

## Original Article

# Establishment and verification of influencing factors and prediction model of early intestinal paralysis after radical operation of endometrial cancer

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**Abstract:** Radical operation is a primary treatment modality for endometrial carcinoma (EC). While effective, it is associated with postoperative complications, including postoperative paralytic ileus (POI). In this retrospective study, clinicopathological data from 587 EC patients who received radical surgery were analyzed. First, logistic regression analysis was used to identify influencing factors for postoperative POI in EC patients. Subsequently, a risk prediction model was developed based on the identified risk factors. The results showed that a history of cesarean section, prior abdominal surgery, diabetes, intestinal adhesion, and dysmenorrhea were independent risk factors for POI in EC patients after radical surgery. Model validation confirmed good goodness-of-fit and satisfactory predictive performance.

**Keywords:** Endometrial carcinoma, radical operation, postoperative paralytic ileus, risk factors, risk prediction model

## Introduction

Endometrial cancer (EC) is a common gynecological malignancy, accounting for approximately 20%-30% of malignant tumors of the female reproductive system in China [1]. Radical surgery is a mainstay of clinical treatment for EC. It can effectively remove tumor tissue, prolong survival, and reduce mortality [2]. However, despite its therapeutic benefits, it is associated with significant postoperative complications [3]. Postoperative paralytic ileus (POI) is a common complication following EC surgery. It refers to a temporary gastrointestinal motility disorder after abdominal surgery, characterized by the inability to effectively propel intestinal contents and/or tolerate oral intake. The exact pathogenesis of POI remains unclear, although current evidence suggests that it is associated with neural dysfunction, inflammatory responses, and pharmacological factors [4]. POI can prolong hospital stays, increase healthcare expenditures and potentially lead to enterogen-

ic infection or multiple organ failure, adversely affecting clinical outcomes [5].

Surgical stress can induce autonomic nervous system dysfunction and activate inflammatory cells [6]. In addition, general anesthesia, opioid use, electrolyte imbalance, and fluid overload may aggravate this reaction, eventually leading to intestinal wall edema and gastrointestinal dysfunction. Therefore, it is of great significance to construct a risk prediction model and implementing targeted preventive measures to reduce the incidence of POI.

Previous studies have identified several risk factors for POI. Grass et al. retrospectively analyzed the data of 513 patients undergoing colon surgery and reported that operation time longer than 3 h, surgical approach, and an American Society of Anesthesiology (ASA) score of 3-4 were significant risk factors for POI [7]. Vather et al. conducted a prospective study of 327 patients undergoing rectal surgery and found that perioperative fluid overload, preoperative

malnutrition, intraoperative bowel manipulation, and delayed postoperative ambulation were risk factors for POI [8]. However, due to disease heterogeneity and individual variability, the risk factors for POI in EC patients following radical surgery remain inconclusive. Therefore, this study aims to analyze risk factors for POI in EC patients after operation and to construct a risk prediction model to provide evidence for early identification and prevention of POI.

## Materials and methods

### General information

From January 2015 to January 2024, patients with EC who received radical surgery at our institution were retrospectively collected and analyzed. This study was reviewed and approved by the Ethics Committee of The Second Affiliated Hospital of Nanchang University. All procedures were conducted in accordance with the Declaration of Helsinki and relevant ethical guidelines for medical research involving human subjects.

Inclusion criteria: ① Patients undergoing initial surgical treatment, with no prior hormone therapy, radiotherapy, or neoadjuvant chemotherapy; ② Preoperative pathological diagnosis of endometrial malignancy confirmed by diagnostic curettage or hysteroscopy, with postoperative pathological results confirming endometrial cancer; ③ Patients undergoing laparotomy or laparoscopic surgery; ④ Patients aged  $\geq 18$ ; ⑤ Reliable and complete clinical and pathological data.

Exclusion criteria: ① Presence of POI before operation; ② History of neurological diseases; ③ Concomitant intestinal injury, anastomotic leakage, or mechanical intestinal obstruction; ④ Occurrence of respiratory diseases or multiple organ failure during the perioperative period.

This study involved the development and internal validation of a prediction model. The adequacy of the sample size was assessed primarily based on the number of endpoint events available for model development. According to methodological recommendations for prediction modeling, to obtain stable and reliable parameter estimates and to minimize overfitting, a minimum of 10 events per candidate predictor variable (EPV  $\geq 10$ ) is generally re-

quired [9]. The primary endpoint of this study was the occurrence of POI.

Given that POI typically occurs in the early postoperative period, all patients were systematically followed throughout their hospitalization until discharge. The diagnosis of POI was based on daily ward round records, nursing notes, imaging reports, and progress notes. To ensure data completeness, perioperative records for all patients were reviewed using the electronic medical record system. Patients who were transferred to another facility or discharged against medical advice before their POI status could be determined were considered as having missing data for this endpoint.

According to the predefined inclusion and exclusion criteria, a retrospective screening was performed on an initially identified cohort of 651 patients. Of these, 24 patients were excluded due to incomplete clinical data or missing postoperative follow-up information, and an additional 40 patients were excluded as they met other exclusion criteria. Consequently, a total of 587 patients with complete data were included in the final analysis.

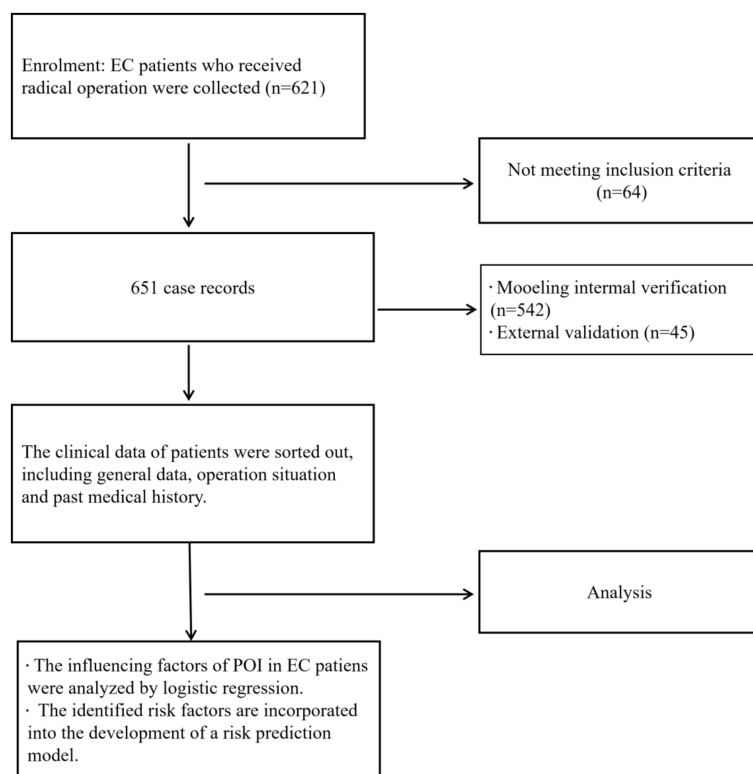
The included patients were randomly assigned into the training or validation set by stratified random sampling. A total of 253 patients developed POI (228 in the training set and 25 in the validation set), while 334 patients did not (314 in the training set and 20 in the validation set). The patient enrollment and allocation process is illustrated in **Figure 1**.

### Methods

The definition of “radical surgery” was in line with the International Federation of Gynecology and Obstetrics (FIGO) guidelines for EC and followed the standard practice of our institution [10]. All procedures were performed by an experienced gynecologic oncology team.

According to the diagnostic criteria for PPOI used in this study, POI was defined as the persistence of two or more of the following symptoms beyond 96 hours postoperatively: ① Moderate-to-severe nausea or vomiting within the preceding 12 hours, corresponding to a score  $>4$  on a 10-point self-report nausea scale; ② Intolerance to solid food during the

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**Figure 1.** Flowchart of the study design. Notes: EC, Endometrial cancer; POI, Postoperative paralytic ileus.

last two meals, defined as a patient-reported oral intake of <25% of the offered meals; ③ Absence of flatus or stool passage within the first 24 hours; ④ Moderate-to-severe abdominal distension upon physical examination, as determined by percussion; ⑤ Radiological evidence of ileus on abdominal X-ray or CT within the past 24 hours, demonstrated by at least two of the following features: gastric distension, air-fluid levels, or dilation of small or large bowel loops [11].

Clinical data were extracted from the hospital electronic medical record system, including age, body mass index (BMI), total protein, albumin, high-density lipoprotein (HDL), number of pregnancies, tumor stage, history of caesarean section (yes/no), ligation (yes/no), anesthesia technique (general anesthesia or continuous epidural anesthesia combined with general anesthesia), opioid drug use on postoperative day 1 (yes/no), total postoperative opioid dosage (TOD; TOD = morphine equivalent/drug weight), postoperative patient controlled intravenous analgesia (yes/no), surgical procedure (laparotomy or laparoscopic surgery), total hys-

terectomy (yes/no), extensive hysterectomy (yes/no), ovariectomy (yes/no), pelvic lymphadenectomy (yes/no), para-aortic lymph node dissection (yes/no), sentinel lymph node biopsy (yes/no), operation time, duration of anesthesia, tumor diameter, lymph node metastasis (yes/no), diabetes (yes/no), hypertension (yes/no), intestinal adhesion (yes/no), dysmenorrhea (yes/no), menopause (yes/no), history of abdominal surgery (yes/no). Among them, dysmenorrhea was evaluated using the visual analog scale (VAS), with pain intensity rated from 0 to 10, where 0 indicates no pain, 1-2 mild pain, 3-4 moderate pain, and  $\geq 5$  severe pain.

Duplicate records and cases with incomplete data were excluded. Relevant information was cross-checked, and original paper medical records were reviewed when electronic

data were incomplete or ambiguous. All verified data were recorded in a predesigned data collection form.

### Statistical method

SPSS 26.0 was used for statistical analyses. Categorical variables were expressed as frequencies and percentages (%). Continuous variables were first assessed for normality using the Shapiro-Wilk test. Data conforming to normal distribution were expressed as the mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ). The incidence of POI in EC patients after radical operation was defined as the dependent variable (1= occurrence, 0= non-occurrence). Logistic regression models were applied to identify risk factors associated with POI. Internal validation of the prediction model was performed using the bootstrap resampling method with 1,000 resamples. Receiver operating characteristic (ROC) curves were constructed, and the area under the ROC curve (AUC) was compared using the DeLong test. Drawing decision curve analysis (DCA) is used to evaluate the clinical benefit, and the difference was statistically significant with  $P < 0.05$ .

## Results

### *Incidence of POI in EC patients after radical operation*

Among the 587 EC patients included in this study, 253 developed POI after radical operation, with an overall POI incidence of 43.1%.

### *Comparison of baseline data between POI and non-POI patients in the testing cohort*

There were no significant differences between the two groups in terms of age, BMI, total protein, albumin, HDL, tumor stage, ligation, opioid use on postoperative day 1, surgical procedure, total hysterectomy, radical hysterectomy, ovariectomy, sentinel lymph node biopsy, or hypertension (all  $P > 0.05$ ).

In contrast, the number of precursors, history of caesarean section, anesthesia technique, TOD, use of postoperative PCIA, pelvic lymphadenectomy, para-aortic lymph node dissection, lymph node metastasis, operative time, duration of anesthesia, tumor diameter, lymph node metastasis, diabetes, intestinal adhesion, dysmenorrhea, menopause and history of abdominal surgery differed significantly between the two groups (all  $P < 0.05$ ; **Table 1**).

### *Univariate analysis of factors associated with POI in EC patients*

Univariate analysis showed that a history of caesarean section, anesthesia technique, TOD, pelvic lymphadenectomy, para-aortic lymph node dissection, sentinel lymph node biopsy, operation time, duration of anesthesia, tumor diameter, diabetes, intestinal adhesion, dysmenorrhea and history of abdominal surgery were significantly associated with the occurrence of POI in EC patients after radical operation ( $P < 0.05$ , **Table 2**).

### *Multivariate analysis of factors associated with POI in EC patients*

Logistic regression analysis showed that anesthesia technique, TOD, operation time, intestinal adhesion, and history of abdominal surgery were independent risk factors for POI in EC patients after radical operation ( $P < 0.05$ , **Table 3**).

### *Construction of forecasting model and ROC curve analysis*

Based on multivariate logistic regression analysis, anesthesia technique, TOD, operation time, intestinal adhesion, and history of abdominal surgery were selected as independent predictors and incorporated into a nomogram prediction model (**Figure 2**). The regression coefficients ( $\beta$  values) were used to construct the risk score, and the predictive equation was defined as follows:  $\text{Logit}(P) = 1.208 \times [\text{anesthesia technique}] + 6.405 \times [\text{TOD}] - 0.080 \times [\text{operation time}] + 1.618 \times [\text{intentional adhesion}] + 1.195 \times [\text{history of abdominal surgery}]$ .

The total score for each patient ranged from 0 to 163 points. The cumulative score was converted into the predicted probability of POI using the  $\text{Logit}(P)$  equation, and the corresponding risk probability (0.1-0.9) was directly displayed on the "Risk" axis of the nomogram, enabling intuitive conversion from total score to predicted risk.

### *Predictive performance of independent risk factors and their combined detection for POI in EC patients*

ROC curves were plotted for the identified risk factors and their combined detection, and corresponding AUCs were calculated (**Table 4**). All identified factors demonstrated predictive value for the postoperative occurrence of POI in EC patients after radical operation, with their combined prediction (incorporating anesthesia technique, TOD, operation time, intestinal adhesion and history of abdominal surgery) demonstrating the best discriminative performance, with an AUC of 0.964 (95% CI: 0.944-0.984). The optimal cut-off value was 0.53, yielding a sensitivity of 88.00% and a specificity of 91.90% (**Figure 3A**). Model verification also demonstrated excellent predictive performance with an AUC of 0.967 (95% CI: 0.945-0.990). At a cutoff of 0.464, the model yielded a sensitivity of 81.40% and a specificity of 94.60% (**Figure 3B**). The DeLong test showed that the AUC of their joint detection was significantly higher than that of anesthesia technique ( $Z = -5.461$ ,  $P < 0.001$ ), TOD ( $Z = -6.138$ ,  $P < 0.001$ ), operation time ( $Z = 10.719$ ,  $P = 0.002$ ), intestinal adhesion ( $Z = 11.737$ ,  $P < 0.001$ ), and history of abdominal surgery ( $Z = 1.233$ ,  $P < 0.001$ ).

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**Table 1.** Comparison of baseline data between two groups of patients

	POI group N=228	Non-POI group N=314	t/ $\chi^2$	P
Age, years	55.69±4.63	55.53±4.82	0.388	0.698
BMI (kg/m <sup>2</sup> )	24.89±2.45	24.66±2.16	1.156	0.248
Total protein (g/L)	68.59±4.14	68.73±4.25	0.383	0.702
Albumin (g/L)	41.98±3.59	42.37±3.36	1.296	0.196
HDL (mmol/L)	1.18±0.12	1.19±0.14	0.871	0.384
Number of pregnancies (n)	2.83±0.32	2.70±0.18	6.009	<0.001
Carcinoma staging (n, %)				
Stage I	125 (54.82%)	191 (60.83%)	3.041	0.385
Stage II	44 (19.30%)	52 (16.65%)		
Stage III	33 (14.47%)	46 (14.65%)		
Stage IV	26 (11.40%)	25 (7.96%)		
History of caesarean section (n, %)				
No	131 (57.46%)	215 (68.47%)	6.943	0.008
Yes	97 (42.54%)	99 (31.53%)		
Ligation (n, %)				
No	137 (60.09%)	181 (57.64%)	3.842	0.050
Yes	91 (39.91%)	83 (26.43%)		
Anesthesia technique (n, %)				
Continuous epidural anesthesia combined with general anesthesia	92 (40.35%)	198 (63.06%)	32.265	<0.001
General anesthesia	136 (59.65%)	106 (33.76%)		
Opioid use on postoperative day 1 (n, %)				
No	74 (32.46%)	105 (33.44%)	0.058	0.810
Yes	154 (67.54%)	209 (66.56%)		
TOD (mg/kg)	2.36±0.34	1.95±0.36	13.397	<0.001
Patient controlled intravenous analgesia after operation (n, %)				
No	111 (46.68%)	118 (37.58%)	6.676	0.010
Yes	117 (51.32%)	196 (62.42%)		
Surgical procedure (n, %)				
Laparotomy	82 (35.96%)	98 (31.21%)	1.346	0.246
Laparoscopic surgery	146 (64.04%)	216 (68.79%)		
Total hysterectomy (n, %)				
No	6 (2.63%)	16 (5.10%)	2.059	0.151
Yes	222 (97.37%)	298 (94.90%)		
Extensive hysterectomy (n, %)				
No	186 (81.58%)	251 (79.97%)	0.228	0.633
Yes	42 (18.42%)	63 (20.06%)		
Ovariectomy (n, %)				
No	6 (2.63%)	9 (2.87%)	0.027	0.869
Yes	222 (97.37%)	305 (97.13%)		
Pelvic lymphadenectomy (n, %)				
No	101 (44.30%)	116 (36.94%)	2.977	0.084
Yes	127 (55.70%)	198 (63.06%)		
Para-aortic lymph node dissection (n, %)				
No	144 (63.16%)	212 (67.52%)	1.113	0.291
Yes	84 (36.84%)	102 (32.48%)		
Sentinel lymph node biopsy (n, %)				
No	192 (84.21%)	279 (88.85%)	2.501	0.114
Yes	36 (15.79%)	35 (11.15%)		

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Operation time (min)	140.47±24.39	185.61±20.47	23.367	<0.001
Duration of anesthesia (min)	176.14±28.91	185.23±27.36	3.728	<0.001
Tumor diameter (min)	32.57±4.67	27.64±4.18	12.637	<0.001
Diabetes (n, %)				
No	210 (92.11%)	265 (84.39%)	7.248	0.007
Yes	18 (7.89%)	49 (15.61%)		
Hypertension (n, %)				
No	160 (70.18%)	217 (69.11%)	1.145	0.285
Yes	58 (25.44%)	97 (30.89%)		
Intestinal adhesion (n, %)				
No	50 (21.93%)	172 (54.78%)	58.933	<0.001
Yes	178 (78.07%)	142 (45.22%)		
Dysmenorrhea (n, %)				
No	65 (28.51%)	250 (79.62%)	141.750	<0.001
Yes	163 (71.49%)	64 (20.38%)		
Menopause (n, %)				
No	113 (49.56%)	191 (60.83%)	6.808	0.009
Yes	115 (50.44%)	123 (39.17%)		
History of abdominal surgery (n, %)				
No	98 (42.98%)	216 (68.79%)	36.098	<0.001
Yes	130 (57.02%)	98 (31.21%)		

POI, Postoperative paralytic ileus; BMI, body mass index; HDL, high density lipoprotein; TOD, morphine equivalent/drug weight.

**Table 2.** Univariate analysis of factors affecting POI in EC patients

Variables	$\beta$	Z	P	OR (95% CI)
Age	0.007	0.353	0.724	1.007 (0.968-1.048)
BMI (kg/m <sup>2</sup> )	0.038	1.073	0.283	1.039 (0.969-1.113)
Total protein				
Albumin	-0.026	-1.072	0.284	0.975 (0.930-1.022)
HDL	-0.069	-0.187	0.851	0.933 (0.453-1.923)
Number of pregnancies	0.111	1.232	0.218	1.118 (0.936-1.334)
Carcinoma staging				
Stage I				1.000 (Reference)
Stage II	0.424	1.539	0.124	1.528 (0.891-2.621)
Stage III	-0.187	-0.592	0.554	0.829 (0.446-1.541)
Stage IV	0.615	1.716	0.086	1.849 (0.916-3.731)
History of caesarean section				
No				1.000 (Reference)
Yes	0.447	2.075	0.038	1.564 (1.025-2.385)
Ligation				
No				1.000 (Reference)
Yes	-0.247	-1.165	0.244	0.781 (0.516-1.183)
Anesthesia technique				
Continuous epidural anesthesia combined with general anesthesia				1.000 (Reference)
General anesthesia	1.097	5.076	<0.001	2.995 (1.961-4.576)
Opioid use on postoperative day 1				
No				1.000 (Reference)
Yes	0.058	0.262	0.793	1.059 (0.689-1.630)
TOD (mg/kg)	2.235	7.687	<0.001	9.342 (5.285-16.515)
Patient controlled intravenous analgesia after operation				
No				1.000 (Reference)
Yes	-0.324	-1.538	0.124	0.723 (0.478-1.093)

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Surgical procedure				
Laparotomy				1.000 (Reference)
Laparoscopic surgery	-0.325	-1.463	0.143	0.722 (0.467-1.117)
Total hysterectomy				
No				1.000 (Reference)
Yes	0.369	0.593	0.553	1.446 (0.428-4.888)
Extensive hysterectomy				
No				1.000 (Reference)
Yes	0.079	0.302	0.762	1.082 (0.648-1.808)
Ovariectomy				
No				1.000 (Reference)
Yes	-1.575	-5.811	<0.001	0.207 (0.122-0.352)
Pelvic lymphadenectomy				
No				1.000 (Reference)
Yes	0.019	0.085	<0.001	1.019 (0.663-1.565)
Para-aortic lymph node dissection				
No				1.000 (Reference)
Yes	3.873	12.392	<0.001	48.065 (26.051-88.681)
Sentinel lymph node biopsy				
No				1.000 (Reference)
Yes	3.873	12.392	<0.001	48.065 (26.051-88.681)
Operation time (min)				
	-0.084	-10.143	<0.001	0.920 (0.905-0.935)
Duration of anesthesia (min)				
	-0.011	-2.801	0.005	0.990 (0.982-0.997)
Tumor diameter (mm)				
	0.268	8.703	<0.001	1.307 (1.230-1.388)
Diabetes				
No				1.000 (Reference)
Yes	-0.828	-2.351	0.019	0.437 (0.219-0.871)
Hypertension				
No				1.000 (Reference)
Yes	-0.410	-1.712	0.087	0.664 (0.415-1.061)
Intestinal adhesion				
No				1.000 (Reference)
Yes	1.470	6.140	<0.001	4.350 (2.721-6.955)
Dysmenorrhea				
No				1.000 (Reference)
Yes	2.266	9.363	<0.001	9.639 (5.998-15.489)
Menopause				
No				1.000 (Reference)
Yes	0.407	1.942	0.052	1.503 (0.996-2.267)
History of abdominal surgery				
No				1.000 (Reference)
Yes	1.065	4.934	<0.001	2.901 (1.900-4.428)

POI, Postoperative paralytic ileus; EC, Endometrial cancer; BMI, body mass index; HDL, high density lipoprotein; TOD, morphine equivalent/drug weight.

The calibration curves indicated good agreement between predicted and observed outcomes (**Figure 4**). Decision curve analysis (DCA) showed that the predictive model provided significant clinical net benefits across a threshold probability range of 0.10-0.50 (**Figure 5**).

### Discussion

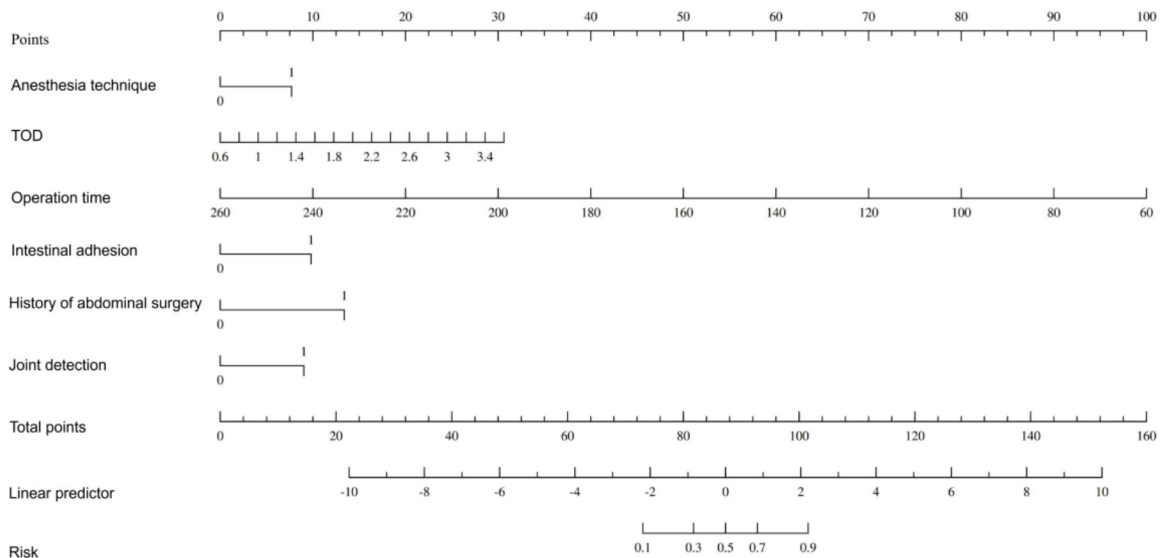
POI refers to a transient impairment of gastrointestinal motility following surgical intervention in the absence of mechanical obstruction, representing a common complication after ab-

## Prediction model for early intestinal paralysis after endometrial cancer radical surgery

**Table 3.** Multivariate analysis of independent risk factors for POI in EC patients

Variables	$\beta$	Z	P	OR (95% CI)
Anesthesia technique				
0				1.000 (Reference)
1	1.208	3.208	<0.001	3.348 (1.600-7.005)
TOD	6.405	4.437	<0.001	6.117 (2.808-13.326)
Operation time	-0.080	-8.600	<0.001	0.884 (0.841-0.930)
Intestinal adhesion				
0				1.000 (Reference)
1	1.618	4.086	<0.001	5.042 (2.320-10.955)
History of abdominal surgery				
0				1.000 (Reference)
1	1.195	3.174	0.002	3.302 (1.579-6.905)
Intercept	6.728	4.027	<0.001	-

POI, Postoperative paralytic ileus; EC, Endometrial cancer; TOD, morphine equivalent/drug weight.



**Figure 2.** The nomogram model for predicting POI in EC patients. Notes: TOD, morphine equivalent/drug weight; EC, Endometrial cancer; POI, Postoperative paralytic ileus.

**Table 4.** Predictive performance of independent factors on POI in EC patients after radical operation

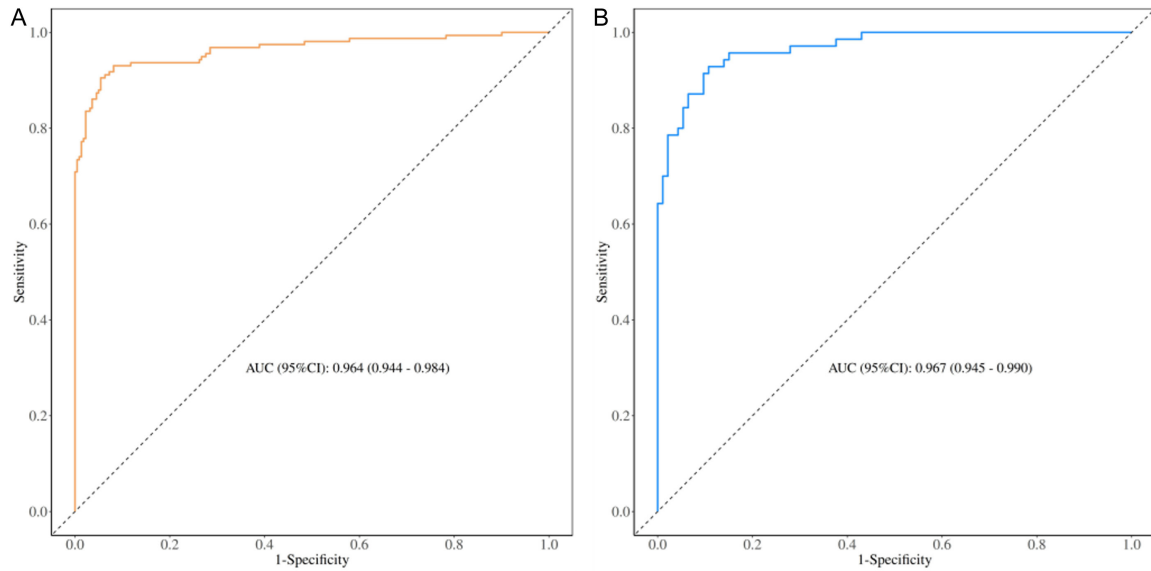
Factor	AUC	95% CI	Sensitivity (%)	Specificity (%)
Anesthesia technique	0.633	0.584-0.683	60.10	66.50
TOD	0.752	0.701-0.803	62.70	82.80
Operation time	0.914	0.890-0.938	81.90	71.10
Intestinal adhesion	0.664	0.618-0.710	78.10	54.80
History of abdominal surgery	0.629	0.580-0.679	68.90	77.00
Joint detection	0.964	0.944-0.984	88.00	91.90

POI, Postoperative paralytic ileus; EC, Endometrial cancer; AUC, Area Under the Curve; TOD, morphine equivalent/drug weight.

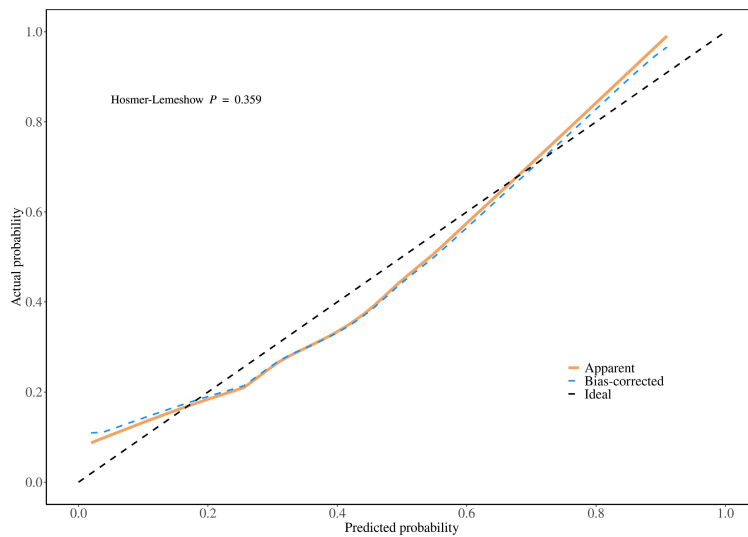
dominal procedures [12]. In patients undergoing radical surgery for EC, POI delays the recovery of gastrointestinal function, which may

compromise nutritional intake and subsequently weaken the host immune response [13]. Furthermore, POI can disrupt the intestinal bar-

## Prediction model for early intestinal paralysis after endometrial cancer radical surgery



**Figure 3.** ROC curve of the prediction model for predicting POI after EC surgery. Note: AUC, Area Under the Curve; POI, Postoperative paralytic ileus; EC, Endometrial cancer; ROC, Receiver's operating characteristic.



**Figure 4.** Calibration curves of the prediction model.

rier function, potentially leading to bacterial translocation and postoperative infections, thereby complicating clinical management and increasing the overall treatment burden. It has been reported that the American health care system spends approximately \$15 billion annually on POI management [14]. In China, the reported incidence of POI is about 3%-32% [15]. In this study, POI occurred in 40.1% of patients after operation, indicating that POI represents a clinically significant concern in our institution. Moreover, the incidence of POI in

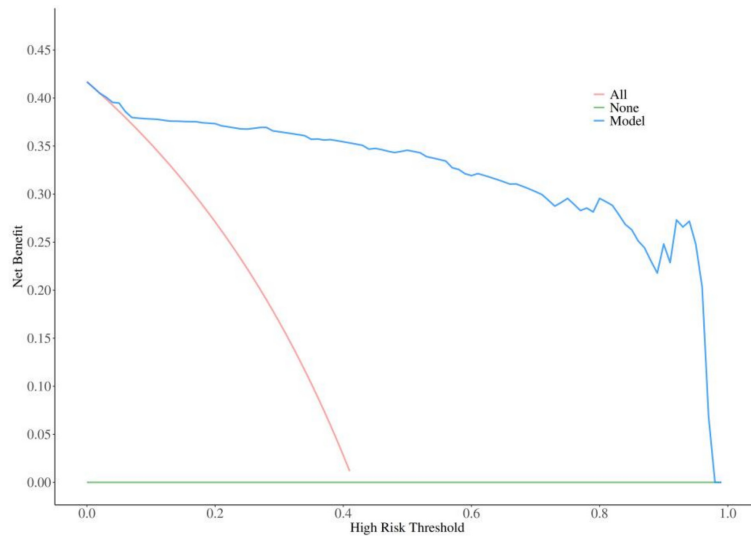
this study was higher than that reported in some previous studies, which may be attributable to differences in patient characteristics, regional variation, and sample size.

In 2022, Henneberry et al. identified preeclampsia, general anesthesia, estimated blood loss greater than 1 L, and perioperative blood transfusion as potential risk factors for POI in patients undergoing cesarean delivery [16]. Similarly, a comprehensive meta-analysis by Hou et al. indicated that opioid use, perioperative blood transfusion, general anesthesia, adhesiolysis, and prolonged operative time were

associated with an elevated risk of POI following hysterectomy [17]. Building on these findings, the present study comprehensively analyzed demographic characteristics, medical history, and surgery-related variables from 587 EC patients and conducted a predictive model, which demonstrated good predictive performance.

The occurrence of POI is mediated by multiple factors, including neuromodulation, hormone and inflammatory mechanism, as well as the

## Prediction model for early intestinal paralysis after endometrial cancer radical surgery



**Figure 5.** DCA of the prediction model. Note: DCA, decision curve analysis.

effects of anesthetic and sedative agents [18-20]. A single-center retrospective study by Matsui et al. showed that right-sided colon resection, preoperative chemotherapy, preoperative antithrombotic therapy, and postoperative complications with a CD grade  $\geq 3$  were independent risk factors for POI in patients with colorectal cancer [21]. Several studies have identified key risk factors for POI following abdominal tumor surgery, including advanced age, open surgical approach, prolonged operative duration (>3 hours), preoperative bowel preparation, perioperative infection, and blood transfusion [22]. In our study, comprehensive clinical data from EC patients who underwent radical surgery were collected, including demographic data, nutritional status-related indicators, surgical methods and contents, lymph node dissection, and comorbidities. Multivariate analysis revealed that anesthesia technique, TOD, operation time, intestinal adhesion, and history of abdominal surgery were independent risk factors for POI in EC patients after radical operation. From a mechanistic perspective, surgical trauma induces ATP release, which promotes the proliferation of intestinal glial cells and triggers an inflammatory cascade, ultimately resulting in intestinal mucosal injury and the development of POI [23]. Furthermore, intraoperative intestinal manipulation with surgical instruments stimulates neural pathways, leading to sympathetic overactivation and suppression of vagal activity, thereby impairing gastrointestinal motility

[24]. Concurrently, tissue dissection or electrocautery during surgery activates inflammatory cells, such as macrophages in the muscle layer of intestinal wall, which further promote inflammation through paracrine signaling and contribute to the pathogenesis of POI [25]. Consequently, prolonged operative duration is positively associated with an increased risk of POI.

The elevated incidence of POI observed in patients with intestinal adhesions may be explained by similar pathophysiology [26, 27]. During radical EC surgery, the presence of intestinal adhesions

often necessitates extensive adhesiolysis, which not only prolongs operative time but also increases the risk of iatrogenic bowel injury - both well-established contributors to POI [28]. Furthermore, patients with intestinal adhesions frequently require higher doses of narcotic medications, which are known to exert inhibitory effects on gastrointestinal motility and increase the risk of POI [29]. These findings collectively underscore the clinical importance of minimizing operative duration, limiting opioid exposure, and reducing gastrointestinal manipulation during radical surgical procedures.

General anesthesia combined with epidural anesthesia can inhibit stress, reduces cortisol secretion, and help maintain immune homeostasis by modulating T-helper cell differentiation [30]. Specifically, this combined approach provides superior analgesia compared to general anesthesia alone and more effectively suppresses the harmful physiological stimulation induced by surgery. Consequently, it is associated with a significant reduction in the incidence of POI during postoperative recovery. Opioids such as fentanyl, morphine and pethidine exert inhibitory effects on gastrointestinal motility primarily through activation of opioid receptors in enteric neural pathways, leading to suppressed peristalsis [31]. In addition, opioids can induce the release of nitric oxide and inhibit gastrointestinal neurotransmitters, further impairing intestinal function and induce POI through immunomodulation. This mechanistic

framework is consistent with our finding that a higher proportion of patients in the POI group received a TOD  $\geq 2.2$  mg/kg compared to those in the non-POI group.

Previous abdominal surgery predisposes patients to intra-abdominal adhesion, which increase the technical difficulty of subsequent procedures, prolong the operation time, and often necessitates extensive adhesiolysis. These factors collectively elevate the risk of iatrogenic intestinal injury, thereby increasing the likelihood of POI. Furthermore, the gastrointestinal tract in patients with prior abdominal surgery is often more susceptible to injury due to pre-existing adhesions and altered anatomy. This heightened vulnerability can result in more significant tissue trauma during radical surgery, further increasing the risk of POI in this population. Accordingly, detailed assessment of prior abdominal surgical history should be performed during preoperative evaluation in EC patients [32, 33]. When a history of abdominal surgery is identified, surgical strategies should be adjusted with heightened precision and care to minimize tissue manipulation and sympathetic nervous system activation [34]. It is worth noting that the standard management of POI also includes measures such as pain control, maintaining electrolyte balance through intravenous infusion, dietary restriction, and selective placement of gastrointestinal drainage tubes. Therefore, the development and implementation of evidence-based, standardized protocols for POI prevention and management are essential to optimize postoperative recovery and improve overall surgical outcomes.

In addition, the univariate analysis results of this study showed that there were significant differences in the number of pregnancies, pelvic lymphadenectomy, operation time, tumor diameter, diabetes, hypertension and menopausal history between the two groups. These factors may influence the risk of POI by prolonging operative duration and amplifying surgical trauma. For instance, a larger tumor diameter can increase surgical complexity, promote the release of inflammatory mediators, and raise the risk of intraoperative nerve injury. However, these variables did not remain independent risk factors in multivariate analysis. One possible explanation is that patients pre-

senting with such characteristics often undergo more meticulous surgical manipulation, which may reduce excessive stimulation of sympathetic nerve during operation [35]. Furthermore, the single-center design and relatively limited sample size of this study may have reduced the statistical power to detect independent associations. Therefore, the generalizability of these findings warrants further validation in large-scale, multicenter studies.

In this study, a predictive model based on multivariate logistic regression analysis was developed, and its discrimination ability was assessed using ROC curve analysis, yielding an AUC of 0.964, indicating excellent predictive accuracy. This study proposes a novel approach for individualized risk assessment of POI following endometrial cancer surgery. However, as a single-center retrospective analysis, the sample size in this study is inherently limited compared to that achievable in multicenter collaborations. Consequently, the stability and broader clinical applicability of the proposed model require further validation. Future multicenter, prospective studies with larger cohorts are necessary to perform external validation and to fully assess the model's translational and clinical utility.

### Conclusion

Anesthesia technique, total opioid dosage, operation time, intestinal adhesion and a history of abdominal surgery are independent risk factors for POI in EC patients after radical operation. The logistic regression model established in this study demonstrate acceptable predictive potential. Clinicians may use this information to identify high-risk patients and implement targeted preventive measures in advance to reduce the incidence of POI.

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### Disclosure of conflict of interest

None.

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