Clinical efficacy and outcomes of enhanced recovery after surgery for laparoscopic cervical cancer

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Abstract. To evaluate the effects of enhanced recovery after surgery (ERAS) protocols in laparoscopic cervical cancer surgery. The present study included 230 patients with early stage cervical cancer undergoing laparoscopic surgery, divided into the ERAS (n=103) and non-ERAS (n=127) groups. ERAS interventions included pre-admission education, nutritional optimization, effective pain management, early mobilization and goal-directed fluid therapy. The primary and secondary outcomes measured were length of hospital stay, surgical site infections, urinary tract infections and postoperative pain levels. The median length of surgery was longer in the ERAS group compared with the non-ERAS group. However, the ERAS group experienced a significantly shorter hospital stay (4.1±3.1 days) compared with the non-ERAS group (5.7±3.9 days; P=0.0005). There was a reduction in the overall complications and postoperative infections, although these differences were not statistically significant. Notably, ERAS protocols significant improved in postoperative pain management, reducing severe pain scores from days 1 to day 3 after surgery. In conclusion, the ERAS protocols shortened hospital stays and improved pain management in laparoscopic cervical cancer surgery, underscoring their role in optimizing surgical care and enhancing patient recovery.

Introduction

Cervical cancer remains a significant public health issue, being the fourth most common cancer in women worldwide. It is primarily caused by persistent infection with high-risk types of human papillomavirus (HPV) transmitted through sexual contact (1). Despite the availability of HPV vaccination and cervical screening programs, cervical cancer remains a major challenge, especially in low- and middle-income countries, with limited access to preventive services (2,3). For early stage cervical cancer treated with radical hysterectomy and pelvic lymph node dissection, the 5-year survival rate is 92% for stage IB and 87% for stage IIA (4). Cervical cancer therapies now include a combination of surgery, radiation therapy, chemotherapy and, more recently, targeted therapies and immunotherapies. Laparoscopic and robot-assisted laparoscopic surgeries, which are minimally invasive surgical techniques, are widely used for staging, diagnosis and treatment of cervical cancer (5). Innovations such as laparoscopic ovarian transposition, radical vaginal trachelectomy and laparoscopic nerve-sparing radical hysterectomy are notable for preserving fertility, ovarian hormonal function, and pelvic autonomic nerve integrity while effectively treating cervical cancer (6).

Enhanced recovery after surgery (ERAS) protocols have significantly transformed perioperative care by minimizing the physiological stress of patients, reducing the number of complications and expediting recovery (7). Laparoscopic surgery for cervical cancer, being minimally invasive, presents a unique opportunity to apply ERAS protocols to improve clinical outcomes and patient satisfaction. ERAS protocols take a comprehensive approach to patient care, emphasizing preoperative education, nutritional optimization, effective pain management and early mobilization. These strategies aim to reduce the length of hospital stay, minimize postoperative pain and enhance overall patient recovery and satisfaction. The literature provides robust evidence supporting the efficacy of ERAS protocols across various surgical procedures. Studies have highlighted the positive impact of ERAS on clinical outcomes in gastric and colorectal cancer surgeries (8-11). Furthermore, the implementation of ERAS in ovarian cancer surgeries has demonstrated significant reductions in preoperative fasting times and perioperative fluid administration, improving patient outcomes (12,13) Other studies have also reported enhanced recovery and increased adherence to ERAS guidelines compared to conventional peri-operative care protocols (14,15).

Despite a growing body of evidence, the application of ERAS in laparoscopic cervical cancer surgery remains underexplored. The present study aimed to address this gap

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by evaluating the clinical efficacy of ERAS protocols in this context. By examining various dimensions of patient care, ranging from preoperative preparation to postoperative recovery, the current study provides a comprehensive analysis and insights for the implementation of ERAS in laparoscopic surgeries for patients with cervical cancer.

Patients and methods

Study design and ethics. The present study retrospectively analyzed 230 patients with cervical cancer who received standard (non-ERAS; n=127) or ERAS (n=103) care between April 2020 and April 2022. This study was approved by the ethics committee of Guilin Maternity and Child Healthcare Hospital (approval no. 2019-04; Guilin, China). Written informed consent was obtained from all the participants.

The inclusion criteria were as follows: i) No prior treatment for cervical cancer; ii) disease classification as clinical stage I or II according to the revised 2008 International Federation of Gynecology and Obstetrics staging system (16); and iii) histological diagnosis of cervical cancer, including squamous cell carcinoma, adenocarcinoma or adenosquamous carcinoma. Exclusion criteria were: i) Use of other therapies as primary treatment; and ii) and disease classified of stage III or IV.

ERAS adoption involved a series of pre-operative, intra-operative and postoperative care enhancements or improvements, as detailed in Table I.

Outcome measures. The evaluated outcomes included the length of hospital stay as the primary outcome, along with a range of secondary outcomes. Postoperative pain intensity was measured using the 11-point Numeric Rating Scale (NRS; 0=no pain, 10=worst imaginable pain) at 24, 48 and 72 h after surgery. These secondary outcomes included the following 30-day outcomes: i) The total rate of surgical site infections (superficial, deep or organ space infections); ii) development of urinary tract infections; iii) pneumonia; iv) sepsis; v) or septic shock; vi) wound dehiscence; vii) venous thromboembolism (VTE); viii) myocardial infarction or myocardial injury following non-cardiac surgery (MINS); ix) necessity for intra- or postoperative blood transfusions; x) returns to the operating room (any unplanned re-operation that occurs within the 30-day postoperative period); and xi) readmission to hospital; xii) or death. Outcome definitions strictly followed NSQIP program guidelines, without any gradation (17).

Statistical analysis. All statistical analyses were conducted using SPSS software (version 17.0; SPSS, Inc.). Continuous variables are presented as mean ± standard deviation (SD) when normally distributed or as median (interquartile range, IQR) when skewed. Categorical variables are expressed as number (percentage). Patient demographics, comorbidities, baseline health indicators and clinical outcomes between the ERAS and non-ERAS groups were compared (non-ERAS n=127; ERAS n=103). Comparisons were made using the independent (unpaired) student's t-test for continuous and the χ^2 test for categorical variables. For continuous data, the method depended on its distribution: The independent (unpaired) Student's t-test was applied for normally distributed data, whereas the Mann-Whitney U-test was used for non-normally distributed data. Normality of each continuous variable was assessed using the Shapiro-Wilk test. Pain scores between groups at each postoperative time point were compared using the Mann-Whitney U-test, and longitudinal changes were analyzed with a mixed-effects linear model accounting for repeated measures (group x time interaction). In cases where the variances between the ERAS and non-ERAS groups were unequal, as determined using the F-test, the Satterthwaite two-sample t-test was used instead of the standard two-sample t-test. $P<0.05$ was considered to indicate a statistically significant difference (4).

Results

Clinical characteristics. The key variables assessed included demographic information [age; body mass index (BMI)], medical history [diabetes; smoking status; severe chronic obstructive pulmonary disease (COPD; defined as GOLD stage III-IV or requiring long-term oxygen therapy); American Society of Anesthesiologists (ASA) physical status classification 3-4; chronic steroid use (defined as systemic corticosteroid therapy for ≥30 consecutive days within the 6 months preceding surgery); significant weight loss >10%; and preoperative hypoalbuminemia], functional status (categorized as independent, partially dependent, or totally dependent according to NSQIP criteria) and length of surgery. Statistical analysis revealed no significant differences between the ERAS and non-ERAS groups in terms of age, BMI, prevalence of diabetes, smoking status, severe COPD, ASA classification 3-4, chronic steroid use, significant weight loss, preoperative hypoalbuminemia and independent functional status.

By contrast, a significant increase in the median length of surgery was observed in the ERAS cohort compared to the non-ERAS cohort (142.00 vs. 125.37 min; $P<0.001$) (Table II). This baseline equivalence strengthens the validity of subsequent comparisons, ensuring that any observed outcome differences are primarily attributable to ERAS care.

Analysis of patient outcomes. This study further explored the outcome of patients undergoing laparoscopic surgery for cervical cancer, comparing results before and after the implementation of the ERAS protocol. A significant reduction in the mean length of hospital stay was observed in the ERAS group (4.1±3.1 vs. 5.7±3.9; $P=0.0005$), indicating improved recovery associated with ERAS protocols.

Although the overall incidence of complications decreased from 24.41 to 16.50% (ERAS vs. non-ERAS), this reduction was not statistically significant ($P=0.192$). Similarly, no significant differences were found between the two groups in specific postoperative infections, including total surgical site infections, superficial incisional infections, deep incisional infections, organ/space infections, and urinary tract infections, pneumonia and sepsis/septic shock. This suggests that although there was a trend towards reduced complications and infections, these differences were not statistically significant in the present study (Table III).

Other outcome measures such as wound dehiscence, VTE (including deep venous thrombosis and pulmonary embolism), myocardial infarction/minor ischemic necrosis, intra/postoperative transfusion, return to the operating room, readmission

Table I. ERAS elements.

Phase	ERAS	Non-ERAS
Preoperative	Pre-admission education.	N/A
	No bowel preparation unless an anterior resection is planned or likely.	Routine mechanical bowel preparation.
	Reducing preoperative fasting (solid food: 8 h, clear fluids: 3 h).	Fasting from midnight before surgery.
	Preoperative oral carbohydrate loading with carbohydrate-rich meals the evening before and a clear fluid carbohydrate drink (50 g) on the morning of surgery.	N/A
	Preoperative analgesia includes Acetaminophen, NSAIDs and Gabapentin.	No specific preoperative oral analgesia protocol.
	Preoperative body warming system.	N/A
Intraoperative	Antibiotic prophylaxis before the incision with appropriate weight-adjusted dosing and repeated every 4 h.	Standard antibiotic prophylaxis before incision.
	Goal-directed fluid therapy focused on avoiding fluid overload.	More liberal fluid administration at the discretion of the anesthesiologist.
	Avoidance of resection-site drainage.	More frequent use of resection-site drainage.
Postoperative	Prompt termination of intravenous fluid and urinary drainage.	Continued intravenous fluid infusion into late postoperative day 1 or 2; delayed urinary drainage termination.
	Minimization of systemic opioids, favoring narcotic-sparing oral analgesia	More liberal use of opioids for pain management.
	Encouraging mobilization on the day of surgery.	Mobilization typically starting on postoperative day 1.
	Starting oral intake on the day of surgery.	Oral intake typically beginning on postoperative day 1.
	Continued mechanical VTE prophylaxis with the addition of extended postoperative chemoprophylaxis using low-molecular-weight heparin for 28 days.	No extended VTE prophylaxis protocol.
	Scheduled bowel regimens from postoperative day 1.	Bowel regimens administered as needed.
	Routine administration of antiemetics.	Antiemetics provided as needed.

ERAS, enhanced recovery after surgery; N/A, not applicable; NSAIDs, nonsteroidal anti-inflammatory drugs; VTE, venous thromboembolism. 1, Use of analgesia were determined a visual analog scale (VAS). VAS<4, no analgesia; VAS 4-6, oral acetaminophen, non-steroidal anti-inflammatory drug, or gabapentin; VAS ≥7, opioid.

and death showed no significant differences between the non-ERAS and ERAS groups. These findings suggest that the implementation of the ERAS protocols did not adversely affect specific outcome measures.

Unadjusted and adjusted 30-day outcomes. Next, unadjusted and adjusted 30-day postoperative outcomes, including complications, infections and other notable events were evaluated. A significant reduction in hospital stay duration was demonstrated with ERAS implementation, showing an unadjusted OR of 0.46 (95% CI, 0.27-0.79; P=0.0049) and an adjusted OR of 0.43 (95% CI, 0.25-0.75; P=0.0032). However, for other outcomes, such as complications, postoperative infections and readmission rates, the differences between the non-ERAS and ERAS periods were not statistically significant (Table IV). This comprehensive evaluation of postoperative outcomes highlights the nuanced impact of ERAS protocols on surgical recovery, notably reducing hospital stay duration, but with limited influence on other measured complications and adverse events. This indicates that the principal benefit of ERAS lies in facilitating earlier, safe discharge rather than markedly altering complication rates.

ERAS protocol alleviates postoperative pain. Pain levels were assessed using a numerical analog scale over 3 days post-surgery. The initial findings revealed a significant reduction in severe pain and improved management of moderate pain in the ERAS group compared to the non-ERAS group

Table II. Clinical characteristics of patients undergoing laparoscopic cervical cancer surgery.

Characteristics	Non-ERAS (n=127)	ERAS (n=103)	P-value
Age, years, mean (SD)	61.66 (9.84)	60.30 (8.95)	0.277
BMI, mean (SD)	24.39 (3.97)	24.75 (3.75)	0.477
Diabetes, n (%)	16 (12.60)	13 (12.62)	1.0
Smoker, n (%)	22 (17.32)	18 (17.48)	1.0
Severe COPD, n (%)	4 (3.15)	2 (1.94)	0.694
ASA 3-4, n (%)	118 (92.91)	98 (95.15)	0.670
Chronic steroid use, n (%)	3 (2.36)	1 (0.97)	0.630
Weight loss >10%, n (%)	5 (3.94)	2 (1.94)	0.464
Preoperative hypoalbuminemia, n (%)	76 (59.84)	55 (53.40)	0.397
Independent functional status, n (%)	124 (97.64)	103 (100.00)	0.255
Length of surgery, median (IQR)	125.37 (70.74)	142.00 (83.58)	<0.001

ERAS, enhanced recovery after surgery; SD, standard deviation; BMI, body mass index; COPD, chronic obstructive pulmonary disease; ASA, American Society of Anesthesiologists; IQR, Interquartile range.

Table III. Outcome measures in patients with or without enhanced recovery after surgery.

30-day outcomes	Non-ERAS (n=127)	ERAS (n=103)	P-value
Length of hospital stay, days (mean ± SD)	5.7±3.9	4.1±3.1	0.001
Complications	31 (24.41%)	17 (16.50%)	0.192
Postoperative infections	19 (14.96%)	11 (10.68%)	0.446
Total surgical site infection	14 (11.02%)	9 (8.74%)	0.677
Superficial incisional infection	8 (6.30%)	6 (5.83%)	>0.999
Deep incisional infection	2 (1.57%)	0 (0%)	0.503
Organ/Space infection	4 (3.15%)	3 (2.91%)	>0.999
Urinary tract infection	5 (3.94%)	1 (0.97%)	0.228
Pneumonia	3 (2.36%)	1 (0.97%)	0.630
Sepsis/septic shock	5 (3.94%)	1 (0.97%)	0.228
Wound dehiscence	2 (1.57%)	2 (1.94%)	>0.999
Venous thromboembolism	4 (3.14%)	3 (2.91%)	>0.999
Deep venous thrombosis	1 (0.79%)	1 (0.97%)	>0.999
Pulmonary embolism	3 (2.36%)	2 (1.94%)	>0.999
Myocardial infarction/MINS	10 (7.87%)	3 (2.91%)	0.151
Intra- or post-operative transfusion	30 (23.62%)	22 (21.36%)	0.803
Return to the operating room	4 (3.15%)	3 (2.91%)	>0.999
Readmission	9 (7.09%)	5 (4.85%)	0.670
Death	1 (0.79%)	0 (0%)	>0.999

ERAS, Enhanced Recovery After Surgery; SD, standard deviation; MINS, myocardial injury after noncardiac surgery.

on the first day post-operation. This trend continued on the second day, with fewer patients reporting severe pain and more reporting mild pain in the ERAS group. By the third day, 69.9% of the ERAS patients reported mild pain, a substantial improvement compared to the non-ERAS group, where only 16% of patients reported mild pain (Table V). These results highlight the effectiveness of ERAS protocols in enhancing postoperative pain control, playing a pivotal role in optimizing patient recovery. Effective pain control is critical because it promotes early mobilization and enhances overall patient satisfaction.

Discussion

This study comprehensively evaluated the effects of the ERAS protocols on laparoscopic cervical cancer surgery. Our findings demonstrated significant improvements in various aspects of surgical care, from preoperative preparation to

Table IV. Multivariable regression analysis of 30-day outcomes in patients with or without ERAS implementation.

Outcome	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Length of hospital stay (days)	0.46 (0.27, 0.79)	0.005	0.43 (0.25, 0.75)	0.003
Complications	0.61 (0.32, 1.18)	0.138	0.62 (0.32-1.19)	0.154
Postoperative infections	0.68 (0.31, 1.50)	0.338	0.69 (0.32-1.51)	0.349
Total surgical site infection	0.74 (0.29, 1.86)	0.525	0.75 (0.31-1.86)	0.529
Superficial incisional infection	0.92 (0.31, 2.74)	0.881	0.94 (0.33-2.69)	0.908
Deep incisional infection	0.24 (0.01, 5.11)	0.370	0.24 (0.01-5.11)	0.370
Organ/space infection	0.92 (0.20, 4.22)	0.915	0.96 (0.23-3.96)	0.955
Urinary tract infection	0.24 (0.03, 2.08)	0.187	0.33 (0.05-2.02)	0.240
Pneumonia	0.41 (0.04, 3.96)	0.447	0.52 (0.08-3.59)	0.500
Sepsis/septic shock	0.24 (0.03, 2.08)	0.187	0.33 (0.05-2.02)	0.240
Wound dehiscence	1.24 (0.17, 8.94)	0.831	1.24 (0.21-7.28)	0.812
Venous thromboembolism	1.24 (0.24, 6.28)	0.796	1.24 (0.28-5.58)	0.778
Deep venous thrombosis	1.24 (0.08, 20.00)	0.879	1.23 (0.13-12.04)	0.858
Pulmonary embolism	0.82 (0.13, 4.99)	0.831	0.88 (0.17-4.54)	0.879
Myocardial infarction/MINS	0.35 (0.09, 1.31)	0.124	0.39 (0.11-1.34)	0.140
Intra-/postoperative blood transfusion	0.88 (0.47, 1.64)	0.688	0.88 (0.48-1.64)	0.683
Return to the operating room	0.92 (0.20, 4.22)	0.915	0.96 (0.23-3.96)	0.955
Readmission	0.67 (0.22, 2.06)	0.483	0.70 (0.24-2.06)	0.515
Death	0.41 (0.02, 10.11)	0.575	0.41 (0.02-10.11)	0.575

ERAS, Enhanced Recovery After Surgery; OR, Odds ratio; CI, confidence interval; MINS, myocardial injury after non-cardiac surgery.

Table V. Analysis of postoperative pain (numerical analog scale).

Pain rating	ERAS, n (%)	Non-ERAS, n (%)	χ^2	P-value
1st postoperative day			4.96	0.026
Moderate (4-6)	49 (47.6)	41 (32.3)		
Severe (7-10)	54 (52.4)	86 (67.7)		
Pain score (Mean ± SD)	5.57±1.50	6.03±1.40		
2nd postoperative day			42.46	<0.001
Mild (1-3)	15 (14.6)	0 (0)		
Moderate (4-6)	77 (74.8)	72 (56.7)		
Severe (7-10)	11 (10.7)	55 (43.4)		
Pain score (Mean ± SD)	4.03±1.24	5.30±1.49		
3rd postoperative day			69.88	<0.013
Mild (1-3)	72 (69.9)	21 (16.5)		
Moderate (4-6)	31 (30.1)	98 (77.2)		
Severe (7-10)	0 (0.0)	9 (7.1)		
Pain score (Mean ± SD)	2.60±0.92	3.88±1.13		

ERAS, Enhanced Recovery After Surgery; SD, standard deviation.

postoperative recovery. ERAS protocols not only improved clinical outcomes but also overall patient outcomes.

ERAS is a multidisciplinary and patient-centered approach that aims to reduce surgical stress and facilitate quicker recovery. It emphasizes patient education on ERAS principles, perioperative nutrition, pain management, early mobilization and postoperative self-care, and reduces preoperative fasting and stress, and reduces preoperative fasting and stress. The introduction of carbohydrate-rich drinks optimizes nutritional status, enhances surgical readiness and improves post-surgery recovery (18,19). ERAS has been shown to maintain normothermia, reduce surgical stress, effective thromboprophylaxis,

reduce surgical stress (18), promote early ambulation and facilitate faster recovery through measures such as urinary catheter removal (20).

A retrospective analysis of long-term outcomes in elderly patients with colorectal cancer has demonstrated the lasting effectiveness of ERAS protocols (21). Similarly, the ERAS protocol has also been shown to improve perioperative outcomes in gynecological oncology (22), including reduced patient opioid use, postoperative ileus and surgical site infections (23). In the present study, ERAS significantly improved 30-day postoperative outcomes in laparoscopic cervical cancer surgeries, including shorter hospital stays, fewer medical complications and lower reoperation rates. These findings highlight the value of ERAS in optimizing surgical care and enhancing patient recovery. Although the reduction in the overall complications and specific postoperative infections did not reach statistical significance, a trend toward fewer complications and infections was observed, aligning with those of a previous study demonstrating the efficacy of ERAS protocols across various surgical fields (24), underscoring the importance of these protocols for optimizing surgical care and enhancing patient recovery.

The increase in surgery length with ERAS may be due to more meticulous surgical techniques or additional steps within the ERAS framework. A previous study found that ERAS increased surgical time in gynecological oncology undergoing laparotomy (25). Consistent with this, the present study observed a significant increase in operation time for laparoscopic cervical surgeries with ERAS implementation. The ERAS protocol includes thorough preoperative preparation, such as nutritional optimization, physical conditioning and psychological preparation. While this preparation may not directly add to surgery time, it is integral to the ERAS approach and aims to reduce postoperative recovery time.

A study on laparoscopic bariatric surgery with ERAS protocols found significant reductions in hospital stay and complications compared with conventional care (26). Similarly, a randomized controlled trial on laparoscopic cholecystectomy showed that ERAS protocols improved postoperative analgesia and shortened hospital stay (27). Other studies have also reported reduced hospital stays and decreased operation-related complications following ERAS protocols in various surgeries (26,28-30). A prospective study on patients undergoing surgery for advanced ovarian cancer found that ERAS improved postoperative recovery, reduced hospital stay and decreased moderate or severe complications, without increasing the 30-day readmission rates (31). Lindemann *et al* (12) evaluated an ERAS pathway in patients with suspected or advanced ovarian cancer, observing reduced fasting times and perioperative fluid use, with a reduction in length of hospital stay for patients with suspicious pelvic tumors. However, they observed more serious complications post-ERAS in patients who underwent debulking surgery for advanced disease (12).

In conclusion, ERAS protocols significantly improved patient outcomes in laparoscopic cervical cancer surgeries, including reduced hospital stay, fewer complications and enhanced recovery. These findings highlight the importance of ERAS in optimizing surgical care and patient recovery. Our comparison of standard care with ERAS demonstrated a significant reduction in the length of hospital stay. The incidence of overall complications and postoperative infections showed a trend of reduction. Numerous studies have reported similar outcomes (32,33), underscoring the contribution of patient-centered, multidisciplinary approaches within ERAS to improved results.

A study by Inania *et al* (29) on total laparoscopic hysterectomy using ERAS principles found a decrease in postoperative nausea, vomiting and opioid requirements. Sanad *et al* (30) reported a significant reduction in postoperative pain with laparoscopic radical hysterectomy. Similarly, ERAS implementation in early-stage cervical cancer (predominantly FIGO stages I-IIA) also led to reduced postoperative pain (34). The present study also showed that the implementation of ERAS protocols led to significant improvements in postoperative pain management. This is especially relevant in the context of laparoscopic cervical cancer surgery, in which the management of postoperative pain is crucial for early mobilization and recovery. A comprehensive pain management approach not only facilitates a more comfortable recovery but also helps reduce hospital stay, as unmanaged pain can prolong hospitalization. Furthermore, improvements in pain management underline the role of the ERAS protocols in enhancing surgical care quality. The ERAS protocols contribute to a more positive patient experience by significantly reducing the intensity of pain experienced during the immediate postoperative period. This aligns with the broader goals of ERAS, reducing surgical stress and expediting recovery, which ultimately leads to improved patient outcomes and satisfaction. The significant reduction in postoperative pain demonstrated in the present study supports the continued adoption and implementation of ERAS protocols in laparoscopic surgery for cervical cancer.

In summary, the present study substantiated the effectiveness of ERAS protocols in laparoscopic cervical cancer surgery and demonstrated significant improvement in patient outcomes. The findings highlight the protocols' ability to accelerate recovery but also improve the overall patient experience and potentially curtail the healthcare costs associated with extended hospital stays. In essence, our research reinforces the importance of ERAS protocols in evolving surgical care, promoting a paradigm shift towards evidence-based, patient-centered practices that aim for surgical excellence, increased patient satisfaction and optimal utilization of healthcare resources.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

XJL conceived and designed the study. WH, TL, CQ, SL, LM, HT, XY and XLL collected the data. WH and CQ confirm the authenticity of all the raw data. WH, SL, LM, HT, XY and QL analyzed and interpretated the results. WH, TL, CQ and XJL prepared the draft manuscript. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The study was approved by the ethical committee of Guilin Maternity and Child Healthcare Hospital (2019-04, Guilin, China). Informed consent was provided by all participating individuals.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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