DOCTORAL THESIS

A preoperative risk-scoring system to predict lymph node metastasis in endometrial cancer and stratify patients for lymphadenectomy.

（子宮体癌におけるリンパ節転移の予測およびリンパ節郭清を要する患者の識別のための術前スコアリングシステム）

March, 2023

（2023 年 3 月）

Kazuaki Imai
今井一章
Department of obstetrics and Gynecology,
Yokohama City University Hospital
横浜市立大学　大学院医学研究科　生殖生育病態医学

（Research Supervisor : Hisamori Kato, Director）
神奈川県立がんセンター　婦人科部長
（研究指導教員：加藤　久盛　部長）

（Doctoral Supervisor：Etsuko Miyagi, Professor）
（指導教員：宮城　悦子　教授）

Gynecologic Oncology 142 (2016) 273–277

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

A preoperative risk-scoring system to predict lymph node metastasis in endometrial cancer and stratify patients for lymphadenectomy

Kazuaki Imai [a,*], Hisamori Kato [a], Kayoko Katayama [b], Kazuho Nakanishi [a], Aiko Kawano [a], Ayaka Iura [a], Katsuyuki Konnai [a], Ryo Onose [a], Fumiki Hirahara [c], Etsuko Miyagi [c]

[a] Department of Gynecology, Kanagawa Cancer Center, Yokohama, Kanagawa, Japan
[b] Cancer Prevention and Cancer Control Division, Kanagawa Cancer Center Research Institute, Yokohama, Kanagawa, Japan
[c] Department of Obstetrics and Gynecology, Yokohama City University Hospital, Minami-ku, Yokohama, Japan

HIGHLIGHTS

- Our preoperative scoring system can accurately predict rate of lymph node metastasis in endometrial cancer.
- Lymphadenectomy can be safely omitted for endometrial cancer patients with no risk of lymph node metastasis.
- Our scoring system can determine extent of lymphadenectomy for patients with risk of lymph node metastasis.

ARTICLE INFO

Article history:
Received 26 February 2016
Received in revised form 1 June 2016
Accepted 3 June 2016
Available online 15 June 2016

Keywords:
Uterine cancer
Lymph node metastasis
Pelvic lymphadenectomy
Para-aortic lymphadenectomy
Cancer antigen 125
Myometrial invasion

ABSTRACT

Objective. This study aimed to validate the preoperative scoring system adopted in the Kanagawa Cancer Center (KCC) to stratify endometrial cancer patients for lymphadenectomy according to the risk of developing lymph node metastasis (LNM).

Methods. The records of 432 and 221 uterine cancer patients treated in the KCC and Yokohama City University (YCU), respectively, were retrospectively analyzed. The KCC classified patients for LNM risk based on tumor volume, myometrial invasion, histological grade, and serum CA125 levels, while YCU used only myometrial invasion. Lymphadenectomy was omitted for 156 patients with 0 LNM risk, while pelvic lymphadenectomy (PLX) or PLX with para-aortic lymphadenectomy (PLAX) were performed for those with low and high LNM risk, respectively. The predicted and actual LNM rates were compared between the KCC and YCU patients, and cancer recurrence and overall survival were analyzed.

Results. There was no difference in survival between patients with LNM score 0 who were or were not treated with lymphadenectomy. None (0%) developed LNM and only 1 (0.6%) had recurrence. Patients who underwent PLX but not PLAX (low LNM score) had a low tumor recurrence rate in the para-aortic nodes (1.3%). The KCC scoring system was significantly more accurate than the YCU system in predicting LNM in the high-risk group ($P < 0.05$) and demonstrated that PLAX was unnecessary in almost 50% of the YCU cases.

Conclusion. The KCC preoperative scoring system is useful to predict LNM risk, and thereby prevent unnecessary lymphadenectomy or to determine its extent in endometrial cancer patients.

1. Introduction

Endometrial cancer is the most frequently occurring gynecologic malignancy in the world and has the top fifth mortality among cancers affecting women in Japan [1]. According to the International Federation of Gynecology and Obstetrics (FIGO) system, in 2007 in Japan, the five-year survival rates of uterine cancer patients with FIGO stages I, II, and III were 95.3%, 89.8%, and 75.6%, respectively, but have been decreasing thereafter. Patients with early stage cancer have relatively good prognosis due to timely surgical treatment [2], which includes total abdominal hysterectomy, bilateral salpingo-oophorectomy, and, frequently, pelvic lymphadenectomy (PLX) and/or retroperitoneal, i.e., para-aortic, lymphadenectomy (PLAX). Lymph nodes (pelvic lymph node and para-aortic lymph node) are the most common sites of tumor spread in endometrial cancer; therefore, the FIGO recommends that lymphadenectomy should be performed for all patients to ensure accurate staging and determine appropriate postoperative treatment. However, lymphadenectomy may cause complications such as postoperative

* Corresponding author at: Kanagawa Cancer Center, 2-3-2, Nakao, Asahi-ku, Yokohama 241-8515, Japan.
E-mail address: wing-of-kazu-kun@excite.co.jp (K. Imai).

http://dx.doi.org/10.1016/j.ygyno.2016.06.004
0090-8258/

deep vein thrombosis or leg lymphedema, and an increasing number of studies have reported that it may be omitted for patients with a low risk of lymph node metastasis (LNM) [3–5]. On the other hand, patients with a high LNM risk benefit from lymphadenectomy, including PLAX, which has been shown to contribute to prognosis improvement [6].

Pelvic lymphadenectomy in uterine cancer has diagnostic significance, but its therapeutic impact has not been yet established. The results of a randomized comparative study conducted in Italy and the UK indicated that PLX significantly improved surgical staging, but did not increase disease-free or overall survival [7,8]. A multicenter questionnaire survey conducted by the Japanese Gynecologic Oncology Group (JGOG) in 2005 revealed that the majority of institutions (72%) performed PLX; however, PLAX or para-aortic lymph node biopsy was performed in 20% and 12% of institutions, respectively [9]. At the same time, a questionnaire survey conducted among gynecological tumor specialists in the United States showed that 69% of institutions performed PLAX [10]. These data indicate that there is no global consensus on the clinical significance and extent of lymphadenectomy in uterine cancer. In view of this, a recent study has proposed personalized treatment of uterine cancer based on a risk-scoring system predicting lymphatic metastasis after hysterectomy in endometrial carcinoma, which is to be used to identify patients with low and high risks of LNM and to determine the extent of lymphadenectomy [11]. Ideally, only the patients requiring extended surgery should undergo lymphadenectomy, while for the others it can be omitted to avoid unnecessary operation-associated risks because lymphadenectomy, PLAX in particular, prolongs surgery duration and increases intraoperative bleeding, post-operative complications, and costs of care [12]. Therefore, it is very important to establish a standard preoperative risk classification system in endometrial cancer to predict LNM preoperatively.

In the Kanagawa Cancer Center (KCC), we have been providing personalized treatment of uterine cancer since 1998 by using our preoperative scoring system that allows the identification of patients with a low risk of developing LNM based on tumor volume, myometrial invasion, histological type, and serum CA125 levels [13]. The KCC system enabled us to preoperatively identify patients at risk of developing cancer metastases to pelvic and para-aortic lymph nodes, and thus to decide who would benefit from lymphadenectomy and determine the anatomic extent of lymph node dissection (PLX only, or PLX and PLAX). Our hypothesis was that complete lymphadenectomy should not be routinely performed and that the KCC scoring system would be a clinically valid tool for preoperative patient stratification for surgery. The objective of this retrospective cohort study was to validate the KCC system by comparing it with that adopted in Yokohama City University (YCU), which used myometrial invasion as a single criterion of LNM risk.

2. Methods

2.1. Patients

A total of 485 and 262 uterine cancer patients who had undergone the initial surgery at the KCC and YCU, respectively, between January 2005 and December 2011 were screened. The inclusion criteria were as follows: endometrial cancer of FIGO stages I–III without ovarian cancer, histological type other than sarcoma, and no extrauterine spread. The exclusion criteria were as follows: FIGO stage IV, complication with sarcoma and/or ovarian cancer, death of another cancer, unknown follow-up prognosis, and/or cancer progression due to extrauterine metastasis. As a result, 432 KCC and 221 YCU patients were included in the study (Fig. 1).

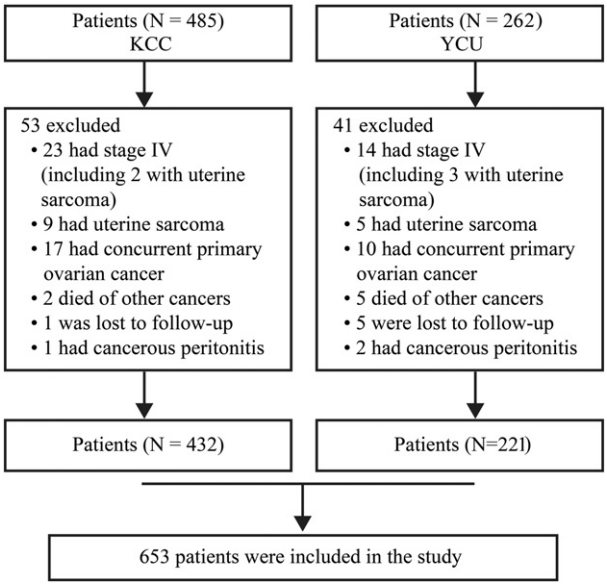

Fig. 1. Study design. KCC, Kanagawa Cancer Center; YCU, Yokohama City University.

2.2. KCC scoring system

In the KCC, we determine the surgical treatment for uterine cancer using our scoring system that classifies patients into three groups according to LNM risk (Table S1). Four criteria, each assigned 1 score, were used: (1) tumor volume > 6 cm^3 (calculated based on three dimensions provided by the preoperative MRI test or intraoperative visual findings), (2) myometrial invasion above 50% (by preoperative MRI or intraoperative visual examination), (3) histological type other than G1 endometrioid adenocarcinoma on preoperative endometrial tissue examination, and (4) serum CA125 level higher than 70 U/ml for premenopausal and 25 U/ml for menopausal women; the cut-off values for tumor volume and serum CA125 value were based on previous studies by Nakayama et al. performed in the KCC [14,15]. Patients with no LNM risk (score 0) received only the standard therapy comprising abdominal total hysterectomy (ATH) and bilateral salpingo-oophorectomy (BSO) without lymphadenectomy, while those with moderate LNM risk (scores 1–2) were treated with ATH, BSO, and PLX, and those with high LNM risk (scores 3–4) had ATH, BSO, PLX, and PALX. In addition, if preoperative diagnostic imaging (CT and/or MRI) indicated swollen lymph nodes in patients with no LNM risk, PLX was added to the treatment. Patients with a high post-operative risk of cancer recurrence were treated with chemotherapy; the regimen consisted of paclitaxel (180 mg/m^2) plus carboplatin (AUC5) for not more than 3 months post-operatively. Patients who demonstrated strong symptoms of peripheral neuropathy were switched from paclitaxel to docetaxel (70 mg/m^2).

On the other hand, in YCU, all patients suspected of myometrial invasion prior to surgery underwent PLAX, and no standards were adopted for the dissection range, which was determined empirically.

2.3. Study design

The patients were divided into the lymphadenectomy and no-lymphadenectomy groups and the overall survival was compared. KCC and YCU patients in the lymphadenectomy group who scored 0 (i.e., for whom lymphadenectomy could be omitted) were analyzed for LNM rate, and KCC patients who scored 1–2 and underwent PLX were evaluated for the rate, pattern, and site of tumor recurrence in para-aortic lymph nodes (PAN). In addition, the accuracy of histological diagnosis of metastasis to pelvic lymph node (PEN) and PAN in the lymphadenectomy group was compared between the KCC and YCU cases. Moreover, given the difference in the preoperative criteria for lymphadenectomy between the two centers, the patients who underwent PLAX in the YCU were classified according to the KCC criteria to determine whether the application of the KCC system could assist in patient stratification for PALX and improve the accuracy of LNM

prognosis. Finally, the rates of overall five-year survival for KCC patients were analyzed. The study was conducted on the basis of medical records provided by the KCC and the YCU after the approval by the respective ethics committees.

2.4. Statistical analysis

KCC and YCU patients were compared using Fisher's exact test, χ^2 test, *t*-test, and Mann-Whitney *U* test; a P-value less than 0.05 was considered statistically significant. Survival rates were estimated using the Kaplan-Meier method. All statistical analyses were performed using SPSS for Windows, version 13.0 (Cary, NC, USA) and the EZR (Easy R) package [16].

3. Results

Patients' demographic characteristics are presented in Table 1. There was no significant difference in the mean age and body mass index (BMI), and median parity between patients treated in the KCC and the YCU. Among the preoperative scoring indexes, only the distribution of endometrial tumor histological type showed a significant difference (P = 0.008), whereas tumor volume, myometrial invasion, and serum CA125 levels were similar between patients of the two centers. However, a significant difference in FIGO classification was detected between KCC and YCU patients (P = 0.005).

Table 2 shows the characteristics of patients with preoperative score 0 (no LNM risk). In total, 178 patients treated in both hospitals scored 0; this indicated no need for lymphadenectomy; among them, 22 (12.4%) underwent lymphadenectomy but had no LNM and 25 (14.6%) had postoperative chemotherapy. Kaplan-Meier analysis revealed no significant difference in survival between patients who were and were not treated with lymphadenectomy (P = 0.652; Fig. S1).

Table 1
Patients' demographic and clinical characteristics.

Parameters	KCC	YCU	P-value
	N = 432	N = 221	
Age at surgery (years), mean (SD)	58 (11.1)	59 (10.7)	0.739
Parity (number)	2 (0–7)	2 (0–4)	0.272
BMI (kg/m^2), mean (SD)	23.9 (5.26)	24.3 (5.4)	0.329
Tumor volume (cm^3)	9 (0–1728)	12 (0–600)	0.216
Myometrial invasion, no. (%)			
<1/2	286 (66.2)	152 (68.8)	0.538
≥1/2	146 (33.8)	69 (31.2)	
Preoperative serum CA125 (IU/ml)	19 (3.2–2864)	20 (5–3613)	0.312
Preoperation histological subtype, N (%)			0.008
Endometrioid adenocarcinoma G1	250 (57.9)	145 (65.6)	
Endometrioid adenocarcinoma G2	82 (19.0)	35 (15.8)	
Endometrioid adenocarcinoma G3	40 (9.3)	7 (3.2)	
Serous adenocarcinoma	12 (2.8)	4 (1.8)	
Clear cell adenocarcinoma	18 (4.2)	4 (1.8)	
Carcinosarcoma	8 (1.9)	5 (2.3)	
Others	22 (5.1)	21 (9.5)	
FIGO stage, N (%)			0.005
IA	244 (56.5)	156 (70.6)	
IB	72 (16.7)	25 (11.3)	
II	38 (8.8)	11 (5.0)	
IIIA	24 (5.6)	16 (7.2)	
IIIB	6 (1.4)	0 (0)	
IIIC1	27 (6.2)	8 (3.6)	
IIIC2	21 (4.9)	5 (2.3)	
KCC score			
0	119	60	
1–2	181	104	
3–4	132	57	
Extent of lymphadenectomy, N (%)			<0.001
No lymphadenectomy	150 (34.7)	109 (49.3)	
PLX only	179 (41.4)	64 (29.0)	
PLX + PLAX	103 (23.8)	48 (21.7)	

KCC, Kanagawa Cancer Center; YCU, Yokohama City University.

Table 2
Characteristics of patients for whom lymphadenectomy could be omitted (score 0).

Lymphadenectomy LNM site	KCC	YCU	Total
	N = 118	N = 60	N = 178
No lymphadenectomy, N (%)	110 (93.2)	46 (76.7)	156 (87.6)
Recurrence	1 (0.9)	0	1 (0.6)
PLX, N (%)	8 (6.8)	10 (16.6)	18 (10.1)
PEN metastasis	0	0	0
PLAX, N (%)	0 (0)	4 (6.7)	4 (2.3)
PEN or PAN metastasis	0	0	0
Adjuvant therapy			
None, N (%)	101 (85.6)	52 (86.7)	153 (85.4)
Chemotherapy, N (%)	17 (14.4)	8 (13.3)	25 (14.6)

KCC, Kanagawa Cancer Center; YCU, Yokohama City University; LNM, lymph node metastasis; PLX, pelvic lymphadenectomy; PEN, pelvic lymph node; PLAX, para-aortic lymphadenectomy; PAN, para-aortic lymph node.

Among the 149 KCC patients with scores 1–2 (moderate LNM risk) who underwent PLX, 13 (8.7%) had cancer recurrence (some in more than one site), including 2 (1.3%) with PAN metastasis (Table 3). Other sites of recurrence were the peritoneal cavity, PEN, vaginal stump, inguinal lymph nodes (intrapelvic), and lung (extrapelvic).

Table 4 compares KCC and YCU patients who underwent lymphadenectomy. There was no difference in the PEN metastasis between the patients of the two centers after PLX (9.0% and 6.3%, respectively; P = 0.787), indicating comparable accuracy in identifying patients who would not benefit from PLX. However, a significant difference was observed for patients treated with PLAX. Thus, among the 103 patients who underwent PLAX in the KCC, 32 (31.1%) showed metastasis to PEN and 20 (19.4%) to PAN, while among the 48 patients who were underwent PLAX in the YCU, metastases to PEN and PAN were found in 7 (14.6%) and 3 (6.3%), respectively. Statistical analysis indicated that the accuracy of predicting metastases to PEN and PAN for PLAX-treated patients was significantly higher in the KCC than in YCU (P = 0.039 and P = 0.049, respectively).

Table 5 shows the results of KCC preoperative scoring for the patients treated with PLAX in the YCU. While 48 patients underwent PLAX in the YCU, the application of the KCC system could decrease this number to 25 (patients with scores 3–4), i.e., almost to 50%; among these patients, 3 had PAN metastasis. These data indicate that patient stratification based on the KCC system significantly increased the accuracy of predicting PAN metastasis (from 6.3% to 12.0%; P < 0.01).

The overall five-year survival rates for patients with FIGO stages I, II, and III disease treated in the KCC and YCU were 97.2% and 96.5%, 91.5% and 72.7%, and 82.8% and 81.3%, respectively (Fig. S2). These data indicate higher survival for KCC patients, especially those with stage II

Table 3
Initial failure patterns and sites in Kanagawa Cancer Center patients with score 1–2 treated with PLX.

	PLX
	N = 149
Recurrence, N (%)	13 (8.7)
Initial failure pattern, N (%)	
Intrapelvic recurrence only	8 (5.4)
Extrapelvic recurrence only	4 (2.7)
Intrapelvic and extrapelvic recurrence	1 (0.7)
Initial failure site, N (%)	
Intrapelvic	
Abdominal cavity	7 (4.7)
Vagina	3 (2.0)
Inguinal node	1 (0.7)
PEN	1 (0.7)
Extrapelvic	
Lung	3 (2.0)
PAN	2 (1.3)

PLX, pelvic lymphadenectomy; PEN, pelvic lymph node; PAN, para-aortic lymph node.

Table 4
Rates of lymph node metastasis in patients treated with systematic lymphadenectomy.

Lymphadenectomy Metastasis node site	KCC N = 282	YCU N = 112	P-value
PLX, N	179	64	
PEN metastasis, N (%)	16 (9.0)	4 (6.3)	0.787
PLAX, N	103	48	
PEN metastasis, N (%)	32 (31.1)	7 (14.6)	0.039
PAN metastasis, N (%)	20 (19.4)	3 (6.3)	0.049
PEN metastasis only, N (%)	15 (14.6)	5 (10.4)	
PEN and PAN metastasis, N (%)	17 (16.5)	2 (4.2)	
PAN metastasis only, N (%)	3 (3.0)	1 (2.1)	

KCC, Kanagawa Cancer Center; YCU, Yokohama City University; PLX, pelvic lymphadenectomy; PEN, pelvic lymph node; PLAX, para-aortic lymphadenectomy; PAN, para-aortic lymph node.

disease, compared with YCU patients, further validating the utility of our preoperative scoring system. The corresponding survival rates reported in Japan in 2007 were 95.3%, 89.8%, and 75.6%, respectively [2]. Other reports have indicated that overall five-year survival of patients with FIGO stage III in hospitals routinely performing PLAX was 79–85% [17,18], which is consistent with that observed after KCC system-based personalization.

4. Discussion

The results of the analysis performed in this study indicate good prognosis for the patients in the no-lymphadenectomy group identified according to the KCC preoperative scoring system (score 0, no LNM risk), strongly suggesting that lymphadenectomy for these patients can be safely omitted. Moreover, this scoring system allowed the determination of the extent of lymphadenectomy and prevention of unnecessary PLAX.

In a previous study, Mitamura et al. have also demonstrated the safety of lymphadenectomy omission using a scoring system based on clinical parameters similar to those of the KCC [19]: tumor volume less than 36 cm^3, G1 or G2 endometrioid adenocarcinoma, CA125 levels below 28 and 70 U/ml for patients aged >50 and ≤50 years, respectively, and no myometrial invasion. As a result, they have reported a low recurrence rate (1.8%) and 100% five-year survival rate, although the analyzed sample size (51 patients) was small [19]. In our study, only 1 among the 156 patients in the lymphadenectomy-omitted group had recurrence (0.6%); it was an extremely rare case wherein the extirpated uterine left no remaining lesions, but the patient had rapid spread of systemic LNM despite very early cancer stage and the absence of other recurrence risk factors; she died 58 months post-surgery. The five-year survival rate in the no-lymphadenectomy group was 99.1%, which is similar to that reported by Mitamura et al. [19]. However, we used a more stringent cut-off value for tumor volume (6 cm^3 versus 36 cm^3 in [19]) that allowed us to not only identify cases where lymphadenectomy may be omitted, but also to determine the scope of lymph node dissection and, thus, avoid needless PLAX.

Several other retrospective studies examined low-risk factors for LNM in patients with endometrial cancer and indicated that lymphadenectomy may be avoided in these patients. Thus, Mariani et al. have reported that patients with G1/G2 endometrioid adenocarcinoma, <50% of myometrial invasion, and tumor size < 2 cm have low LNM risk [3,20], while Milam et al. have shown that LNM occurs in 0.8% of such patients [21]. Schink et al. have reported that tumor size is important to assess LNM risk, as evidenced by the LNM rate of 15% and 4% observed in patients with tumors above and below 2 cm, respectively [22]. In the present study, 22 of the 178 patients with 0 LNM risk were treated with lymphadenectomy; however, no significant difference between the lymphadenectomy and no-lymphadenectomy groups was observed in the survival rate, and none of the patients in both groups (0%) had LNM, indicating that lymphadenectomy could be safely omitted for the patients who scored 0 according to the KCC system.

Table 5
Diagnostic rate of lymph node metastasis based on KCC scoring of PLAX-treated YCU patients.

	Before using scoring	After using scoring	P-value
PLAX, N	48	25	
PAN metastasis, N (%)	3 (6.3)	3 (12.0)	<0.01
Both PEN and PAN metastasis, N	2	2	
PAN metastasis only, N	1	1	

It should be also emphasized that patients who, as a result of KCC scoring, underwent PLX but not PLAX (scores 1–2) had a low rate of tumor recurrence in PAN (1.3%; Table 3). Furthermore, comparison of LNM rates between KCC and YCU patients (Table 4) and the application of the KCC system to patients treated by PLAX in YCU (Table 5) demonstrated high rate of metastasis prediction by the KCC scoring system, indicating that PLAX was unnecessary in almost 50% of YCU cases. Although Todo et al. have reported that for 316 patients who underwent PLX, cancer recurrence in PAN was somewhat higher (5.1%) compared to that observed in the current study [23], our results strongly suggest that PLAX may be safely omitted for endometrial cancer patients with KCC scores 1–2.

A number of previous studies have investigated the rate of metastasis to PAN in endometrial cancer. A recent large-scale retrospective study conducted in Japan has reported a PAN metastasis rate of 18% [6], while another study in the USA has detected PAN metastasis in 14% of 281 patients, excluding the low-risk group (endometrioid adenocarcinoma of grade G1/G2 with myometrial invasion < 50%, and tumor size < 2 cm) [3]. In a large study of 15,234 patients allocated to the high-risk group using the Mayo Clinic criteria (myometrial invasion > 50%, tumor grade G3, and tumor size > 2 cm), LNM was detected in 6.4% cases [24]. In our study, patients to be treated with PLAX were identified using the KCC system and the prediction rate of PAN metastasis (19.4%) was comparable or even greater than that reported by previous studies, underscoring high prognostic accuracy of our system. The prediction rate of PAN metastasis was significantly improved after the application of the KCC scoring system to YCU patients (Table 5), allowing the omission of unnecessary risk-associated treatment (PLAX), which is an objective of personalized medicine; as a result, the quality of life for endometrial cancer patients undergoing surgery was improved. Compared with YCU, the KCC demonstrated significantly higher accuracy in predicting PAN metastasis for patients who underwent PLAX because it used preoperative patient stratification based on four LNM risk factors, whereas YCU used only one (myometrial invasion) reflecting the practice generally adopted in Japan. Among the risk factors for PAN metastasis, tumor volume, serum CA125 value, myometrial invasion > 50%, cervical invasion, positive peritoneal cytology, G3 histological differentiation, lymphovascular space invasion, and PEN metastasis are considered important [25,26]. The development of a reliable system to correctly stratify patients for PLX and PLAX based on preoperatively evaluable important risk factors should contribute to treatment efficiency and allow avoidance of unnecessary risks.

Over the last few years, sentinel lymph node (SLN) biopsy has rapidly become a standard of care in endometrial cancer as an alternative approach to complete lymphadenectomy for cancer staging, especially in patients with low and intermediate risk of LNM [27,28]. The aim of SLN mapping is to identify metastatic cancer cells in the draining lymph nodes closest to the tumor, which would determine the extent of surgery, thus preventing unnecessary interventions and morbidity. However, in a significant proportion of patients, sentinel nodes, especially the ones in the para-aortic area, cannot be mapped, and for them, our preoperative scoring system would have a particular diagnostic relevance, since complete lymphadenectomy may be avoided.

Our study has provided the validation of the preoperative scoring system adopted in the KCC to identify endometrial cancer patients

requiring lymphadenectomy and to determine the extent of the treatment; however, it had some limitations. First, we did not evaluate postoperative chemotherapy and radiotherapy, which are a part of multimodal cancer treatment. Second, for patients with preoperative scores 1–2, the prognostic accuracy of PEN metastasis after PLX was lower compared to that of PEN and PAN metastasis after PLAX; therefore, the indications to perform PLX should be additionally examined.

In conclusion, in this study we validated our unique preoperative scoring system, which not only provides accurate stratification of endometrial cancer patients for lymphadenectomy but also allows the determination of the scope of lymph node dissection (PLX only or PLX and PALX). KCC preoperative scoring can be applied to identify patients without LNM risk and omit unnecessary lymphadenectomy, thus decreasing the chances of concurrent complications. The KCC system has also demonstrated high accuracy in predicting cancer recurrence in PAN and can be used to minimize the rate of unnecessary PLAX. In the recent strive to adhere to the principles of personalized treatment, the need for lymphadenectomy as a part of surgical treatment for uterine cancer should be carefully evaluated, and the preoperative scoring adopted by the KCC may be a useful clinical tool to perform patient stratification for lymphadenectomy.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ygyno.2016.06.004.

Conflict of interest statement

The authors declare no conflict of interest.

Acknowledgements

Editorial support, in the form of medical writing, collating author comments, copyediting, fact checking, and referencing, was provided by Editage, a division of Cactus Communications.

References

[1] K. Katanoda, M. Hori, T. Matsuda, A. Shibata, Y. Nishino, M. Hattori, et al., An updated report on the trends in cancer incidence and mortality in Japan, 1958–2013, Jpn. J. Clin. Oncol. 45 (2015) 390–401.
[2] A. Daisuke, An annual patient report in fiscal year 2007, Acta Obstet. Gynaecol. Jpn 67 (2015) 1215–1226.
[3] A. Mariani, M.J. Webb, G.L. Keeney, T.G. Lesnick, K.C. Podratz, Surgical stage I endometrial cancer: predictors of distant failure and death, Gynecol. Oncol. 87 (2002) 274–280.
[4] A. Mariani, S.C. Dowdy, W.A. Cliby, B.S. Gostout, M.B. Jones, Wilson TO, et al., Prospective assessment of lymphatic dissemination in endometrial cancer: a paradigm shift in surgical staging, Gynecol. Oncol. 109 (2008) 11–18.
[5] D.S. Chi, R.R. Barakat, M.J. Palayekar, D.A. Levine, Y. Sonoda, K. Alektiar, et al., The incidence of pelvic lymph node metastasis by FIGO staging for patients with adequately surgically staged endometrial adenocarcinoma of endometrioid histology, Int. J. Gynecol. Cancer 18 (2007) 269–273.
[6] Y. Todo, H. Kato, M. Kaneuchi, H. Watari, M. Takeda, N. Sakuragi, Survival effect of para-aortic lymphadenectomy in endometrial cancer (SEPAL study): a retrospective cohort analysis, Lancet 375 (2010) 1165–1172.
[7] ASTEC Study Group, H. Kitchener, A.M. Swart, Q. Qian, C. Amos, M.K. Parmar, Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study, Lancet 373 (2009) 125–136.
[8] P. Benedetti Panici, S. Basile, F. Maneschi, A. Alberto Lissoni, M. Signorelli, G. Scambia, et al., Systematic pelvic lymphadenectomy vs. no lymphadenectomy in early-stage endometrial carcinoma: randomized clinical trial, J. Natl. Cancer Inst. 100 (2008) 1707–1716.
[9] Y. Watanabe, D. Aoki, R. Kitagawa, S. Takeuchi, S. Sagae, N. Sakuragi, et al., Status of surgical treatment procedures for endometrial cancer in Japan: results of a Japanese Gynecologic Oncology Group Survey, Gynecol. Oncol. 105 (2007) 325–328.
[10] E.E. Partrige, J.M. Jessup, E.S. Donaldson, P.T. Taylor, M. Randall, P. Braley, et al., 1996 patients care evaluation study (PCF) of cancer of corpus uteri, National Cancer Database (NCDB), American College of Surgery, Gynecol. Oncol. 72 (1999) 445.
[11] M.M. AlHilli, K.C. Podratz, S.C. Dowdy, J.N. Bakkum-Gamez, A.L. Weaver, M.E. McGree, et al., Risk-scoring system for the individualized prediction of lymphatic dissemination in patients with endometrioid endometrial cancer, Gynecol. Oncol. 131 (2013) 103–108.
[12] S.C. Dowdy, B.J. Borah, J.N. Bakkum-Gamez, A.L. Weaver, M.E. McGree, L.R. Haas, et al., Prospective assessment of survival, morbidity, and cost associated with lymphadenectomy in low-risk endometrial cancer, Gynecol. Oncol. 127 (2012) 5–10.
[13] H. Nakayama, Y. Holi, K. Konnai, M. Ikeda, A. Yamamoto, R. Numazaki, et al., Original individualized treatment strategies in endometrial cancer, Jpn J. Gynecol. Oncol. 27 (2009) 392–400 (in Japanese).
[14] H. Nakayama, N. Matsushita, E. Miyagi, R. Onose, H. Kato, D. Doi, et al., Prognostic factor in endometrial cancer, Obstet. Gynecol. Pract. 48 (1999) 1117–1121 (in Japanese).
[15] H. Nakayama, N. Matsushita, E. Miyagi, R. Onose, H. Kato, Do serum CA125 levels predict poor prognosis in patient with endometrial cancer? Acta Obstet. Gynaecol. Jpn 51 (1999) 1150–1156 (in Japanese).
[16] Y. Kanda, Investigation of the freely available easy-to-use software 'EZR' for medical statistics, Bone Marrow Transplant. 48 (2013) 452–458.
[17] A. Mariani, M.J. Webb, L. Galli, K.C. Podratz, Potential therapeutic role of para-aortic lymphadenectomy in node-positive endometrial cancer, Gynecol. Oncol. 76 (2000) 348–356.
[18] H. Watari, T. Mitamura, M. Moriwaki, M. Hosaka, Y. Ohba, S. Sudo, et al., Survival and failure pattern of patients with endometrial cancer after extensive surgery including systematic pelvic and para-aortic lymphadenectomy followed by adjuvant chemotherapy, Int. J. Gynecol. Cancer 19 (2009) 1585–1590.
[19] H. Mitamura, H. Watari, Y. Todo, T. Kato, Y. Konno, M. Hosaka, et al., Lymphadenectomy can be omitted for low-risk endometrial cancer based on preoperative assessments, J. Gynecol. Oncol. 25 (2014) 301–305.
[20] A. Mariani, M.J. Webb, G.L. Keeney, M.G. Haddock, G. Calori, K.C. Podratz, Low-risk corpus cancer: is lymphadenectomy or radiotherapy necessary? Am. J. Obstet. Gynecol. 182 (2000) 1506–1519.
[21] M. Milam, J. Java, J. Walker, L. Parker, D. Metzinger, R. Coleman, Incidence of nodal metastasis in endometrioid endometrial cancer risk groups: a Gynecologic Oncology Group multicenter review, Gynecol. Oncol. 120 (2011) S4, http://dx.doi.org/10.1016/j.ygyno.2010.12.012.
[22] J.C. Schink, A.W. Rademaker, D.S. Miller, J.R. Lurain, Tumor size in endometrial cancer, Cancer 67 (1991) 2791–2794.
[23] Y. Todo, H. Kato, S. Minobe, K. Okamoto, Y. Suzuki, S. Sudo, et al., Initial failure site according to primary treatment with or without para-aortic lymphadenectomy in endometrial cancer, Gynecol. Oncol. 121 (2011) 314–318.
[24] R. Vargas, J.A. Rauh-Hain, J. Clemmer, R.M. Clark, A. Goodman, W.B. Growdon, et al., Tumor size, depth of invasion, and histological grade as prognostic factors of lymph node involvement in endometrial cancer: a SEER analysis, Gynecol. Oncol. 133 (2014) 216–220.
[25] K. Hirahatake, H. Hareyama, N. Sakuragi, M. Nishiya, S. Makinda, S. Fujimoto, A clinical and pathological study on paraaortic lymph node maetastasis in endometrial carcinoma, J. Surg. Oncol. 65 (1997) 82–87.
[26] Y. Todo, N. Sakuragi, R. Nishida, T. Yamada, Y. Ebina, R. Yamamoto, et al., Combined use of magnetic resonance imaging, CA 125 assay, histological type, and histological grade in the prediction of lymph node metastasis in endometrial carcinoma, Am. J. Obstet. Gynecol. 188 (2003) 1265–1272.
[27] B. Marcos, D. Gil, L. Fabrice, H. Denis, M. Patrice, M. Henri, et al., Detection rate and diagnostic accuracy of sentinel-node biopsy in early stage endometrial cancer: a prospective multicentre study (SENTI-ENDO), Lancet Oncol. 12 (2011) 469–476.
[28] A. Papadia, S. Imboden, F. Siegenthaler, M.L. Gasparri, S. Mohr, S. Lanz, et al., Laparoscopic indocyanine green sentinel lymph node mapping in endometrial cancer, Ann. Surg. Oncol. (Jan 20 2016) http://dx.doi.org/10.1245/s10434-016-5090-x (Epub ahead of print).

論文目録

Ⅰ　主論文

A preoperative risk-scoring system to predict lymph node metastasis in endometrial cancer and stratify patients for lymphadenectomy.
Imai K, Kato H, Katayama K, Nakanishi K, Kawano A, Iura A, Konnai K, Onose R, Hirahara F, Miyagi E.：Gynecologic Oncology Vol.142, Page 273-277. 2016

Ⅱ　参考論文

Combination of conservative treatment and temporary bilateral laparoscopic uterine artery clipping with hysteroscopic transcervical resection for cervical pregnancy: A retrospective study. Imai K, Fukushi Y, Nishimura M, Ohara Y, Suzuki Y, Ota H, Nakajima A, Wada S, Fujino T. J Gynecol Obstet Hum Reprod. 50(4) 101735.2021

Laparoscopically Diagnosed and Treated Ruptured Metastatic Ovarian Tumor.　Nishimura M, Matsumoto S, Ohara Y, Imai K, Wada S, Fujino T.　Gynecol Minim Invasive Ther. 9(2) 88-90.2020

Analysis of risk factors of postlaparoscopic shoulder pain. Wada S, Fukushi Y, Nishimura M, Matsumoto S, Takimoto K, Imai K, Ota H, Tsuzuki Y, Nakajima A, Fujino T. J Obstet Gynaecol Res. 46(2) 310-313.2020

Laparoscopic Management of Cesarean Scar Pregnancy. Ohara Y, Wada S, Fukushi Y, Nishimura M, Imai K, Fujino T. J Minim Invasive Gynecol. 26(5) 798-799.2019

Complications Related to the Initial Trocar Insertion of 3 Different Techniques: A Systematic Review and Meta-analysis. Nishimura M, Matsumoto S, Ohara Y, Minowa K, Tsunematsu R, Takimoto K, Imai K, Tsuzuki Y, Ota H, Nakajima A, Fukushi Y, Wada S, Fujino T, Ito YM. J Minim Invasive Gynecol. 26(1) 63-70.2019

Negative peritoneal washing cytology during interval debulking surgery predicts overall survival after neoadjuvant chemotherapy for ovarian cancer. Iura A, Takita M, Kawano A, Imai K, Konnai K, Onose R, Kato H. J Gynecol Oncol. 29(5) e70.2018