

# Risk Prediction Model for Surgical Treatment of Ruptured Corpus Luteum in the Ovary

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## Abstract

**Objective:** To explore the related factors of surgical treatment of patients with corpus luteum rupture and establish a risk prediction model of surgical treatment of corpus luteum rupture. **Methods:** 222 patients with corpus luteum rupture treated in Jingzhou First People's Hospital from January 2015 to March 2022 were analyzed retrospectively, including 45 cases of surgery and 177 cases of conservative treatment. The training set and validation set were randomly assigned according to 7:3. We collected the basic information, laboratory and ultrasonic examination data of 222 patients. Logistic regression analysis was used to determine the independent risk factors and combined predictors of surgical treatment of corpus luteum rupture. The risk prediction model was established and the nomogram was drawn. The discrimination and calibration of the prediction model were verified and evaluated by receiver operating characteristic (ROC) curve, calibration curve and Hosmer-Lemeshow goodness of fit test; Decision curve analysis (DCA) was used to evaluate the clinical effectiveness of the prediction model. **Results:** Univariate logistic regression showed that whole abdominal pain (OR: 2.314, 95% CI: 1.090 - 4.912), abdominal muscle tension (OR: 2.379, 95% CI: 1.112 - 5.089), adnexal mass  $\geq$  4 cm (OR: 3.926, 95% CI: 1.771 - 8.266), hemoglobin  $<$  12 g (OR: 11, 95% CI: 4.724 - 25.616), pelvic effusion depth  $\geq$  3 cm under ultrasound (OR: 10.606, 95% CI: 4.602 - 24.445) and positive cervical lifting pain (OR: 3.960, 95% CI: 1.831 - 8.563) were suspected risk factors for surgical treatment of corpus luteum rupture; Multivariate logistic regression analysis showed that hemoglobin  $<$  12 g (OR: 5.398, 95% CI: 1.985 - 14.682), pelvic effusion depth  $\geq$  3 cm under ultrasound (OR: 6.256, 95% CI: 1.607 - 24.354) and positive cervical lifting pain (OR: 2.995, 95% CI: 1.19 - 7.538) were independent risk factors for surgical treatment of corpus luteum rupture ( $P < 0.05$ ). The nomogram is drawn according to the prediction variables, and the prediction model is constructed. The prediction model predicted that the area under the ROC curve (AUC) of patients with corpus luteum rupture in the training set was 0.841, 95% CI (0.759, 0.922), and the area under the ROC

curve (AUC) of patients with corpus luteum rupture in the validation set was 0.919, 95% CI (0.821, 0.999). **Conclusion:** The nomogram prediction model containing three predictive variables (hemoglobin, depth of pelvic effusion under ultrasound and cervical lifting pain) can be used to predict the risk of surgical treatment in patients with corpus luteum rupture.

## Keywords

Corpus Luteum Rupture, Surgical Treatment, Prediction Model

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## 1. Introduction

Ovary luteal rupture is one of the most common gynaecological emergencies [1], usually with an acute onset and mostly unilateral rupture, with the right side being the most common [2]. Ovarian rupture of the corpus luteum can occur at all ages in women of childbearing age [3]. The most common clinical presentation is sudden onset of lower abdominal pain on one side, with atypical accompanying symptoms and non-specific ancillary investigations. If the diagnosis is not made early, timely and accurately, the condition is easily delayed and some patients may experience massive intra-abdominal bleeding, leading to haemorrhagic shock and even life-threatening. There are no clear guidelines on the choice of treatment for ruptured corpus luteum at home or abroad, and currently, there are clinical categories of surgical and conservative treatment, with each option having its own advantages and disadvantages [4]. Both open and laparoscopic surgery may result in long-term complications such as ovarian damage, pelvic adhesions and skin scarring, especially with the widespread use of monopolar and bipolar energy devices in laparoscopic surgery. The ensuing electrical and thermal radiation may cause irreversible damage to ovarian reserve function and may have long-term effects on patients with a ruptured corpus luteum who have a need for fertility. The trauma caused by thermal radiation is insidious and not easily detected intraoperatively, with symptoms often appearing around 2 weeks after the procedure [5].

There is currently no method of assessing the risk associated with surgery in the treatment of ruptured corpus luteum in national and international studies. The aim of this study is to investigate the factors influencing the surgical treatment of patients with ruptured corpus luteum and to develop a predictive model to provide an effective predictive tool for identifying high-risk patients, to further scientifically guide subsequent treatment, and to strictly control the indications for surgery so as to draw up individualized and more optimal treatment plans.

## 2. Subjects and Methods

### 2.1. Study Subjects

222 patients with ruptured corpus luteum admitted to the First People's Hospital

of Jingzhou City from January 2015 to March 2022 were selected, of which 45 were operated and 177 were conservatively treated. To establish and validate the prediction model the study population was randomly divided into two parts according to 7:3, with 172 cases ( $\approx 70\%$ ) in the training cohort and 50 cases ( $\approx 30\%$ ) in the validation cohort. Inclusion criteria: 1) admission with sudden onset of abdominal pain, ultrasound suggestive of a mass in the adnexal region and pelvic effusion; 2) diagnosis confirmed by postoperative pathology or conservative dynamic observation. Exclusion criteria: 1) previous history of pathological pelvic masses considered (untreated); 2) positive blood  $\beta$ -HCG; 3) no liver, kidney or haematological disease and no recent use of anticoagulant drugs.

## 2.2. Data Collection

Data were collected through a computer terminal, using the hospital's electronic medical record system and digital case system, according to a pre-designed clinical information questionnaire. One patient was included in the surgery group after 1 day of conservative treatment, when abdominal pain increased and was referred for surgery. Data collected included treatment modality, age, body mass index ( $\text{BMI} = \text{weight (kg)}/\text{height (m)}^2$ ), marital status, regularity of menstruation (cycles of 21 - 35 days were considered regular), predisposing factors, smoking status (yes defined as  $\geq 1$  cigarette per day), alcohol consumption status (yes defined as  $\geq 1$  drink per week, history of previous pelvic surgery, whether abdominal muscle tension, cervical lifting pain on post-admission examination Laboratory and ultrasound indicators include hemoglobin (Hb), white blood cells (WBC), platelets (PLT), international standardized ratio (INR), C-reactive protein (CRP), and ultrasound monitoring of pelvic fluid depth and adnexal mass size through vagina (with sexual history) or rectum (without sexual history).

## 2.3. Statistical Methods

SPSS (Version 26.0; IBM, Armonk, New York) and Stata (Version 15.0; Stata Corporation) were used to analyse the data. Count data were statistically described using frequencies and two groups were compared according to data characteristics using Pearson's chi-square test, continuous corrected chi-square test and Fisher's exact test, respectively. Variables with  $P < 0.05$  were included in the multi-factor logistic regression analysis using one-way logistic regression with forced, forward, backward and stepwise regressions to obtain a total of four clinical prediction models, with the best model selected based on the AIC and likelihood ratio tests and plotted on column plots. The prediction models were assessed in terms of discrimination, calibration and net clinical benefit, with discrimination assessed by the area under the subject operating characteristic curve (ROC curve) (AUC); calibration assessed by the calibration curve and Hosmer-Lemeshow goodness of fit test; and clinical validity assessed by decision curve analysis (DCA). Differences were considered statistically significant at  $P < 0.05$ .

### 3. Results

#### 3.1. Comparison of the Basic Clinical Characteristics of the Patients in the Training and Validation Sets

The p-values for body mass index, shock index and international normalized ratio in the training and validation sets were calculated using Fishers exact probability method as 0.553, 0.401 and 1, respectively; the p-values for regularity of menstruation, history of pelvic surgery, alcohol consumption and NRS pain score were calculated using the continuous corrected chi-square test as 1, 1, 0.275 and 0.719, respectively; the remaining variables were calculated using the Pearson chi-square test, none of the differences were statistically significant ( $P > 0.05$ ), see [Table 1](#).

#### 3.2. Univariate and Multivariate Analysis for Predicting Risk of Luteal Rupture Surgery

Univariate analysis showed that there were six suspected risk factors associated with surgery for ruptured corpus luteum, namely cervical lifting pain, site of pain, abdominal muscle tension, haemoglobin, ultrasound monitoring of pelvic fluid depth and size of adnexal masses ( $p < 0.05$ , see [Table 2](#)). The statistically significant influencing factors from the univariate analysis were included in the multi-factor logistic regression analysis, which showed that cervical lifting pain, haemoglobin and ultrasound monitoring of pelvic fluid depth were statistically significant ( $p < 0.05$ , see [Table 2](#)).

#### 3.3. Construction of the Prediction Model

A multivariate logistic regression prediction model was constructed using the mode of treatment for patients with ruptured corpus luteum as the dependent variable (assigned values: conservative = 0, surgery = 1) and three predictor variables screened by multivariate logistic regression analysis as the independent variables (assigned values shown in [Table 1](#)). The results showed that cervical lifting pain, haemoglobin and ultrasound monitoring of pelvic fluid depth were risk factors for surgical treatment of patients with ruptured corpus luteum ( $p < 0.05$ ), and four clinical prediction models were constructed. Columnar plots, known as Nomograms, were also constructed based on the predictor variables ([Figure 1](#)). The column line graph allows the corresponding value of each variable to be scored, and then the scores of all variables are added together to obtain a total score, and a vertical line is drawn down from the total score to mark the estimated probability of surgical treatment risk for patients with ruptured corpus luteum.

#### 3.4. Validation of the Prediction Model

The validation of the prediction model was based on the model discrimination and calibration, and the model discrimination was assessed by plotting the ROC curve of the prediction model predicting the risk of surgical treatment for patients

**Table 1.** Comparison of clinical basic information, laboratory and ultrasound examination between training set and verification set.

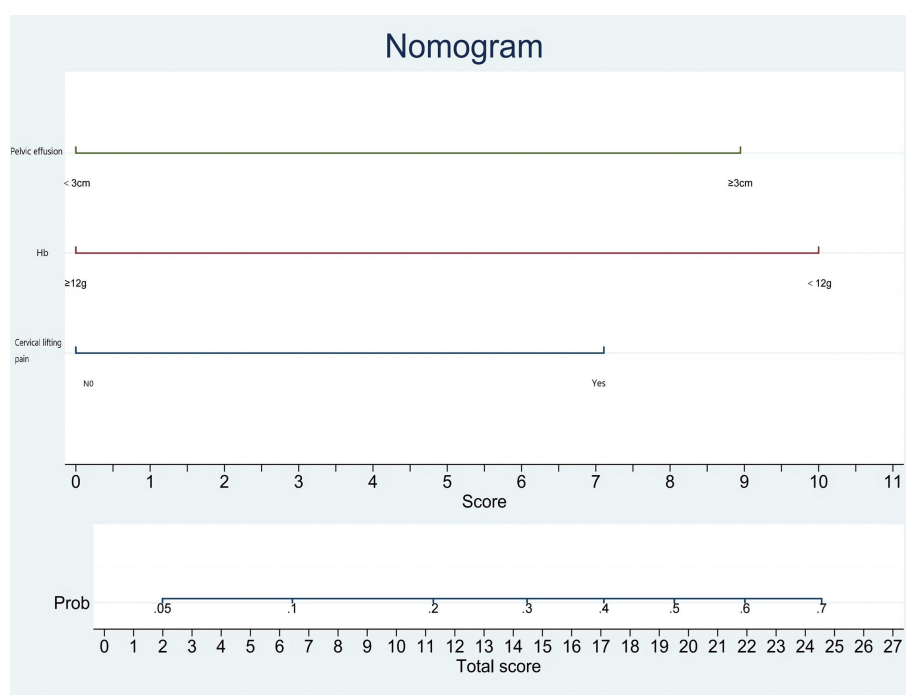
Variable	Training cohort (n = 172)	Validation cohort (n = 50)	$\chi^2$	P	Variable	Training cohort (n = 172)	Validation cohort (n = 50)	$\chi^2$	P
<b>Treatment</b>					<b>Marital status</b>				
conservative (0)	136	41	0.206	0.65	unmarried (0)	108	28	0.753	0.386
surgical (1)	36	9			married (1)	64	22		
<b>Age (y)</b>					<b>Menstrual regularity</b>				
<35 (0)	164	49	0.184	0.403	yes (0)	165	48	0	1
≥35 (1)	8	1			no (1)	7	2		
<b>BMI (kg/m<sup>2</sup>)</b>					<b>NRS Pain level (points)</b>				
<18.5 (0)	98	27		0.622	1 - 3 (1)	111	34	0.629	0.719
18.5 - 24 (1)	73	22			4 - 6 (2)	47	11		
>24 (2)	1	1			7 - 10 (3)	14	5		
<b>Predisposing factors</b>					<b>Cervical lifting pain</b>				
other (0)	67	18	0.143	0.705	no (0)	107	27	1.091	0.296
sex (1)	105	32			yes (1)	65	23		
<b>Smoking</b>					<b>Pain site</b>				
no (0)	155	40	3.711	0.054	lower abdomen (0)	95	30	0.358	0.55
yes (1)	17	10			whole abdomen (1)	77	20		
<b>History of pelvic surgery</b>					<b>Abdominal muscle tension</b>				
no (0)	166	48	0	1	no (0)	91	23	0.74	0.39
yes (1)	6	2			yes (1)	81	27		
<b>Alcohol</b>					<b>International standardized ratio</b>				
no (0)	159	49	1.194	0.275	<1.2 (0)	167	49		1
yes (1)	13	1			≥1.2 (1)	5	1		
<b>Shock index</b>					<b>C-reactive protein (mg/L)</b>				
0 - 1 (0)	171	49		0.401	<5 (0)	47	10	1.089	0.297
1 - 2 (1)	1	1			≥5 (1)	125	40		
<b>Hemoglobin (g/L)</b>					<b>Adnexal tumors (cm)</b>				
≥12 (0)	120	39	1.292	0.256	<4 (0)	106	35	1.172	0.279
<12 (1)	52	11			≥4 (1)	66	15		
<b>Leukocyte (10<sup>9</sup>/L)</b>					<b>Pelvic effusion depth (cm)</b>				
<10 (0)	94	28	0.028	0.866	<3 (0)	123	39	0.827	0.363
≥10 (1)	78	22			≥3 (1)	49	11		
<b>Platelets (10<sup>9</sup>/L)</b>									
<100 (0)	166	49	0.005	0.944					
≥100 (1)	6	1							

**Table 2.** Univariate and multivariate logistic regression analysis of the risk of surgical treatment of ovarian corpus luteum rupture.

Variable	Univariate logistic regression							Multivariate logistic regression							
	B	S.E	Wald	Sig	OR	95% CI for OR		B	S.E	Wald	Sig	OR	95% CI for OR		
						Lower	Upper						Lower	Upper	
<b>Age (y)</b>															
<35	-0.641	1.086	0.349	0.555	0.527	0.063	4.423								
≥35															
<b>BMI (kg/m<sup>2</sup>)</b>															
<18.5															
18.5 - 24	-0.096	0.372	0.066	0.797	0.909	0.439	1.883								
>24															
<b>Marital status</b>															
unmarried	0.238	0.382	0.386	0.534	1.268	0.599	2.683								
married															
<b>Menstrual regularity</b>															
yes	0.433	0.859	0.254	0.614	1.541	0.286	8.291								
no															
<b>Predisposing factor</b>															
other	0.629	0.411	2.347	0.126	1.876	0.839	4.196								
sex															
<b>Smoking</b>															
no	-1.263	0.755	2.800	0.094	0.283	0.064	1.242								
yes															
<b>Alcohol</b>															
no	0.075	0.674	0.012	0.911	1.078	0.288	4.038								
yes															
<b>History of pelvic surgery</b>															
no	-19.919	16408.711	0	0.999	0	-19.91	16408.711								
yes															
<b>Cervical lifting pain</b>															
no	1.376	0.394	12.23	0.000	3.960	1.831	8.563	1.097	0.471	5.424	0.02	2.995	1.19	7.538	
yes															
<b>Pain site</b>															
lower abdomen	0.839	0.384	4.776	0.029	2.314	1.090	4.912	0.537	0.488	1.21	0.271	1.71	0.657	4.451	
whole abdomen															
<b>Abdominal muscle tension</b>															
no	0.867	0.388	4.994	0.025	2.379	1.112	5.089	0.796	0.478	2.774	0.096	2.217	0.869	5.66	
yes															
<b>Hemoglobin (g/L)</b>															
≥12	2.398	0.431	30.91	0.000	11.000	4.724	25.616	1.686	0.51	10.911	0.001	5.398	1.985	14.682	
<12															
<b>Leukocyte (10<sup>9</sup>/L)</b>															
<10	0.236	0.375	0.396	0.529	1.267	0.607	2.644								
≥10															
<b>Platelets (10<sup>9</sup>/L)</b>															
≥100	-0.663	0.887	0.559	0.455	0.515	0.091	2.931								
<100															

## Continued

<b>International standardized ratio</b>														
<1.2	0.959	0.933	1.056	0.304	2.608	0.419	16.231							
≥1.2														
<b>C-reactive protein (mg/L)</b>														
<5	0.546	0.461	1.401	0.237	1.726	0.699	4.263							
≥5														
<b>Benign adnexal tumors (cm)</b>														
<4	1.342	0.393	11.663	0.001	3.826	1.771	8.266	-0.58	0.696	0.695	0.405	0.56	0.143	2.191
≥4														
<b>Pelvic effusion depth (cm)</b>														
<3	2.361	0.426	30.723	0.000	10.606	4.602	24.445	1.834	0.693	6.991	0.008	6.256	1.607	24.354
≥3														
<b>NRS Pain level (points)</b>														
1 - 3														
4 - 6	0.498	0.274	3.316	0.069	1.646	0.963	2.815							
7 - 10														



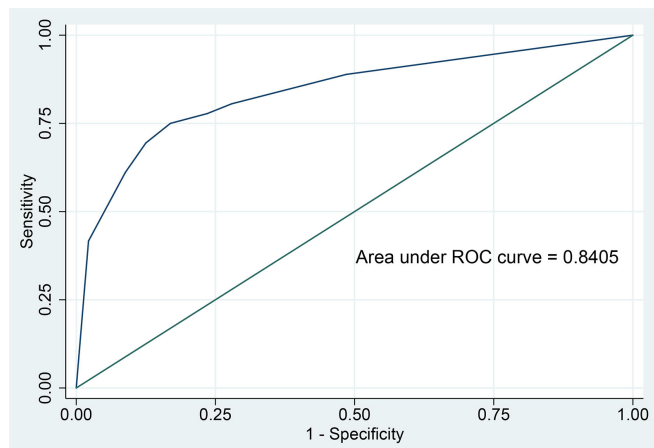
**Figure 1.** Nomogram of surgical risk in patients with ovarian corpus luteum rupture.

with ruptured corpus luteum. The AUC for the training cohort was 0.841 [95% CI (0.760, 0.922)] with a cut-off value of 0.263 (**Figure 2(a)**); the AUC for the validation cohort was 0.919 [95% CI (0.826, 0.999)] with a cut-off value of 0.128 (**Figure 2(b)**), indicating that the prediction model had good discriminatory power. Meanwhile, the Hosmer-Lemeshow goodness-of-fit test showed a good fit (training cohort  $P = 0.93$ ; validation cohort  $P = 0.41$ ), indicating that the pre-

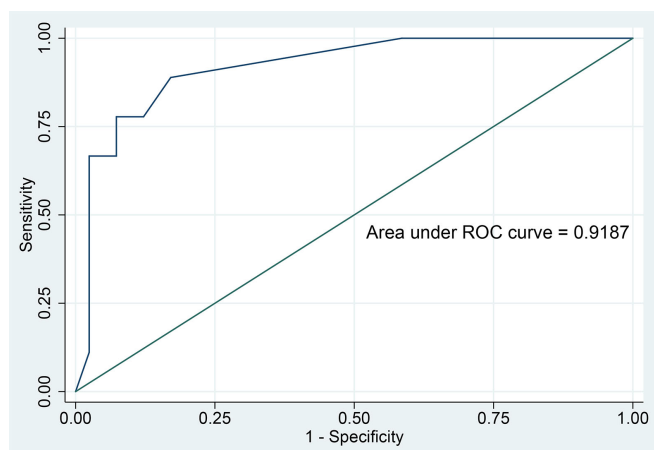
dicted probabilities of the model were generally consistent with the actual probabilities and had a good calibration. In addition, the calibration curves for the training and validation cohorts showed moderate agreement and the prediction model had good calibration ability (Figure 3). In summary, the Nomogram of the prediction model has good prediction capability.

### 3.5. Clinical Application

The clinical validity of the prediction model was assessed using the DCA for the column line graph of the probability of occurrence of surgical treatment for patients with ruptured corpus luteum is shown in Figure 4. The results show that using this column line graph to predict the risk of surgical treatment for patients with ruptured corpus luteum in the current study would have been more beneficial than implementing an intervention program for all patients if the threshold probabilities for patients and physicians were each >20%, and that the net benefit of the prediction model was significantly higher in this range than in two extreme cases, where all patients received clinical interventions.



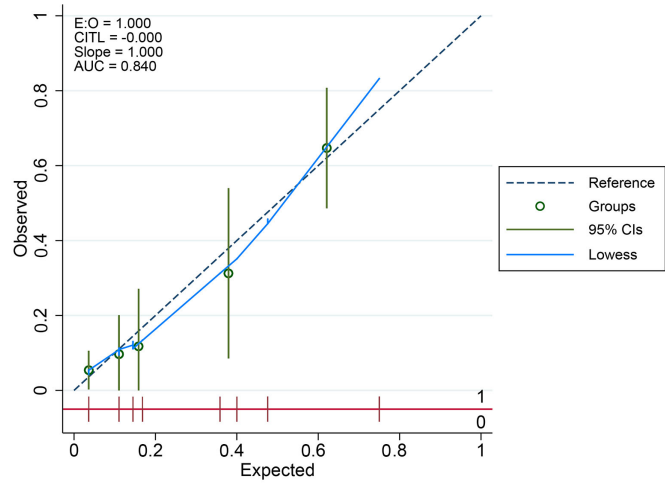
(a)



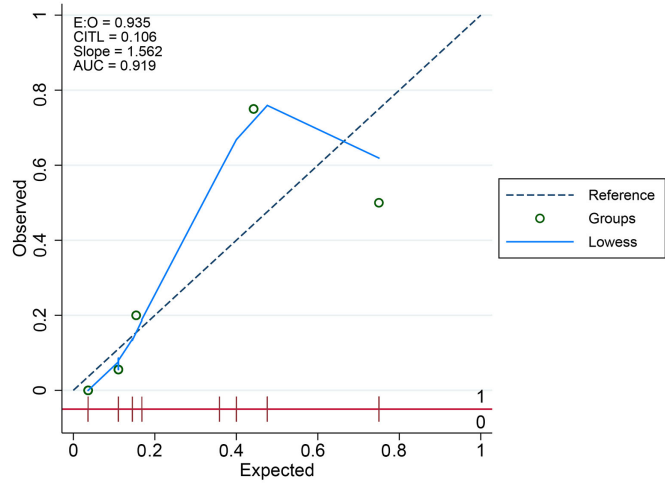
(b)

**Figure 2.** ROC curve of prediction model in training cohort and validation cohort. (a) Training cohort; (b) Validation cohort.



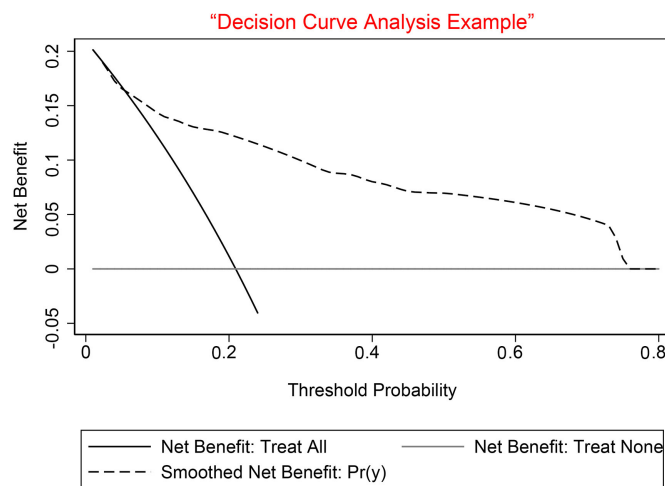


(a)

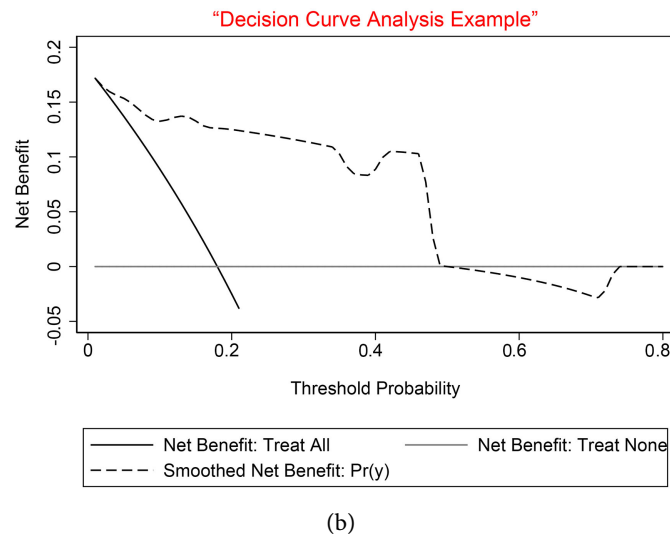


(b)

**Figure 3.** Calibration curve of prediction model in training cohort and validation cohort. (a) Training cohort; (b) Validation cohort.



(a)



**Figure 4.** DCA curve of prediction model in training cohort and validation cohort. (a) Training cohort; (b) Validation cohort.

#### 4. Discussion

In recent years, nomograms have been widely used for risk prediction in oncology and chronic diseases, both nationally and internationally because of their high utility and reliability [6] [7]. They can be used to visualize and quantify the occurrence and prognosis of various diseases. However, there is no literature on the assessment of the risk of surgical treatment in patients with ruptured corpus luteum.

This study establishes and validates a new tool to predict the risk of surgical treatment in patients with ruptured corpus luteum by obtaining three surgically relevant and readily available influencing factors through multivariate logistic regression. The incorporation of these risk factors into a concise nomogram enables individualised prediction of the risk of surgical treatment in patients with ruptured corpus luteum. This study provides a relatively accurate predictive tool for predicting the risk of surgical treatment in patients with ruptured corpus luteum. The AUCs of the training and validation cohorts were 0.841 and 0.919 ( $p < 0.05$ ) respectively, indicating that the constructed nomogram had good predictive ability. In addition, the DCA curves also suggested that the prediction model has good clinical validity.

This study showed that haemoglobin  $< 12$  g, pelvic fluid depth  $> 3$  cm on ultrasound and cervical lifting pain (+) were independent risk factors for the risk of surgery in patients with ruptured corpus luteum. In a retrospective study by Seok *et al.* [8], the results showed that CT suggestive of active bleeding from the lesion and depth of pelvic effusion made a significant difference in the choice of treatment modality with ORs of 3.773 and 1.318 respectively ( $p < 0.01$ ). In the ROC curve with the depth of pelvic blood collection as the test variable, the best cut-off value (cut-off) was measured at 5.8 cm, where the sensitivity was 73.7% and the specificity was 58.6% ( $P = 0.004$ ). The conclusions of the article suggest

that surgery is 5.786 times more risky than conservative treatment for patients with ruptured corpus luteum with active bleeding measured by CT to a depth of >5.8 cm in the pelvis. This finding is consistent with the findings of this study. A study by Mi Ju Kim *et al.* [9] showed that the surgical group had more pelvic blood loss ( $325 \pm 250$  ml vs  $206 \pm 146.5$  ml,  $p = 0.002$ ) and lower haemoglobin ( $11.3 \pm 1.4$  g/dL vs  $12.2 \pm 1.2$  g/dL;  $p = 0.007$ ) on preoperative assessment compared to the conservative treatment group and CT suggested a high volume of pelvic effusion (single deepest depth in the literature) ( $6.7 \pm 2.2$  cm vs.  $5.1 \pm 1.5$  cm,  $p = 0.006$ ), all differences being statistically significant and consistent with the findings of this study. However, active bleeding from the lesion requires enhanced CT for effective assessment [10] [11], which is less feasible for primary care and emergency patients, and ultrasound monitoring is more clinically appropriate in comparison. In a study by Wei *et al.* [4], it was shown that for both functional and non-functional ruptured ovarian cysts, the surgical group had a larger cyst volume and more pelvic fluid compared to the conservative treatment group, and the difference was statistically significant, consistent with the results of this study. This study also suggests that cervical lifting pain can be an independent risk factor for assessing the need for surgical treatment, but this has not been reported.

In 1993, the rate of surgery for patients with ruptured corpus luteum could reach 83% [12], but with continuous advances in all aspects of medical technology, conservative treatment has become the trend [3]. However, surgery remains the only treatment option for patients with unstable vital signs, unremitting symptoms, progressive worsening of anaemia and imaging suggestive of increased pelvic effusion [13]. Platelet anemia, systemic lupus erythematosus, renal failure, and coagulation abnormalities due to oral anticoagulants can all lead to severe abdominal bleeding in patients with luteal rupture [14] [15] [16] [17], while case reports suggest that deficiency of  $\alpha$ -1 trypsin can even lead to recurrent luteal rupture [18].

Although this study was the first to establish a predictive model for the risk of surgical treatment in patients with ruptured corpus luteum, the degree of differentiation and calibration was fair, and the DCA curve suggested that the predictive model had good clinical validity. However, there are still shortcomings in this study. Firstly, the study excluded patients with early pregnancy and coagulation disorders, and only provided risk prediction for the surgical treatment of luteal rupture in normal non-pregnant women of childbearing age. Secondly, this study is a single-centre retrospective study and the predictive validity of the line graph prediction model needs to be validated with more external data, especially in multicentre, large-sample cohort studies with different regions and ethnicities; thirdly, this study did not refer to the basal haemoglobin level of patients, nor did it refer to the dynamic detection of haemoglobin changes in patients whose vital signs were basically stable after admission and who did not want to undergo surgery for the time being, so the assessment of haemoglobin on actual blood loss is not well guided. Finally, the model in this study included

fewer risk factors. Therefore, more risk factors should be included in the next validation studies to further improve the predictive power of the model.

In conclusion, this study found that total abdominal pain, abdominal muscle tension, adnexal mass  $\geq 4$  cm, haemoglobin  $< 12$  g, pelvic fluid depth  $\geq 3$  cm on ultrasound, and positive cervical lift pain were suspected risk factors for surgical treatment of patients with ruptured corpus luteum. Using multivariate logistic regression analysis, we screened the three best risk factors and created a nomogram with relatively high accuracy to predict the risk of surgical treatment for patients with ruptured corpus luteum and to provide individualised treatment for patients.

### Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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