Thai Journal of Obstetrics and Gynaecology
January 2018, Vol. 26, pp. 59-67

GYNECOLOGY

Association Between Preoperative Serum Markers and Lymph Node Metastasis in Endometrioid Adenocarcinoma of Endometrium

Roseleeya Aleediman, M.D.*,
Kamaitorn Tientong, M.D.*,**.

** Department of Obstetrics and Gynecology, Rajavithi Hospital, Bangkok 10400, Thailand*
*** College of Medicine, Rangsit University, Bangkok, Thailand*

ABSTRACT

Objectives: Serum markers play many roles in various cancers. Our aim is to investigate whether preoperative serum markers can be used for predicting lymph node (LN) metastasis in endometrioid adenocarcinoma of endometrium.

Materials and Methods: Clinical characteristics of all patients with pure endometrioid adenocarcinoma of endometrium who underwent complete surgical staging at Rajavithi hospital, between 1 January 2010 and 31 December 2014 were retrospectively reviewed. Preoperative serum markers including hemoglobin (Hb), neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), multiplication of neutrophil and monocyte counts (MNM), platelet counts, mean platelet volume (MPV) and serum albumin levels were investigated. Sensitivity, specificity, positive predictive value, negative predictive value of serum markers to predict lymph node metastasis were evaluated.

Results: Two hundred eighty-three patients who meet the study inclusion criteria were included. There were 40/283 (14.3%) of LN metastasis. LN metastasis was significantly associated with lower Hb level ($p < 0.001$) and higher NLR, PLR, MNM and platelet count ($p = 0.018$, $p = 0.004$, $p = 0.008$ and $p = 0.03$ respectively). The best cut off values to identify lymph node metastasis were 11.85 for Hb (72.5% sensitivity, 59.7% specificity), 2.29 for NLR (60.0% sensitivity, 61.7% specificity), 10.37 for PLR (67.5% sensitivity, 56% specificity), 0.0068 for MNM (70% sensitivity, 56% specificity) and 297,500 for platelet count (62.5% sensitivity, 57% specificity).

Conclusion: Preoperative lower Hb level, higher NLR, PLR, MNM and platelet count were significantly related with lymph node metastasis. They could be used in clinical practice to rule in patients with low risk for LN metastasis without extra costs.

Keywords: Endometrioid adenocarcinoma of endometrium, lymph node metastasis, hemoglobin, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio.

Correspondence to: *Kamaitorn Tientong, M.D., Department of Obstetrics and Gynecology, Rajavithi hospital Phyathai Road, Rajathevee, Bangkok 10400, Thailand, Telephone: (+66)813754048, E-mail: tulkamaitorn@gmail.com*

การศึกษาความสัมพันธ์ระหว่างค่าผลเลือดก่อนการผ่าตัดและภาวะการแพร่กระจายทางหลอดน้ำเหลืองในมะเร็งเยื่อบุโพรงมดลูกชนิด เนื้อเยื่อ endometrioid

โรสลียา อะลีดิมัน, กมัยธร เทียนทอง

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาประสิทธิภาพค่าความแม่นยำของการใช้ค่าผลเลือดก่อนการผ่าตัด ในการทำนายการแพร่กระจายทางหลอดน้ำเหลืองในมะเร็งเยื่อบุโพรงมดลูกชนิด endometrioid*

วัสดุและวิธีการ: *เป็นการศึกษาย้อนหลังโดยการคัดเลือกผู้ป่วยมะเร็งเยื่อบุโพรงมดลูกชนิด endometrioid ซึ่งได้รับการผ่าตัดและเลาะต่อมน้ำเหลืองเพื่อกำหนดระยะของโรค ในโรงพยาบาลราชวิถี ในช่วงวันที่ 1 มกราคม พ.ศ. 2553 จนถึงวันที่ 31 ธันวาคม พ.ศ. 2557 โดยค่าผลเลือดก่อนการผ่าตัดที่ใช้ในการวิเคราะห์ประกอบด้วย ความเข้มข้นของเม็ดเลือดแดง สัดส่วนของนิวโทรฟิลล์ต่อลิมโฟไซด์ สัดส่วนของเกร็ดเลือดต่อลิมโฟไซด์ การเพิ่มจำนวนเท่าตัวของนิวโทรฟิลล์และโมโนไซด์ จำนวนเกร็ดเลือด ค่าเฉลี่ยปริมาตรเกร็ดเลือด และระดับอัลบูมินในเลือด*

ผลการศึกษาวิจัย: *มีผู้เข้าเกณฑ์การวิจัยนี้ทั้งหมด 283คน โดยมี 40 คนมีการแพร่กระจายของโรคไปยังหลอดน้ำเหลือง พบว่าการแพร่กระจายไปยังหลอดน้ำเหลืองสัมพันธ์กับภาวะความเข้มข้นของเม็ดเลือดแดงต่ำ ($p<0.001$) สัดส่วนของนิวโทรฟิลล์ต่อลิมโฟไซด์ สัดส่วนของเกร็ดเลือดต่อลิมโฟไซด์ ค่าการเพิ่มจำนวนเท่าตัวของนิวโทรฟิลล์และโมโนไซด์ และจำนวนเกร็ดเลือด ($p=0.018$, $p=0.004$, $p=0.008$ and $p=0.03$ ตามลำดับ) ที่สูงขึ้นอย่างมีนัยสำคัญทางสถิติ โดยค่าที่เหมาะสมที่ใช้นำมาวิเคราะห์เพื่อหาค่าความแม่นยำของการแพร่กระจายไปหลอดน้ำเหลืองของตัวแปรต่างๆ มีดังนี้ ค่าความเข้มข้นเม็ดเลือดแดง คือ 11.85 โดยมีค่าความไวร้อยละ 72.5 และค่าความจำเพาะร้อยละ 59.7, สัดส่วนของนิวโทรฟิลล์ต่อลิมโฟไซด์ คือ 2.29 โดยมีค่าความไวร้อยละ 60.0 และค่าความจำเพาะร้อยละ 61.7, สัดส่วนของเกร็ดเลือดต่อลิมโฟไซด์คือ 10.37 โดยมีค่าความไวร้อยละ 67.5 และค่าความจำเพาะร้อยละ 56, ค่าการเพิ่มจำนวนเท่าตัวของนิวโทรฟิลล์และโมโนไซด์ คือ 0.0068 โดยมีค่าความไวร้อยละ 70 และค่าความจำเพาะร้อยละ 56 และจำนวนเกร็ดเลือด คือ 297,500 โดยมีค่าความไวร้อยละ 62.5 และค่าความจำเพาะร้อยละ 57*

สรุป: *ค่าความเข้มข้นเม็ดเลือดแดงที่ต่ำ และสัดส่วนของนิวโทรฟิลล์ต่อลิมโฟไซด์ สัดส่วนของเกร็ดเลือดต่อลิมโฟไซด์ การเพิ่มจำนวนเท่าตัวของนิวโทรฟิลล์และโมโนไซด์ รวมทั้งจำนวนเกร็ดเลือดที่สูง เป็นตัวบ่งชี้การแพร่กระจายทางหลอดน้ำเหลืองในมะเร็งเยื่อบุโพรงมดลูกชนิด เนื้อเยื่อ endometrioid ได้อย่างมีนัยสำคัญทางสถิติ*

คำสำคัญ: *มะเร็งเยื่อบุโพรงมดลูก, การแพร่กระจายของมะเร็งไปยังต่อมน้ำเหลือง, ความเข้มข้นของฮีโมโกลบิน, อัตราส่วนของเซลล์เม็ดเลือดขาว, อัตราส่วนของเกร็ดเลือดและเซลล์เม็ดเลือดขาว*

Introduction

Endometrial cancer (EMC) is the most common malignancy of female genital tract in more developed countries. In the United States, it was estimated that 54,870 new uterine cancers occurred in 2015[1]. On the contrary, incidence of this disease decreases in less developed countries. At Rajavithi hospital, EMC is the second most common cancer in gynecology. It was estimated that 167 new cases occurred in 2015.

Patients with EMC have been treated with surgical staging since 1988 which includes hysterectomy, bilateral salpingo-oophorectomy, peritoneal washing for cytology, and pelvic and paraaortic lymph node (LN) sampling using explorative laparotomy or laparoscopy. However, there is a controversial issue about the role of lymphadenectomy in surgical management of EMC. Because some retrospective studies have suggested that systematic lymphadenectomy be beneficial, a full pelvic and paraaortic lymphadenectomy were previously done in all patients[2-4]. After that, two randomized clinical trials concluded that routine lymph node dissection did not improve the outcome of patients with early-stage EMC[5-6]. On the other hand, lymphadenectomy can identify true staging, guide the appropriate adjuvant treatment, and eradicate metastatic LN. To avoid systematic overtreatment, NCCN guideline recommends a more selective and tailored lymphadenectomy approach[7]. Computerized Tomography (CT) and Magnetic Resonance Imaging (MRI) do not have good sensitivity for detecting metastatic LN in EMC[8], but Positron Emission Tomography (PET)/CT scan has been used for preoperatively lymphatic spreading. In patients with deeply invasive grade 2 on preoperative MRI, grade 3, serous, and clear cell, preoperative PET/CT has moderate sensitivity (78%–79%) with good specificity (98%–99%), positive predictive value (91%–92%), and negative predictive value (95%–97%)[9-11]. Although PET/CT is moderate sensitivity for detecting metastatic LN, it is not used in routine practice in Thailand because of high expense. Therefore, we try to find the simple, inexpensive preoperative blood test to evaluate correlation with LN metastasis.

The host immune responses play important roles in the local environments of the tumors. Interactions between tumor cells and host immune responses cause tumor progression and growth[12]. Circulating cytokines and chemokines from tumor cells trigger systemic alterations of inflammatory responses, such as a low hemoglobin level, an increase in neutrophil counts, a slight increase in platelet counts, and a decline in lymphocyte counts[13]. Elevated neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR)] and multiplication of neutrophil and monocyte counts (MNM) have been investigated as prognostic and predictive markers in patients with various cancers[14-16]. Moreover, low-pretreatment hemoglobin (Hb) and thrombocytosis were associated with unfavorable prognosis in a number of epithelial malignancy including EMC[17]. Based on the theory that mean platelet volume (MPV) is an indicator of platelet activation, larger MPV was found to be a marker for predicting advanced-stage endometrial cancers in one study[18]. Therefore, this retrospective study was designed to investigate whether preoperative serum markers can be used for predicting LN metastasis in endometrioid adenocarcinoma of endometrium.

Materials and Methods

The study population consisted of patients with pathologically pure endometrioid adenocarcinoma of endometrium who underwent hysterectomy, salpingo-oophorectomy, pelvic and/or paraaortic LN sampling and peritoneal cytology at Rajavithi hospital, between 1 January 2010 and 31 December 2014. Patients with acute inflammatory disease, myeloproliferative disorders, autoimmune disease, hepatitis, splenectomy and synchronous malignancy were not included in the study. Patients using aspirin or clopidogrel which could affect platelet count and/or function were also excluded.

The study protocol was approved by the ethics committee of Rajavithi hospital, Thailand. Clinicopathological data, including age, body mass index (BMI), parity, menopausal status, diabetes, histopathological grade, surgical International Federation of Gynaecology and Obstetrics (FIGO) stage (revised in 2009), tumor diameter, myometrial invasion, lymphovascular space invasion (LVSI), lower uterine and cervical stromal involvement were retrospectively reviewed.

Preoperative hematological parameters were documented from medical records. Complete blood counts (CBCs) were obtained within one month before the operation using Coulterls780 and Xn1000 automatic analyzer in all patients. Serum albumin was collected as well within three months before the operation using Cobas8000 modular analyzer. The NLR was defined as the absolute neutrophil count divided by the absolute lymphocyte count, PLR was defined as the absolute platelet count divided by the absolute lymphocyte count and the MNM was defined as the multiplication of neutrophil counts and monocyte counts then divided by 10,000.

All statistical analyses were performed using the Statistical Package for Social Sciences version 16.0 software (SPSS Inc, Chicago, IL, USA). Categorical variables were analyzed using Pearson's chi-square test and Fisher's exact test. Continuous variables were shown as the mean ± standard deviation and compared using the student's t-test. The differences in each serum markers were compared using the Mann-Whitney U tests. Sensitivity and specificity for different serum markers cutoffs were calculated with receiver-operating curves. Receiver-operating curve analysis was plotted to investigate optimal cutoff values that maximized sensitivity and specificity. $P < 0.05$ was considered to be statistically significant.

Results

A total of 283 patients who meet the study inclusion criteria were included. Table 1 shows clinicopathological characteristics of the patients according to LN metastasis. Of the 283 patients, 213 patients (75.3%) underwent both pelvic and paraaortic LN sampling and 70 patients (24.7%) underwent only pelvic LN sampling. 40 patients (14.1%) had pelvic and/or paraaortic LN metastasis, and 243 patients (85.9%) did not have. Age, BMI, parity, menopausal status and diabetes were not different in group of LN positive and negative for malignancy. In the group of LN metastasis, there were significant higher in high grade of surgical specimen, FIGO staging, lower uterine and cervical involvement, depth of myometrial invasion, presence of LVSI and positive peritoneal cytology.

CBCs were collected in all patients, but data of serum albumin were missed in 50 patients (17.7%). Table 2 shows the comparison between each serum markers and LN metastasis. LN metastasis was significantly associated with lower Hb level ($p<0.001$) and higher NLR, PLR, MNM and platelet count ($p=0.018$, $p=0.004$, $p=0.008$ and $p=0.03$, respectively). MPV and serum albumin were quite higher in LN negative group, but there were no significant difference.

Receiver operating characteristics (ROC) curve findings, indicating the utility of the Hb, NLR, PLR, MNM and platelets count as predictive markers for lymph node metastasis in endometrioid adenocarcinoma of endometrium are shown in Fig. 1 and Table 3. Diagnostic sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of preoperative serum markers by the ROC curve are shown in Table 4. The best cut off values to identify LN metastasis were 11.85 for Hb (72.5% sensitivity, 59.7% specificity, 22.8% PPV, 93.0% NPV), 2.29 for NLR (60.0% sensitivity, 61.7% specificity, 20.15% PPV, 90.4% NPV), 10.37 for PLR (67.5% sensitivity, 56% specificity, 20.15% PPV, 91.3% NPV), 0.0068 for MNM (70% sensitivity, 56% specificity, 20.74% NPV, 91.9% NPV) and 297,500 for platelet count (62.5% sensitivity, 57% specificity, 19.2% PPV, 90.2% NPV). Accuracy of Hb, NLR, PLR, MNM, platelet count are 61.5%, 61.5%, 57.6%, 58.0%, 57.6% respectively.

Table 1. Clinicopathological characteristics of patients with endometrioid adenocarcinoma of endometrium according to LN metastasis.

Characteristics	Total (n = 283)		Pelvic + Paraaortic LN				p value
			Positive (n =40)		Negative (n = 243)		
	n	%	n	%	n	%	
Age (years)							0.113
< 40	15	5.3%	0	0%	15	6.2%	
40-60	178	62.9%	23	57.5%	155	63.8%	
> 60	90	31.8%	17	42.5%	73	30.0%	
BMI (kg/m^2)							0.782
Underweight (< 18.5)	9	3.2%	2	5.0%	7	2.9%	
Normal (≥ 18.5 – 24.99)	98	34.6%	15	37.5%	83	34.2%	
Overweight (≥ 25-29.99)	105	37.1%	15	37.5%	90	37.0%	
Obesity (≥ 30)	71	25.1%	8	20.0%	63	25.9%	
Parity							0.899
0	93	32.9%	14	35.0%	79	32.5%	
1	46	16.3%	7	17.5%	39	16.0%	
≥ 2	144	50.9%	19	47.5%	125	51.4%	
Menopausal status							0.248
premenopause	78	27.6%	8	20.0%	70	28.8%	
menopause	205	72.4%	32	80.0%	173	71.2%	
DM	89	31.4%	13	32.5%	76	31.3%	0.877
Grading of surgical specimen							< 0.001*
G1	135	47.7%	9	22.5%	126	51.9%	
G2	100	35.3%	14	35.0%	86	35.4%	
G3	48	17.0%	17	42.5%	31	12.8%	
Staging							< 0.001*[F]
1	193	68.2%	0	0%	193	79.4%	
2	33	11.7%	0	0%	33	13.6%	
3	53	18.7%	38	95.0%	15	6.2%	
4	4	1.4%	2	5.0%	2	0.8%	
Tumor diameter (cm)							< 0.001[M]
Mean ± S.D.	4.36 ± 2.39		6.63 ± 2.41		3.99 ± 2.18		
Median (min-max)	4 (0.1-13)		6.75 (0.5-13)		4 (0.1-12.5)		
Lower uterine involvement	93	32.9%	24	60.0%	69	28.4%	< 0.001*
Cervical involvement	56	19.8%	14	35.0%	42	17.3%	0.009*
Myometrial invasion							< 0.001*
≤ ½	171	60.4%	9	22.5%	162	66.7%	
> ½	112	39.6%	31	77.5%	81	33.3%	

Table 1. Clinicopathological characteristics of patients with endometrioid adenocarcinoma of endometrium according to LN metastasis. (Cont.)

Characteristics	Total (n = 283)		Pelvic + Paraaortic LN				p value
			Positive (n =40)		Negative (n = 243)		
	n	%	n	%	n	%	
LVSI							< 0.001*
Positive	95	33.6%	32	80.0%	63	25.9%	
Negative	188	66.4%	8	20.0%	180	74.1%	
Peritoneal washing							< 0.001*
positive	18	6.4%	9	22.5%	9	3.7%	
negative	224	79.2%	27	67.5%	197	81.1%	
no data	41	14.5%	4	10.0%	37	15.2%	

BMI: body mass index; DM; diabetes mellitus; LVSI: lymphovascular space invasion. p-value from Chi-Square test, F = p-value from Fisher's Exact Test, M = Mann-Whitney U test, * Significant at the 0.05 level

Table 2. the comparison between each serum markers and LN metastasis.

Serum markers	Pelvic + Paraaortic				p value
	Positive (n=40)		Negative (n=243)		
	Mean	S.D.	Mean	S.D.	
Hb	11.11	1.82	12.23	1.56	< 0.001*^{T}
NLR	3.36	2.20	2.55	1.62	0.018*^{M}
PLR	15.75	9.61	11.71	7.42	0.004*^{M}
MNM	0.00719	0.00113	0.00671	0.00106	0.008*^{M}
Plt count	322.40	77.61	294.81	92.49	0.030*^{M}
MPV	9.30	1.18	9.63	1.15	0.095^{T}
Albumin	4.14	0.44	6.32	29.41	0.293^{M}

Hb: hemoglobin; NLR: neutrophil/lymphocyte ratio; PLR: platelet/lymphocyte ratio; MNM: multiplication of neutrophil and monocyte counts; Plt: platelet; MPV:mean platelet volume. M = Mann-Whitney U test, T=p-value from Independent t-test, *Significant at the 0.05 level

Table 3. Area under the curve and cut-off value in the ROC curve for serum markers.

Variables	Cut-off value	AUC	p-value	95% CI
Hb	≥ 11.85	0.698	< 0.001	0.611-0.785
NLR	≥ 2.285	0.617	0.018	0.517-0.717
PLR	≥ 10.368	0.643	0.004	0.543-0.742
MNM	≥ 0.006815	0.632	0.008	0.533-0.730
Plt	≥ 297.5	0.607	0.030	0.513-0.701

Hb: hemoglobin; NLR: neutrophil/lymphocyte ratio; PLR: platelet/lymphocyte ratio; MNM: multiplication of neutrophil and monocyte counts; Plt: platelet; AUC: area under the curve.

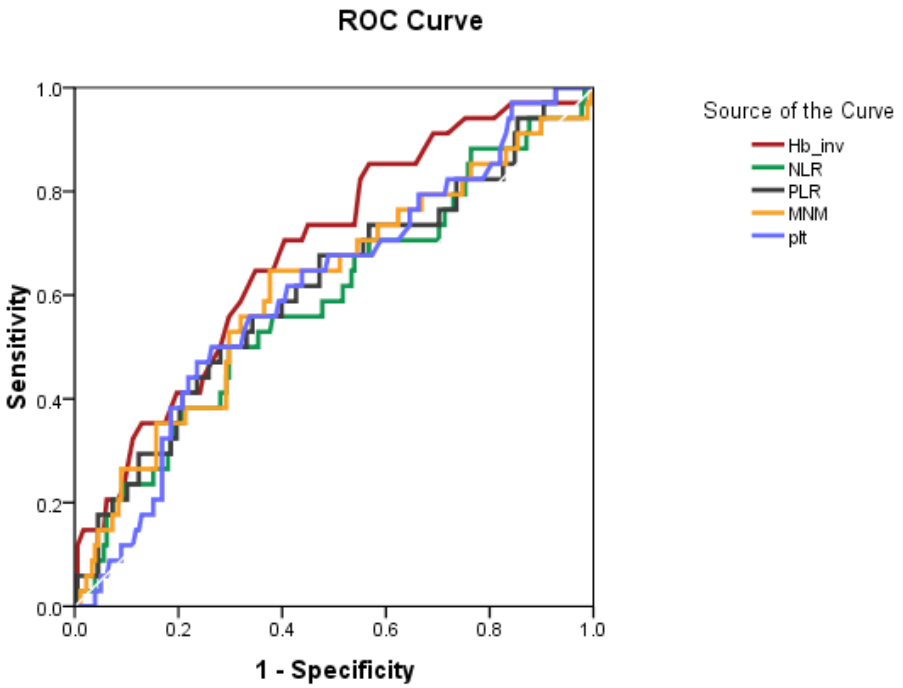

Fig. 1. Flow chart of participants' progress through the study.

Table 4. Diagnostic Sensitivity, specificity, PPV, NPV and accuracy of Serum markers.

serum markers	Cut-off value	Sensitivity (95%CI)	Specificity (95%CI)	PPV (95%CI)	NPV (95%CI)	Accuracy
Hb	< 11.85	72.50%	59.67%	22.83%	92.95%	61.48%
	≥ 11.85	56.11-85.40	53.21-65.89	15.86-31.12	87.73-96.43%	
NLR	≥ 2.285	60.00%	61.73%	20.51%	90.36%	61.48%
	< 2.285	43.33%-75.14%	55.30%-67.87%	13.61%-28.97%	84.82%-94.39%	
PLR	≥ 10.368	67.50%	55.97%	20.15%	91.28%	57.60%
	< 10.368	50.87%-81.43	49.48%-62.31	13.72%-27.95%	85.54%-95.27%	
MNM	≥ 0.006815	70.00%	55.97%	20.74%	91.89%	57.95%
	< 0.006815	53.47%-83.44%	49.48%-62.31%	14.25%-28.56%	86.27%-95.74%	
Plt	≥ 297.5	62.50%	56.79%	19.23%	90.20%	57.60%
	< 297.5	45.80%-77.27%	50.13%-63.11%	12.85%-27.07%	84.35%-94.41%	

Hb: hemoglobin; NLR: neutrophil/lymphocyte ratio; PLR: platelet/lymphocyte ratio; MNM: multiplication of neutrophil and monocyte counts; Plt: platelet; PPV: positive predictive value; NPV: negative predictive value.

Discussion

LN sampling is the necessary procedure of surgical staging in EMC because it can make true staging, guide the appropriate adjuvant treatment, and eradicate metastatic LN. This procedure causes complications such as vessel injury, postoperative lymphedema. To avoid systematic overtreatment, NCCN guideline recommends a more selective and tailored lymphadenectomy approach according to intraoperative finding[19]. However, risk factors for

predicting LN metastasis are cell type, grade, depth of myometrial invasion, LVSI and cervical involvement which are clearly detected after surgical procedure[20]. Thus, many studies have investigated about noninvasive preoperative methods with high accuracy and sensitivity to detect LN metastasis. To date, no preoperative test whether it is PET/CT scan, MRI or any preoperative blood tests is able to detect LN micrometastasis.

Tumor cells can produce cytokines, such as interleukins, interferon gamma and tumor necrosis factor which induce hemolysis, suppress erythropoiesis and inhibit the response of erythroid progenitor cells to erythropoietin[21]. Platelets have been associated with malignant diseases, based on alteration of coagulation and abnormal hemostasis in cancer patients[18]. The presence of neutrophilia, leukocytosis and thrombocytosis represents a nonspecific response to cancer-related inflammation[22]. Neutrophilia provides a suitable environment and secrets most circulating vascular endothelial growth factors, and finally it causes cancer progression[23].

At present, a few studies have investigated the accuracy of systemic inflammatory response (SIR) markers for LN metastasis in endometrial cancer. One retrospective study reviewed the correlation of SIR markers with LN metastasis compared with serum CA-125 in endometrioid adenocarcinoma of endometrium after surgical staging. Preoperative SIR markers including CBCs, CRP, fibrinogen and serum albumin were obtained. This study found that preoperative NLR, PLR, CRP, albumin, and fibrinogen levels were not superior to CA-125 for the prediction of LN metastasis, but that among the markers, only NLR and PLR reached comparable sensitivities (63.3% and 64.5%, respectively) (24). Serum CRP, fibrinogen and CA 125 were not used in routine preoperative blood tests in our country. This study has some limitations. First, only 26% of patients underwent both pelvic and paraaortic lymphadenectomy and 8.8% of patients did not undergo pelvic and paraaortic lymphadenectomy. Second, CRP and fibrinogen values were missing for several patients.

In the present study, a total of 283 patients were included. All of our patients were surgical staging with pelvic and/or paraaortic LN sampling. Of the 283 patients, 213 patients (75.3%) underwent both pelvic and paraaortic LN sampling and 70 patients (24.7%) underwent only pelvic LN sampling. Serum markers were moderate sensitivity to detect LN metastasis in endometrioid adenocarcinoma of endometrium especially Hb, PLR and MNM. Furthermore, negative predictive values (NPV) of Hb, NLR, PLR, MNM and platelet count to predict LN metastasis were more than 90%. These serum markers were acceptable, simple to obtain and calculate. They could be used in clinical practice to rule in patients with low risk for LN metastasis without extra costs. If using these serum markers with other blood test (CA125) or imaging (PET/CT, MRI), it will improve the good performance to rule in patients with low risk for LN metastasis.

Our study has some limitations. First, it was retrospective in nature based on a single institution. Second, there was difference in timing of collecting preoperative hematological parameters in each patient. Lastly, data of serum albumin were missing up to 17.7% of patients. Although the association of these serum markers between the patients with positive or negative lymph nodes was statistically significant, the differences of these values were only small and may be not clinically important. If we had been able to collect all data, the test value would have been improved for using in clinical practice.

Conclusion

Preoperative lower Hb level, higher NLR, PLR, MNM and platelet count were significantly related with lymph node metastasis. They could be used in clinical practice to rule in patients with low risk for LN metastasis without extra costs.

Potential conflicts of interest

The authors declare no conflict of interest.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J Clin 2015;65:5-29.

2. Kilgore LC, Partridge EE, Alvarez RD, Austin JM, Shingleton HM, Noojin F, et al. Adenocarcinoma of the endometrium: survival comparisons of patients with and without pelvic node sampling. Gynecol Oncol 1995;56:29–33.
3. Havrilesky LJ, Cragun JM, Calingaert B, Synan I, Secord AA, Soper JT, et al. Resection of lymph node metastases influences survival in stage IIIC endometrial cancer. Gynecol Oncol 2005;99:689–95.
4. Todo Y, Kato H, Kaneuchi M, Watari H, Takeda M, Sakuragi N. Survival effect of para-aortic lymphadenectomy in endometrial cancer (SEPAL study): a retrospective cohort analysis. Lancet 2010;375:1165–72.
5. ASTEC study group, Kitchener H, Swart AMC, Qian Q, Amos C, Parmar MKB. Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study. Lancet 2009;373:125–36.
6. Benedetti Panici P, Basile S, Maneschi F, Alberto Lissoni A, Signorelli M, Scambia G, et al. Systematic pelvic lymphadenectomy vs. no lymphadenectomy in early-stage endometrial carcinoma: randomized clinical trial. J Natl Cancer Inst 2008;100:1707–16.
7. Soliman PT, Frumovitz M, Spannuth W, Greer MJ, Sharma S, Schmeler KM, et al. Lymphadenectomy during endometrial cancer staging: practice patterns among gynecologic oncologists. Gynecol Oncol 2010;119:291–4.
8. Clark LH, Soper JT. Endometrial Cancer and the Role of Lymphadenectomy. Obstet Gynecol Surv 2016;71:353–60.
9. Signorelli M, Guerra L, Buda A, Picchio M, Mangili G, Dell'Anna T, et al. Role of the integrated FDG PET/CT in the surgical management of patients with high risk clinical early stage endometrial cancer: detection of pelvic nodal metastases. Gynecol Oncol 2009;115:231–5.
10. Crivellaro C, Signorelli M, Guerra L, De Ponti E, Pirovano C, Fruscio R, et al. Tailoring systematic lymphadenectomy in high-risk clinical early stage endometrial cancer: the role of 18F-FDG PET/CT. Gynecol Oncol 2013;130:306–11.
11. Kim HJ, Cho A, Yun M, Kim YT, Kang WJ. Comparison of FDG PET/CT and MRI in lymph node staging of endometrial cancer. Ann Nucl Med 2016;30:104–13.
12. Mantovani A, Allavena P, Sica A, Balkwill F. Cancer-related inflammation. Nature 2008;454:436–44.
13. Tavares-Murta BM, Mendonça MAO, Duarte NL, da Silva JA, Mutão TS, Garcia CB, et al. Systemic leukocyte alterations are associated with invasive uterine cervical cancer. Int J Gynecol Cancer 2010;20:1154–9.
14. Cho H, Hur HW, Kim SW, Kim SH, Kim JH, Kim YT, et al. Pre-treatment neutrophil to lymphocyte ratio is elevated in epithelial ovarian cancer and predicts survival after treatment. Cancer Immunol Immunother 2009;58:15–23.
15. Margolis KL, Rodabough RJ, Thomson CA, Lopez AM, McTiernan A, Women's Health Initiative Research Group. Prospective study of leukocyte count as a predictor of incident breast, colorectal, endometrial, and lung cancer and mortality in postmenopausal women. Arch Intern Med 2007;167:1837–44.
16. Cho H, Kim J-H. Multiplication of neutrophil and monocyte counts (MNM) as an easily obtainable tumour marker for cervical cancer. Biomarkers 2009;14:161–70.
17. Tamussino KF, Gücer F, Reich O, Moser F, Petru E, Scholz HS. Pretreatment hemoglobin, platelet count, and prognosis in endometrial carcinoma. Int J Gynecol Cancer 2001;11:236–40.
18. Oge T, Yalcin OT, Ozalp SS, Isikci T. Platelet volume as a parameter for platelet activation in patients with endometrial cancer. J Obstet Gynaecol 2013;33:301–4.
19. Soliman PT, Frumovitz M, Spannuth W, Greer MJ, Sharma S, Schmeler KM, et al. Lymphadenectomy during endometrial cancer staging: practice patterns among gynecologic oncologists. Gynecol Oncol 2010;119:291–4.
20. Cho H, Kim YT, Kim J-H. Accuracy of preoperative tests in clinical stage I endometrial cancer: the importance of lymphadenectomy. Acta Obstet Gynecol Scand 2010;89:175–81.
21. Khan FA, Shukla AN, Joshi SC. Anaemia and cancer treatment: a conceptual change. Singapore Med J 2008;49:759–64.
22. Bhatti I, Peacock O, Lloyd G, Larvin M, Hall RI. Preoperative hematologic markers as independent predictors of prognosis in resected pancreatic ductal adenocarcinoma: neutrophil-lymphocyte versus platelet-lymphocyte ratio. Am J Surg 2010;200:197–203.
23. Kusumanto YH, Dam WA, Hospers GAP, Meijer C, Mulder NH. Platelets and granulocytes, in particular the neutrophils, form important compartments for circulating vascular endothelial growth factor. Angiogenesis 2003;6:283–7.
24. Suh DH, Kim HS, Chung HH, Kim JW, Park NH, Song YS, et al. Pre-operative systemic inflammatory response markers in predicting lymph node metastasis in endometrioid endometrial adenocarcinoma. Eur J Obstet Gynecol Reprod Biol 2012;162:206–10.