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The risk factors for postoperative ileus following posterior thoraco-lumbar spinal fusion surgery

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ABSTRACT

Objective: Postoperative ileus (PI) is a common complication following posterior thoraco-lumbar spinal fusion surgery. It usually slows patient's recovery and increases postoperative morbidity. However, the risk factors associated with PI in patients undergoing posterior thoraco-lumbar spinal fusion surgery are still unclear. The purpose of this study is to investigate the potential risk factors for PI in those patients.

Patients and methods: A prospective study was conducted and 426 patients received posterior thoraco-lumbar spinal fusion surgery between March 2017 and February 2018 were included in this study. The associations between different clinical factors and PI were analyzed. A logistic regression analysis was performed to detect independent risk factors for PI. The cut-off value, sensitivity and specificity of these independent factors were calculated by receiver operating characteristic (ROC) curve.

Results: In this study, 8.2% (35/426) of these patients were identified with PI. The average length of post-operative hospital stay was 12.54 ± 6.06 days in patients with PI compared with 8.91 ± 3.81 days in patients without PI ($P = 0.001$). These results indicated that surgical duration, PLIF approach, blood loss and length of postoperative diet restriction were potential risk factors for PI in patients with thoraco-lumbar spinal fusion surgery. The cut-off values of surgical duration, blood loss and length of postoperative diet restriction were 4.375 h, 750 ml and 9.5 h, respectively. Combination of surgical duration, PLIF approach, blood loss and length of postoperative diet restriction has the highest predictive value for PI (AUC = 0.910, $P < 0.001$).

Conclusion: Based on the study, surgical duration, PLIF approach, blood loss and length of postoperative diet restriction were the independent risk factors for PI in patients with posterior thoraco-lumbar spinal fusion surgery. Combined those factors has the highest risk for developing PI.

1. Introduction

Postoperative ileus (PI) is a recognized complication following posterior thoraco-lumbar fusion surgery. And it may be defined as pathophysiological state of a reversible nonmechanical blockage of the gastrointestinal tract that frequently occurs following surgery [1]. The symptoms associated with PI include discomfort in the form of bloating, a mix of abdominal pain, nausea and vomiting, inability to tolerate an oral diet, increased transit time for the passage of flatus and stool [2]. A large amount of patients experienced symptoms of gastrointestinal morbidity following posterior thoraco-lumbar fusion surgery, despite timely and adequate prevention [3]. Timely and adequate preventing PI is important for patients after spinal surgery [4]. PI has been reported to slow patient's recovery and increase postoperative morbidity, leading to increase the length of hospital stay, dissatisfaction with surgical care and even death [2,5]. It is important to determine the risk factors related to PI in patients with posterior thoraco-lumbar spine surgery for preventing PI. Although few studies focus on the risk factors associated with PI in patients underwent posterior thoraco-lumbar fusion [1,3,4], the correlation between clinical parameters and PI is still unclear.

In this study, we investigate the correlations between clinical parameters and PI in patients undergoing posterior thoraco-lumbar fusion surgery, and to identify the independent risk factors for PI.

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2. Materials and methods

2.1. Patients

This prospective study was approved by the medical research ethics committee of the First Affiliated Hospital of Nanchang University (No. NDYFY20170112). All participants provided written informed consent before surgery. All the methods were performed in accordance with relevant guidelines and regulations. In this study, a total of 426 patients received general anesthesia for posterior thoraco-lumbar fusion surgery between March 2017 and February 2018 were included. Additionally, all patients received patient controlled analgesia during postoperative period. Patients presenting with concomitant pathologies that could potentially affect the evaluation of the risk factors were excluded from this study, such as patients with spinal trauma, infection, malignancy or metastasis to the spine; patients who had used opioid analgesics and prokinetic drug 2 weeks before the surgery; patients with serious cardiovascular, pulmonary, renal, hepatic and hematologic diseases; patients with preoperative ileus.

2.2. Data collection

At present, no accepted standardized definition about PI was reported. Indeed, gastric and small intestinal peristalsis would recover within a few hours after surgery, and the colon peristalsis would restore between 24 and 48 h after surgery. Thus, the duration of PI greater than 48 h was considered to be pathologic [6,7]. In this study, PI was defined as no tolerance of an oral diet and missing bowel movements / passage of flatus or stool until postoperative day 2 [8,9].

The following parameters were recorded: patient demographics (gender, age and body mass index), comorbidities (diabetes mellitus, high blood pressure, previous abdominal and spine surgery), surgery related factors (surgical indications, duration of preoperative dietary restriction, surgical type, number of fusion segments, length of skin incision, surgical duration, blood loss and blood transfusion), postoperative factors (duration of postoperative dietary restriction, date of first gas passage, date of first bowel movement, vomiting, preoperative and postoperative day three laboratory findings, length of postoperative hospital stay). Dietary restriction means no food and fluids in this study. The incidence of PI in patients underwent posterior thoraco-lumbar fusion surgery was evaluated, and the risk factors of PI were analyzed.

2.3. Statistical analysis

All analysis was performed by SPSS Version 22 (SPSS Inc. Chicago IL). Qualitative variables were expressed as frequency and percentages, and were assessed by the *Chi-square test* or *Fisher's exact test*. Continuous variables were presented as means ± standard deviation and analyzed by independent samples *t tests*. Binary logistic regression model was used to identify the independent risk factors for PI. Receiver operating characteristic (ROC) curve was used to assess the predictive value of risk factors for PI following posterior thoraco-lumbar fusions surgery. All $P < 0.05$ were considered statistically significant.

3. Results

3.1. Patient demographics

A total of 426 patients undergoing posterior thoraco-lumbar spinal fusion surgery were included in this study. Of these patients, 35 individuals were identified with PI. The overall incidence of PI in this study was 8.2% (35/426). Table 1 shows the demographics of patients with and without PI. Patients with PI after posterior thoraco-lumbar spinal fusion surgery experienced an increased length of postoperative hospital stay (12.54 ± 6.06 vs. 8.91 ± 3.81 days, $P = 0.001$).

Table 1
The demographics of patients with and without postoperative ileus following posterior thoraco-lumbar spinal fusion surgery.

Factors	With PI (n = 35)	Without PI (n = 391)	*P* value
Gender			0.773
Female	18 (51.4%)	211 (54.0%)	
Male	17 (48.6%)	180 (46.0%)	
Age (yr)	54.8 ± 13.71	56.78 ± 12.05	0.359
BMI (kg/m2)	24.22 ± 4.02	23.03 ± 3.11	0.096
Comorbidities			
Diabetes mellitus	4 (11.4%)	33 (8.4%)	0.538
High blood pressure	9 (25.7%)	78 (19.9%)	0.518
Prior abdominal surgery	2 (5.7%)	43 (11.0%)	0.561
Prior spinal surgery	3 (8.6%)	25 (6.4%)	0.720
Length of postoperative hospital stay (d)	12.54 ± 6.06	8.91 ± 3.81	0.001
Length of postoperative ileus (h)	57.34 ± 6.67	24.36 ± 8.07	< 0.001

PI: postoperative ileus; BMI: body mass index.

Table 2
The differences among surgical related factors in patients with and without postoperative ileus following posterior thoraco-lumbar spinal fusion surgery.

Risk Factors	With PI (n = 35)	Without PI (n = 391)	*P* value
Surgical indications			0.261
Degenerative disc disease	19 (54.3%)	227 (58.0%)	
Degenerative spondylolisthesis	5 (14.3%)	84 (21.5%)	
Stenosis	11 (31.4%)	80 (20.5%)	
Surgical approach			< 0.001
TLIF	2 (5.7%)	169 (43.2%)	
PLIF	33 (94.3%)	222 (56.8%)	
Number of fusion segments			< 0.001
1	10 (28.6%)	262 (67.0%)	
2	11 (31.4%)	118 (30.2%)	
≥3	14 (40.0%)	11 (2.8%)	
Surgical duration (h)	5.06 ± 1.89	2.87 ± 0.85	< 0.001
Preoperative diet restriction (h)	16.17 ± 2.57	16.61 ± 2.81	0.373
Postoperative diet restriction (h)	13.29 ± 4.25	11.61 ± 4.72	0.044
Blood loss (ml)	1111.43 ± 684.42	373.81 ± 198.17	< 0.001
Blood transfused (ml)	707.14 ± 768.51	75.06 ± 156.89	< 0.001
Length of skin incision (cm)	13.86 ± 5.17	8.96 ± 2.54	< 0.001
Use of PCA	35 (100%)	391 (100%)	1.000

PI: postoperative ileus; PCA: patient controlled analgesia.

3.2. Risk factors for PI

The differences between clinical parameters and PI were investigated and the results were presented in Tables 2 and 3. Based on the analysis, those who undergoing posterior lumbar interbody fusion (PLIF) surgery were at a higher risk for PI than those receiving transforaminal lumbar interbody fusion (TLIF) surgery ($P < 0.001$). In addition, the number of fusion segments, surgical duration, length of postoperative diet restriction, length of skin incision, intraoperative blood loss and blood transfusion were significantly associated with PI.

Furthermore, binary logistic regression analysis was carried out to identify the independent risk factors for PI in patients with posterior thoraco-lumbar fusion surgery (Table 4). The results showed that surgical duration, PLIF approach, blood loss and length of postoperative diet restriction were the independent risk factors for PI ($P < 0.05$, respectively).

Table 3
The differences among laboratory findings of preoperative and postoperative day 2 in patients with and without postoperative ileus following posterior thoraco-lumbar spinal fusion surgery.

Laboratory findings	With PI (n = 35)	Without PI (n = 391)	P value
Preoperative laboratory findings			
White **blood count (*10^9/L)**	6.42 ± 1.68	6.43 ± 2.35	0.970
Red **blood count (*10^{12}/L)**	4.37 ± 0.73	4.35 ± 0.57	0.807
Hemoglobin (g/L)	130.37 ± 20.24	131.08 ± 17.58	0.822
Blood platelet (*10^9/L)	219.83 ± 55.97	217.78 ± 67.97	0.863
CRP (mg/L)	10.42 ± 22.50	6.75 ± 15.01	0.187
ESR (mm/h)	16.91 ± 20.25	15.41 ± 14.07	0.669
Serum protein (g/L)	66.67 ± 6.24	66.81 ± 5.73	0.886
Serum albumin (g/L)	41.75 ± 5.73	42.09 ± 3.97	0.638
Blood glucose (mmol/L)	5.49 ± 1.10	5.56 ± 2.37	0.861
Serum Calcium (mmol/L)	2.37 ± 0.14	2.39 ± 0.14	0.394
Serum Potassium (mmol/L)	3.96 ± 0.33	3.95 ± 0.42	0.886
PT (s)	10.95 ± 0.79	10.83 ± 0.68	0.331
APTT(s)	26.73 ± 4.33	26.89 ± 4.32	0.844
Postoperative laboratory findings			
White **blood count (*10^9/L)**	11.64 ± 3.97	11.05 ± 3.56	0.377
Red **blood count (*10^{12}/L)**	3.53 ± 0.89	3.62 ± 0.76	0.526
Hemoglobin (g/L)	103.82 ± 21.87	107.35 ± 19.77	0.338
Blood platelet (*10^9/L)	177.67 ± 61.46	198.73 ± 71.45	0.105
CRP (mg/L)	38.78 ± 37.23	33.80 ± 33.68	0.558
ESR (mm/h)	47.46 ± 41.64	41.64 ± 31.14	0.485
Serum protein (g/L)	51.56 ± 8.49	54.62 ± 6.45	0.056
Serum albumin (g/L)	31.59 ± 6.52	33.75 ± 4.38	0.076
Blood glucose (mmol/L)	7.78 ± 2.44	7.34 ± 10.02	0.827
Serum Calcium (mmol/L)	2.12 ± 0.21	2.19 ± 0.14	0.075
Serum Potassium (mmol/L)	3.90 ± 0.37	3.86 ± 0.40	0.606
PT (s)	12.04 ± 1.50	11.37 ± 0.92	0.062
APTT(s)	29.89 ± 6.15	30.17 ± 5.73	0.837

PI: postoperative ileus; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; PT: prothrombin time; APTT: activated thromboplastin time.

Table 4
The risk factors for postoperative ileus in patients with posterior thoraco-lumbar spinal fusion surgery.

Risk factors	Odds ratio	95 % Confidence Interval	*P* value
Surgical duration	2.186	1.237-3.887	0.007
PLIF	5.439	1.063-27.139	0.040
Estimated blood loss	1.003	1.000-1.006	0.002
Postoperative diet restriction	1.114	1.005-1.241	0.043

PLIF: posterior lumbar interbody fusion.

3.3. Values of risk factors for predicting PI

The ROC curve was analyzed to determine the values of risk factors for predicting PI in patients with posterior thoraco-lumbar spinal fusion surgery. The accuracy was analyzed by the area under the curve (AUC). The results were demonstrated in Fig. 1 and Table 5. Intraoperative blood loss had the highest predictive accuracy for PI among those factors (AUC = 0.846, $P < 0.001$), with a sensitivity of 65.7% and specificity of 46.3%. The cut-off values of the surgical duration, blood loss and length of postoperative diet restriction for the prediction were 4.375 h, 750 ml and 9.5 h, respectively. Thus, patients with the surgical duration > 4.375 h, blood loss > 750ml and length of postoperative diet restriction > 9.5 h have a high risk for PI.

3.4. Combination of different factors for predicting PI

In order to identify the predictive accuracy of combined different risk factors for predicting PI in patients with posterior thoraco-lumbar spinal fusion surgery, the ROC curves for combined risk factors were analyzed (Fig. 2 and Table 6). Combination of surgical duration and blood loss were more accurate for predicting PI than other two combinations of risk factors (AUC = 0.866). Additionally, combination of surgical duration, blood loss and PLIF approach were more accurate for predicting PI than other three combinations of risk factors (AUC = 0.902). Finally, combination of surgical duration, blood loss, PLIF approach and length of postoperative diet restriction had the highest predictive value for PI in patients (AUC = 0.910), with a sensitivity of 68.6% and specificity of 94.9%.

4. Discussion

PI is a physiologic response to posterior thoraco-lumbar/lumbar spinal fusion surgery. Lots of patients experienced symptoms of PI during the postoperative period, despite timely and adequate prevention [2,3]. PI has been reported to slow patient's recovery and increase postoperative morbidity, resulting in an increased duration of postoperative hospital stay and dissatisfaction with surgical care [5]. Given that, identifying available risk factors for PI is benefit for early intervention and prevention of it.

In a retrospective study, Fineberg et al [4] investigated more than 200,000 patients, and found that the incidences of PI after different types of spinal fusion were ranged from 2.6% to 8.4%. Hyun et al [2] demonstrated an incidence as great as 13.4% for PI after posterior spinal fusion. In the present study, we defined postoperative day 2 as the suitable cut-off value for PI, which was suggested by Stienen et al [9] based on a systematic review, and 8.2% (35/426) of the patients were identified with PI after posterior thoraco-lumbar spinal fusion surgery.

The pathogenesis of PI is multi-factorial, including inflammatory, neurological and pharmacological factors. Increased surgical duration always accompanies with a greater degree of tissue injury and resulted in inflammatory response [10,11]. Al Maaieh et al [12] confirmed that increased duration of surgery associated with PI after lateral lumbar interbody fusion. Huang et al [13] found that duration of operation over 4 h was an independent risk factor for PI. In line with previous studies, the surgical duration was increased in patients with PI and identified as an independent risk factor for PI in our study. The cutoff value of it was 4.375 h, which indicated the surgical duration > 4.375 h was a risk factor for PI following posterior thoraco-lumbar spinal fusion surgery.

The stimulation of parasympathetic and sympathetic will affect the gastrointestinal function. The activation of different neural reflexes has been reported to dependent on the degree of the nociceptive stimulus applied during the surgery [14]. Compared with PLIF approach, TLIF allows a unilateral approach to the disc space, which resulted in less surgical duration and blood loss, also less nerve root stimulation [15]. Stienen et al [10] showed that the incidences of PI following lateral lumbar fusion surgery were not significantly different between PLIF and TLIF approaches. Different from previous studies, the incidence of PI in this study associated with the surgical approaches, and PLIF approach was found to be an independent factor for PI after posterior thoraco-lumbar fusion surgery.

The decrease of hemoglobin concentration will increase sympathetic and endocrine stress response, which leads to gastrointestinal edema and motility inhibition [16]. Fineberg et al [4] indicated that the preoperative vitamin deficiency anemia and chronic blood loss anemia were independent risk factors for PI in patients with lumbar spinal fusion surgery. Motasem et al [13] revealed the average surgical blood loss was 910.7 ± 1066 ml in patients with PI compared with 450 ± 746 ml in patients without PI. Artinyan et al [17] demonstrated that increased surgical blood loss related with increased duration of ileus. In line with previous studies, the intraoperative blood loss was increased in patients with PI and identified as an independent risk factor for PI in patients with posterior thoraco-lumbar spinal fusion surgery. The cutoff value of it was 750 ml. It suggested that blood

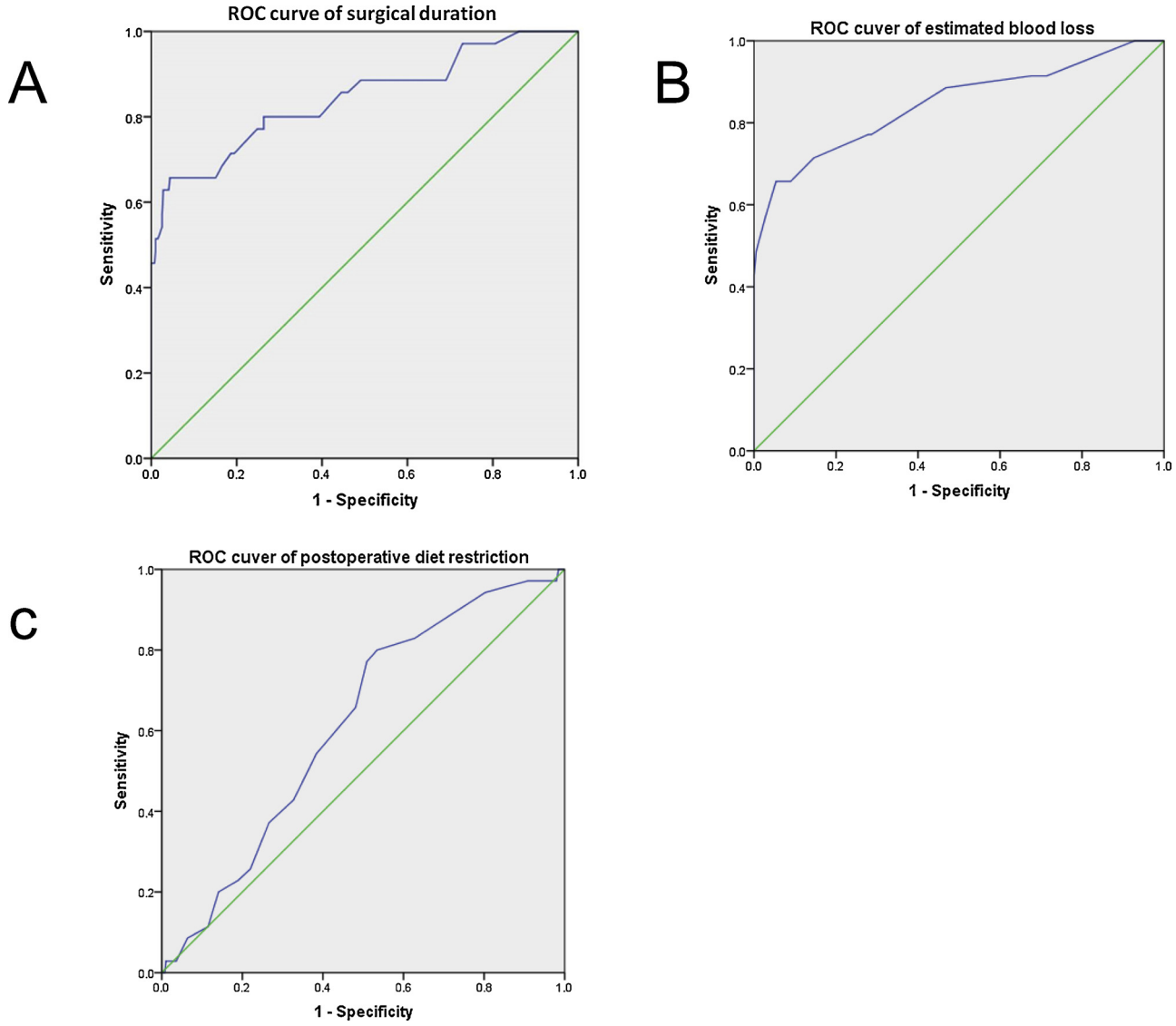

Fig. 1. The receiver operating characteristic (ROC) curves of risk factors for predicting postoperative ileus in patients with posterior thoraco-lumbar fusion surgery. A. ROC curve of surgical duration, B. ROC curve of blood loss, C. ROC curve of length of postoperative diet restriction.

Table 5
The cut off values, sensitivities and specificities of risk factors for postoperative ileus in patients with posterior thoraco-lumbar spinal fusion surgery.

Risk factors	Cut-off value	Sensitivity	Specificity	AUC	*P*
SD (h)	4.375	65.7%	56.5%	0.843	< 0.001
EBL (ml)	750	65.7%	46.3 %	0.846	< 0.001
PDR (h)	9.5	80.0%	46.6 %	0.616	0.023

SD: surgical duration; EBL: estimated blood loss; PDR: postoperative diet restriction.

loss > 750 ml predicted patient at a high risk of PI.

Early start of oral nutrition or enteral nutrition can effectively increase the blood supply of gastrointestinal mucosa, and promotes the gastrointestinal motility, resulting in early first defecation and short hospital stay [18,19]. Kirilina et al. [20] found that early nutritional support with new balanced mixtures could effectively prevent and treat PI in patients with lumbar spine surgery. Sun et al. [21] revealed that drinking water immediately after waking and enteral nutrition initiated 6 h after surgery would improve the function of gastrointestinal. In accordance with previous studies, the length of postoperative diet restriction was increased in patients with PI and identified as a risk factor for PI in this study, with a cut off value > 9.5 h. It indicated that early start of oral nutrition within 9.5 h could potentially reduce the risk of PI in thoraco-lumbar spinal fusion patients.

In order to identify the predictive accuracy of combined risk factors for predicting PI in patients with posterior thoraco-lumbar spinal fusion surgery, we also analyzed the combined risk factors for PI in the present study. Compared with the single factor, combined risk factors had higher predictive values for predicting PI. In addition, combined surgical duration, PLIF approach, blood loss and length of postoperative diet restriction had the highest predictive value for predicting PI. It indicated that combination of risk factors appeared to be more useful for predicting PI.

To our knowledge, this is the first study to identify the length of postoperative diet restriction as an independent risk factor for PI in patients with posterior thoraco-lumbar spinal fusion surgery. Although the results were interesting, the limitations of this study still existed. First of all, this is a single-center study, and a relative small sample may result in bias to the outcomes. Secondly, we didn't include preoperative and postoperative anaesthetics for the analysis. In previous study, using of anaesthetics was reported to be an independent risk factor for PI [7]. In this study, all patients received general anesthesia and patient controlled analgesia after surgery. Thirdly, the sensitivities and specificities

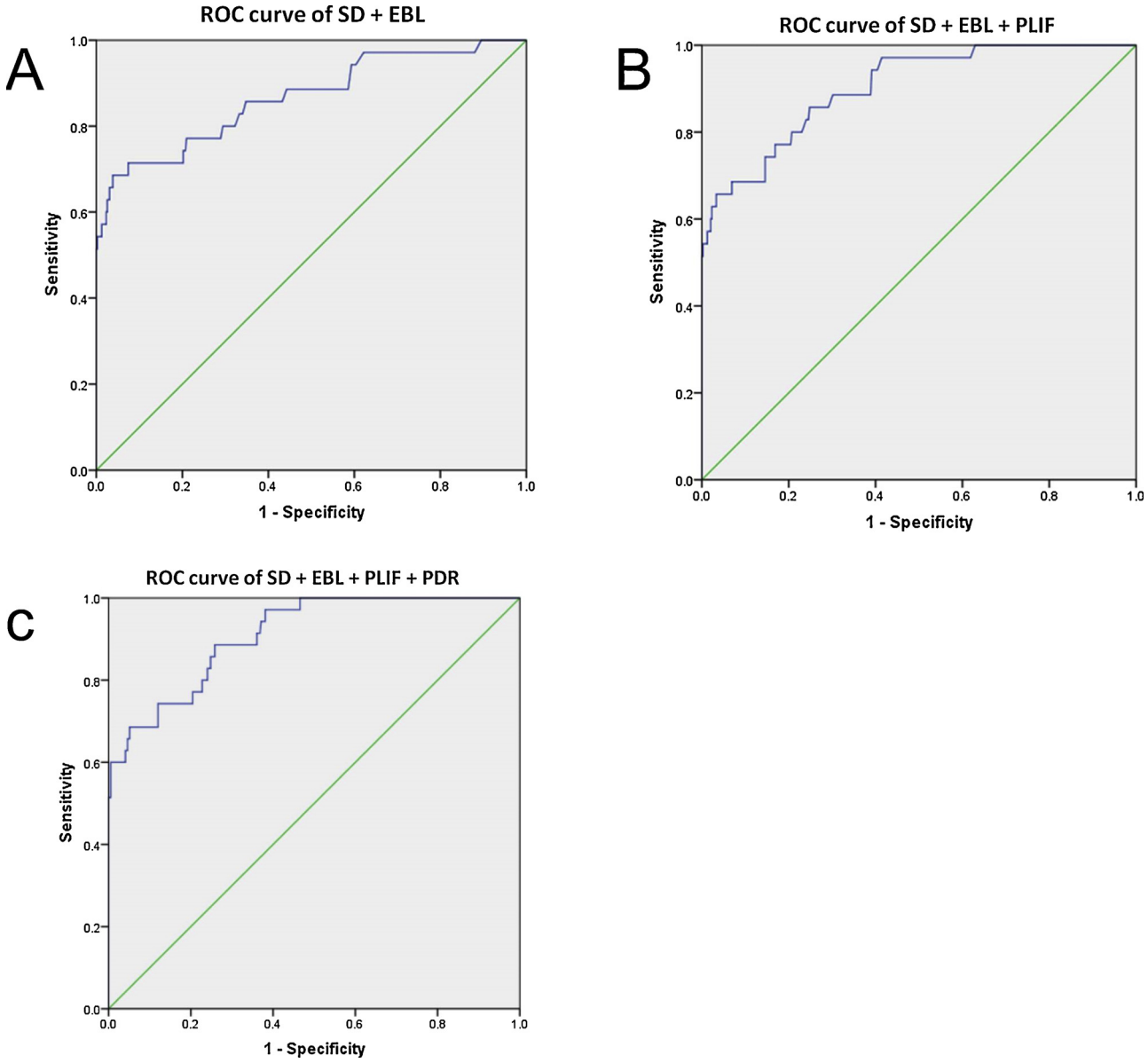

Fig. 2. The receiver operating characteristics (ROC) curves of different combined risk factors for predicting postoperative ileus in patients with posterior thoraco-lumbar fusion surgery**. A.** ROC curve of combined surgical duration and blood loss, B. ROC curve of combined combined surgical duration, blood loss and PLIF approach, C. ROC curve of combined combined surgical duration, blood loss, PLIF approach and length of postoperative diet restriction.

Table 6
The combination of different risk factors for postoperative ileus in patients with posterior thoraco-lumbar fusion surgery.

Risk factors	Sensitivity	Specificity	AUC	p
SD + EBL	68.6%	96.2%	0.866	< 0.001
LOS + EBL + PLIF	65.7%	96.7%	0.902	< 0.001
LOS + EBL + PLIF + PDR	68.6%	94.9%	0.910	< 0.001

SD: surgical duration; EBL: estimated blood loss; PLIF: posterior lumbar interbody fusion; PDR: postoperative diet restriction.

of these risk factors for PI were not high enough. Further study with large sample and multi-center investigation is necessary to make sure the efficacy of these risk factors for predicting PI in patients with posterior thoraco-lumbar spinal fusion surgery.

5. Conclusions

In summary, based on the analysis, we identified surgical duration > 4.375 h, length of postoperative diet restriction > 9.5 h, PLIF approach and blood loss > 750 ml as independent risk factors for PI in patients with posterior thoraco-lumbar spinal fusion surgery. And combined those factors had the highest risk for developing PI. However, further study with large sample and multi-center investigation is necessary to verify the efficacy of these risk factors for predicting PI in patients following posterior thoraco-lumbar spinal fusion surgery.

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