Development and Validation of Predictive Models for Vaginal Birth After Cesarean Delivery in China

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Source of support: The present study was supported by the National Key R&D Program of China (No. 2016YFC1000405, 2017YFC1001402, 2018YFC1004104, and 2018YFC10029002), the National Natural Science Foundation (No. 81830045, 81671533, 81571518, and 81971415), and the general program of the Guangdong Natural Science Foundation (No. 2020A1515010273)

Background: The rate of delivery by cesarean section is rising in China, where vaginal birth after cesarean (VBAC) is in its early stages. There are no validated screening tools to predict VBAC success in China. The objective of this study was to identify the variables predicting the likelihood of successful VBAC to create a predictive model.

Material/Methods: This multicenter, retrospective study included 1013 women at ≥28 gestational weeks with a vertex singleton gestation and 1 prior low-transverse cesarean from January 2017 to December 2017 in 11 public tertiary hospitals within 7 provinces of China. Two multivariable logistic regression models were developed: (1) at a first-trimester visit and (2) at the pre-labor admission to hospital. The models were evaluated with the area under the receiver operating characteristic curve (AUC) and internally validated using k-fold cross-validation. The pre-labor model was calibrated and a graphic nomogram and clinical impact curve were created.

Results: A total of 87.3% (884/1013) of women had successful VBAC, and 12.7% (129/1013) underwent unplanned cesarean delivery after a failed trial of labor. The AUC of the first-trimester model was 0.661 (95% confidence interval [CI]: 0.61–0.712), which increased to 0.758 (95% CI: 0.715–0.801) in the pre-labor model. The pre-labor model showed good internal validity, with AUC 0.743 (95% CI: 0.694–0.785), and was well calibrated.

Conclusions: VBAC provides women the chance to experience a vaginal delivery. Using a pre-labor model to predict successful VBAC is feasible and may help choose mode of birth and contribute to a reduction in cesarean delivery rate.

MeSH Keywords: Cesarean Section, Repeat • Pregnancy Complications • Trial of Labor • Vaginal Birth after Cesarean

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/927681

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Background

The rate of delivery by cesarean section has increased world-wide. From 1970 to 2016, the cesarean section rate in the United States increased from 5% to 31.9% [1,2]. In Germany, studies reported that the cesarean section rate increased from 25.3% in 2002 to 33% in 2012 [3]. In China, the cesarean rate increased from 28.8% in 2008 to 34.9% in 2014 [4]. These rates are far from the World Health Organization (WHO) recommended cesarean section rate of 10% to 15% of total births [5]. The increase in cesarean rate is due partly to an increased rate of repeat cesarean delivery (RCD). Currently, the high cesarean section rate and the complications involved with cesarean delivery are serious public health problems, and it is crucial to reduce both. The promotion of vaginal birth after cesarean (VBAC) is one way to reduce the overall number of cesarean deliveries worldwide.

In 1982, the American College of Obstetrics and Gynecology recommended VBAC as a safe and acceptable birthing option [6]. In 1985, the National Consensus Conference on Aspects of Cesarean Birth in Canada recommended that women with no indication for cesarean section be offered a trial of labor [7]. Many studies have shown that, with strict indications for VBAC, its success rate could reach 60% to 80% [2,3]. However, from 1996 to 2010, the rate of VBAC decreased from 28% to 8%, which was thought to be largely related to the high legal risks for obstetricians and midwives when offering VBAC [8].

The National Institutes of Health of the United States [6] and the American Association of Obstetricians and Gynecologists [9] encouraged and guaranteed support for pregnant women with cesarean section history to attempt trial of labor after cesarean delivery (TOLAC) when conditions permit [2]. For women with a previous cesarean delivery (CD), the decision to proceed with RCD or TOLAC is based on multiple factors. The assessment of individual risks and the likelihood of VBAC success is, therefore, critical in identifying appropriate candidates for TOLAC [10]. There are several published models available to predict the probability of a successful VBAC in women who undergo TOLAC [11–13].

In 2016, the enactment of the 2-child policy in China was expected to increase the rate of cesarean section because of RCDs [14], and women with cesarean section history were facing the difficult decision of choosing delivery modes. China was at the early stage of dealing with TOLAC. There were no large multicenter studies of VBAC screening tools to provide a consistent and validated ability to predict the success of VBAC in China. Although some VBAC nomograms and prediction models have been developed in other countries, their accuracy decreased when applied to different datasets [15–17], which may be due in part to geographic diversity or to the models being calibrated to lower predicted probabilities of success [11].

The aim of this study was to analyze and identify variables affecting VBAC success and to develop 2 predictive tools for VBAC, the first for use during the first trimester and the second at the pre-labor hospital admission, using multicenter, retrospective clinical data from hospitals in China. Our goal is to help obstetricians make accurate clinical treatment decisions and decrease the high rate of RCD in China.

Material and Methods

This was a retrospective, multicenter, electronic medical records-based study conducted at 11 public tertiary hospitals, including 7 provinces, municipalities, and autonomous regions in China (Guangdong, Beijing, Xinjiang, Shanxi, Henan, Hubei, and Chongqing). The cohort comprised 14 734 pregnant women with uterine scarring from CD who delivered again between January 2017 and December 2017. Exclusion criteria were major fetal congenital abnormalities, antepartum fetal death, multiple pregnancies, uterine scarring caused by myomectomy, and missing essential medical record data including delivery week, delivery mode, and amount of blood loss. From the 11 958 women enrolled, 10 945 chose RCD, and 1013 women whose gestational week was ≥28 with a vertex singleton gestation, 1 prior low-transverse cesarean [2], and without other contradictions for vaginal birth underwent TOLAC. Figure 1 shows a flow diagram of the patient enrollment process.

We collected multiple obstetric data through chart review at each hospital, including general maternal features, current pregnancy information, past medical history, and fetal features. Some maternal and neonatal outcomes were also gathered.

Postpartum hemorrhage is defined as an estimated blood loss of more than 500 mL for vaginal deliveries and 1000 mL for cesarean deliveries. In this study, placenta accrete spectrum consisted of placenta accreta, placenta increta, and placenta percreta diagnosed by a clinician before delivery. Preeclampsia was diagnosed according to the guidelines of the International Society for the Study of Hypertension in Pregnancy [18]. The diagnostic criteria of neonatal asphyxia in China are (i) an Apgar score at 5 min ≤7, and effective breathing has not been established; (ii) pH <7.15 in umbilical artery blood sample; (iii) other causes of lower Apgar score have been excluded; (iv) prenatal risk factors that may lead to asphyxia have been considered. Items (i) to (iii) are necessary conditions and (iv) is a reference indicator [17].

Oxytocin induction was performed as follows: 2.5 U of oxytocin was added to 500 mL of 0.9% normal saline. An amount of 1 to 2 mU/min of oxytocin was administered IV, and the adjustment interval was 15 to 30 min, according to the intensity of uterine contractions. Oxytocin was increased by 1 to 2
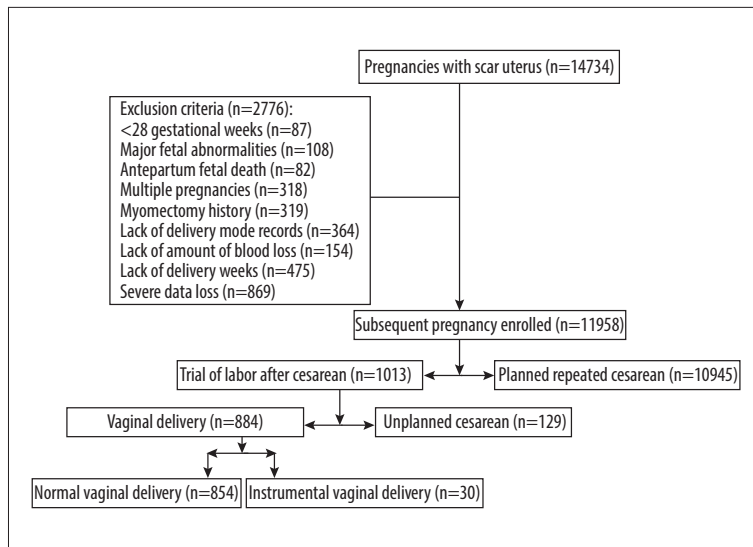
Figure 1. Flow diagram of the patients' enrollment process.

Table 1. Maternal and neonatal outcomes.

Variables	Cesarean (n=129)		Vaginal birth (n=884)		P
24-h blood loss (mL)	395	(300, 498)	309.33	(265, 373.02)	0
PPH	4	(3.1%)	68	(7.7%)	0.065
Blood transfusion	5	(3.9%)	31	(3.5%)	0.83
Rupture of uterus	3	(2.3%)	1	(0.1%)	0.007
Injury of bladder	0		14	(1.6%)	0.237
Antibiotics after birth	126	(97.7%)	256	(29%)	0
Oxytocin after birth	124	(96.1%)	801	(90.6)	0.038
Prostaglandin after birth	51	(39.5%)	379	(42.9%)	0.474
Ergonovine after birth	6	(4.7%)	22	(2.5%)	0.155
Maternal mortality	0		0		
1-min Apgar score	9	(9, 10)	9	(9, 10)	0.16
Asphyxia	3	(2.3%)	28	(3.2%)	0.105
Neonatal mortality	1	(0.8%)	0		1

PPH – postpartum hemorrhage.

mU/min each time, as appropriate. The maximum dose of oxytocin usually did not exceed 20 mU/min [19].

We sought to build predictive models of VBAC success at 2 timepoints. The first timepoint was in the first trimester according to the features noted at the first-trimester visit. The second timepoint was at the pre-labor and delivery hospital visit, when all features before delivery were considered. At each timepoint, 2 models were established: (1) was a full model using all variables and (2) a simple model using independent risk factors (*P*<0.05) whose adjusted odds ratios were significant.

This study was approved by the Medical Ethics Committee of each hospital, with Medical Research No. 2016(0406) approved on April 6, 2016. All of the methods were performed in accordance with the relevant ethical guidelines and regulations, and the statements of informed consent for participation were signed by participants or their legally authorized representatives.

Statistics analysis

Statistical analysis was performed using R software (version 3.6.1) and IBM SPSS v25.0. Missing values were imputed using the Random Forests algorithm. Quantitative data were

Table 2. Characteristics of the pregnant women.

Variables	Cesarean (n=129)		Vaginal birth (n=884)		P
Age (years)*	32	(30, 35)	32	(28, 35)	0.38
Height (cm)*	160	(155, 162)	159.35	(156, 162)	0.891
Pre-weight (kg)*	55	(49, 61)	54	(48.5, 60)	0.118
Pre-BMI (kg/m^2)*					0.019
<18	9	(7%)	84	(9.5%)	
18–24	85	(65.9%)	607	(68.7%)	
24–30	29	(13.2%)	183	(20.7%)	
≥30	6	(4.7%)	10	(1.1%)	
Nationality*					1
Han population	128	(99.2%)	874	(98.9%)	
Other	1	(0.8%)	10	(1.1%)	
Gravity*	3	(2, 4)	3	(2, 3)	0.26
Parity*	1	(1, 1)	1	(1, 1)	0.024
Abortion*	1	(0, 1)	1	(0, 1)	0.14
Drug abortion*	0	(0, 0)	0	(0, 0)	0.12
Artificial abortion*	0	(0, 1)	0	(0, 1)	0.07
Spontaneous abortion*	0	(0, 0)	0	(0, 0)	0.016
Vaginal deliver history*	8	(6.2%)	117	(13.2%)	0.023
Preterm history*	15	(11.6%)	202	(22.9%)	0.004
PROM history*	4	(3.1%)	37	(4.2%)	0.81
PP history*	3	(2.3%)	12	(1.4%)	0.42
Placenta abruption history*	1	(0.8%)	2	(0.2%)	0.34
Emergency cesarean history*	56	(43.4%)	386	(43.7%)	0.96
Weight gain (kg)	13	(10, 16)	12	(10, 15)	0.17
Weight (kg)	69	(63, 75)	66.7	(61, 74)	0.03
BMI (kg/m^2)					0.004
<18	2	(1.6%)	1	(0.1%)	
18–24	21	(16.3%)	174	(19.7%)	
24–30	76	(58.9%)	574	(64.9%)	
≥30	30	(23.3%)	135	(15.3%)	
ART	2	(1.6%)	18	(2%)	1
Interval months					0.07
Gestational days	276	(271, 280.5)	273	(266, 279)	0
Source					0.048
Hospital	108	(83.7%)	792	(89.6%)	

Table 2 continued. Characteristics of the pregnant women.

Variables	Cesarean (n=129)		Vaginal birth (n=884)		P
Referral	21	(16.3%)	92	(10.4%)	
PROM	43	(33.3%)	187	(21.2%)	0.002
Antepartum hemorrhage	3	(2.3%)	71	(8%)	0.017
Tenderness of lower uterine segment	12	(9.3%)	168	(19%)	0.007
PP	0		3	(0.3%)	1
PAS	3	(2.3%)	3	(0.3%)	0.03
Polyhydramnios	1	(0.8%)	9	(1%)	1
Oligohydramnios	6	(4.7%)	18	(2%)	0.068
Macrosomia	5	(3.9%)	16	(1.8%)	0.12
FGR	2	(1.6%)	16	(1.8%)	1
Preeclampsia	5	(3.9%)	14	(1.6%)	0.073
GDM	22	(17.1%)	136	(15.4%)	0.625
ICP	2	(1.6%)	4	(0.5%)	0.17
Thyroid disease	0		9	(1%)	0.613
Balloon induction	12	(9.3%)	25	(2.8%)	0
Oxytocin induction	19	(14.7%)	29	(3.3%)	0
Artificial rupture of membrane induction	5	(3.9%)	37	(4.2%)	0.869
BPD (cm)	92	(89, 94)	91	(88, 93)	0.06
FL (cm)	71	(69, 72)	70	(68, 71)	<0.05
HC (cm)	323	(316.5, 330)	322	(314, 328)	0.067
AC (cm)	335	(328, 343)	328	(318.25, 339)	<0.05
Neonatal weight	3320	(3012.5, 3500)	3100	(2800, 3350)	<0.05

* Variables were included in first trimester full model. AC – abdominal circumference; ART – artificial assisted reproductive technology; BMI – body mass index; BPD – biparietal diameter; FGR – fetal growth restriction; FL – femur length; GDM – gestational diabetes mellitus; HC – head circumference; ICP – intrahepatic cholestasis of pregnancy; PA – placenta accrete spectrum; Pre-weight – weight before pregnancy; Pre-BMI – body mass index before pregnancy; PP – placenta previa; PROM – premature rupture of membrane.

examined for normal distribution, and normally distributed variables were represented as mean±SD, and the *t* test was used. Non-parametric continuous variables were represented as median and interquartile range, and the Mann-Whitney U test was applied. Categorical variables were reported as frequencies (percentages), and the differences between the groups were compared using the χ^2 test or Fisher exact test, in cases of small numbers, as appropriate. Multivariable logistic backward regression models were built as simple models to assess women's personalized likelihood for VBAC success. Validation of the robustness of full and simple models were done using 5-fold cross-validation. Cross-validation was a process involving splitting the dataset into randomized training and test sets.

The model was trained on a training set and tested on the test set, and the area under the receiver operating characteristic curve (AUC) was compared across random splits. The AUC was used to assess the discrimination of the predictive models. The calibration of the models was evaluated by plotting the calibration curve. To provide the clinician with a quantitative tool predicting the individual likelihood for successful VBAC, a nomogram was developed on the basis of the simple model. Clinical impact curves were proposed to assess the clinical usefulness of the prediction nomogram. The reported statistical significance levels were all 2-sided, with P<0.05 considered statistically significant.

Table 3. The most significant variables included in the 2 models.

Variables	Cesarean (n=129)		Vaginal birth (n=884)		First trimester model aOR (95% CI)		P	Pre-labor model aOR (95% CI)		P
Gravity	3	(2,4)	3	(2,3)	0.81	(0.674–0.973)	*	0.77	(0.634–0.934)	**
Parity	1	(1,1)	1	(1,1)	2.465	(1.21–5.025)	*	3.235	(1.496–6.997)	**
Spontaneous abortion	0	(0,0)	0	(0,0)	3.291	(1.207–8.976)	*	3.917	(1.391–11.026)	**
Pre-weight	55	(49,61)	54	(48.5,60)	0.975	(0.955–0.995)	*			
Preterm history	15	(11.6%)	202	(22.9%)	2.345	(1.32–4.166)	**			
Source (Hospital)	108	(83.7%)	792	(89.6%)				0.398	(0.226–0.702)	**
PROM	43	(33.3%)	187	(21.2%)				0.562	(0.36–0.876)	*
Antepartum hemorrhage	3	(2.3%)	71	(8%)				4.046	(1.205–13.584)	*
PAS	3	(2.3%)	3	(0.3%)				0.081	(0.012–0.541)	*
Neonatal weight	3320 (3012.5, 3500)		3100 (2800, 3350)					0.999	(0.998–0.999)	***
Oxytocin induction	19	(14.7%)	29	(3.3%)				0.273	(0.139–0.537)	***
Preeclampsia	5	(3.9%)	14	(1.6%)				0.271	(0.082–0.898)	*

aOR – adjusted odds ratios; CI – confidence interval; PAS – placenta accrete spectrum; Pre-weight – weight before pregnancy; PROM – premature rupture of membrane. *** $P<0.001$; ** $P<0.01$; * $P<0.05$.

Results

The study included 11 958 pregnant women with uterine scarring from cesarean section who delivered again. Among these women, 91.5% (10 945/11 958) opted for RCDs and 8.5% (1013/11 958) opted for TOLAC. From the 1013 women attempting a TOLAC, 87.3% (884/1013) achieved a vaginal delivery, which included 854 cases of normal vaginal delivery and 30 cases of instrumental vaginal delivery, and 12.7% (129/1013) underwent an unplanned cesarean delivery (Figure 1). Table 1 shows the maternal and neonatal outcomes in the unplanned cesarean and successful vaginal delivery groups. The median blood loss in the unplanned cesarean delivery group was higher than that in the successful vaginal delivery group (395 mL vs. 309.33 mL, respectively, $P<0.05$). The rates of uterine rupture and administration of antibiotics and oxytocin were also higher in the unplanned cesarean delivery group than in the successful vaginal delivery group (2.3% vs. 0.1%, 97.7% vs. 29%, and 96.1% vs. 90.6%, respectively, $P<0.05$). Postpartum hemorrhage, blood transfusion, bladder injury, and outcomes of the newborn were similar between the 2 groups.

Table 2 shows the characteristics of the pregnant women. There were 17 variables collected at the first-trimester visit and an additional 28 variables collected at the hospital pre-labor and delivery visit. Table 3 summarizes the most significant variables included in the 2 simple models at these 2 timepoints.

Figure 2 shows the receiver operating characteristic curves of the 4 models. At each timepoint (first-trimester and pre-labor visits), 2 models were established: (1) a full model using all variables and (2) a simple model using independent risk factors. At the first-trimester visit, the AUC of the full model was 0.672 (95% confidence interval [CI]: 0.622–0.723) and the AUC of the simple model was 0.661 (95% CI: 0.61–0.712). The full and simple models achieved 5-fold cross-validation mean AUCs of 0.607 (95% CI: 0.546–0.659) and 0.652 (95% CI: 0.599–0.703), respectively. At the pre-labor visit, the AUCs of the full and simple models were 0.8 (95% CI: 0.763–0.838) and 0.758 (95% CI: 0.715–0.801), respectively; and the full and simple models achieved 5-fold cross-validation mean AUCs of 0.703 (95% CI: 0.653–0.752) and 0.743 (95% CI: 0.694–0.785), respectively. The calibration curve of the pre-labor model for the probability of vaginal birth demonstrated agreement between prediction and observation (Figure 3).

In Figure 4, the pre-labor model is presented as a graphical calculator (nomogram). The clinical impact curve for the pre-labor model is presented in Figure 5. Of 1000 patients, the red solid line shows the total number who were deemed high risk for each risk threshold. The blue dashed line shows how many of those were true positives (cases).
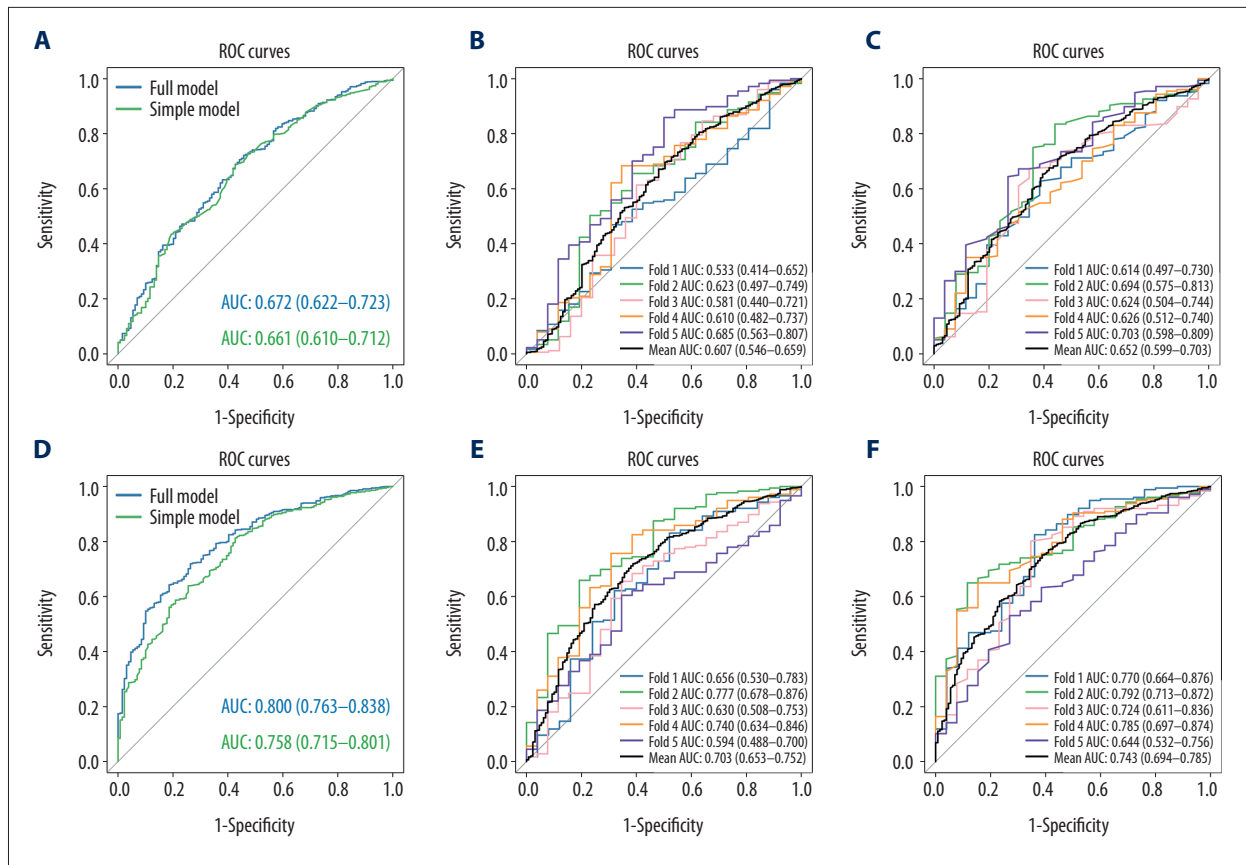
Figure 2. The receiver operating characteristic (ROC) curves of the 4 models. The first trimester period: (**A–C**); 5-fold cross validation of full model; 5-fold cross validation of first trimester model. The pre-labor period: (**D–F**); 5-fold cross validation of full model; 5-fold cross validation of pre-labor model.
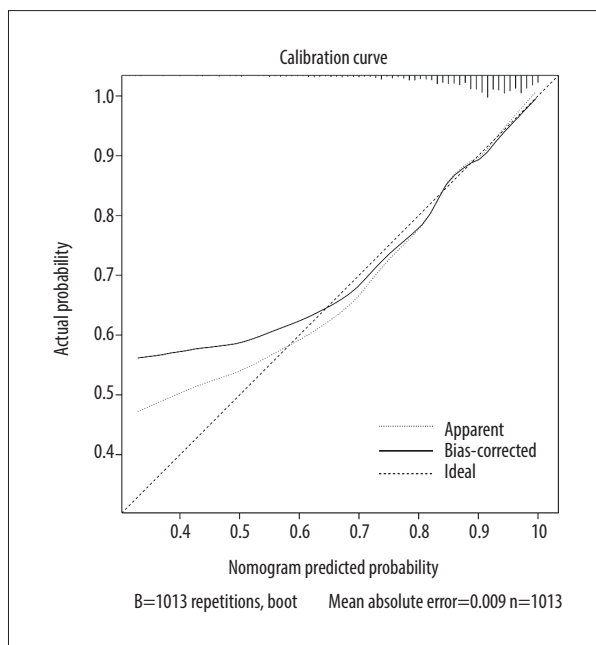

Figure 3. The calibration curve of the pre-labor model.

Discussion

In this multicenter retrospective study, the proportion of successful deliveries by TOLAC was 87.3% (884/1013). The prediction of the simple model with 5 variables at the first-trimester visit was limited, with an AUC of 0.661 (95% CI: 0.61–0.712). The pre-labor model increased the prediction accuracy, with an AUC of 0.758 (95% CI: 0.715–0.801) and a validation curve that adhered more closely to the ideal validation line from the addition of variables before labor. Logistic multivariate analysis indicated that gravity, parity, number of spontaneous abortions, source of patient referral, premature rupture of membrane, antepartum hemorrhage, placenta accrete spectrum, preeclampsia, neonatal weight, and oxytocin induction influenced the success of VBAC. The total incidence rate of uterine rupture was 0.39% (4/1013). There were no maternal deaths in the 2 groups and there was 1 neonatal death in the cesarean group.

Although China is in the early stages of dealing with TOLAC, the success rate of VBAC in China found in the present study should help increase the frequency with which TOLAC is offered. Our results are also comparable with other reports. Fonseca et al.
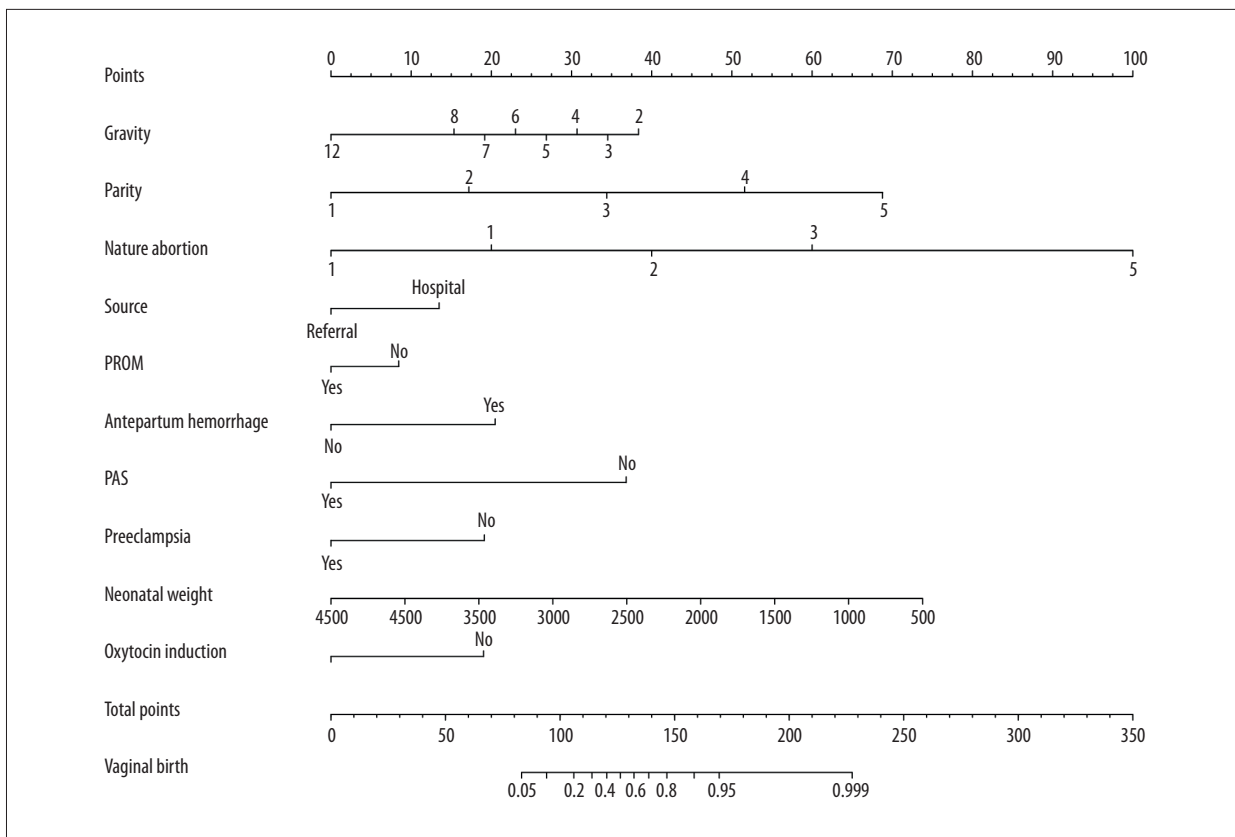
Figure 4. The nomogram of the pre-labor model. The nomogram converts each risk predictor into a 0 to 100 scale that is proportional to the derived adjusted log odds. These points are added across predictors to derive the ''total points'', which are converted to predict the probabilities of vaginal birth.
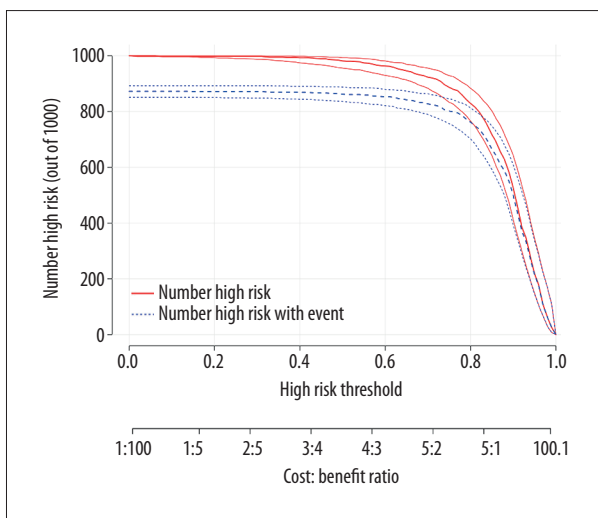

Figure 5. The clinical impact curve for the pre-labor model. Of 1000 patients, the red solid line shows the total number who would be deemed high risk for each risk threshold. The blue dashed line shows how many of those would be true positives (cases).

in Columbia reported that, of 203 women who had a TOLAC, 174 (85.7%) had a successful delivery [6]. Haumonte et al. reported a 65% (240/367) VBAC success rate in France [20]. Xu et al. reported that 85.2% (456/535) of women had successful VBAC in China [21]. Lipschuetz et al. reported the success rate of VBAC was 77.4% (5787/7473) in a study in Israel [22]. As these studies show, VBAC is feasible for most pregnant women, even in China where there is a high rate of CD. Women with a previous CD should be recommended TOLAC to reduce the rate and complications of RCD.

At present, many researchers have collected clinical data to construct predictive models that can provide physicians with a useful tool to accurately predict the success of VBAC for a given woman. Grobman et al. developed a nomogram with an AUC of 0.754 (95% CI: 0.742–0.766) from the first prenatal check-up [21], which increased to 0.774 (95% CI: 0.764–0.784) when the features at the delivery unit were added. Lipschuetz et al. used machine learning to build a tool that had an AUC of 0.745 (95% CI: 0.728–0.762) in a first-trimester model, which increased to an AUC of 0.793 (95% CI: 0.778–0.808) in the pre-labor model [22]. Some researchers reported that the accuracy of the predictive models decreased when they were applied to

other datasets [15,23,24], which could have been due in part to geographic diversity or that the model had been calibrated to lower predicted probabilities of success [11]. Therefore, in the present study, it was necessary to develop predictive models using clinical data collected from pregnant women in China.

To the best of our knowledge, this was the first multicenter retrospective study using screening tools to predict the success of VBAC in China. Our results agreed with previously published models in which adding variables that were available before delivery increased the predictive accuracy of VBAC. It is worth noting that some of the predictors of VBAC in the present study had already been described in the literature. The presence of preeclampsia [20], induction of labor [20], advanced gestational age [12,25], and increased fetal weight [25] decreased the chance of VBAC. Parity [12] and no maternal complications [26] increased the success of VBAC. Contrary to the results of Denham et al. [26], we found that previous antepartum hemorrhage was associated with more VBAC occurrence. In our study, we found that some new variables, including less gravity and more spontaneous abortions, were related to the success of VBAC, while referral patients complicated with premature rupture of membranes or placenta accrete spectrum were not conducive to vaginal delivery. These results should be investigated in more extensive, prospective trials. Whether there are other factors influencing the success of VBAC also requires further study.

Although the Bishop score was commonly used as a discriminatory tool to predict the success of VBAC in some published models [13,22], this implied that the opportunity of VBAC may have been offered to women with a high Bishop score. Many women with unfavorable cervices chose RCD directly. For those women with unfavorable cervices, induction of labor may improve the cervical condition. The American College of Obstetrics and Gynecology Practice Bulletin (Number 205) recommends that the induction of labor remain an option for women undergoing TOLAC [2]. In this study, we used oxytocin induction and a mechanical method of cervical ripening for women with unfavorable cervices intending to TOLAC. Our pre-labor model considered numerous variables in addition to cervical status, given the large number of women with unfavorable cervices having VBAC after induction of labor.

Our study had several strengths. The study was based on the multicenter database from 11 public tertiary hospitals, including 7 provinces, municipalities, and autonomous regions in China in 2017, which effectively avoided the selection bias of single-center and small-sample studies. Therefore, to some extent, the data could be generalized to more heterogeneous populations. The model's ease of use by obstetricians is enhanced by its representation as a graphical nomogram, and its validity was tested with results showing moderate discrimination and good calibration. The clinical impact curves visually show the estimated numbers of pregnant women who were deemed vaginal birth and true positives with different threshold probabilities.

However, our study had some limitations. First, this is a retrospective study. Second, data from different centers were not always ideal and complete. Therefore, we excluded cases with important missing data. Other missing values were imputed using the Random Forests algorithm. More complete data may provide more accurate outcomes.

Conclusions

In conclusion, VBAC provides a chance for women to experience a vaginal delivery after CD. Additionally, using a pre-labor model to predict successful VBAC by comprehensively assessing the previous and current pregnancy and fetal features is feasible. The prediction nomogram based on gravity, parity, number of spontaneous abortions, source of patient referral, premature rupture of membranes, antepartum hemorrhage, placenta accrete spectrum, preeclampsia, neonatal weight, and oxytocin induction could help obstetricians and pregnant women in the decision-making process about the mode of birth after CD and can reduce of the rate of RCD.

Conflict of interest

None.

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