

Prognostic Value of the Cutoffs for HALP in Endometrial Cancer

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Objectives: Using preoperative hemoglobin, albumin, lymphocyte, and platelet (HALP) scores, a cutoff value of HALP in endometrial cancer was identified, and the significance of HALP value in endometrial cancer prognosis was evaluated to guide the management of patients.

Materials and Methods: This study included 626 patients with endometrial cancer who underwent surgery at the First Affiliated Hospital of Chongqing Medical University between June 2015 and June 2020. A Cox regression model was used to analyze the correlation between HALP endometrial cancer recurrence and death, and the receiver operating characteristic curve was used to determine the optimal cutoff value of HALP for predicting the lymph node metastasis (LNM), recurrence, and death of endometrial cancer. Survival analysis was performed using the Kaplan-Meier method and log-rank test.

Results: Univariate analysis revealed that HALP was associated with a lower risk of recurrence and death of endometrial cancer. Multivariate analysis indicated that HALP was an independent protective factor for predicting recurrence and death in endometrial cancer. The thresholds of HALP for predicting LNM, recurrence, and death in endometrial cancer patients are around 33.8. Kaplan-Meier survival curves showed that the recurrence-free and the overall survival rates were significantly lower in the low-HALP group than that in the high-HALP group ($P < 0.001$).

Conclusions: Preoperative HALP values in patients with endometrial cancer are important in predicting LNM, recurrence, and death of patients. HALP scores combined with traditional pathologic factors can better guide the prognostic management of patients.

Key Words: endometrial cancer, HALP score, prognosis, critical value
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Recent studies have shown that endometrial cancer is among the most common malignant tumors in gynecology, and its incidence is increasing in various countries.¹ Although patients have a 5-year survival rate of over 80%, the risk of recurrence and death remains high. Consequently, we should screen out patients with poor prognoses as soon as possible to initiate

treatment earlier and more aggressively, thereby improving quality of life and reducing the risk of recurrence and mortality. Although pathologic parameters such as the age, pathologic type, International Federation of Gynecology and Obstetrics (FIGO) stage, and lymph node status can be used to predict the prognosis of endometrial cancer patients,^{2,3} we still need to find simpler and more accurate indicators.

More and more studies have shown that systemic inflammation and nutritional status are related to cancer prognosis, and higher inflammatory markers are associated with poorer outcomes. Inflammatory-related indicators are widely used to predict the prognosis of various cancers, such as the systemic inflammatory response index, neutrophil/lymphocyte ratio, platelet count/lymphocyte ratio, etc.^{4,5} The HALP score based on hemoglobin (g/L), albumin (g/L), lymphocytes (/L), and platelets (/L) has been associated with improved survival rates for gastric cancer and lung cancer patients in recent years. The HALP score has been validated as a reliable prognostic indicator in many studies, including bladder cancer, gastric cancer, colorectal cancer, etc.^{6,7} (Preoperative HALP score has been confirmed as an independent predictor of non-small cell carcinoma, and it is useful for evaluating the prognosis of such patients). However, no studies have confirmed that the HALP score has a role in the prognosis of endometrial cancer.

Therefore, the aim of this study is to analyze the value of HALP score in predicting postoperative recurrence and death in patients with endometrial cancer and to determine the optimal threshold of HALP for more prognostic postoperative management of patients with endometrial cancer.

MATERIALS AND METHODS

Patient Selection

Chongqing Medical University Ethics Committee approved this retrospective study (Ethics approval number: 2020-166). Clinical data collected were from patients with stage I to III endometrial cancer who underwent surgery at the First Affiliated Hospital of Chongqing Medical University from June 2015 to June 2020. The clinicopathological indicators included age, body mass index, FIGO stage, histologic type (histotypes), lymphatic vessel space invasion (LVSI), cervical stromal invasion, myometrial invasion, depth of myometrial invasion, hemoglobin, albumin, lymphocytes, and platelets (HALP). Patients are included and excluded based on the following criteria. Criteria for inclusion are the following: (1) patients have received standard surgical treatment; (2) the postoperative pathologic examination of patients with endometrial cancer diagnosed as FIGO stage I to III⁸; (3) patients with HALP in their routine blood test results before surgery; (4) patients with complete clinical, pathologic, and follow-up information. Criteria for exclusion are the following: (1) patients did not receive standard surgical treatment; (2) the patients received radiotherapy or chemotherapy before

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The authors declare no conflicts of interest.

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surgery; (3) other malignancies in patients; (4) patient data are missing; (5) patients' loss; (6) patients with chronic and acute inflammation, as well as infections that affect prognosis.⁹ Patients received standard surgical treatment, including at least total hysterectomy with bilateral salpingo oophorectomy, with nodal staging (sentinel lymph node + pelvic ± para-aortic lymphadenectomy).^{9,10} Pathologic evaluation of the patient specimens was conducted within 20 minutes by the Pathology Experiment Center of Chongqing Medical University. A low-risk histotype (histotype I) includes G1 or G2 endometrioid adenocarcinomas, whereas a high-risk histotype (histotype II) includes G3 endometrioid adenocarcinomas, as well as other histotypes, including serous, clear cell, and other tissues.^{11,12} Multidisciplinary discussions and international guidelines determined the postoperative adjuvant therapy (radiation and/or chemotherapy) and its cycle. After surgery, follow-up was done by outpatient and telephone: every 3 months for the first 2 years, every 6 months for the next 3 years, and annually thereafter.¹³ The physical examination should be followed by a reexamination, if necessary. A recurrence of the disease was determined by physical examination, histology, and/or imaging studies (including computed tomography, magnetic resonance imaging, ultrasonography, fluorodeoxyglucose-positron emission tomography, or specific x-rays).¹⁴ According to the site of recurrence, it was divided into vaginal stump recurrence, lymph node recurrence (pelvic or para-aortic lymph nodes), local pelvic recurrence, peritoneal metastasis (peritoneal cancer), and distant metastasis.

Recurrence-free survival (RFS) is defined by the period from the time of complete remission after antitumor therapy to the time of recurrence or the end of follow-up. Overall survival (OS) is the time from the end of antitumor therapy to the time of death from any cause.¹⁵

Ethical Statement

The Ethics Committee of Chongqing Medical University approved this study (Ethics approval number: 2020-166). All patients provided their informed consent before starting the treatment and gave consent to have their data published. As it was a retrospective clinical study, all the patients were contacted by telephone to obtain verbal informed consent, and it was approved by the ethics committee. All data about the patients was anonymized or maintained with confidentiality.

Statistical Analysis

A computer program, SPSS26.00, was used for data processing, and the HALP value was calculated from HALP. (HALP = hemoglobin [g/L] × albumin [g/L] × lymphocytes [L]/platelets [L]). An analysis of the clinicopathological data (including HALP) and the prognosis of patients (recurrence and death) was conducted using univariate cox regression analysis. A multivariate cox regression analysis was performed on the correlated factors after the results were sorted and analyzed. The optimal cutoff value of HALP for predicting lymph node metastasis (LNM), recurrence, and death was determined by ROC curve analysis and the Youden index. On the basis of a cutoff value,¹⁶ patients were divided into high and low-HALP groups; Kaplan-Meier curves were used to draw RFS and OS for patients with high and low-HALP values, as well as for patients undergoing surgery without adjuvant therapy, and to evaluate the impact of HALP value on recurrence and death.¹⁷

Data Availability

The data sets used and/or analyzed in the current study are available from the corresponding author on reasonable request.

RESULT

Patients Characteristic

In this study, 626 patients with endometrial cancer were included based on the inclusion and exclusion criteria, their basic characteristics were summarized in Table 1, and all the inflammation-related indicators were collected 1 week before surgery (Table, Supplemental Digital Content 1, <http://links.lww.com/AJCO/A446>, which demonstrates inflammation-related indicators of patients). A mean age of 53 years was observed among the patients (range 24 to 79 y). The majority had FIGO stage I endometrial cancer (69.6%). The number of patients with type I endometrioid adenocarcinoma was 446 (71.2%). Total of 465 patients received pelvic lymph node

TABLE 1. Patient Characteristics (n = 626)

Characteristic	Patients (N = 626) (%)
Age (y)	
Mean (±SD)	53.64 (±9.28)
Median (range)	53.00 [24-79]
BMI (kg/m ²)	
Mean (±SD)	24.63 (±3.73)
Median (range)	24.24 (16.35-45.72)
FIGO stage, n (%)	
I	436 (69.6)
II	57 (9.1)
III	133 (21.2)
Histotypes, n (%)	
I	446 (71.2)
II	180 (28.8)
LVSI, n (%)	
Positive	143 (22.8)
Negative	483 (77.2)
Cervical stromal invasion, n (%)	
Yes	102 (16.3)
No	524 (83.7)
Myometrial invasion, n (%)	
Yes	197 (31.5)
No	429 (68.5)
Scope of lymphadenectomy, n (%)	
Only pelvic LNs	465 (74.3)
Pelvic + para-aortic LNs	161 (25.7)
No. pelvic LNs removed	
Mean (±SD)	30.29 (±12.25)
Median (range)	30.00 [5-87]
No. para-aortic LNs removed	
Mean (±SD)	11.40 (±7.26)
Median (range)	9.00 [4-41]
LNM	
Only pelvic LNM	80
Pelvic + para-aortic LNM	11
Adjuvant treatment, n (%)	
No adjuvant treatment	251 (40.1)
Radiotherapy only	210 (33.5)
Chemotherapy only	21 (3.4)
Chemoradiotherapy	144 (23)
Recurrence, n (%)	
Yes	81 (12.9)
No	545 (87.1)
Death	
Yes	60 (9.6)
No	566 (90.4)
Follow-up (mo)	
Mean (±SD)	52.00 [7-84]
Median (range)	54.46 ± 18.76

BMI indicates body mass index; FIGO, International Federation of Gynecology and Obstetrics; LN, lymph node; LVSI, lymphatic vessel space invasion.

TABLE 2. Univariate and Multivariate Analysis of Factors Predicting Endometrial Cancer Recurrence

Variables	Univariate analysis			Multivariate analysis		
	Hazard ratio	95% CI	P	Hazard ratio	95% CI	P
Age (≥ 60 vs. <60)	2.215	1.427-3.438	<0.001	1.674	1.047-2.674	0.031
FIGO stage						
I	—	—	<0.001	—	—	0.867
II	2.606	1.171-5.800	0.019	1.297	0.487-3.457	0.603
III	8.148	4.996-13.287	<0.001	1.153	0.457-2.908	0.762
Histotypes (II vs. I)	7.248	4.470-11.754	<0.001	2.927	1.654-5.180	<0.001
Cervical stromal invasion (yes or no)	3.043	1.924-4.811	<0.001	1.251	0.714-2.191	0.433
Myometrial invasion (yes or no)	4.432	2.813-6.983	<0.001	2.107	1.237-3.588	0.006
LVSI (positive vs. negative)	5.224	3.364-8.114	<0.001	2.162	1.290-3.623	0.003
LNM (yes or no)	8.429	5.442-13.056	<0.001	2.630	1.173-5.899	0.019
Adjuvant treatment (yes or no)	2.291	1.371-3.831	0.002	0.600	0.330-1.093	0.095
HALP	0.975	0.963-0.988	<0.001	0.984	0.972-0.996	0.011

FIGO indicates International Federation of Gynecology and Obstetrics; HALP, hemoglobin, albumin, lymphocyte, and platelet; LN, lymph node; LVSI, lymphatic vessel space invasion.

dissection only, whereas 161 patients received pelvic and para-aortic lymph node dissection, the median number of removed lymph nodes was 30 (5 to 87), a total of 91 patients had LNM, 11 of which also had para-aortic LNM, and there were no patients with separate para-aortic LNM. Total of 375 patients received adjuvant therapy (210 with radiotherapy, 21 with chemotherapy, and 144 with chemoradiation). Patients were followed up for a median period of 54.46 ± 18.76 (7.91) months. During the follow-up period, 81 (12.9%) patients relapsed, in total, 60 people died (9.6%), of whom 55 died from relapse and 5 died from other causes. The HALP values ranged from 5.73 to 185.60 (median 41.16).

Univariate and Multivariate Analyses of Death and Recurrence

The univariate analysis of recurrence revealed (Table 2), age ($P < 0.001$), FIGO stage (stage I $P < 0.001$, stage II $P = 0.019$, and stage III $P < 0.001$), histotype ($P < 0.001$), cervical stromal invasion ($P < 0.001$), myometrial invasion ($P < 0.001$), LVSI ($P < 0.001$), LNM ($P < 0.001$), adjuvant treatment ($P = 0.002$), and HALP score ($P < 0.001$) were all associated with recurrence in endometrial cancer patients, the 9 factors with P -value < 0.05 including age, FIGO stage, histotypes, cervical stromal invasion, myometrial invasion, LVSI, LNM, adjuvant treatment, and HALP were put into the multivariate

cox regression analysis of relapse rates. The multivariate analysis revealed (Table 2) that age ($P = 0.031$), histotypes ($P < 0.001$), myometrial invasion ($P = 0.006$), LVSI ($P = 0.003$), and LNM ($P = 0.019$) were the independent risk factors for the recurrence of endometrial cancer patients, and HALP ($P = 0.011$) was an independent protective factor. The univariate analysis of death in patients with endometrial cancer showed that (Table 3) age ($P < 0.001$), FIGO stage (stage I $P < 0.001$ and stage III $P < 0.001$), histotypes ($P < 0.001$), cervical stromal invasion ($P < 0.001$), myometrial invasion ($P < 0.001$), LVSI ($P < 0.001$), LNM ($P < 0.001$), adjuvant treatment ($P = 0.013$), and HALP ($P = 0.001$) were significantly associated with death in endometrial cancer patients, whereas the 9 factors with P -value < 0.05 including age, FIGO stage, histotypes, cervical stromal invasion, myometrial invasion, LVSI, LNM, adjuvant treatment, and HALP were put into the multifactorial cox regression of patient death in the analysis. The multivariate analysis revealed (Table 3) that age ($P = 0.008$), histotypes ($P = 0.002$), myometrial invasion ($P = 0.001$), and LNM ($P = 0.024$) were the independent risk factors for the death of endometrial cancer patients, and HALP ($P = 0.007$) was an independent protective factor.

Identifying the Optimal Cutoff for HALP

The results of univariate and multivariate analyses indicate that HALP is an independent protective factor for endometrial cancer

TABLE 3. Univariate and Multivariate Analysis of Factors Predicting Endometrial Cancer Death

Variables	Univariate analysis			Multivariate analysis		
	Hazard ratio	95% CI	P	Hazard ratio	95% CI	P
Age (≥ 60 vs. <60)	2.906	1.752-4.820	<0.001	2.083	1.211-3.584	0.008
FIGO stage						
I	—	—	<0.001	—	—	0.848
II	2.439	0.893-6.658	0.082	1.299	0.395-4.272	0.666
III	9.431	5.268-16.885	<0.001	1.325	0.444-3.955	0.614
Histotypes (II vs. I)	6.989	3.985-12.257	<0.001	2.749	1.438-5.255	0.002
Cervical stromal invasion (yes or no)	3.302	1.953-5.583	<0.001	1.290	0.690-2.413	0.425
Myometrial invasion (yes or no)	4.815	2.814-8.238	<0.001	2.710	1.481-4.962	0.001
LVSI (positive vs. negative)	4.033	2.430-6.695	<0.001	1.476	0.816-2.668	0.198
LNM (yes or no)	9.735	5.835-16.244	<0.001	3.001	1.159-7.767	0.024
Adjuvant treatment (yes or no)	2.094	1.167-3.756	0.013	0.539	0.276-1.052	0.070
HALP	0.976	0.961-0.990	0.001	0.982	0.969-0.995	0.007

FIGO indicates International Federation of Gynecology and Obstetrics; HALP, hemoglobin, albumin, lymphocyte, and platelet; LN, lymph node; LVSI, lymphatic vessel space invasion.

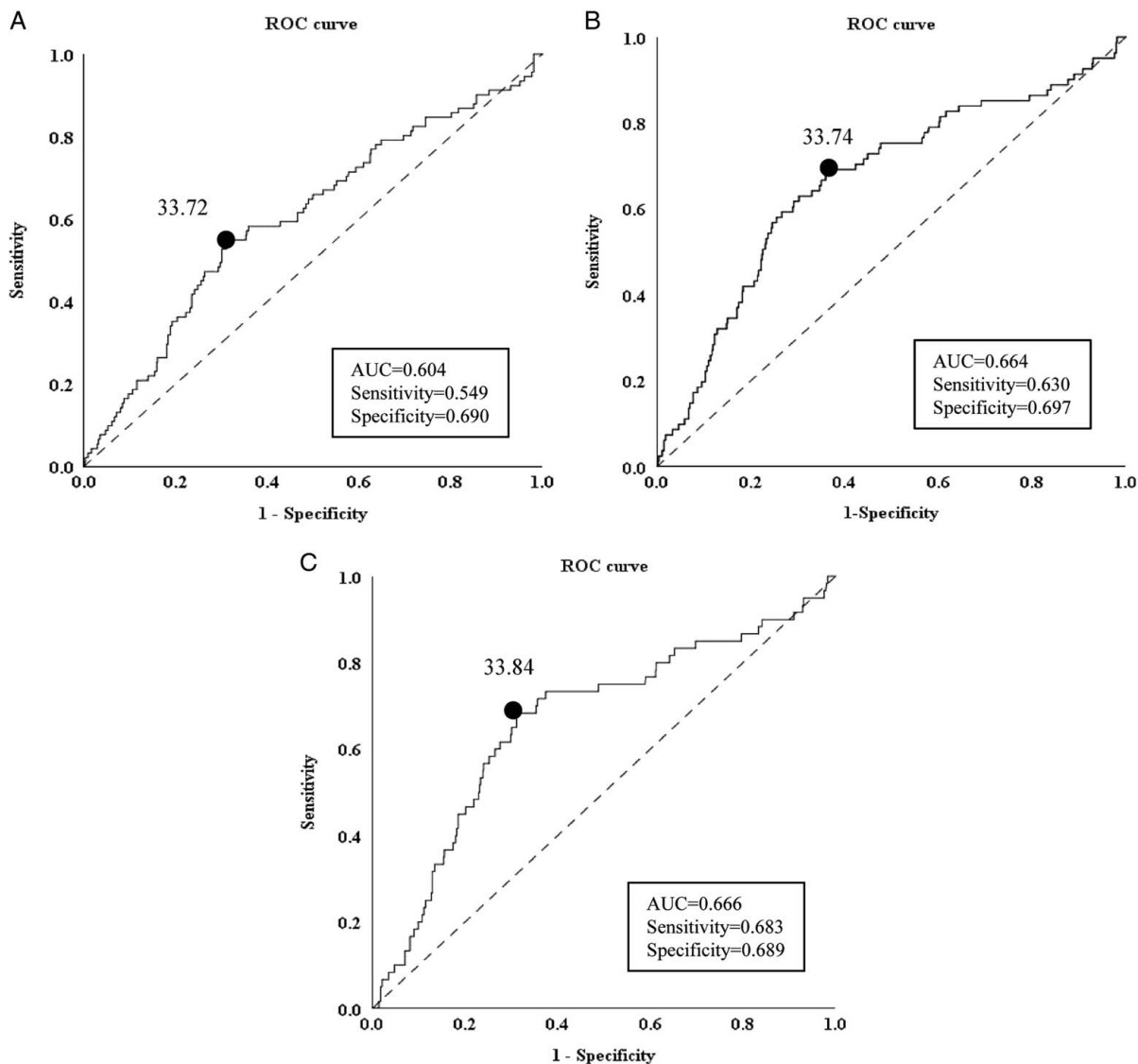


FIGURE 1. (A) The cutoff value of hemoglobin, albumin, lymphocyte, and platelet (HALP) for predicting endometrial cancer lymph node metastasis. (B) The cutoff value of HALP for predicting endometrial cancer recurrence. (C) The cutoff value of HALP for predicting endometrial cancer death. (Black dot: the area under the curve at this point is the largest, which indicates the optimal cutoff value of the HALP. Dotted line: reference line; solid line: HALP curve.) AUC indicates area under the curve; ROC, receiver operating characteristic curve.

recurrence and death. On the basis of the ROC curve and the calculated Youden index (Fig. 1), the optimal cutoff values of HALP for predicting LNM, recurrence, and death in patients were 33.72 (specificity 0.690, sensitivity 0.549, and area under the curve 0.604), 33.74 (specificity 0.697, sensitivity 0.630, and area under the curve 0.664), and 33.84 (specificity 0.689, sensitivity 0.683, and area under the curve 0.666). These 3 results were similar, thus, we determined that 33.8 was the optimal cutoff value of HALP for predicting the prognosis (LNM, recurrence, and death) of endometrial cancer.

Clinical Prognostic Value of Each Predictor and Its Combination

The ROC curve (Fig. 2) showed that the AUC of the combination that composed of age, histotypes, myometrial invasion, LVSI, LNM, and HALP (AUC=0.879, 95% CI, 0.844 to 0.914) was better than other single predictors for

predicting endometrial cancer recurrence, including age (AUC=0.595, 95% CI, 0.526 to 0.664), histotypes (AUC=0.746, 95% CI, 0.686 to 0.806), myometrial invasion (AUC=0.688, 95% CI, 0.624 to 0.752), LVSI (AUC=0.695, 95% CI, 0.628 to 0.762), LNM (AUC=0.714, 95% CI, 0.645 to 0.784), HALP (AUC=0.664, 95% CI, 0.597 to 0.732), the differences were significantly statistically significant ($P < 0.05$). Similarly, we had the same results in the ROC curve predicting death in endometrial cancer patients, the combination (AUC=0.864, 95% CI, 0.818 to 0.909), age (AUC=0.629, 95% CI, 0.551 to 0.707), histotypes (AUC=0.737, 95% CI, 0.668 to 0.806), myometrial invasion (AUC=0.695, 95% CI, 0.622 to 0.767), LNM (AUC=0.733, 95% CI, 0.655 to 0.811), HALP (AUC=0.666, 95% CI, 0.589 to 0.744), and the differences were significantly statistically significant ($P < 0.05$). This indicates that we can combine this approach preoperatively and

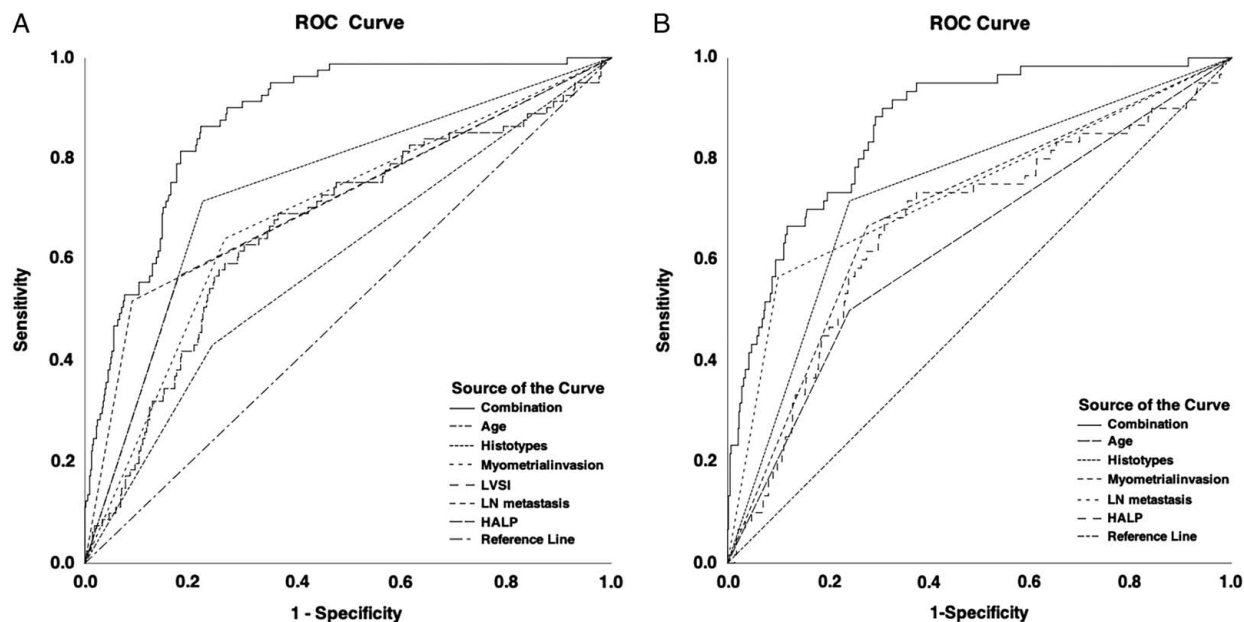


FIGURE 2. (A) The ROC curve of various predictive markers and their combinations for predicting endometrial cancer recurrence. (B) The ROC curve of various predictive markers and their combinations for predicting endometrial cancer death. HALP indicates hemoglobin, albumin, lymphocyte, and platelet; LN, lymph node; LVSI, lymphatic vessel space invasion; ROC, receiver operating characteristic curve.

postoperatively to predict patient prognosis and provide better patient care.

Comparison of Clinicopathological Parameters and Survival Analysis Between high-HALP and Low-HALP Groups

In accordance with the optimal positive threshold for HALP (33.8), patients were divided into high and low-HALP group. Compared between the 2 groups showed, low-HALP group was related to the following factors (Table, Supplemental Digital Content 2, <http://links.lww.com/AJCO/A446>, which demonstrates the comparison of clinicopathological parameters between high-HALP and low-HALP groups), age ($P = 0.043$), FIGO stage (stage I $P < 0.001$, stage II $P = 0.001$, and stage III $P < 0.001$), histotypes ($P < 0.001$), cervical stromal invasion ($P = 0.004$), LVSI ($P = 0.002$), LNM ($P < 0.001$), and adjuvant therapy ($P = 0.004$). We collected the prognostic data of 626 patients with an average follow-up period of 52 (7 to 84) months to investigate the relationship between HALP value and patient prognosis. Thirty patients (7.3%) relapsed and 18 patients (4.4%) died in the high-HALP group, whereas 51 patients (23.6%) relapsed and 42 patients (19.4%) died in the low-HALP group. According to Kaplan-Meier survival analysis (Fig. 3), the 3-year RFS rate for patients in the high-HALP group was 92.9% (95% CI, 0.904 to 0.954), the 5-year RFS rate was 92.5% (95% CI, 0.900 to 0.950), the 3-year OS rate was 95.9% (95% CI, 0.939 to 0.979), and the 5-year OS rate was 94.9% (95% CI, 0.927 to 0.971). In the low-HALP group, the 3-year RFS rate was 77.7% (95% CI, 0.722 to 0.832), the 5-year RFS rate was 75.9% (95% CI, 0.700 to 0.818), the 3-year OS rate was 83.3% (95% CI, 0.784 to 0.882), and the 5-year OS rate was 81.1% (95% CI, 0.758 to 0.864). Meanwhile, our further survival analysis found that when the endometrial cancer patients without adjuvant therapy were divided into the high-HALP and low-HALP groups, the low-HALP patients still had a worse prognosis than the high-HALP group.

DISCUSSION

The incidence and mortality of endometrial cancer have steadily increased in recent years.¹⁸ It is crucial to accurately predict the risk of postoperative recurrence and death in EC patients, as well as to take appropriate intervention measures during the perioperative or postoperative period. Presently, some studies have indicated that nutrition and inflammation are also important.^{19,20} We established the HALP score by administering the preoperative blood indicators hemoglobin (g/L); albumin (g/L); lymphocytes (/L), and platelets (/L). The HALP score can reflect the inflammatory and nutritional status of patients to a certain extent, according to studies. In our univariate and multivariate analyses, we found that the HALP score was an independent predictor of recurrence and death, which implies that when considering the prognosis of patients, we should not only consider their clinicopathologic characteristics, but also their inflammation and nutritional status. Based on the ROC curve and Youden index, we determined the best cutoff value (33.8) for HALP to predict recurrence and death in EC patients and divided them into high and low-HALP groups. As a result of survival analysis, patients in low-HALP group had a significantly lower postoperative RFS rate and an OS rate ($P < 0.001$) than those in high-HALP group. Consequently, we need to pay attention to the clinical prognosis management of patients in the low-HALP group, as the existing adjuvant therapy may not be very effective in controlling the recurrence of these patients, so we may need to adjust the adjuvant therapy appropriately and increase follow-up time. In our stratified analysis, we found that in low-risk patients who did not receive adjuvant therapy (without obvious high-risk clinicopathological features), the prognosis of patients with low HALP was still higher than those with high HALP. Indicating that the HALP score may be a very independent indicator in low-risk patients, so those with low-HALP scores may also require appropriate adjuvant therapy. The question of whether adjuvant therapy can improve the prognosis of patients in the low-risk group remains controversial, and prospective studies are necessary to confirm

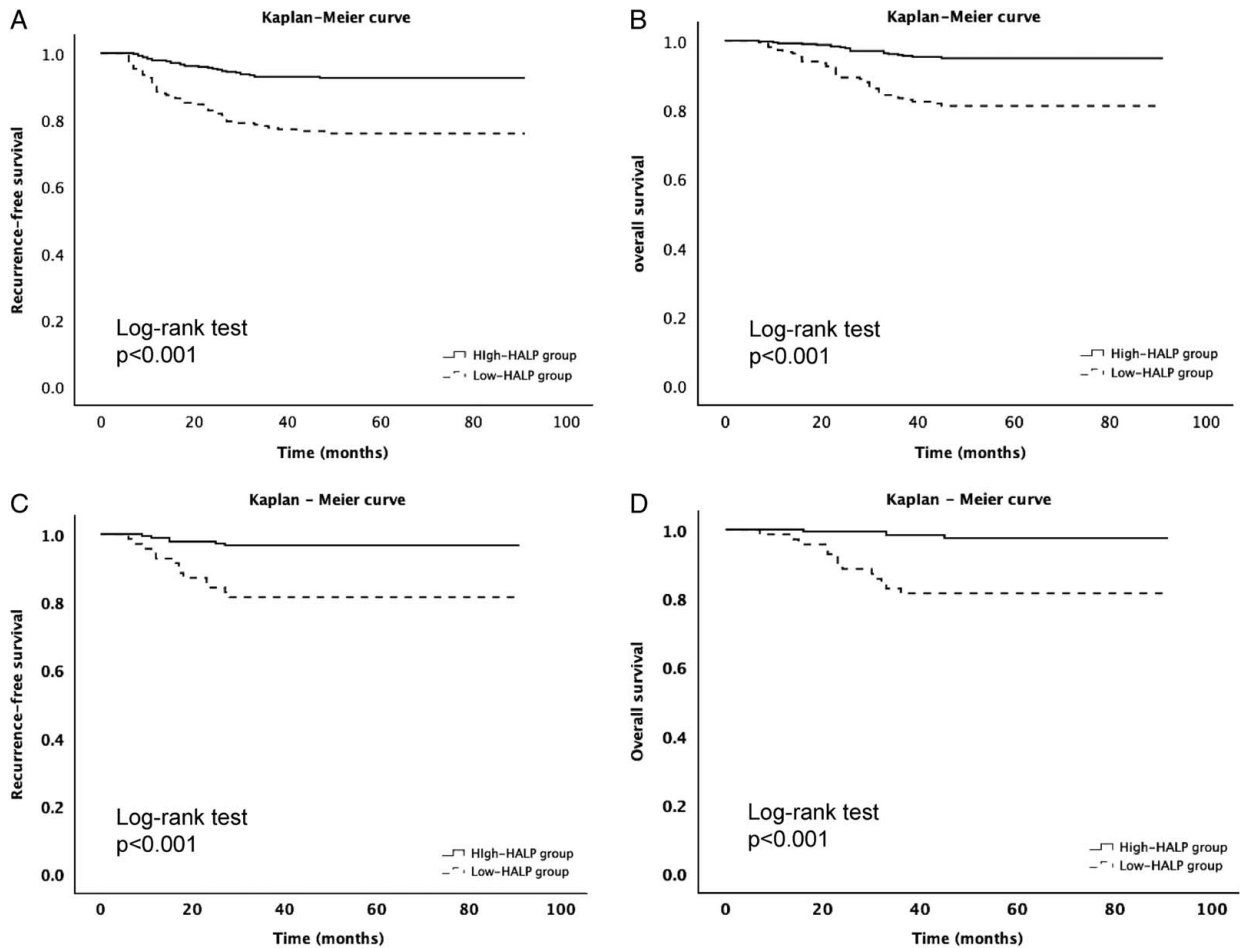


FIGURE 3. (A) The recurrence-free survival for all patients in the high-HALP group and the low-HALP group. (B) The overall survival for all patients in the high-HALP group and the low-HALP group. (C) The recurrence-free survival for patients without adjuvant treatment in the high-HALP group and the low-HALP group. (D) The overall survival for patients without adjuvant therapy in the high-HALP group and the low-HALP group. HALP indicates hemoglobin, albumin, lymphocyte, and platelet.

this conclusion, this study suggests that the HALP score may be used as a basis for screening potentially beneficial populations in such studies.

It is worth mentioning that we found that the HALP score not only has a predictive value for recurrence and death in endometrial cancer patients, but also it has some significance for predicting LNM, and the optimal threshold of it is also concentrated around 33.8. It is well known that nodal status is an important factor affecting patient prognosis. According to our findings, patients with a HALP score of <33.8 may have a higher risk of LNM, and therefore, such patients need to take appropriate measures to some extent, such as sentinel node mapping and systemic lymph node dissection, if necessary. After all, they are important intervention for patients with endometrial cancer who have a high risk of LNM.²¹ Patients with a HALP score of >33.8 have less risk of LNM and may be a beneficial group to be exempted from lymph node dissection. Of course, the HALP score alone is not accurate enough to predict LNM. A recent study reported that sentinel node mapping and pathologic ultrastaging can improve the detection rate of low-volume disease (micro-metastases and isolated tumor cells), which can help diagnose and tailor appropriate adjuvant treatments for patients with endometrial cancer.^{22,23} Our proposed HALP score can be used in this

regard as an adjuvant indicator for the initial preoperative prediction of LNM, thus better guiding the preoperative and postoperative management of patients.

Currently, the Cancer Center for Endometrial Cancer has classified endometrial cancer into 4 distinct types: OLE, microsatellite instability-hypermutated, copy number abnormal, items low and copy number abnormalities high.^{24,25} Classifications of this type have considerable feasibility and application value in clinical practice, can serve as a useful tool for individualized diagnosis and treatment, and have a significant predictive value for prognosis of patients with EC.²⁶ No matter which of the clinicopathological parameters or the Cancer Center for Endometrial Cancer molecular typing is used, they all reflect the biological behavior of the tumor. However, the HALP score we propose is based on the inflammatory index and nutritional status of patients to predict their prognosis. There is no contradiction between the 2 and they may even be complementary.

It should be noted that in the univariate analysis of this study, postoperative adjuvant therapy (including chemotherapy, radiotherapy, and combined radiotherapy and chemotherapy) was indicated as a risk factor for recurrence and death in patients with endometrial cancer. It is believed that the reason is that most of these patients who receive adjuvant therapy after

surgery are at a later stage and their tumor type and differentiation are poor. When we performed a univariate analysis of high-risk factors for tumor recurrence and death, which was suggested as a “risk factor,” we found a strong “collinearity,” the clinical facts are contradicted.²⁷ When the “collinearity” between the factors was eliminated in multivariate analysis, postoperative adjuvant therapy was confirmed as a “protective factor” for tumor survival. Other literature has also confirmed that postoperative adjuvant therapy can improve tumor survival.²⁸ The second shortcoming of this study is that it was a retrospective study conducted in a single center, which calls for further prospective studies to demonstrate its validity.

In summary, the present study established the HALP score based on preoperative blood markers and explored its prognostic value for endometrial cancer. The optimal threshold of the HALP score could be used to further stratify patients and provide more comprehensive personalized care.

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