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ORIGINAL RESEARCH

The Association of Inflammatory Markers with Maternal-Neonatal Outcome After Cervical Cerclage

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Objective: Cervical cerclage is effective in prolonging the number of weeks gestation in patients with cervical insufficiency(CI). However, valuable predictors with successful cervical cerclage remain limited. It aimed to evaluate the value of the systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI) to predict the outcomes of cervical cerclage.

Methods: This study analyzed 374 participants. Inflammatory markers were calculated using maternal peripheral blood. The association of inflammatory markers and the outcome of cervical cerclage were analyzed. And the optimal cut-off values of inflammatory markers were calculated. Also, the Chi-square test and logistic and linear regression analyses were performed to evaluate inflammatory markers with the maternal outcome and neonatal outcomes.

Results: 374 pregnancies were included in this study. Finally, 268 (71.7%) participants suffered successful cervical cerclage. This study demonstrated that the baseline BMI (cm^2/kg), the bulging membrane, cervical dilation (≥2cm), the amniotic sac herniation, the neutrophils counts, the systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI) were significant difference between the successful and unsuccessful groups (all $P<0.05$). Additionally, maternal blood inflammatory markers, such as WBC, lymphocyte, neutrophils, monocyte, platelet counts, SII, and SIRI, were significantly associated with maternal-neonatal outcomes. Furthermore, the results demonstrated that the SII level had the highest OR (OR=4.626; 95% CI (2.500–8.560)), as well as the following: SIRI level (OR = 3.795; 95% CI (1.989–7.242)), cervical dilation (≥2cm) (OR =3.477; 95% CI (1.458–10.844)), and amniotic sac herniation (OR = 1.796; 95% (0.473–4.975)).

Conclusion: This study demonstrated that the baseline SII level and SIRI level are important biochemical markers for predicting the outcome of cervical cerclage and maternal-neonatal outcomes with non-invasive procedures. They can help to provide personalized treatment before surgery and enhance postoperative surveillance.

Keywords: cervical cerclage, maternal-neonatal, outcome, inflammatory markers, peripheral blood

Introduction

Globally, approximately 15 million pregnancies are born yearly, indicating a global preterm birth rate of about 11%.[1] It is reported that nearly 1 million babies die because of preterm birth under 5 years,[1] causing problems for families and society. Although cervical insufficiency is relatively rare, accounting for less than 0.5% of all pregnancies,[2] it remains the leading risk factor for preterm birth (PTB), and the incidence could be up to 2.0%.[3] Cervical cerclage is the only effective way to treat cervical insufficiency. It is reported that cervical cerclage is effective in prolonging the number of weeks gestation in patients with cervical insufficiency compared with traditional treatments such as bed rest and oral fetal

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preservation drugs.[4] Cervical cerclage strengthens the cervix by providing mechanical support for the cervix, which prevents the extension of the lower part of the uterus in the second trimester to achieve the purpose of fetal preservation and reduce the risk of PTB by about 20% in pregnant women with cervical insufficiency.[5–8] Unfortunately, despite the importance of this surgery, valuable predictors with successful cervical cerclage remain limited, especially using non-invasive methods.

Cervical cerclage is widely used in clinical practice. However, postoperative abortion and preterm birth still occur, and the mechanism remains unclear. Richard Brown et al[9] demonstrated that it might be related to inflammation and preconception BMI. It is reported that 80% of acute cervical insufficiency may be related to intranet-amniotic infection.[9] Similarly, another study[10] proposed that the interleukin-10, interleukin-6, mannose-2, and gene promoter representing the inflammatory gene increase in patients with cervical insufficiency, which increases the incidence of preterm birth. Recently, some studies revealed that intrauterine infection and inflammation are important risk factors for postoperative prognosis after cervical cerclage.[11–13] More importantly, they may increase the risk of long-term disability in preterm infants.[14] Therefore, numerous studies have found that the levels of interleukin (IL)-1, IL-6, and IL-8 in the amniotic fluid can be used to evaluate the success of cervical cerclage.[11–13] However, these studies have been limited to small samples and invasive methods.

Importantly, recent studies have revealed that the blood neutrophil-lymphocyte ratio (NLR) is an independent diagnostic and prognostic factor of clinical inflammatory diseases, including preterm labor and gestational diabetes (GDM).[15,16] Fortunately, the systemic immune-inflammation index (SII) and systemic inflammation response index (SIRI), derived from blood cell counts, are novel and comprehensive inflammatory predictors that can affect suitably the local immune status and systemic inflammation throughout the human body.[17–19] What is more, current studies have confirmed that SII and SIRI can better reflect the chronic inflammatory state in the body than NLR and other inflammatory indicators.[20,21] Therefore, they can serve as valuable predictors of systemic inflammation with more diagnostic effectiveness and stability. Furthermore, easy access to blood samples provides convenience for investigating the peripheral inflammation in disease. Nevertheless, the relationships of SII and SIRI with the outcome after cervical cerclage remain unknown.

In the present study, we analyze the associations between the inflammatory markers, including SII and SIRI, and the clinical outcomes with maternal-neonatal outcomes after cervical cerclage. We aimed to evaluate whether the inflammatory markers in maternal blood are valuable biomarkers to predict the outcomes of cervical cerclage with a non-invasive method.

Materials and Methods

Participants

This study analyzed 374 participants from Fujian Provincial Maternity and Child Health Hospital, Affiliated Hospital of Fujian Medical University (FMCH) from January 1, 2018, to May 31, 2022. According to the guidelines, women were recruited to the study if they had cervical cerclage and indications for cervical cerclage.[22] Pregnant women were excluded due to the following criteria: (1) multifetal pregnancies, (2) severe medical and surgical complications; (3) fetal anomalies; (4) patients with incomplete clinical data. This study was approved by the Hospital Ethics Committee (2021KLR601). Detailed data on maternal-neonatal outcomes were collected from computerized obstetric records, neonatal databases, and handwritten records.

The Procedure of Cervical Cerclage

Our previous article elaborated on the specific surgical steps and preoperative management of cervical cerclage surgery.[23] Prophylactic antibiotics (intravenous Cefmetazole 1g) were given, and spinal anesthesia was performed before cerclage. The type of cerclage is McDonald for all participants. All cerclages were inserted by the same operating team using a standard technique. According to the American College of Obstetricians, antibiotics were given. And Gynecologists were changed by the maternal blood or endocervical culture results.[24] Also, a single course of antenatal betamethasone

was used for women between 23 and 34 weeks of pregnancy to reduce neonatal RDS. Delivery was suggested if chorioamnionitis, fetal distress, ongoing preterm labor, or other criteria for an emergent delivery were met.

Definition

Successful cervical cerclage was defined as the birth of a neonate discharged from the hospital without identifiable morbidity. Unsuccessful cervical cerclage resulted in miscarriage, intrauterine death, neonatal death, or neonatal morbidity. And significant neonatal morbidity was defined as the presence of any of the following: intra-ventricular hemorrhage (VIH), necrotic enterocolitis (NEC), patent ductus arteriosus (PDA), retinopathy of prematurity, RDS, or sepsis.

Blood Cell Count Assay

The blood samples were collected before the cervical cerclage procedure during the face-to-face interviews and were sent to the laboratory. White blood cell (WBC) counts, neutrophil, lymphocyte, monocyte, and platelet counts were detected with flow cytometry (XE-3000, SYSMES, Kobe, Japan). The SII (platelet count×neutrophil count/lymphocyte count) and SIRI (monocyte count×neutrophil count/lymphocyte count) were calculated with absolute neutrophil count ($\times 10^9$ /L), monocyte count ($\times 10^9$ /L), lymphocyte count ($\times 10^9$ /L) and platelet count ($\times 10^9$ /L).[25,26]

Statistical Analysis

The measurement data were calculated with chi-square tests, and the counting data were *t*-tests using SPSS version 26.0 (IBM, Armonk, NY, USA). The area under the receiver operating characteristic (ROC) curve (AUC) was used to assess the predictive efficiency of inflammatory markers (SII and SIRI) with successful cervical cerclage. Also, the Spearman rank correlation coefficient was used to determine relationships between inflammatory markers (SII and SIRI) and maternal-neonatal outcomes. Multiples logistic regression analysis was performed to evaluate risk factors associated with the prognosis of the cervical cerclage. The results were presented as odds ratio (OR) and 95% confidence interval (CI). In all statistical tests, the differences were considered statistically significant at P-values<0.05.

Results

The Clinical Characteristic of Maternal-Neonatal Outcomes

374 pregnancies were included in this study. The maternal data and neonatal characteristics are presented in Table 1. The mean age of the participants was 31.1±0.2 years, and the mean body mass index (BMI) was 22.8±0.2 (cm^2/kg). And then, the mean gestational age at the time of cerclage, PPROM, and delivery was $23^{+5}(15^{+1}–27^{+2})$ weeks, $36^{+2}(22^{+3}–41^{+1})$ weeks, and $34^{+5}(17^{+3}–41^{+3})$ weeks, respectively. Moreover, the mean interval between cerclage and delivery was 88.1 ±2.3 days. Of the patients, 13 (3.5%) had a postpartum hemorrhage, 20 (5.3%) had gestational hypertension and 50 (13.4%) had gestational diabetes (GDM). As for neonatal outcomes, 41 (11.0%) newborns died. Besides, most newborns have a good outcome delivered in the appreciable period (≥28 weeks). The mean birth weight was 2688.9±46.8g. There were some severe neonatal complications such as RDS (63/333, 4.1%), IVH (18/333, 5.5%), NEC (14/333, 4.2%), retinopathy of prematurity (19/333, 5.7%), PDA (23/333, 6.9%) and sepsis (15/333, 4.5%) in this study.

The Inflammatory Markers are Predictive Risk Factors for Unsuccessful Cervical Cerclage

Finally, 268 (71.7%) participants suffered successful cervical cerclage. This study demonstrated that the baseline BMI (cm^2/kg), the bulging membrane, cervical length (<1.5cm), cervical dilation (≥2cm), the amniotic sac herniation, the neutrophils counts, the SII and the SIRI were significantly different between the successful and unsuccessful groups (all P<0.05). As shown in Table 2, the maternal age, recurrent abortion, times of gravitas, times of parity, WBC, lymphocyte, monocyte, and platelet counts were not significantly different.

Table 1 Clinical Characteristics of the Study Population

Characteristics		Number of Cases (%)
Mother	Maternal age (years)	31.1±0.2(20–50)
	BMI (cm^2/kg)	22.8±0.2
	Gravida	3 (0–7)
	Parity	0(0–3)
	Bulging membrane	77 (20.6)
	Cervical length(cm)	
	≤1.5	318 (85.0)
	>1.5	56 (15.0)
	Cervical dilation(cm)	
	≧2	65 (17.4)
	<2	309 (82.6)
	Recurrent Abortion	35 (9.4)
	GA at cerclage (weeks)	23^{+5} (15^{+1}–27^{+2})
	GA at PPROM (weeks)	36^{+2} (22^{+3}–41^{+1})
	GA at delivery (weeks)	34^{+5} (17^{+3}–41^{+3})
	Cerclage to delivery interval (days)	88.1±2.3 (0–189)
	Cesarean delivery	142(38.0)
	GDM	50 (13.4%)
	Gestational hypertension	20(5.3%)
	Herniation of the amniotic sac	105(28.1)
	Postpartum hemorrhage	13(3.5)
	WBC($\times10^9$/L)	10.3±0.1
	Neutrophils($\times10^9$/L)	7.8±0.1
	Lymphocyte ($\times10^9$/L)	1.8±0.1
	Monocyte ($\times10^9$/L)	0.6±0.1
	Platelet ($\times10^9$/L)	239.0±3.1
	SII($\times10^9$/L)	1058.1±24.3
	SIRI($\times10^9$/L)	2.9±0.1
Newborn	GA at delivery (week)	
	<24 wk	19(5.1)
	≥24 to <28 wk	36(9.6)
	≥28 to <32 wk	48(12.8)
	≥32 to <34 wk	23(6.1)

(*Continued*)

Table 1 (Continued).

Characteristics		Number of Cases (%)
	≥34 to <37 wk	66(17.6)
	37≥wk	182(48.7)
	Birth weight (g)	2688.9±46.8 (690–4675)
	Apgar score (1 min)	9.6±0.1 (3–10)
	Apgar score (5 min)	9.9±0.1 (8–10)
	Apgar score (10 min)	10.0±0.0 (8–10)
	Mortality	41(11.0)
	NICU admission	16(21.9)
	Time in hospital (days)	12.7±1.1 (0–97)
	RDS	63(18.9)
	IVH	18(5.4)
	Sepsis	15(4.5)
	NEC	14(4.2)
	Retinopathy of prematurity,	19(5.7)
	PDA	23(6.9)

Notes: Continuous variables are presented as mean ± SD (range) and categorical variables as n (%). Recurrent abortion was defined as at least three spontaneous abortions.
Abbreviations: BMI, body mass index; GA, gestational age; PPROM, preterm premature rupture of membranes; GDM, gestational diabetes; WBC, white blood cell; SII, systemic immune inflammation index; SIRI, systemic inflammation response index; NICU, neonatal intensive care unit; RDS, respiratory distress syndrome; IVH, intraventricular haemorrhage; NEC, necrotizing enterocolitis; PDA, patent ductus arteriosus.

The Relationships Between the Inflammatory Markers and Maternal-Neonatal Outcomes

According to Table 3, we found that maternal blood inflammatory markers, such as WBC, lymphocyte, neutrophils, monocyte, platelet counts, SII, and SIRI, were significantly associated with maternal outcomes. It suggested that a longer cerclage to delivery interval times with a lower WBC counts, a lower neutrophils counts, a lower monocyte counts, lower SII and lower SIRI levels ($r = -0.307$, $P<0.001$;$r = -0.343$, $P<0.001$;$r = -0.138$, $P=0.008$;$r = -0.332$, $P<0.001$;$r = -0.351$, $P<0.001$).

The associations between maternal blood inflammatory markers and neonatal outcomes are shown in Table 3. Significant relationships were revealed between mothers with a lower WBC counts, a higher neutrophils counts, a lower lymphocyte counts, a higher monocyte counts, a higher platelet counts, a higher SII and higher SIRI levels with an earlier delivery age ($r = -0.176$, $P=0.001$;$r = -0.224$, $P<0.001$;$r = -0.329$, $P<0.001$;$r = -0.278$, $P<0.001$), lower birth weight ($r = -0.163$, $P=0.002$;$r = -0.174$, $P<0.001$;$r = -0.114$, $P=0.030$;$r = -0.319$, $P<0.001$;$r = -0.208$ $P<0.001$), a lower neonatal Apgar score (5 min) ($r = -0.113$, $P=0.038$), a lower neonatal Apgar score (10 min)($r = -0.115$, $P=0.035$;$r = -0.119$, $P=0.029$), a lower rate of NICU admission ($r = 0.129$, $P=0.016$;$r = 0.137$, $P=0.011$), and a lower mortality rate ($r = -0.166$, $P=0.001$;$r = -0.170$, $P=0.001$;$r = 0.102$, $P=0.049$;$r = -0.319$, $P<0.001$;$r = -0.259$, $P<0.001$).

Predictive Value of Inflammatory Markers for Outcomes After Cervical Cerclage

ROC analyses of SII and SIRI were performed to predict the outcomes after cervical cerclage. The SII and SIRI level were evaluated individually (Figure 1A and B). We revealed that AUC for the SII level (0.783) was higher than that for

Table 2 The Association Between Clinical Factors and Cervical Cerclage Outcomes

Variable	Successful (N=268) n (%)	Unsuccessful (N=106) n (%)	P-value
Maternal age (years)	30.7±4.3	31.8±5.0	0.074
BMI(cm^2/kg)	22.5±3.3	23.5±3.6	0.023
Gravida	2(0–8)	3(1–7)	0.105
Parity	0(0–3)	1(0–3)	0.515
Recurrent Abortion	21(7.8%)	14(13.2%)	0.108
Bulging membrane	51(19.0%)	26(24.5%)	0.031
Cervical length(cm)			0.001
<1.5	133(49.6%)	72(67.9%)	
≧1.5	135(50.4%)	34(32.1%)	
Cervical dilation(cm)			<0.001
≧2	24(9.0%)	41(38.7%)	
<2	244(91.0%)	65(61.3%)	
Amniotic sac herniation	56(20.9%)	49(46.2%)	<0.001
WBC(×10^9/L)	10.0±2.1	10.8±2.5	0.253
Neutrophils (×10^9/L)	7.5±1.7	8.4±2.2	<0.001
Lymphocyte (×10^9/L)	1.8±0.5	1.8±1.2	0.413
Monocyte (×10^9/L)	0.6±0.2	0.6±0.2	0.782
Platelet (×10^9/L)	235.8±57.2	243.560.7	0.253
SII (×10^9/L)	915.5±298.0	1400.4±567.0	<0.001
SIRI (×10^9/L)	2.4±1.0	3.8±1.8	<0.001

Note: Categorical data were analysed using chi-squared tests, and continuous data with *t*-tests.
Abbreviations: BMI, body mass index; WBC, white blood cell; SII, systemic immune inflammation index; SIRI, systemic inflammation response index.

the SIRI level (0.739). Also, the optimal cut-off of the SII level was 1226.797, and the optimal cut-off of the SIRI level was 3.201. The logistic regression analysis parameters for detecting successful and unsuccessful cervical cerclage were calculated based on the combinations of SII and SIRI. The model =−4.9234 + 0.0025*SII + 0.3874*SIRI. In particular, we found the combination of SII and SIRI had a higher AUC (0.797), and the optimal cut-off was −0.822 (Figure 1C).

The independent risk factors associated with outcome after cervical cerclage in multivariable logistic regression analysis are shown in Table 4. The results demonstrated that the SII level had the highest OR (OR=4.626; 95% CI (2.500–8.560)), as well as the following: SIRI level (OR = 3.795; 95% CI (1.989–7.242)), cervical dilation (≥2cm) (OR =3.477; 95% CI (1.458–10.844)), and amniotic sac herniation (OR = 1.796; 95% (0.473–4.975)).

Discussion

Recently, cervical insufficiency has increased yearly,[27] and the perinatal mortality rate has also increased, bringing severe economic burden and serious psychological harm to individuals and families. Cervical cerclage is a valuable method to prolong gestational age and prevent mid-trimester pregnancy loss with CI. However, some adverse outcomes, such as preterm premature rupture of membranes and chorioamnionitis, may fail cervical cerclage.[28,29] Unfortunately, there is no clinically effective indicator to predict the efficacy of cervical cerclage. Therefore, there is an urgent need to study some

Table 3 Relationships Between the Inflammatory Markers and Maternal-Neonatal Outcomes

Variable		WBC	Neutrophils	Lymphocyte	Monocyte	Platelet	SII	SIRI
Cerclage to delivery interval (days)	r-value	−0.307	−0.343	0.089	−0.138	0.020	−0.332	−0.351
	p-value	<0.001	<0.001	0.085	0.008	0.693	<0.001	<0.001
Cesarean delivery	r-value	0.028	−0.005	−0.013	0.054	−0.021	−0.05	−0.017
	p-value	0.587	0.916	0.807	0.293	0.685	0.330	0.748
Postpartum hemorrhage	r-value	0.015	0.024	0.021	0.022	−0.092	−0.066	−0.005
	p-value	0.771	0.642	0.686	0.669	0.077	0.204	0.918
GA at delivery (week)	r-value	−0.176	−0.224	0.049	0.021	−0.088	−0.329	−0.278
	p-value	0.001	<0.001	0.347	0.687	0.090	<0.001	<0.001
Birth weight (g)	r-value	−0.163	−0.174	0.068	0.067	−0.114	−0.319	−0.208
	p-value	0.002	<0.001	0.194	0.200	0.030	<0.001	<0.001
Apgar score (1 min)	r-value	−0.073	−0.099	0.007	−0.020	0.048	−0.080	−0.053
	p-value	0.178	0.070	0.899	0.711	0.376	0.141	0.327
Apgar score (5 min)	r-value	−0.077	−0.104	−0.054	−0.011	−0.072	−0.113	−0.079
	p-value	0.159	0.056	0.324	0.834	0.187	0.038	0.146
Apgar score (10 min)	r-value	−0.044	−0.079	−0.057	0.014	−0.115	−0.119	−0.021
	p-value	0.415	0.148	0.295	0.793	0.035	0.029	0.696
NICU admission	r-value	−0.092	0.129	−0.039	−0.044	−0.002	0.142	0.137
	p-value	0.087	0.016	0.469	0.416	0.968	0.008	0.011
Mortality	r-value	−0.166	−0.170	0.102	−0.037	−0.039	−0.319	−0.259
	p-value	0.001	0.001	0.049	0.437	0.455	<0.001	<0.001

Note: Analysis was performed using Spearman's rank correlation analysis.
Abbreviations: GA, gestational age; WBC, white blood cell; SII, systemic immune inflammation index; SIRI, systemic inflammation response index; NICU, neonatal intensive care unit.

reliable indicators to predict the outcome of cervical cerclage and provide guidance measurements to improve the success rate.

In this study, 268 (71.7%) participants obtained successful cervical cerclage, proving that cervical cerclage can reduce the rate of preterm birth. And then, the neonatal mortality rate in the present study was 11.0%, which is similar to other studies, ranging from 12.7–47.5%.[30,31] Interestingly, this study found that inflammatory markers, such as the neutrophils counts, the SII, and the SIRI, in the maternal peripheral blood were significantly associated with the success rate of

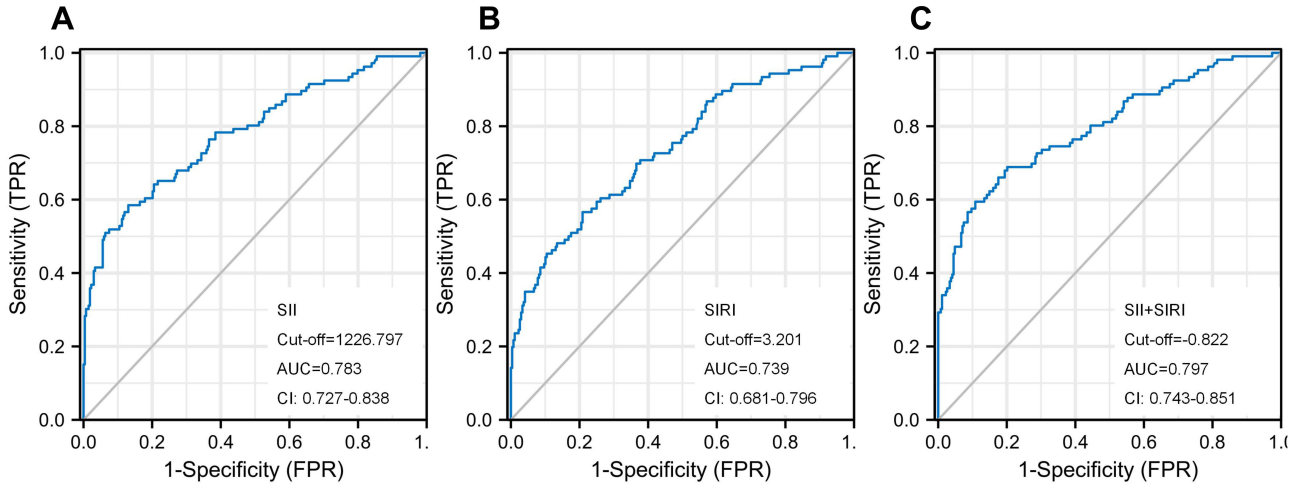

Figure 1 ROC curve analysis of the SII and SIRI level to predict the outcome of cervical cerclage. (**A**) Cut-off, the optimal SII according to the ROC curve. (**B**) Cut-off, the optimal SII according to the ROC curve. (**C**) Cut-off, the optimal the combination with SII and SIRI level according to the ROC curve.
Abbreviations: SII, systemic immune inflammation index; SIRI, systemic inflammation response index; AUC, the area under the ROC curve; ROC, receiver operator characteristic; CI, confidence interval.

Table 4 Independent Risk Factors for Predicting the Unsuccessful Cervical Cerclage

Factors	OR	95% CI	p-value
BMI(cm^2/kg)	1.022	0.841–1.494	0.053
Bulging membrane	1.546	0.428–4.641	0.694
Cervical dilation(≥2cm)	3.477	1.458–10.844	0.007
Amniotic sac herniation	1.796	0.473–4.975	0.032
Neutrophils ($\times10^9$/L)	1.119	0.903–4.480	0.240
SII ($\times10^9$/L) (≥1226.797)	4.626	2.500–8.560	<0.001
SIRI ($\times10^9$/L) (≥3.201)	3.795	1.989–7.242	<0.001

Abbreviations: BMI, body mass index; SII, systemic immune inflammation index; SIRI, systemic inflammation response index; CI, confidence interval.

cervical cerclage. Moreover, we found that the AUC for the SII level (0.783) was higher than that for the SIRI level (0.739). Also, the optimal cut-off of the SII level was 1226.797, and the optimal cut-off of the SIRI level was 3.201.

Furthermore, we found the combination of SII and SIRI had a higher AUC (0.797) by ROC analysis. Finally, multivariable logistic regression analysis demonstrated that the SII and SIRI levels were independent risk factors associated with outcome after cervical cerclage. These non-invasive markers could assist in making clinical decisions to manage cervical cerclage.

As we know, infection is a significant etiologies in up to 50% of cases in PTB.[32] It has recently been suggested that preoperative inflammatory indicators may predict pregnancy outcomes after cervical cerclage. Because the cervical opening is often accompanied by infection, uterine contraction, or rupture of the fetal membranes, which often leads to poor postoperative prognosis for cervical insufficiency. It is reported that up to 40% of PTB cases had inflammation of the uterine cavity or membranes, which is considered the pathological basis for the occurrence of PTB.[33] Recently, some studies revealed that intrauterine infection and inflammation are important risk factors for postoperative prognosis after cervical cerclage.[11–13] Importantly, WBC counts and C-reactive protein (CRP) in maternal peripheral blood have been reported to reflect infection in women with preterm labor or premature rupture of membranes.[34,35] Importantly, recent studies have revealed that the blood neutrophil-lymphocyte ratio (NLR) is an independent diagnostic and prognostic factor of clinical inflammatory diseases, such as preterm labor and gestational diabetes (GDM).[15,16] Yilmaz et al[15] points out that NLR level was significantly higher in GDM women compared with without GDM. Logistic regression analysis showed that elevated NLR was an independent variable for predicting GDM in pregnancy. Our previous research also suggested that platelet-lymphocyte ratio (PLR) can be a valuable predictor of cerclage failure.[36] However, unfortunately, our previous study did not elaborate on the relationship between inflammatory markers in maternal peripheral blood and maternal and child outcomes.

Many scholars have recently suggested that the number of neutrophils, platelets, and lymphocytes from peripheral blood is closely associated with various tumors and inflammatory diseases.[37,38] Accumulated evidence suggests that inflammation and immune responses play a crucial role in cancer development, including tumor development, malignant transformation, invasion, metastasis, and even combination therapy and immune defense responses.[39] Another study mentions that six biological factors play a crucial role in the cancer response.[40] Inflammatory markers and cell-to-cell matrix interactions constitute a tumor microenvironment (TME) that influences tumorigenesis and development.[40]

Recent studies have shown that SII and SIRI are comprehensive indicators based on peripheral platelet, neutrophil, monocyte, and lymphocyte counts that more fully reflect the balanced state of local immunity and systemic inflammatory response.[17–19] SII, a new prognostic indicator of systemic immune inflammation], is associated with many tumors and inflammatory diseases, including pancreatitis and novel coronavirus pneumonia.[41–43] Elevated SII levels suggest a poor prognosis.[44] Similarly, SIRI is a new type of inflammatory index. And numerous studies have shown that it can be a good predictor of prognosis in patients with tumors. Its ability to predict prognosis has certain advantages over a traditional inflammatory index, tumor markers, and pathological tumor stages.[45–47] Wei et al[48] reported that a high SIRI level is associated with a poor disease prognosis. And those cancer patients with high levels of SIRI suggested poor prognosis

with shortened survival, accelerated tumor progression, and high rates of recurrence or metastasis. SII and SIRI are easy to obtain and less cost-effective, so they are gradually applied to clinical research. What is more, current studies have confirmed that SII and SIRI can better reflect the chronic inflammatory state in the body than NLR and other inflammatory indicators.[20,21]

Additionally, our results indicate that cervical dilation and amniotic sac herniation are independent potential risk factors to predict the subsequent cervical cerclage outcome. Fortner et al[49] demonstrated that pregnancies with cervical dilatation were more significant than 2 cm suggested with a higher rate of PTB and delivered before 27 weeks of pregnancy on average, which is consistent with our study. According to our research, higher WBC counts, higher neutrophils counts, lower lymphocyte counts, higher monocyte counts, higher platelet counts, a higher SII, and higher SIRI levels significantly represent poor prognostic maternal-neonatal outcome, with an earlier delivery age, lower birth weight, a lower neonatal Apgar score (5 min), a lower neonatal Apgar score (10 min), a lower rate of NICU admission, and a lower mortality rate.

There are some limitations to this study. Firstly, this study did not explore twin and multiple pregnancies because the surgical indications for twin and multiple pregnancies are unclear. So the conclusions in this study do not apply to twin and multiple pregnancies. Secondly, some inflammatory indicators were not included, such as NLR, platelet to lymphocyte (PLR), and lymphocyte to monocyte rate (LMR). Thirdly, this is a retrospective study, so temporality cannot be ascertained. Therefore, a prospective study and a randomized controlled trial are necessary for the future.

In conclusion, this study demonstrated that the baseline SII level and SIRI level in maternal peripheral blood emerged as important biochemical markers for predicting the outcome of the cervical cerclage. Moreover, our data prove they are closely related to maternal-neonatal outcomes. We advocate maternal peripheral blood from non-invasive procedures and combined measurement of baseline SII level and SIRI level as a suitable and practical method to predict the outcome of cervical cerclage. Our results may offer additional prognostic information in clinical, which helps to provide a personalized treatment before surgery and enhance postoperative surveillance.

Patient Consent for Publication

The Hospital Ethics Committee of Fujian Provincial Maternity and Children's Hospital, an affiliated hospital of Fujian Medical University, approved the study (2022KYLLR03050) and complied with the Declaration of Helsinki. And all individuals participating in this study signed written informed consent.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the report has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

All authors declare that they have no competing interests in this work.

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