[23]

Statistical Analysis

Statistical analysis was performed with the statistical package for the SPSS 21 (IBM SPSS Statistics, IBM Corporation, Armonk, NY, USA). The Kolmogorov-Smirnov test was used to test whether two samples come from the same distribution (parametric or nonparametic). Categorical measurements were summarized as numbers and continuous measurements were summarized as mean and standard deviation. Odds Ratio values were given for the results that are significant as a result of these analyzes. Pearson (Spearman) test for data correlations, Student t-test (independent samples t-test) for normally distributed data in paired group analyses, Mann-Whitney U test for non-parametric data, Anova for normally distributed data in multi-group analysis, Kruskal-Wallis test for non-parametric data were done. OS and PFS results were estimated using the Kaplan Mayer method and Cox proportional hazard regression was used to assess associations between OS and PFS for each study group. Variables univariately associated with OS and PFS were estimated in multivariable analyses. Binary logistic regression analyses for each group that cohort lymph node groups measured baseline patients covariates (including age, menopausal status, age, recurrence, myometrial invasion, lymphovascular space invasion (LVSI), cervical stroma invasion, peritoneal cytology, presence of positive pelvic nodes and count, presence of positive paraaortic nodes and count, grade, histologic type, tumor size and mayo risk score). Cox regression analysis were used in the research to reveal the model of the relationship between independent variables and dependent variables. In addition, survival were estimated according to the Kaplan meier estimator. When comparing the survival times of the groups, evaluation is made with the Log Rank test. For the significance level of the tests, $p<0.05$ was accepted.

Results

A total of 182 patients were included in the study, 92 patients underwent sentinel lymph node mapping (SLNM cohort) and 90 patients underwent extensive pelvic and paraaortic lymphadenectomy (SCL cohort). All patients in both groups were operated laparoscopically. The clinical and pathological characteristics of the patients are summarized in Table I.

The mean age of the patients in the non-sentinel and sentinel groups was 65.4±10.3 and 59.2±9.0 ($p=0.001$), respectively. Postmenopausal patients were predominantly in the non-sentinel group ($p=0.005$). There was no difference between the histological subtypes of patients in both groups ($p=0.606$), and most patients had endometrioid histology. The remaining features were more advanced in favor of the non-sentinel group, including adjuvant therapy (Table I).

The mean number of pelvic lymph nodes removed in the SLNM cohort was 17.3±9.0, while it was 21.8±11.5 in the SCL cohort. ($p<0.005$). In patients whose pelvic lymph nodes were evaluated, positive lymph nodes were detected in 4.3% (4/92) in the sentinel group and 17,7% (16/90) in the non-sentinel group ($p=0.004$). More paraaortic lymph nodes were removed in the SCL cohort compared to the SLNM cohort (7.4±6.7 $vs.$ 0.6±1.7, $p<0.001$, Table II). While metastatic paraaortic lymphatics were detected in 10% of the SCL cohort, they were not found in the sentinel group.

The overall median follow-up time after surgery was 3.6 years in the SLNM cohort and 5.2 years in the SCL cohort. Postoperative adjuvant therapy was used in patients who underwent SLNM and SCL at a rate of 30/92 (32.6%) and 57/90 (63.3%), respectively (Table I, $p=0.001$). In Binary logistic regression analysis of the two groups, age $p=0.010$ OR=0.914 (95% CI 0.8-0.9), number of pelvic lymph nodes $p=0.026$ OR=1.073 (95% CI 1.0-1.1), and paraaortic number of lymph nodes $p=0.001$ OR=0.463 (95% CI 0.3-0.6) was found to be significant, while other parameters were not statistically significant.

In the os cox regression analysis of the two groups (-2 Log Likelihood 44.367 $p=0.046$), no

Table I. The clinical and pathological characteristics of the patients.

Characteristic		Non-sentinel n=90	Sentinel n=92	p-value
Age (year) mean (SD)		65.4±10.3	59.2±9.0	0.001
Menopause				0.005
	Premenapause	6	19	
	Postmenapause	84	73	
Histologic type				0.606
	Endometrioid	79	84	
	Musinous	1	1	
	Mixed	0	1	
	Serous	9	6	
	Clear cell	1	0	
Tumor size mm		40.2±21.3	32.2±18.7	0.008
FIGO Grade				0.001
	Grade I	40	67	
	Grade II	28	15	
	Grade III	22	10	
FIGO Stage				0.007
	I	60	79	
	II	6	6	
	III	22	6	
	IV	2	1	
Malignant peritoneal cytology		14	5	0.022
Myometrial invasion				0.001
	None	8	12	
	<50%	51	72	
	≥50%	31	8	
LVSI				0.036
	No	77	87	
	Yes	13	5	
Cervical stromal invasion				0.024
	No	72	84	
	Yes	18	8	
Lymph node metastasis				0.002
	No	71	87	
	Yes	19	5	
Adjuvant therapy				0.001
	Follow-up	33	62	
	Brachytherapy	17	8	
	Chemotherapy	1	6	
	chemotherapy±bracytherapy	31	13	
	Bracytherapy+ external radiotherapy	8	3	
DFS month		51.2±25.0	36.5±13.3	0.001
OS month		52.2±24.3	36.7±13.4	0.001

SD: Standard deviation. FIGO: International Federation of Gynecology and Obstetrics. LVSI: Lymph-vasculer space invasion. DFS: Disease free survival. OS: Overall survival.

statistically significant parameter was found (lymphatic metastasis p=0.915 HR = 0.898 (95% CI 0.1-6.4), myometrial invasion p=0.904 HR=1.135 (95% CI 0.1–8.9), malignant peritoneal cytology p=0.71 HR =0.64 (95% CI 0.1–6.7), pelvic lymph node count p=0.362 HR=0.947 (95% CI 0.8-1.0), paraaortic lymph node count p=0.575 HR= 1.045 (95% CI 0.9-1.2), tumor size p=0.921 HR=0.998 (95% CI 0.9-1.0) , grade p=0.946 HR=1.04 (95% CI 0.3-3.2), and stage p=0.179 H=2.3 (95% CI 0.6-7.8)). And also, in the free-disease survival cox regression analysis of the two groups (-2 Log Likelihood 44.277 p=0.049), no parameter was

**Table II.** Lymphadenectomy characteristics of each groups and mayo risk score model.

Characteristic		Non-sentinel n=90	Sentinel n=92	p-value
Pelvic LND mean		21.8±11.5	17.3±9.0	0.005
Positive pelvic lymph nodes				0.004
	No	74	88	
	Yes	16	4	
Sentinel lymph node		0	4.1±2.3	0.001
Paraaortic LND		7.4±6.7	0.6±1.7	0.001
Positive paraaortic lymph nodes				0.002
	No	81	92	
	Yes	9	0	
Mayo risk				0.021
	1	11	23	
	2	79	69	

LND: Lymph node dissection.

found to be statistically significant. When the two groups within surgery for all patients and the subgroup of node-negative patients were compared, recurrence rates were not found statistically significant and but, death rates were found statistically significant (p=0.035 and 0.039). Recurrences sites for each groups were not found statistically significant (Table III).
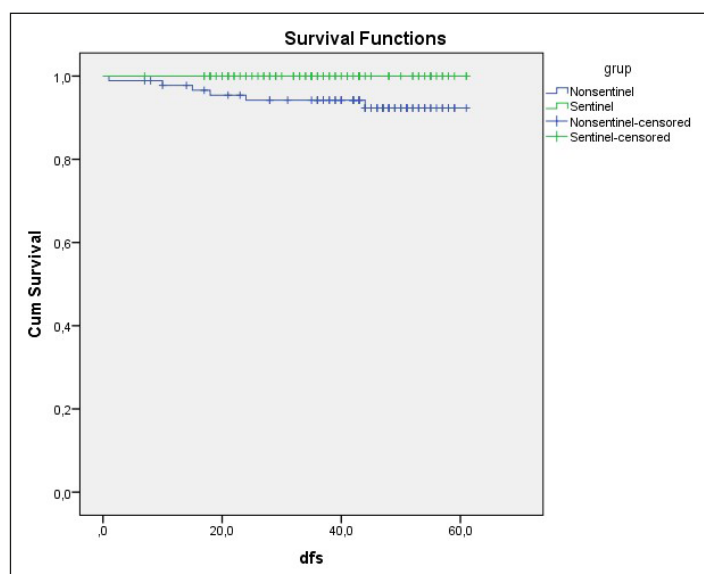
In the Kaplan-Meier analysis of both groups, the long rank of 0.019 was statistically significant on overall survival and progression-disease survival (Figure I and II).
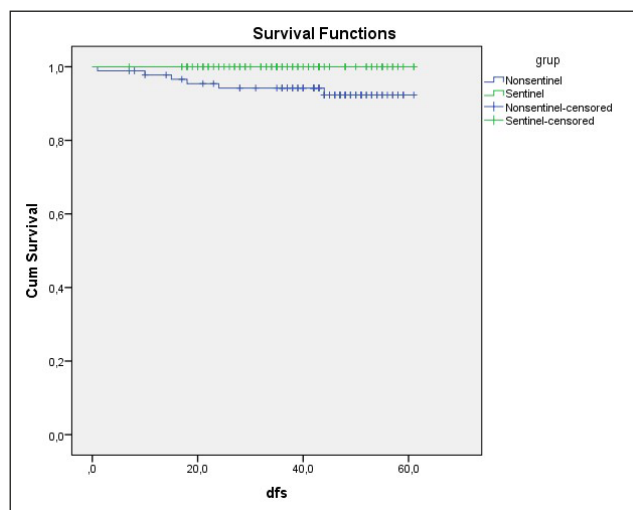
Figure 1. In the Kaplan-Meier analysis of both groups, the long rank of 0.019 was statistically significant on overall survival.

Table III. Comparison of outcomes of the two different surgical approaches within surgery for all patients and the subgroup of node-negative patients.

Outcome		Non-sentinel n=90	Sentinel n=92	p-value
All patients				0.372
	Death	6	0	0.035
	Recurrence	3	5	0.487
Recurrence site				0.343
	Cuff	1	0	
	Pelvic	2	3	
	None	87	89	
Node-negative patients				
	Death	4	0	0.039
	recurrences	3	5	0.945

Figure 2. In the Kaplan-Meier analysis of both groups, the long rank of 0.019 was statistically significant on progression-disease survival.

Discussion

A definitive answer to the question of whether lymphadenectomy is performed for staging or curative purposes in endometrial cancer has not yet been found. It is clear that lymphadenectomy clarifies the stage and shapes adjuvant therapy, but its contribution to survival has not been demonstrated. The fact that comprehensive lymphadenectomy is not only diagnostic but also therapeutic has been discussed in many articles. Clinically demonstrated in small cohort studies in a population of patients with node-positive disease that removal of occult nodal metastases contributes to survival[24,25]. Kilgore et al[26] reported that multisite pelvic lymph node sampling improved OS in a retrospective analysis of 649 patients. This survival advantage has been shown to persist even when patients with stage 3 or deep myometrial invasion receive adjuvant therapy. Based on Surveillance, Epidemiology, and End Results (SEER) data including 4178 women with endometrial cancer, any lymphadenectomy as well as a more extensive lymphadenectomy was reported to improve 5-year OS even in patients with negative lymph nodes[27]. The results of these retrospective reports are in conflict with the MRC ASTEC study, which is a prospective randomized study, in which it was reported that there was no difference in survival between patients who underwent systematic lymphadenectomy and those who did not[18]. In another study of 514 patients with stage I endometrial carcinoma, the patient was randomized into those who underwent systematic pelvic lymphadenectomy and those who did not. It has been reported that patients who underwent lymphadenectomy benefit from increased detection of lymph node metastases, but the 5-year DFS and overall survival (OS) rates are similar. (81% and 86% in those who underwent lymphadenectomy and 82% and 90% in those who did not undergo lymphadenectomy, p=0.7 and 0.5, respectively)[19]. All of these studies did not include the SLNM method, which shows lymph nodes at high risk for disease spread. Schiavone et al. compared the patients who underwent lymphadenectomy with the Sentinel Lymph Node Mapping algorithm and the patients who underwent a complete systematic lymphadenectomy, and they found no difference in 2-year Disease free survival (DFS) rates between the two cohorts (77% vs. 71%, respectively). The frequency of regional (pelvic or vaginal) recurrence was 9.7% in the SLNM group, 9.1% in the lymphadenectomy group alone; The frequency of isolated nodal recurrence was 16.1% versus 24.2%, respectively[28]. Multinu et al. evaluated survival outcomes of the patients with deeply invasive endometrial carcinoma who underwent full systematic lymphadenectomy versus SLNM technique. The results were not associated with DFS and specifically there was no difference in nodal recurrence between the groups[29].

Since the ultra-staging procedure is applied in SLNM, it is obvious that lymph nodes are evaluated in more detail, as a result, more metastatic lymph nodes can be detected, and the rate of adjuvant therapy is higher in patients who underwent ultra-staging[30]. However, another question that

needs to be answered is; whether detection of micrometastases or isolated tumor cells has prognostic significance. The prognostic significance of these low-volume tumor burdens revealed by SLNB and ultra-staging should be clarified by new studies to be conducted in the future. Another discussion topic in SLNB; It is unclear whether nodal metastases are limited to the pelvic region or whether they are accompanied by para-aortic nodal involvement. Approximately half of patients with positive pelvic lymph nodes have involvement in both the pelvic and paraaortic regions[31-33]. The dilemma here is the uncertainty in the status of the paraaortic lymph nodes and the resulting confusion in determining the boundaries of the radiotherapy field when adjuvant radiotherapy is planned due to lymph node positivity in patients who underwent only pelvic SLNM[15].

The SHREC trial is the largest prospective trial investigating the Sentinel lymph node (SLN) algorithm in high-risk endometrial cancers (HREC) and is the first trial to systematically investigate a pelvic SLN algorithm. In this study, the pelvic SNL algorithm, in the hands of experienced surgeons, has been reported as having the potential to safely replace systemic lymphadenectomy in HREC without the need for para-aortic dissection[7].

Our study of SLNM in patients with endometrial carcinoma included 182 patients and used a comparative cohort of patients who had undergone systematic lymphadenectomy to evaluate survival outcomes among these groups. A statistically significant difference in 5-year DFS and OS rates was noted between these clinically similar groups (p=0.001). While evaluating all patients with positive and negative lymph nodes in our study, lymphadenectomy type was a significant factor for DFS or OS in univariate or multivariate analysis (p=0.005 *vs*. p= 0.002, respectively). Considering only patients with negative lymph nodes, the SLNM cohort was associated with a reduced DFS and OS (p=0.008 and p=0.005, respectively). This difference may be due to the longer follow-up times of patients with comprehensive lymph node sampling.

The primary strength of our study is that the only difference in surgical staging is the lymph node evaluation technique and all surgical staging procedures were performed by the same team. The limitations of our study are that firstly it is a retrospective study, secondly all histological types with endometrial cancer were included in the study and lastly, we cannot comment on isolated paraaortic lymph node metastases; however, there was no increased rate of nodal recurrence in the SLNM cohort.

Conclusions

The SLNM cohort was associated with a reduced DFS and OS, but this difference is thought to be due to longer follow-up times for patients with comprehensive lymph node sampling. On the aother hand, There was no difference in survival in lymph node positive cases.

ORCID ID
Mehmet Kulhan: 0000-0002-5478-7510.
Ahmet Bilgi: 0000-0001-8682-1739.
Fazıl Avcı: 0000-0002-9244-9168.
Nur Gozde Kulhan: 0000-0002-7463-9101.
Cetin Celik: 0000-0002-9881-7814.
Mustafa Gazi Ucar: 0000-0002-6888-0206.

References

1) Creasman WT, Odicino F, Maisonneuve P, Quinn MA, Beller U, Benedet JL, Heintz AP, Ngan HY, Pecorelli S. Carcinoma of the corpus uteri. FIGO 26th Annual Report on the Results of Treatment in Gynecological Cancer. Int J Gynaecol Obstet 2006; 95 Suppl 1: S105-143.

2) Creasman WT, Morrow CP, Bundy BN, Homesley HD, Graham JE, Heller PB. Surgical pathologic spread patterns of endometrial cancer. A Gynecologic Oncology Group Study. Cancer 1987; 15 Suppl 8: 2035-2041.

3) Boente MP, Yordan EL Jr, McIntosh DG, Grendys EC Jr, Orandi YA, Davies S, Beck D, Graham JE Jr, Miller A, Marshall R, Dolan T, Kirschner C, Reddy S, Wilbanks GD. Prognostic factors and long-term survival in endometrial adenocarcinoma with cervical involvement. Gynecol Oncol 1993; 51: 316-322.

4) Miklos P, Klacko M, Babala P, Masak L, Ondrus D, Waczulikova I. Transvaginal ultrasound examination of myometrial infiltration by endometrial cancer. Bratisl Lek Listy 2014; 115: 14-18.

5) Tanaka T, Ueda S, Miyamoto S, Terada S, Konishi H, Kogata Y, Fujiwara S, Tanaka Y, Taniguchi K, Komura K, Ohmichi M. Oncologic outcomes for patients with endometrial cancer who received minimally invasive surgery: a retrospective observational study. Int J Clin Oncol 2020; 25: 1985-1994.

6) Bogani G, Murgia F, Ditto A, Raspagliesi F. Sentinel node mapping vs. lymphadenectomy in endometrial cancer: A systematic review and meta-analysis. Gynecol Oncol 2019; 153: 676-683.

7) 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; 116: 77-85.

8) Renz M, Marjon N, Devereaux K, Raghavan S, Folkins AK, Karam A. Immediate intraoperative sentinel lymph node analysis by frozen section is predictive of lymph node metastasis in endometrial cancer. J Robot Surg 2020; 14: 35-40.

9) Lee GW, Park JY, Kim DY, Suh DS, Kim JH, Kim YM, Kim YT, Nam JH. 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 2021; 41: 605-611.

10) Cheng-Yen Lai J, Lai KJ, Yi-Yung Yu E, Hung ST, Chu CY, Wang KL. Sentinel lymphatic mapping among women with early-stage cervical cancer: A systematic review. Taiwan J Obstet Gynecol 2018; 57: 636-643.

11) Barczynski B, Fraszczak K, Bednarek W. Sentinel lymph node mapping in endometrial cancer after 2020 ESGO-ESTRO-ESP consensus update: what will happen in the next few years? Ginekol Pol 2022; 93: 321-328.

12) Ignatov A, Papathemelis T, Ivros S, Ignatov T, Ortmann O, Eggemann H. Comparison of survival of patients with endometrial cancer undergoing sentinel node biopsy alone or systematic lymphadenectomy. Arch Gynecol Obstet 2020; 302: 995-1000.

13) Volpi L, Sozzi G, Capozzi VA, Ricco' M, Merisio C, Di Serio M, Chiantera V, Berretta R. Long term complications following pelvic and para-aortic lymphadenectomy for endometrial cancer, incidence and potential risk factors: a single institution experience. Int J Gynecol Cancer 2019; 29: 312-319.

14) Dizdar O, Oguz A, Kucukoztas N, Dursun P, Altundag O, Ayhan A. Paraaortic Lymph Node Dissection in Endometrial Cancer; Is It Necessary? UHOD 2014; 24: S279-280

15) Jingjing H, Rui J, Hui P. Adjuvant chemoradiotherapy vs. radiotherapy alone in early-stage high-risk endometrial cancer: a systematic review and meta-analysis. Eur Rev Med Pharmacol Sci 2019; 23: 833-840.

16) Khazaei Z, Hasanpour Dehkordi A, Amiri M, Adineh H, Sohrabivafa M, Darvishi I. The incidence and mortality of endometrial cancer and its association with body mass index and human development index in Asian population. WCRJ 2018; 5: 1174.

17) Lheureux S, Oza AM. Endometrial cancer-targeted therapies myth or reality? Review of current targeted treatments. Eur J Cancer 2016; 59: 99-108.

18) 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. Lancet 2009; 373: 125-36.

19) Benedetti Panici P, Basile S, Maneschi F, Alberto Lissoni A, Signorelli M, Scambia G, Angioli R, Tateo S, Mangili G, Katsaros D, Garozzo G, Campagnutta E, Donadello N, Greggi S, Melpignano M, Raspagliesi F, Ragni N, Cormio G, Grassi R, Franchi M, Giannarelli D, Fossati R, Torri V, Amoroso M, Crocè C, Mangioni C. Systematic pelvic lymphadenectomy vs. no lymphadenectomy in early-stage endometrial carcinoma: randomized clinical trial. J Natl Cancer Inst 2008; 100: 1707-1716.

20) Jayot A, Owen C, Bendifallah S, Kolanska K, Boudy AS, Touboul C, Darai E. Relevance of sentinel lymph node biopsy in early endometrial cancer: A series of 249 cases. Eur J Obstet Gynecol Reprod Biol 2021; 258: 208-215.

21) Tanaka T, Terai Y, Fujiwara S, Tanaka Y, Sasaki H, Tsunetoh S, Yamamoto K, Yamada T, Ohmichi M. The detection of sentinel lymph nodes in laparoscopic surgery can eliminate systemic lymphadenectomy for patients with early stage endometrial cancer. Int J Clin Oncol 2018; 23: 305-313.

22) Barlin JN, Khoury-Collado F, Kim CH, Leitao MM Jr, Chi DS, Sonoda Y, Alektiar K, DeLair DF, Barakat RR, Abu-Rustum NR. The importance of applying a sentinel lymph node mapping algorithm in endometrial cancer staging: beyond removal of blue nodes. Gynecol Oncol 2012; 125: 531-535.

23) Mariani A, Webb MJ, Keeney GL, Haddock MG, Calori G, Podratz KC. Low-risk corpus cancer: is lymphadenectomy or radiotherapy necessary? Am J Obstet Gynecol 2000; 182: 1506-1519.

24) Mahdi H, Lockhart D, Moselmi-Kebria M. Prognostic impact of lymphadenectomy in uterine clear cell carcinoma. J Gynecol Oncol 2015; 26: 134-140.

25) Alagkiozidis I, Weedon J, Grossman A, Wang P, Mize B, Wilson K, Shah T, Economos K, Salame G, Abulafia O, Lee YC. Extent of lymph node dissection and overall survival in patients with uterine carcinosarcoma, papillary serous and endometrioid adenocarcinoma: A retrospective cohort study. Int J Surg 2015; 24: 9-13.

26) Kilgore LC, Partridge EE, Alvarez RD, Austin JM, Shingleton HM, Noojin F 3rd, Conner W. Adenocarcinoma of the endometrium: survival comparisons of patients with and without pelvic node sampling. Gynecol Oncol 1995; 56: 29-33.

27) Mahdi H, Kumar S, Al-Wahab Z, Ali-Fehmi R, Munkarah AR. Prognostic impact of lymphadenectomy in uterine serous cancer. BJOG 2013; 120: 384-391.

28) Schiavone MB, Scelzo C, Straight C, Zhou Q, Alektiar KM, Makker V, Soslow RA, Iasonos A, Leitao MM, Abu-Rustum NR. Survival of Patients with Serous Uterine Carcinoma Undergoing Sentinel Lymph Node Mapping. Ann Surg Oncol 2017; 24: 1965-1971.

29) Schlappe BA, Weaver AL, McGree ME, Ducie J, Zahl Eriksson AG, Dowdy SC, Cliby WA, Glaser GE, Abu-Rustum NR, Mariani A, Leitao MM Jr. Multicenter study comparing oncologic outcomes after lymph node assessment via a sentinel lymph node algorithm versus comprehensive pelvic and paraaortic lymphadenectomy in patients with serous and clear cell endometrial carcinoma. Gynecol Oncol 2020; 156: 62-69.

30) Plante M, Stanleigh J, Renaud MC, Sebastianelli A, Grondin K, Grégoire J. Isolated tumor cells identified by sentinel lymph node mapping in endometrial cancer: Does adjuvant treatment matter? Gynecol Oncol 2017; 146: 240-246.

31) Kumar S, Podratz KC, Bakkum-Gamez JN, Dowdy SC, Weaver AL, McGree ME, Cliby WA, Keeney GL, Thomas G, Mariani A. Prospective assessment of the prevalence of pelvic, paraaortic and high paraaortic lymph node metastasis in endometrial cancer. Gynecol Oncol 2014; 132: 38-43.

32) Ruiz R, Gorostidi M, Jaunarena I, Cobas P, Lekuona A. Maximizing sentinel node detection in endometrial cancer with dual cervical and transcervical fundal indocyanine green injection: 5-year single-center prospective study. Eur J Obstet Gynecol Reprod Biol 2021; 261: 59-64.

33) Taşkın S, Sarı ME, Altın D, Ersöz CC, Gökçe A, Yüksel S, Kankaya D, Ortaç F. Risk factors for failure of sentinel lymph node mapping using indocyanine green/near-infrared fluorescent imaging in endometrial cancer. Arch Gynecol Obstet 2019; 299: 1667-1672.