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A nomogram for predicting prognosis of patients with cervical cerclage

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ABSTRACT

Introduction: Cervical insufficiency is an increased risk of midterm miscarriage and early preterm birth which increase the risk of fetal loss. This study aimed to construct a nomogram for patients with cervical insufficiency after cervical cerclage, which may assist clinicians to have individualized treatment for patients with cervical insufficiency.

Methods: A study was done retrospectively from January 2013 through July 2022 in our hospital. The primary outcomes were delivered at more than 28, 30, 32, or 34 gestational weeks. Kaplan-Meier curves were applied to analyze 17 variables. All patients were randomly split (147:64) into development and validation cohorts. Based on the multivariate Cox regression analysis, a nomogram was constructed through the 'rms' package in R.

Results: A total of 211 patients with cervical insufficiency were enrolled: 121 had historyindicated cerclage; 58 had ultrasound-indicated cerclage and 32 had emergency cerclage. Times of gestations, times of miscarriages, IVF, abdominal pain, diagnostic classification, preoperative and postoperative management were demonstrated to impact overall extended days when delivering at more than 28 gestational weeks was set as the primary outcome. Except for preoperative and postoperative management, the above other five variables impacted the primary outcomes of delivering at more than 30, 32, or 34 gestational weeks. Postoperative tocolytics had an impact on the prognosis of patients who delivered at more than 30 gestational weeks. In development cohort data, a nomogram was established to predict overall extended days of patients with cervical cerclage. In present study, C-index was 0.662 in the development cohort and 0.687 in the validation cohort respectively, suggesting that the model presented some satisfied prediction. Moreover, the clinical decision curves for patients with delivering at more than 28, 30, 32 or 34 weeks set as primary outcomes also displayed that this nomogram demonstrated good clinical predictive usefulness. *Conclusions:* The nomogram developed in this study may be a valuable tool assisting clinicians to

Conclusions: The nomogram developed in this study may be a valuable tool assisting clinicians to evaluate outcomes of patients with cervical insufficiency after cervical cerclage, which helps them develop individualized management for the patients.

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1. Introduction

Cervical insufficiency is defined that the cervix becomes shorter and dilates too early in the absence of uterine contractions, causing early preterm delivery and midterm fetal loss. Complications of cervical insufficiency count for about 1 % of pregnancies [1] and 8 % of recurrent pregnancy loss in patients who underwent mid-trimester fetal loss [2].

Cervical insufficiency was classified into three categories: history-indicated cervical insufficiency; ultrasound-indicated cervical insufficiency and emergency cervical insufficiency. Cervical cerclage provides mechanical support to keep the cervix close. In February 2014, The American College of Obstetricians and Gynecologists (ACOG) recommended cervical cerclage as the only effective treatment for cervical insufficiency in addition to conservative treatment such as restriction of activity and bed rest [3].

The nomogram is a potential valuable tool, and one of merits is to estimate individualized risk based on patient characteristics. The nomogram was reported to present higher accuracy, good clinical utility and more precise prognostic predictions than traditional staging systems [4]. In addition, nomogram may be superior to clinicians' assessment of the prognosis of disease [5].

Currently, few previous studies assessed the prognosis of patients with cervical insufficiency after cervical cerclage, and only one research predicted the possibility of extremely preterm birth in women with singleton pregnancies undergoing cervical cerclage [6]. There was no data that estimated the prognosis of patients after cervical cerclage with prolonged gestational weeks up to more than 30, 32, or 34 gestational weeks. In the present work, a nomogram was constructed to assess the prognosis of patients with cervical insufficiency after management of cervical cerclage, which aimed to assist clinicians develop individualized management for the patient.

2. Methods

2.1. Study design and data source

221 patients with cervical insufficiency were enrolled from January 2013 through July 2022 in our hospital, of which ten cases were excluded because one patient carried fetal malformation, and nine patients did not deliver. All patients were singleton pregnancies. All clinical information was from medical records without a missing case. Since there were too less cases with chronic morbidities to analyze. We excluded chronic morbidities and events related to iatrogenic preterm birth in this cohort (e.g., preeclampsia, FGR, obstetric cholestasis, abruptio, etc). This work was approved by the Ethical Committee of our hospital (KL 901334). All patients were performed with Mc Donald techniques. Neuraxial analgesia was performed for all patients. Bladder was empty by foley catheter before procedure. All patients were placed in steep Trendelenburg position to allow gravity to retract the membranes. We prepared vagina and cervices with saline solution, avoid contact with the fetal membranes if exposed. For emergent clinically indicated cerclages, we applied sterilized cotton ball to push the prolapsed membranes in the uterine cavity gently. Ring forceps was used to fix the cervix before the suture. There was no intraoperative rupture of membranes. We analyzed input variables including the age of diagnosis, times of gestations, times of parturitions, times of miscarriages, preterm delivery, menstruation, in vitro fertilization (IVF), abdominal pain, cervical surgery, vaginal culture, diagnostic classification, preoperative white blood counts (WBC), post-operative WBC and C-reactive protein (CRP), prophylactic pharmacotherapy, preoperative and preoperative tocolytics. And we studied outcome variables including gestational weeks of delivery, extended days after cervical cerclage, and pregnancy status of 28, 30, 32 and 34 gestational weeks.

2.2. Inclusions and exclusions

All patients with cervical insufficiency were diagnosed between 12 through 24 weeks of gestation [7]. Patients with the following conditions were excluded, including patients with fetal malformation, preterm premature rupture of membranes, clinical chorioamnionitis, massive vaginal bleeding (placenta previa and placental abruption), active uterine contractions, and evident infection. All patients underwent McDonald cervical cerclage successfully under lumbar anesthesia, followed by routine postoperative prophylactic antibiotics and tocolytics. Sutures were removed at 36^{+0} to 37^{+0} gestational weeks or immediately at the onset of preterm labor.

2.3. Statistical analysis

IBM SPSS version 26.0 was used to analyze and Kaplan-Meier curves were performed for the comparison of variables. A two-tailed p < 0.05 was considered to be statistically significant. Finally, all patients were randomly divided (147: 64) into development cohort and validation cohort. Based on the multivariate Cox regression analysis in the development cohort, a nomogram was constructed through the 'rms' package in R. In R software, to assess the predictive performance of the nomogram, we calculated the C-indexes of the development cohort and the validation cohort, and produced calibration curves and clinical decision curves, respectively.

3. Results

3.1. Patient characteristics

211 women with cervical insufficiency who underwent cervical cerclage were enrolled. Times of gestations, times of miscarriages,

IVF, abdominal pain, diagnostic classification, preoperative pharmacotherapy, and preoperative and postoperative tocolytics were demonstrated to impact overall extended days when delivery at more than 28 gestational weeks was set as the primary outcome [Table 1, Fig. 1(a-h)]. Except for preoperative and postoperative management, the above other five variables impacted the primary outcomes of delivering at more than 30, 32, or 34 gestational weeks. Post-operative tocolytics had an impact on the prognosis of patients delivering at more than 30 gestational weeks. (Table 2, Figs. S1–3).

3.2. Three cerclage subtypes

Based on the diagnostic classification of the cervical insufficiency, the patients were divided into history-indicated cervical insufficiency (n = 121), ultrasound-indicated cervical insufficiency (n = 58) and emergency cervical insufficiency (n = 32). The effects of variables of three cerclage subtypes were analyzed respectively (Table 3). In cases of history-indicated cervical insufficiency, gestation and abdominal pain were the main independent factors (P < 0.05, Table 3). Among patients with ultrasound-indicated insufficiency, IVF presented poorer prognoses when delivering more than 30, 32 or 34 gestational weeks were set as a primary

Table	1
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Clinical characteristics of patients with cervical cerclage when delivery at more than 28 gestational weeks.

Variables	Numbers (N)	Overall extended days Median survival days (95 % CI)	Kaplan-Meier p value
Age			0.369
Age<30 years old	130	149.0 (120.1–178.0)	
$30 \le Age < 35$ years old	49	141.8 (134.7–153.3)	
Age \geq 35 years old	32	128.0 (110.8–145.2)	
Gestation	211		< 0.001
Parturition	211		0.551
Miscarriage	211		< 0.001
Premature	211		0.550
Menstruation			0.634
Regular menstruation	173	139.0 (128.8–149.2)	01001
Irregular menstruation	38	144.0 (134.4–153.6)	
IVF	00		0.019
Natural conception	174	144.0 (137.0–151.0)	0.019
In vitro fertilization	37	104.0 (82.9–125.1)	
Cervical surgery	57	104.0 (02.9-123.1)	0.352
No	183	132.0 (123.6–140.4)	0.332
Yes	28	150.0 (146.3–153.7)	
	20	130.0 (140.3-133.7)	< 0.001
Abdominal pain	159	147.0 (140.6, 159.1)	<0.001
No		147.0 (140.6–153.1)	
Yes	52	108.0 (92.2–123.8)	0.005
Vaginal culture	150		0.835
No infection	170	138.0 (128.6–147.4)	
Infection	41	144.8 (126.7–171.3)	
Diagnostic classification			< 0.001
History-indicated cerclage	121	152.0 (157.4–156.6)	
Ultrasound-indicated cerclage	58	102.0 (92.8–111.2)	
Emergency cerclage	32	108.0 (73.6–142.4)	
Preoperative WBC			0.121
≤10^9/L	85	126.0 (115.2–136.8)	
>10^9/L	126	146.0 (138.9–152.7)	
Postoperative WBC			0.386
≤10^9/L	99	130.0 (112.2–147.8)	
>10^9/L	112	141.0 (132.6–149.4)	
Postoperative CRP			0.995
$\leq 10 \text{ mg/L}$	129	141.0 (129.6–152.4)	
>10 mg/L	82	128.0 (111.4–144.6)	
Prophylactic pharmacotherapy			0.025
No-prophylactic pharmacotherapy	97	150.0 (140.1–159.9)	
Tocolytics	89	122.0 (96.5–141.5)	
Antibiotics	2	70.0	
Combined pharmacotherapy	23	126.0 (106.7–145.4)	
Preoperative tocolytics			0.005
No-prophylactic tocolytics	97	150.0 (141.1–158.9)	
Dydrogesterone tablets	14	152.0 (110.6–193.4)	
Infusion therapy	70	112.0 (91.1–132.9)	
Combination	30	114.0 (104.3–123.7)	
Postoperative tocolytics			0.019
Dydrogesterone tablets	5	127.0 (41.7–212.3)	
Infusion therapy	93	110.0 (92.2–127.8)	
Combination	113	149.0 (139.7–158.2)	

IVF in vitro fertilization, WBC white blood cell, CRP C-reactive protein, Infusion therapy ritodrine hydrochloride injection.

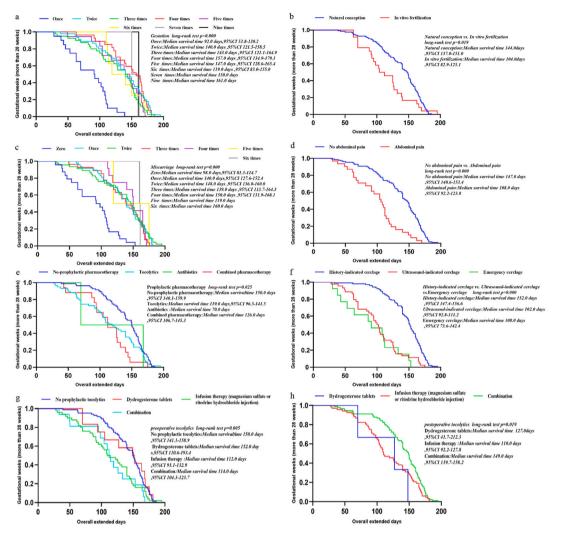


Fig. 1. Curves of extended days of patients delivered at more than 28 gestational weeks.

a. Compared to multiparous women, primiparous patients had a worse prognosis. b. Patients conceived through in vitro fertilization extended shorter gestational days than patients with natural conception. c. Primiparous women had a worse outcomes than patients with history of miscarriage for extending gestational weeks. d. Patients without abdominal pain had longer gestational days than patients with abdominal pain. e. Patients without prophylactic pharmacotherapy had the longest extended gestational days. f. Among three subtypes of cervical cerclages, patients with history-indicated cerclage presented the most favorable outcomes. g. In general, patients without propertive tocolytics had the longer extended gestational days. h. Combination of ritodrine hydrochloride injection and dydrogesterone tablets was better than monotherapy after cerclages.

outcome, while this variable was not an independent factor when gestation more than 28 weeks was set as a primary outcome (Table 3). Among patients with emergency cervical insufficiency, menstruation was one meaningful factor (Table 3). Women with irregular menstruation (periods that start at intervals >38 days) presented less extended days than patients with regular menstrual cycles after cervical cerclage (Fig. 2a). Postoperative CRP level (post-CRP) was also one relevant factor affecting the outcome of emergency cerclage (Table 3). CRP more significantly affected the prognosis when delivering more than 28 or 30 gestational weeks was set as the primary outcome (Fig. 2b). If postoperative-CRP was above 10 mg/L, patients had poorer outcomes when delivering more than 28 or 30 gestational weeks was set as primary outcome. However, women did not present worse outcomes when delivering more than 32 or 34 gestational weeks were set as primary outcome. For emergency cervical cerclage, management of postoperative tocolytics was also an impacted variable (Fig. 2c). Generally, combination of ritodrine hydrochloride injection and dydrogesterone tablets was better than monotherapy.

3.3. The prognostic nomogram

No statistical differences were identified in the factors between development and validation cohorts (P > 0.05, Table S1). In

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Table 2

Clinical characteristics of patients when delivery at more than 30, 32, 34 gestational weeks.

Variables	<i>p</i> value						
	\geq 30 weeks	\geq 32 weeks	\geq 34 weeks				
Age	0.258	0.287	0.402				
Gestation	<0.001	< 0.001	< 0.001				
Parturition	0.513	0.500	0.396				
Miscarriage	<0.001	< 0.001	< 0.001				
Premature	0.641	0.627	0.687				
Menstruation	0.769	0.830	0.932				
IVF	0.022	0.019	0.034				
Cervical surgery	0.418	0.576	0.635				
Abdominal pain	< 0.001	< 0.001	< 0.001				
Vaginal culture	0.826	0.748	0.634				
Diagnostic classification	<0.001	< 0.001	< 0.001				
Preoperative WBC	0.180	0.286	0.218				
Postoperative WBC	0.430	0.526	0.463				
Postoperative CRP	0.873	0.904	0.825				
Prophylactic pharmacotherapy	0.117	0.094	0.127				
Preoperative tocolytics	0.071	0.073	0.106				
Postoperative tocolytics	0.026	0.059	0.144				

Table 3

Clinical characteristics of three groups with cervical insufficiency after cerclage based on delivery at more than three different gestational weeks.

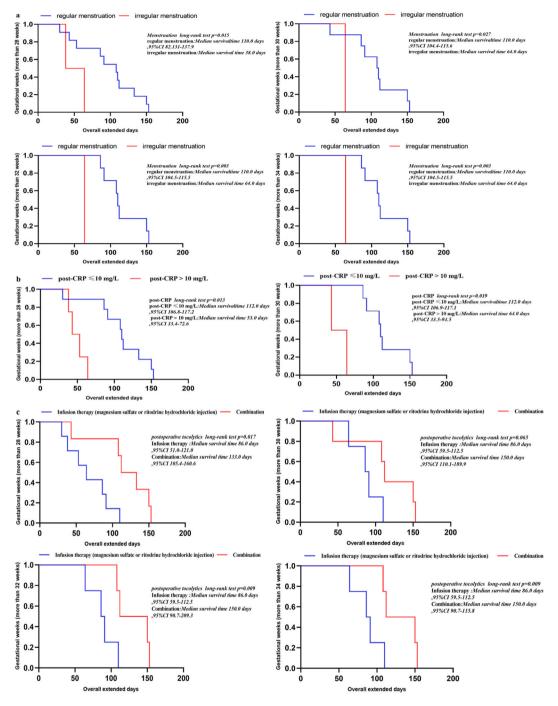
Variables	p value											
History- ≥28	History-i	istory-indication			Ultrasound-indication			Examination-indication				
	≥ 28	≥ 30	\geq 32	\geq 34	≥ 28	≥ 30	\geq 32	\geq 34	≥ 28	\geq 30	\geq 32	≥34
Age	0.166	0.117	0.116	0.187	0.633	0.853	0.664	0.732	0.508	0.813	0.317	0.317
Gestation	0.023	0.029	0.019	0.177	0.231	0.385	0.728	0.753	0.670	0.561	0.773	0.77
Parturition	0.166	0.139	0.120	0.054	0.772	0.860	0.836	0.573	0.924	0.787	0.856	0.856
Miscarriage	0.261	0.141	0.090	0.327	0.179	0.267	0.420	0.451	0.410	0.550	0.760	0.760
Premature	0.366	0.296	0.260	0.325	0.578	0.813	0.972	0.836	0.050	-	-	-
Cervical surgery	0.800	0.923	0.983	0.955	0.696	0.995	0.841	0.697	0.413	0.083	0.083	0.083
Menstruation	0.738	0.868	0.965	0.791	0.127	0.063	0.108	0.205	0.015	0.027	0.003	0.003
IVF	0.850	0.923	0.976	0.807	0.051	0.048	0.035	0.031	0.703	0.751	0.525	0.525
Abdominal pain	0.012	0.007	0.024	0.044	0.152	0.133	0.097	0.978	0.563	0.881	0.872	0.872
Vaginal culture	0.925	0.802	0.715	0.700	0.873	0.953	0.977	0.734	0.705	0.130	0.149	0.149
Pre-WBC	0.946	0.784	0.860	0.779	0.562	0.881	0.826	0.664	0.207	0.551	0.928	0.928
Post-WBC	0.329	0.282	0.288	0.352	0.225	0.329	0.379	0.192	0.192	0.551	0.928	0.928
Post-CRP	0.806	0.801	0.857	0.901	0.583	0.511	0.817	0.909	0.013	0.019	0.061	0.061
Pharmacotherapy	0.292	0.508	0.466	0.627	0.756	0.791	0.739	0.507	0.507	0.881	-	-
Pre-tocolytics	0.274	0.595	0.693	0.756	0.383	0.629	0.374	0.484	-	-	-	-
Post-tocolytics	0.543	0.506	0.522	0.661	0.133	0.140	0.120	0.127	0.017	0.065	0.009	0.009

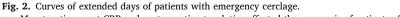
"-" Too little data for statistical significance.

development cohort data, the above five variables (times of gestations, times of miscarriages, IVF, abdominal pain and diagnostic classification) were analyzed in the multivariate Cox regression analysis. Times of gestation, miscarriage, abdominal pain and diagnosis were independent predictive factors for patients with cervical cerclage based on delivering different gestational weeks (P < 0.05, Table 4). A nomogram was developed to predict outcomes of patients with cervical cerclage (Fig. 3a) according to the final multivariate Cox analysis. In present study, the C-index was 0.662 in the development cohort and 0.687 in the validation cohort respectively, implying that the model had satisfied prediction. Good predictive accuracy could be seen between the actual probability and predicted probability from the calibration curves of the development and validation cohorts (Fig. 3b–e, Fig. 4a–d). Moreover, the clinical decision curves (Fig. 3f–i, Fig. 4e–h) in the development and the validation cohorts for 28, 30, 32 or 34 weeks also indicated that this nomogram presented good clinical usefulness.

4. Discussion

Cervical insufficiency is associated to increase risk of miscarriage and early preterm delivery. Cervical cerclage was identified as an effective management for those population. Prior data presented that this treatment performed an important role in prolonging gestational days and improving neonatal outcomes [8]. Especially, emergency cerclage was reported to prolonged the pregnancy and increased survival rate of preterm baby [9,10]. However, limited data analyzed the impact of various factors on patients with cervical cerclage. In addition, no effective prediction tools predicted the prognosis for patients with cervical insufficiency after cervical cerclage. The





a-c. Menstruation, post-CRP and postoperative tocolytics affected the prognosis of patients after emergency cerclage, respectively.

nomogram was constructed to assist clinicians to better manage patients with cervical sufficiency based on delivering different gestational weeks.

In this study, times of gestation, miscarriages, abdominal pain, IVF, diagnosis classifications, prophylactic pharmacotherapy and management of preoperative and postoperative tocolytics were demonstrated as impact factors on outcomes of patients with cervical insufficiency. History of multiple vaginal deliveries easily resulted in cervical and vaginal slackness. Repeated deliveries destroyed the anatomical structure and the biochemical protection of the cervix, causing potential damage to the cervical opening and subclinical infection. Although there is no visible wound in the body of the uterus, the cervical function becomes incomplete and the risk of preterm birth increases [11]. Therefore, a history of multiple deliveries increases a high risk of cervical insufficiency. In our study, the

Table 4

Multivariate	Cox ana	lysis of	prognosis	in the	development cohort.

Variables	Multivariate Cox analysis				
	HR (95 % CI)	p value			
Gestation	0.594 (0.389–0.907)	0.030 *			
Miscarriage	1.490 (1.039-2.136)	0.016 *			
IVF					
Natural conception	Ref				
In vitro fertilization	1.474 (0.798-2.722)	0.216			
Abdominal pain					
Without	Ref				
With	2.271 (1.181-4.367)	0.014 *			
Diagnostic classification					
History-indicated cerclage	Ref				
Ultrasound-indicated cerclage	3.778 (2.202-6.481)	< 0.001 *			
Emergency cerclage	2.595 (1.004-6.706)	0.049 *			

survival curve showed that patients with a history of previous pregnancies had better surgical outcomes than those who had never delivered, suggesting that the cerclage performed a good role in mechanical support for patients with cervical insufficiency due to previous pregnancies. Previous data consistently supported this approach [12-15]. We found that patients who conceived spontaneously presented longer gestational days than patients who underwent IVF. Patients undergoing IVF required more intrauterine surgical intervention, which may increase risk of potential damage to the cervix [16]. Administration of gonadotropins during ovarian stimulation might lead to producing hyper-physiological estradiol levels in the ovaries and prolonged the depletion time of estrogen receptors, so that the high levels of hormones led to a premature opening of the cervix, resulting in poor cervical mucosa in 15%-50 % of patients and an increased risk of cervical insufficiency [17,18]. At the same time, it might be difficult to get pregnant partly due to hyperandrogenism such as polycystic ovarian syndrome. Some studies reported that excessive androgens hurt cervical function, resulting in cervical insufficiency [19]. In conclusion, cervical cerclage did not significantly improve post-operative outcomes among females with IVF, compared to patients who conceived spontaneously. In our study, patients with back soreness and irregular abdominal pain, the extended days of pregnancy were shorter than those patients without such symptoms. It is known that preoperative contractions increase the pressure of the amniotic capsule bulges during surgery and the difficulty of operations. Irregular contractions may gradually turn into regular contractions and result in cervix dilation. Cervical cerclage may stimulate considerably stronger contractions, leading to inevitable miscarriage or even cervical tears. Therefore, gynecologists should exclude contractions, vaginal and uterine cavity infections before they do cervical cerclage. Preoperative pharmacotherapy was unnecessary in patients without obvious intrauterine infections and contractions [20]. The ACOG and others have not made strong recommendations for or against using prophylactic antibiotics and tocolytics for patients with cerclage due to limited evidence [21]. Our study demonstrated extended gestational days in patients with no preoperative pharmacotherapy were longer than in females with prophylactic antibiotics or tocolytics alone or combination of prophylactic antibiotics and tocolytics. These results were not consistent with previous discoveries [21,22]. However, for postoperative tocolytics, combination of ritodrine hydrochloride injection and dydrogesterone tablets was beneficial to the prognosis of cervical cerclage when delivering at more than 28, 30 gestational weeks were set as the primary outcome.

History-indicated cerclage was performed between the 12th and 14th gestational weeks. When cervical length became shorter with gestational age, ultrasound-indicated cerclage was efficiently managed. Emergency cerclage was typically performed in women with advanced cervical dilation, uterine cervix opening, and amniotic sac bulging, regardless of whether the membrane protruded into the vagina or not [17]. In our study, for history-indicated surgeries, the times of gestation and abdominal pain impacted outcomes. Clinicians should be concerned about the patients' previous pregnancies and abdominal pain before history-indicated cerclage to prevent fetal loss again due to cervical insufficiency. For ultrasound-indicated cerclage, IVF was the only impact variable. Patients with natural conception were more likely to deliver after 30, 32 or 34 weeks of gestation than patients with IVF. Among patients with emergent surgeries, high-risk factors, such as irregular menstruation (prolonged menstrual cycles), abnormal postoperative-CRP and postoperative tocolytics were found to be a risk of outcome of cerclage. Patients with irregular menstruation should be managed before they intend to be pregnant. The pretreatment protected the uterine tissue from severe inflammation and deep placental-related oxidative stress. At the same time pretreatment reduced the progesterone resistance and inflammatory reaction of the endometrium. In contrast, the inflammatory cascade did not stimulate uterus and cervix and put them at an increased risk of dysplasia [23,24]. For patients delivering at more than 28 or 30 gestational weeks, postoperative-CRP played an important role in cerclage outcomes. When CRP was more than 10 mg/L, the risk of intrauterine infection increased in the postoperative short term. As proposed by studies, when there was a lack of a positive result of amniotic fluid bacterial cultures, elevated postoperative-CRP were closely related to adverse pregnancy outcome in patients who underwent emergency cervical cerclage [25]. Importantly, we found the combination of tocolytics was the most effective after the emergent cerclage.

In present work, a nomogram was constructed to predict the outcomes of the women with cervical insufficiency when delivering at more than 28, 30, 32 and 34 gestational weeks were set as primary outcomes according to related factors. In present study, the C-index was 0.662 in the development cohort and 0.687 in the validation cohort respectively, implying that the model presented satisfied prediction performance. Besides nomogram predicts outcomes of preterm delivery, an interesting paper presented a generalized

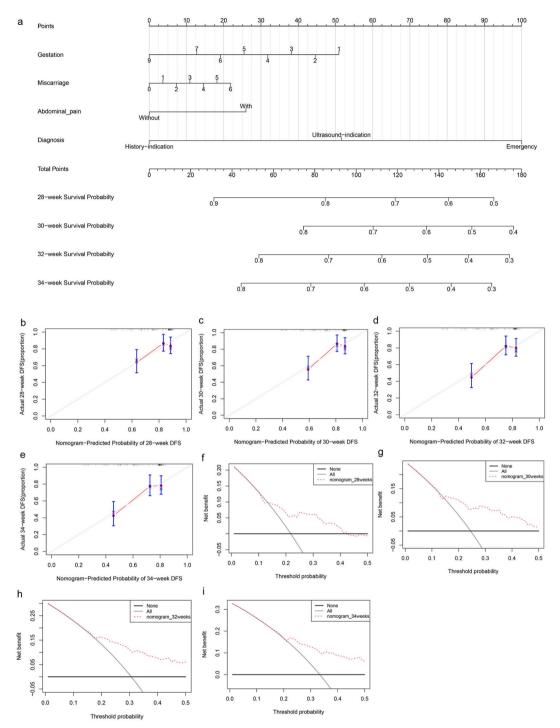


Fig. 3. A prognostic nomogram in the development cohort.

A prognostic nomogram(a) included significant clinical parameters for delivery at more than 28 weeks, 30 weeks, 32 weeks and 34 weeks in patients with cervical cerclage. Calibration curves for delivery at more than 28 weeks (b), 30 weeks (c), 32 weeks (d) and 34 weeks (e) in the development cohort. All calibration curves were close to the ideal 45° dotted line. DCA curves for delivery at more than 28 weeks (f), 30 weeks (g), 32 weeks (h) and 34 weeks (g), 32 weeks (h) and 34 weeks (g), 32 weeks (h) and 34 weeks (i) in the development cohort. Overall, the net benefit of patients was higher than that of other two extreme cases (all and none).

methodology (machine learning models) for building-up an evidence-based risk assessment for preterm birth to be used in clinical practice [26–28].

In our work, a nomogram was the first one to report to predict the prognosis of women with cervical sufficiency according to

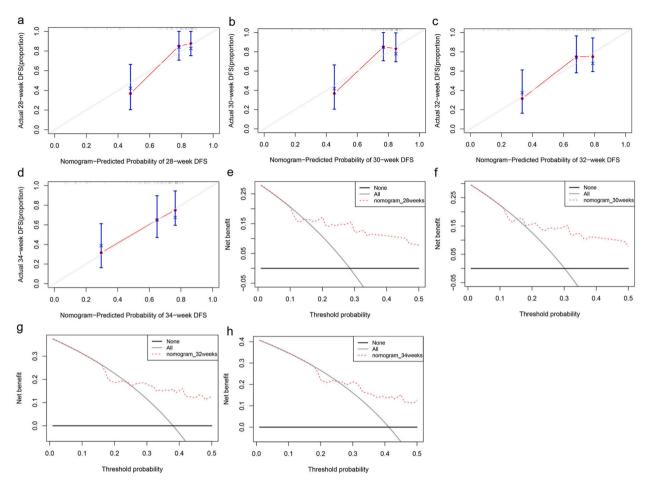


Fig. 4. Calibration curves and DCA curves in the validation cohort.

a-d. Calibration curves for delivery at more than 28 weeks, 30 weeks, 32 weeks and 34 weeks in the validation cohort, respectively. e-h. DCA curves for delivery at more than 28 weeks, 30 weeks, 32 weeks and 34 weeks in the validation cohort, respectively.

different delivering gestational weeks as outcomes of cerclage. The limitation of this study is that this work is retrospective. Prospective research is warranted to be done and supports the impact of relevant factors on the prognosis of cervical cerclage in the future. Secondary, we did not have the data of post-surgery cervical length. We will collect this characteristic in the future when we do relevant research. The third limitation is all patients performed by three different gynecologists. Limited sample size is one of limitations. Future study with a large sample size is needed to further validate this finding.

5. Conclusions

Times of gestations, times of miscarriages, IVF, abdominal pain, cervical insufficiency subtypes, preoperative management, and preoperative and postoperative tocolytics were demonstrated to impact overall extended days of cervical sufficiency after cerclage when delivering at more than 28 gestational weeks was set as the primary outcome. Except for preoperative and postoperative management, the above other five variables impacted the primary outcomes of delivering at more than 30, 32, or 34 gestational weeks. Postoperative tocolytics also impacted the prognosis of patients delivering at more than 30 gestational weeks. For all four outcomes, the times of gestation, miscarriage, abdominal pain and diagnosis were independent predictive factors for patients with cervical cerclage data based on the multivariate Cox regression analysis in the development cohort. The established nomogram may assist clinicians to evaluate outcomes of patients with cervical insufficiency after cervical cerclage, which helps them develop individualized management for the patients.

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Data availability statement

Data will be made available on request.

Details of ethics approval

This retrospective study was approved by Ethical Committee of Suzhou Municipal hospital (KL 901334). The informed consent was waived due to the retrospective nature of the study.

CRediT authorship contribution statement

Jiaqi Xu: Writing – original draft. Tianru Yang: Writing – original draft. Fei Wu: Formal analysis. Ting Chen: Formal analysis. Aifen Wang: Conceptualization, Writing – review & editing. Shunyu Hou: Conceptualization, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e21147.

References

- [1] I.A. McDonald, Cervical cerclage, Clin. Obstet. Gynaecol. 7 (1980) 461-479.
- [2] A.J. Drakeley, S. Quenby, R.G. Farquharson, Mid-trimester loss-appraisal of a screening protocol, Hum. Reprod. 13 (1998) 1975–1980.
- [3] R.M. Ehsanipoor, N.S. Seligman, G. Saccone, et al., Physical examination-indicated cerclage: a systematic review and meta-analysis, Obstet. Gynecol. 126 (2015) 125–135.
- [4] C.S. Cho, M. Gonen, J. Shia, et al., A novel prognostic nomogram is more accurate than conventional staging systems for predicting survival after resection of hepatocellular carcinoma, J. Am. Coll. Surg. 206 (2008) 281–291.
- [5] P.L. Ross, C. Gerigk, M. Gonen, et al., Comparisons of nomograms and urologists' predictions in prostate cancer, Semin. Urol. Oncol. 20 (2002) 82-88.
- [6] M. Lv, C. Chen, L. Qiu, et al., A nomogram to predict extremely preterm birth in women with singleton pregnancies undergoing cervical cerclage, Heliyon 8 (2022), e10731.
- [7] Y. Liao, H. Wen, S. Ouyang, et al., Routine first-trimester ultrasound screening using a standardized anatomical protocol, Am. J. Obstet. Gynecol. 224 (2021) 396, e391-396. e315.
- [8] A.J. Drakeley, D. Roberts, Z. Alfirevic, Cervical stitch (cerclage) for preventing pregnancy loss in women, Cochrane Database Syst. Rev. 1 (2003) (2003) CD003253.
- [9] C.C. Hulshoff, R.P. Bosgraaf, M.E.A. Spaanderman, et al., The efficacy of emergency cervical cerclage in singleton and twin pregnancies: a systematic review with meta-analysis, Am J Obstet Gynecol MFM 5 (2023), 100971.
- [10] C. Chatzakis, A. Efthymiou, A. Sotiriadis, et al., Emergency cerclage in singleton pregnancies with painless cervical dilatation: a meta-analysis, Acta Obstet. Gynecol. Scand. 99 (2020) 1444–1457.
- [11] A. Shennan, B. Jones, The cervix and prematurity: aetiology, prediction and prevention, Semin. Fetal Neonatal Med. 9 (2004) 471-479.
- [12] P.C. Leppert, S.Y. Yu, S. Keller, et al., Decreased elastic fibers and desmosine content in incompetent cervix, Am. J. Obstet. Gynecol. 157 (1987) 1134–1139.
 [13] Final report of the medical research council/royal College of Obstetricians and gynaecologists multicentre randomised trial of cervical cerclage, Br. J. Obstet. Gynaecol. 100 (1993) 516–523.
- [14] J.C. Buckingham, R.A. Buethe Jr., D.N. Danforth, Collagen-muscle ratio in clinically normal and clinically incompetent cervices, Am. J. Obstet. Gynecol. 91 (1965) 232–237.
- [15] T. Rechberger, N. Uldbjerg, H. Oxlund, Connective tissue changes in the cervix during normal pregnancy and pregnancy complicated by cervical incompetence, Obstet. Gynecol. 71 (1988) 563–567.
- [16] L.A. Schieve, B. Cohen, A. Nannini, et al., A population-based study of maternal and perinatal outcomes associated with assisted reproductive technology in Massachusetts, Matern. Child Health J. 11 (2007) 517–525.
- [17] M. Bayrak, A. Gul, G. Goynumer, Rescue cerclage when foetal membranes prolapse into the vagina, J. Obstet. Gynaecol. 37 (2017) 471-475.
- [18] C.S. Sullivan-Pyke, S. Senapati, M.A. Mainigi, et al., In Vitro fertilization and adverse obstetric and perinatal outcomes, Semin. Perinatol. 41 (2017) 345–353.
- [19] Y. Wu, X. Liang, M. Cai, et al., Development and validation of a model for individualized prediction of cervical insufficiency risks in patients undergoing IVF/ ICSI treatment, Reprod. Biol. Endocrinol. 19 (2021) 6.
- [20] V. Berghella, J. Ludmir, G. Simonazzi, et al., Transvaginal cervical cerclage: evidence for perioperative management strategies, Am. J. Obstet. Gynecol. 209 (2013) 181–192.
- [21] G.U. Eleje, A.C. Eke, J.I. Ikechebelu, et al., Cervical stitch (cerclage) in combination with other treatments for preventing spontaneous preterm birth in singleton pregnancies, Cochrane Database Syst. Rev. 9 (2020) CD012871.
- [22] E.S. Miller, W.A. Grobman, L. Fonseca, et al., Indomethacin and antibiotics in examination-indicated cerclage: a randomized controlled trial, Obstet. Gynecol. 123 (2014) 1311–1316.
- [23] J.J. Brosens, M.G. Parker, A. McIndoe, et al., A role for menstruation in preconditioning the uterus for successful pregnancy, Am. J. Obstet. Gynecol. 200 (2009), 615. e611-615. e616.
- [24] I. Brosens, G. Benagiano, Menstrual preconditioning for the prevention of major obstetrical syndromes in polycystic ovary syndrome, Am. J. Obstet. Gynecol. 213 (2015) 488–493.
- [25] E. Aguin, T. Aguin, M. Cordoba, et al., Amniotic fluid inflammation with negative culture and outcome after cervical cerclage, J. Matern. Fetal Neonatal Med. 25 (2012) 1990–1994.

- [26] S. Park, D. Oh, H. Heo, et al., Prediction of preterm birth based on machine learning using bacterial risk score in cervicovaginal fluid, Am. J. Reprod. Immunol. 86 (2021), e13435.
- [27] L.Q. Zhu, H. Chen, L.B. Chen, et al., Effects of emergency cervical cerclage on pregnancy outcome: a retrospective study of 158 cases, Med. Sci. Mon. Int. Med. J. Exp. Clin. Res. 21 (2015) 1395–1401.
 [28] P.A. Della Rosa, C. Miglioli, M. Caglioni, et al., A hierarchical procedure to select intrauterine and extrauterine factors for methodological validation of preterm birth risk estimation, BMC Pregnancy Childbirth 21 (2021) 306.