

# Gestational Age as a Predictor of Pregnancy Outcome After Repeat Cerclage

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## Research article

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# Abstract

**Background:** The role of repeat cerclage (RC) as a remedy for patients with prolapsed membranes after prior cerclage remains controversial. We aimed to investigate whether gestational age (GA) could be used as a valuable factor for predicting pregnancy outcome following RC in women with prolapsed membranes after prior cerclage.

**Methods:** We retrospectively investigated the clinical data of 29 patients who underwent RC resulting from prolapsed membrane after prior cerclage. Receiving operating characteristic (ROC) curve analysis and univariate analysis were performed to determine predictive factors. Patients were divided into two groups according to GA at RC,  $GA < 24.2$  weeks and  $GA \geq 24.2$  weeks. Pregnancy outcomes were compared between groups.

**Results:** The mean GA at prior cerclage was 16.5 weeks; mean GA at RC was 23.6 weeks. The mean GA at delivery was 27.8 weeks with a 69.0% neonatal survival rate. ROC curve and univariate analysis demonstrated that GA at RC was significantly predictive for neonatal survival (area under the curve: 0.928;  $p=0.000$ ). Using a GA cut-off of  $\geq 24.2$  weeks at RC, the sensitivity and specificity of predicting neonatal survival were 93.75% and 61.54%, respectively. There was a significant difference in neonatal survival rate between the  $GA < 24.2$  weeks group and  $GA \geq 24.2$  weeks group (38.5% vs. 93.8%,  $p=0.003$ ). Kaplan–Meier survival curves showed a lower incidence of neonatal death in the  $GA \geq 24.2$  weeks group (6.3%) compared with  $GA < 24.2$  weeks group (61.5%,  $p=0.023$ ).

**Conclusions:** GA could be a valuable factor for predicting pregnancy outcome post-RC in women with prolapsed membrane after prior cerclage.

## Background

Cervical cerclage is a surgical intervention involving the placement of a stitch around the uterine cervix with the aim to prevent cervical shortening and opening, thereby reducing the risk of preterm birth. Women who have a cerclage suture transvaginally for cervical insufficiency remain at high risk of preterm delivery[1, 2]. Amniotic membrane prolapses following prior cerclage is usually considered as cerclage failure; however, repeat cerclage(RC), as an emergency cerclage, also known as rescue cerclage, is a possible intervention to increase the neonatal survival rate[3]. Cervical cerclage has been reported to increase the risk of preterm premature rupture of membranes or chorioamnionitis in some cases, especially prolapse of the amniotic membrane, which can result in miscarriage, infection, and premature birth[4–8]. Therefore, the effectiveness of RC remains controversial and it is necessary to assess whether it is appropriate to perform RC when the amniotic membrane has prolapsed following prior cerclage.

There is a lack of valid predictors for pregnancy outcome following RC. The effectiveness of an initial emergency cerclage is affected by various factors[5–7], among which, gestational age (GA) at cerclage plays an important role in the pregnancy outcome[6]. Based on this, we hypothesized that pregnancy outcome after RC may also be linked to GA at RC. We therefore assessed the association between GA at

RC and pregnancy outcome, in order to identify the most appropriate GA for RC in women with prolapsed membranes.

## Methods

### Patients and study design

Patients who underwent RC at Shengjing Hospital of China Medical University between January 2015 and December 2019 were evaluated in this study. All the patients provided written informed consent. The study inclusion criteria were as follows: singleton pregnancy with GA between 16 and 28 weeks; cervical dilation > 1cm with prolapsed but intact membranes; no uterine contraction; no vaginal bleeding; and no foetal abnormalities. We excluded women with chronic maternal complications such as gestational diabetes, preeclampsia, infectious or autoimmune diseases, chorioamnionitis, and incomplete clinical information.

The RC(McDonald-type) was performed under combined spinal epidural anaesthesia using 5mm Mersilene tape or double No.10 silk suture. The previous cerclage knot was untied, and the prolapsed membrane pushed back into the intrauterine cavity with a saline wet gauze. All cerclage procedures were performed by experienced senior doctors. After the procedure, patients were placed on bed rest and given antibiotics and magnesium sulphate for 48 hours. Data were reviewed from medical records.

### Statistical analysis

The data were compared between the two groups using the analysis of variance or Kruskal–Wallis test. The difference in percentages between the groups were compared using the  $\chi^2$  test or *Fisher's* exact probability test. Non-conditional univariate logistic regression was applied in the univariate analysis. The receiver-operating characteristic (ROC) curve was analysed to assess the discriminative ability of GA at RC. Survival curves were compared using Kaplan–Meier analysis and the log-rank test. A *p*-value < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS 23.0 statistical software.

## Results

This study cohort consisted of 29 patients. RC was performed successfully in all patients. There were no cases of membrane rupture or immediate pregnancy loss during the procedure. Table 1 shows the patient clinical information and pregnancy outcomes after RC. The mean GA at prior cerclage was 16.5 weeks;55.2% (16/29) of patients underwent history indicated cerclage (history of two or more late miscarriage or early preterm births),27.6% (8/29) of patients underwent ultrasound indicated cerclage (short cervix observed with a transvaginal ultrasound scan in women with prior preterm birth), and 17.2% (5/29) of patients underwent physical examination indicated cerclage (cervical dilatation with visible bulging membranes). The mean GA at RC was 23.6 weeks. The average width of the cervical funnel before RC was 2.4cm. The mean GA at delivery was 27.8 weeks with a 69.0% (20/29) neonatal survival

rate. Among the 29 pregnancies, nine ended with immediate neonatal death due to extreme prematurity, 8 patients delivered vaginally after removing the cerclage knot, and the remaining 12 patients delivered by caesarean section due to scarred uterus, foetal malposition, and placenta previa.

Table 1  
Patient clinical information and pregnancy outcomes (n = 29)

Variables	Values
Age (years)	
Type of prior cerclage	33.6 ± 3.7
History indicated (%)	16/29 (55.2%)
Ultrasound indicated (%)	8/29 (27.6%)
Physical examination indicated (%)	5/29 (17.2%)
GA at prior cerclage (weeks)	16.5 ± 3.0
GA at repeat cerclage (weeks)	23.6 ± 2.9
GA at delivery (weeks)	27.8 ± 4.5
Width of cervical funnel before RC (cm)	2.4 ± 0.9
Latency between repeat cerclage and delivery (days)	29.4 ± 25.8
Birthweight (g)	1151.3 ± 766.1
Neonatal survival (%)	20/29 (69.0%)
Values are n, mean ± standard deviation or n/N (%)	

In order to determine the predictors of neonatal survival before RC, we compared clinical factors, including maternal age, type of prior cerclage, type of suture at prior cerclage, GA at prior cerclage, GA at RC, width of the cervical funnel before RC, and neutrophil/lymphocyte ratio (NLR). Among all factors, GA at RC was the only powerful predictor of neonatal survival in the univariate analysis (Odds ratio (OR): 0.393; 95%confidence interval (CI): 0.196–0.787; p = 0.008) (Table 2).

Table 2  
Comparison of clinical factors before RC between neonatal survival and death groups

	Survival (n = 20)	Death (n = 9)	<i>Univariate analysis</i>	
			<i>OR (95%CI)</i>	<i>P</i>
Age (years)	33.4 ± 3.6	34.1 ± 4.2	1.059 (0.851,1.317)	0.608
Type of prior cerclage	-	-	-	-
History indicated (%)	11(55)	5(55.6)	1.023(0.210,4.978)	0.978
Ultrasound indicated (%)	6(30)	2(22.2)	0.816(0.325,2.048)	0.666
Physical examination indicated (%)	3(15)	2(22.2)	1.174(0.604,2.283)	0.636
Type of suture at prior cerclage	-	-	-	-
5-mm mersilene tape	6(30)	1(11.1)	0.540(0.172,1.696)	0.291
No.10 silk suture	14(70)	8(88.9)	3.429(0.348,33.799)	0.291
GA at prior cerclage (weeks)	16.7 ± 3.3	16.2 ± 2.6	0.942(0.717,1.237)	0.667
GA at RC (weeks)	25.0 ± 1.8	20.5 ± 2.6	0.393(0.196,0.787)	0.008
Width of cervical funnel before RC (cm)	2.4 ± 0.9	2.2 ± 1.0	0.778(0.313,1.935)	0.589
NLR before RC	5.3 ± 2.8	7.1 ± 3.4	1.207(0.926,1.574)	0.165

ROC curve analysis demonstrated that GA at RC may be an index for predicting neonatal survival. The area under the ROC curve (AUC) for the prediction of neonatal survival by GA at RC was 0.928 ( $p = 0.000$ ) (Fig. 1). Using a GA cut-off of  $\geq 24.2$  weeks at RC, the sensitivity and specificity for predicting neonatal survival were 93.75% and 61.54% respectively. According to the cut-off, patients were divided into the GA  $\geq 24.2$  weeks at RC group ( $n = 16$ ) and GA  $< 24.2$  weeks at RC group ( $n = 13$ ). Table 3 demonstrates the comparison of clinical factors and pregnancy outcomes between the two groups. There was no significant difference in GA at prior cerclage between the two groups (15.9 vs. 17.1,  $p = 0.299$ ), while the GA at RC differed significantly between two groups (21.0 vs. 25.7,  $p = 0.000$ ). There was no significant difference in GA at delivery, although the GA at delivery was increased in the GA  $\geq 24.2$  weeks group (26.1 vs. 29.2,  $p = 0.067$ ). The GA  $< 24.2$  weeks group showed a worse pregnancy outcome compared to the GA  $\geq 24.2$  weeks group; there was a significant difference in the neonatal survival rate between two groups (38.5% vs. 93.8%,  $p = 0.003$ ).

Table 3  
Comparison of clinical factors and pregnancy outcome according to GA at RC

Variables	GA < 24.2 weeks	GA ≥ 24.2 weeks	<i>P value</i>
Age (years)	34.7 ± 4.2	32.7 ± 3.2	0.155
Type of prior cerclage	6.5 ± 3.0	5.4 ± 3.1	0.351
History indicated (%)	10/13 (84.6%)	6/16 (37.5%)	0.061
Ultrasound indicated (%)	2/13 (15.4%)	6/16 (37.5%)	0.238
Physical examination indicated (%)	1/13 (7.7%)	4/16 (30.8%)	0.343
NLR			
GA at prior cerclage (weeks)	15.9 ± 2.5	17.1 ± 3.4	0.299
GA at repeat cerclage (weeks)	21.0 ± 2.2	25.7 ± 1.3	0.000
GA at delivery (weeks)	26.1 ± 5.3	29.2 ± 3.3	0.067
Width of cervical funnel before RC (cm)	2.4 ± 1.0	2.4 ± 0.8	0.997
Latency between repeat cerclage and delivery (days)	35.3 ± 31.0	24.6 ± 20.5	0.273
Birthweight (g)	921.7 ± 939.7	1337.9 ± 553.3	0.149
Neonatal survival (%)	5/13 (38.5%)	15/16 (93.8%)	0.003

There were nine neonatal deaths in the study. Kaplan-Meier survival curves showed a lower incidence of neonatal death in the GA ≥ 24.2 weeks group (6.3%) compared with the GA < 24.2 weeks group (61.5%) ( $p = 0.023$ , Log Rank test) (Fig. 2). This shows that the rate of neonatal death was significantly worse in patients with GA < 24.2 weeks at RC.

## Discussion

The main finding of this study was that GA at RC is a valuable predictor of pregnancy outcome following RC. ROC curve and univariate analysis indicated that GA at RC was an index for predicting neonatal survival. We found that patients with a lower GA at RC showed a worse pregnancy outcome. GA < 24.2 weeks at RC was associated with earlier delivery and a poorer neonatal survival rate.

Previous studies have shown that pre- and post-cerclage cervical length, positive vaginal culture at cerclage, and amniotic fluid levels of neutrophil elastase and IL-6 are predictors of pregnancy duration[4, 6, 9–13]. Cervical dilatation, volumetric assessment of cervical funnelling, and a history of previous uterine instrumentation are independent predictors of cerclage failure[14–17]. Most studies on predictors of pregnancy outcome have focused on initial cerclage, with few studies reporting the predictors of

pregnancy outcome after RC. A previous report claimed that women with a cervical length  $\geq 2.5\text{cm}$  delivered later than women with a cervical length  $< 2.5\text{cm}$  after the prior cerclage; RC did not delay delivery for women with a cervical length  $< 2.5\text{cm}$ [18]. While in our study, the amniotic membranes of all patients had prolapsed, thus, cervical lengths could not be assessed. Another report demonstrated that the NLR could be used as a reliable factor for predicting pregnancy outcome following RC[19]. However, this study did not come to the same conclusion, possibly due to the different population or limited sample size.

Our current study showed that gestational age  $< 24.2$  weeks at RC indicated a poor pregnancy outcome. This finding supports the use of GA at RC as a useful tool for predicting pregnancy outcome as it may enable obstetricians to predict the effect of RC and counsel patients with amniotic membrane prolapse following prior cerclage.

## Conclusions

To the best of our knowledge, our current study is the first to show that GA is a valuable factor for predicting pregnancy outcome following RC in women with a prolapsed membrane after prior cerclage. However, there are some limitations to this study, including its design as a retrospective investigation of a regional population, as well as the relatively small sample size. Further prospective investigations including a multicentre, large cohort are needed in the future.

## Abbreviations

gestational age, GA; repeat cerclage, RC; receiving operating characteristic, ROC; neutrophil/lymphocyte ratio, NLR; Odds ratio, OR; confidence interval, CI; area under the ROC curve, AUC

## Declarations

Ethics approval and consent to participate

Written informed consent was obtained from the patients. The protocol was approved by the ethics committee of Shengjing Hospital. The reference number: 2020PS819K.

Consent for publication

Written informed consent for publication was obtained from the patients.

Availability of data and material

Data and materials can be available from corresponding author

Competing interests

Not applicable.

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## Authors' contributions

BC wrote the manuscript. XN collected the patients' information. Both of the authors approved the final manuscript.

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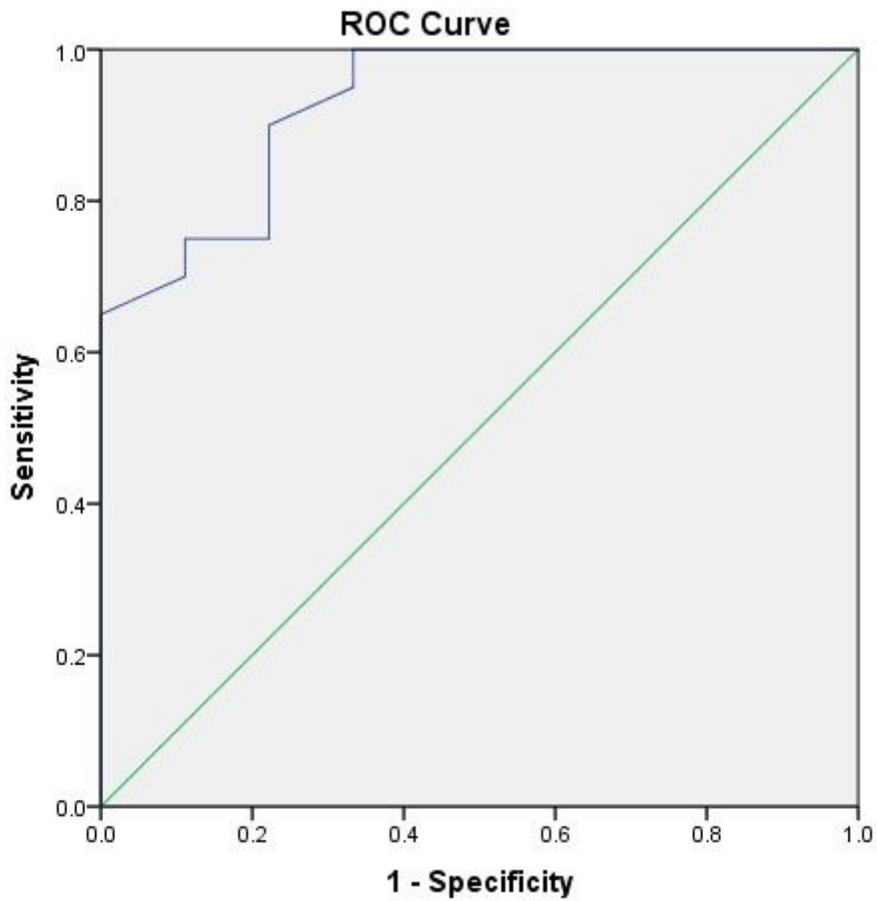
Not applicable.

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## Figures



Diagonal segments are produced by ties.

**Figure 1**

Receiver-operating characteristic (ROC) curve of GA at RC predicting neonatal survival. The area under curve (AUCs) are 0.928 (p=0.000). GA  $\geq$ 24.2 weeks at RC with sensitivity 93.75% and specificity 61.54%.

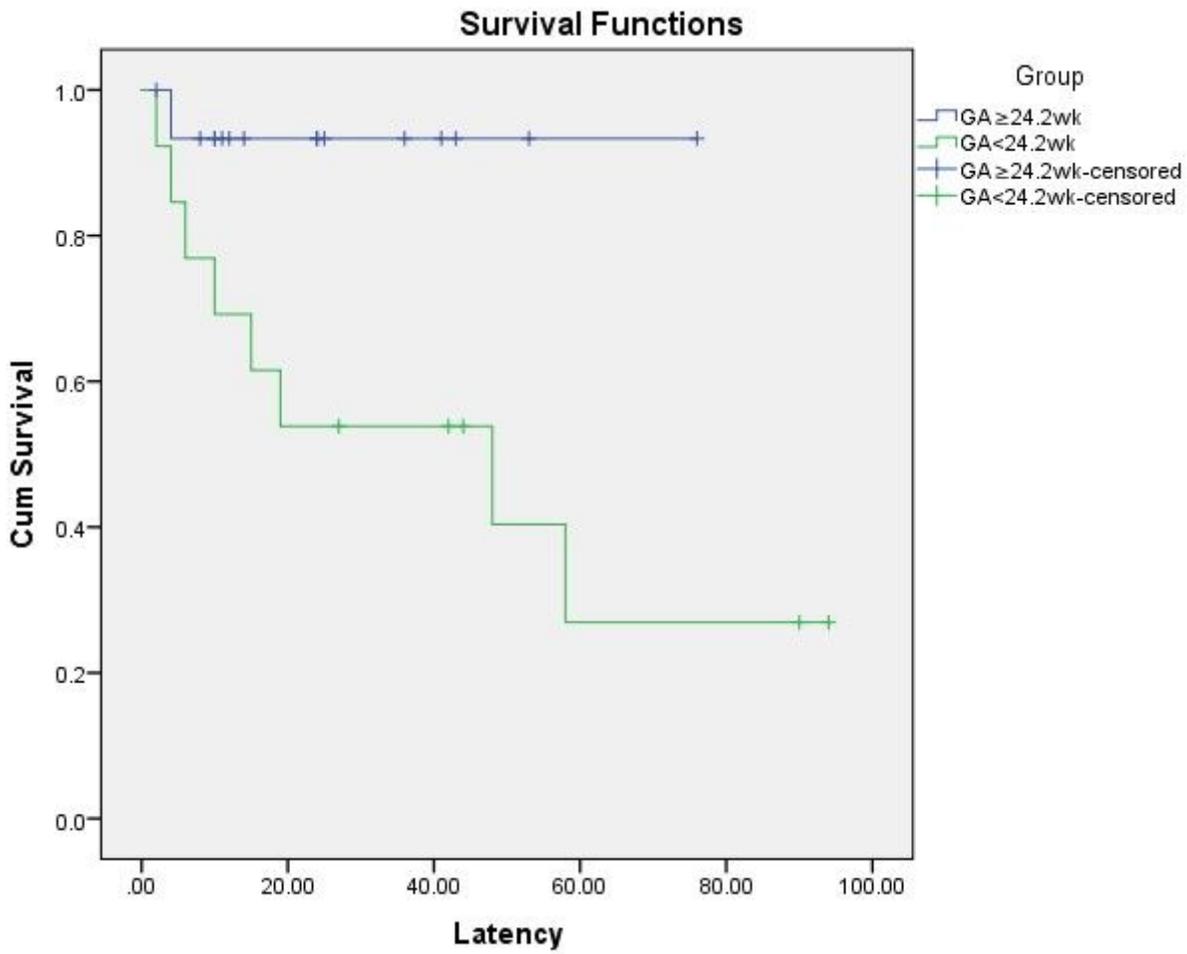


Figure 2

Kaplan-Meier survival curve for neonatal survival with GA at RC  $\geq$  24.2 weeks and < 24.2 weeks