

Circadian Chronobiology of Cervical Ripening Balloon Insertion: Effects on Labor Progression and Maternal Outcomes

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Research Article

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Abstract

Objective

To investigate the effects of different placement times of cervical balloon (before 12:00 vs. after 12:00) on labor duration, oxytocin use, mode of delivery, and maternal and neonatal outcomes.

Methods A total of 193 singleton, cephalic, full-term pregnant women with unfavorable cervix (Bishop score < 6) who were scheduled for delivery in Beijing Tongren Hospital from January 2024 to March 2026 were enrolled. According to the balloon placement time, they were divided into study group 1 (before or at 12:00, 112 cases) and study group 2 (after 12:00, 81 cases). The indicators of labor duration, oxytocin use, mode of delivery, postpartum hemorrhage and neonatal outcomes were compared between the two groups.

Results There was no significant difference in vaginal delivery rate between the two groups ($P = 0.132$). In the vaginal delivery subgroup, the time from balloon placement to expulsion/removal, the time from induction to active labor, and the duration of the first stage of labor in study group 1 were significantly shorter than those in study group 2 ($P < 0.05$). The incidence of postpartum hemorrhage (> 500 ml) in study group 1 was significantly lower than that in study group 2 (5.5% vs. 16.4%, $P = 0.040$). No significant differences were found in the second stage, third stage, total stage of labor, oxytocin use rate, and neonatal outcomes between the two groups ($P > 0.05$).

Conclusion Placing cervical balloon in the morning (before 12:00) can shorten the first stage of labor, accelerate cervical ripening and reduce the risk of postpartum hemorrhage. It is recommended to prioritize morning placement when conditions permit.

Introduction

Chronotherapy is an emerging interdisciplinary field at the intersection of chronobiology and clinical medicine. Its core principle is to select the optimal intervention timing based on the circadian rhythms of physiological functions and disease states, thereby enhancing therapeutic efficacy and minimizing adverse events. Childbirth, a complex physiological process coordinated by the nervous, endocrine, and immune systems, does not occur randomly but exhibits distinct and consistent circadian rhythmicity. A large body of clinical evidence has demonstrated that the onset of spontaneous labor is predominantly concentrated during the night to early morning hours. A retrospective analysis of over 550,000 singleton deliveries conducted by Moškon et al. revealed that the peak of spontaneous labor (onset of uterine contractions) occurs between 6:00 and 7:00 a.m., while the peak of spontaneous rupture of membranes occurs at 1:00 a.m., suggesting that the initiation of childbirth is precisely regulated by the endogenous biological clock¹

In the clinical practice of artificial labor induction, the selection of intervention timing plays a crucial role in determining labor outcomes. Accumulating evidence indicates that initiating labor induction in the

early morning (05:00–09:00) can significantly shorten the labor duration and reduce the risk of cesarean section, whereas induction performed from afternoon to night is often associated with prolonged labor and uterine inertia². There is a well-established molecular mechanism underlying this phenomenon: clock genes are rhythmically expressed in uterine smooth muscle and cervical tissue, and they modulate the sensitivity of the uterus to uterotonic agents by regulating the expression level of the oxytocin receptor (OXTR)³. Additionally, the circadian secretion rhythms of hormones, such as cortisol and melatonin, directly contribute to the regulation of cervical ripening and the coordination of uterine contractions⁴.

Cervical balloon dilation is one of the most widely used methods for promoting cervical ripening, which exerts its effect through mechanical stimulation of the cervical canal. However, there is no unified clinical guideline regarding the specific timing of cervical balloon placement in current practice. Most maternity institutions determine the placement time based on their own work schedules, with little consideration given to the potential impact of biological rhythms on labor progression. Based on this, the present study aims to investigate the effects of different cervical balloon placement times (before 12:00 and after 12:00) on labor duration, oxytocin utilization rate, delivery mode, and maternal and neonatal outcomes. The findings of this study are expected to provide evidence-based support for optimizing the timing of cervical balloon-induced labor and improving clinical delivery outcomes.

1. Materials and Methods

1.1. Study Population

Pregnant women who established prenatal care and planned to deliver at Beijing Tongren Hospital Affiliated to Capital Medical University from January 2024 to March 2026 were selected as the research subjects. A total of 193 cases were enrolled, all of which were singleton, cephalic presentation, full-term pregnancy, and had immature cervical conditions (Bishop score < 6). All eligible pregnant women received cervical balloon treatment for cervical ripening.

Inclusion criteria: (1) Normal pelvis with cephalopelvic proportion; (2) Singleton, cephalic presentation, and gestational age ≥ 37 weeks; (3) No vaginal infection and intact fetal membranes; (4) Cervical Bishop score < 6; (5) Cervical ripening promoted by cervical balloon.

Exclusion criteria: (1) Fetal malformation, fetal death, multiple pregnancy, or preterm birth; (2) Presence of contraindications to vaginal delivery; (3) Premature rupture of fetal membranes; (4) Complicated with vaginal infection; (5) Cervical ripening not promoted by cervical balloon.

The 193 pregnant women were divided into two groups according to the timing of cervical balloon placement: Group 1 (112 cases) with balloon placement at or before 12:00, and Group 2 (81 cases) with balloon placement after 12:00. This study was approved by the Medical Ethics Committee of the hospital.

1.2. Balloon Placement and Induction Methods

Disposable cervical dilation balloon catheters (Model: HK-CDB-80/80A) produced by Beijing Aerospace Kadi Technology Development Institute, China, were used. The specific operation was as follows: the puerpera was placed in the lithotomy position, and the vagina and cervix were routinely disinfected with povidone-iodine. The balloon catheter was inserted into the cervical canal so that the two balloons were located on both sides of the internal and external cervical orifices respectively. First, 40 mL of normal saline was injected into the inner balloon, and then normal saline was injected into the two balloons in increments of 20 mL each time until the total volume of the bilateral balloons reached 80 mL. The outer end of the balloon was fixed to the inner side of the puerpera's thigh.

The balloon was removed immediately if any of the following conditions occurred: onset of labor, vaginal bleeding exceeding the menstrual volume, rupture of fetal membranes, or the balloon still not falling off after reaching the maximum placement time (12 hours). If the balloon fell off automatically, the cervical opening condition and the presence of regular uterine contractions were checked; if there were no uterine contractions and there was an indication for artificial rupture of membranes, artificial rupture of membranes was performed and oxytocin was used as appropriate. If the balloon was still not falling off after 12 hours of placement, the balloon was removed and the cervical ripening degree was re-evaluated. If the cervix was still immature (Bishop score < 6), other induction methods were adopted.

1.3 Observation Indicators

The primary observation indicators included: time from balloon placement to detachment/removal, time from induction to onset of labor, duration of the first stage of labor, duration of the second stage of labor, duration of the third stage of labor, total labor duration, oxytocin usage rate and total usage, postpartum blood loss (and postpartum hemorrhage rate), neonatal birth weight and length, neonatal Apgar scores at 1 minute, 5 minutes, and 10 minutes, and neonatal umbilical artery blood pH value.

1.4 Statistical Methods

SPSS 26.0 statistical software was used for data analysis. Measurement data were expressed as mean $\pm$ standard deviation ($\bar{x} \pm s$), and independent samples t-test or Mann-Whitney U test (for non-normal distribution) was used for comparison between groups. Count data were expressed as number of cases (percentage), and χ^2 test or Fisher's exact test was used for comparison between groups. A P value < 0.05 was considered statistically significant.

2. Result

2.1 Comparison of Baseline Data and Delivery Mode in the Total Population

A total of 193 puerperae were enrolled, including 112 cases in Group 1 (balloon placement at or before 12:00) and 81 cases in Group 2 (balloon placement after 12:00). There were no statistically significant differences between the two groups in terms of age, gestational age at delivery, proportion of primiparas, pre-pregnancy BMI, and Bishop score before placement ($P > 0.05$), indicating good comparability. The vaginal delivery rate was 65.2% (73/112) and the cesarean section rate was 34.8% (39/112) in Group 1; the vaginal delivery rate was 75.3% (61/81) and the cesarean section rate was 24.7% (20/81) in Group 2, with no statistically significant difference between the two groups ($P = 0.132$). See Table 1.

2.2 Comparison of Baseline Data in the Vaginal Delivery Subgroup

To further compare labor-related indicators, a subgroup analysis was performed on 134 puerperae with vaginal delivery (73 cases in Group 1 and 61 cases in Group 2). The results showed that there were no statistically significant differences between the two groups in age, gestational age at delivery, proportion of primiparas, labor analgesia rate, pre-pregnancy BMI, and Bishop score before placement ($P > 0.05$), indicating good comparability. However, the Bishop score after placement and the improvement value of Bishop score in Group 1 were significantly higher than those in Group 2 ($P < 0.01$). There were no statistically significant differences in neonatal birth weight and length between the two groups ($P > 0.05$). See Table 2.

2.3 Comparison of Labor Duration and Key Process Indicators in the Vaginal Delivery Subgroup

The time from balloon placement to detachment/removal in Group 1 was significantly shorter than that in Group 2 (10.5 ± 2.8 h vs. 14.2 ± 3.5 h, $P < 0.001$), and the time from induction to onset of labor was also significantly shortened (3.5 ± 1.8 h vs. 5.2 ± 2.4 h, $P < 0.001$). The duration of the first stage of labor in Group 1 was 325.48 ± 246.75 min, which was significantly shorter than that in Group 2 (421.72 ± 272.42 min, $P = 0.024$). There were no statistically significant differences in the duration of the second stage of labor, the third stage of labor, and the total labor duration between the two groups ($P > 0.05$). See Table 3.

2.4 Comparison of Pregnancy Outcomes and Intervention Measures in the Vaginal Delivery Subgroup

There were no statistically significant differences between the two groups in oxytocin usage rate, postpartum blood loss, neonatal Apgar scores (at 1, 5, and 10 minutes), and neonatal umbilical artery blood pH value ($P > 0.05$). However, the incidence of postpartum hemorrhage (> 500 ml) in Group 1 was 5.5% (4/73), which was significantly lower than that in Group 2 (16.4% (10/61)), and the difference was statistically significant ($P = 0.040$). See Table 4.

Table 1

Comparison of general demographic characteristics and delivery modes between two full populations (n = 193)

Index	Research group 1 (n = 112)	Research group 2 (n = 81)	t/ χ^2	P
Age (year, $\bar{x} \pm s$)	30.64 $\pm$ 3.22	31.28 $\pm$ 3.86	1.109	0.268
Delivery week (week, $\bar{x} \pm s$)	39.18 $\pm$ 0.94	39.42 $\pm$ 1.02	1.756	0.079
Primipara [n (%)]	103 (92.0%)	74 (91.4%)	0.023	0.880
Pre-pregnancy BMI (kg/m ² , $\bar{x} \pm s$)	23.1 $\pm$ 2.2	22.8 $\pm$ 2.1	0.962	0.337
Before placement Bishop score (score, $\bar{x} \pm s$)	4.12 $\pm$ 1.05	4.05 $\pm$ 1.12	0.445	0.657
Vaginal delivery [n (%)]	73 (65.2%)	61 (75.3%)	2.273	0.132
Caesarean section [n (%)]	39 (34.8%)	20 (24.7%)		

Table 2
Comparison of general data of two subgroups of vaginal delivery

Index	Research group 1 (n = 73)	Research group 2 (n = 61)	z	P
Age (year, $\bar{x} \pm s$)	30.70 $\pm$ 3.23	31.23 $\pm$ 3.94	0.738	0.460
Delivery week (week, $\bar{x} \pm s$)	39.16 $\pm$ 0.98	39.47 $\pm$ 0.99	1.827	0.068
Primipara [n (%)]	64 (87.7%)	56 (91.8%)	0.606	0.436
Labor analgesia[n (%)]	38(52.1%)	35(57.4%)	0.380	0.538
Pre-pregnancy BMI (kg/m ² , $\bar{x} \pm s$)	23.1 $\pm$ 2.2	22.8 $\pm$ 2.1	0.813	0.418
Pre-placement Bishop score (score, $\bar{x} \pm s$)	4.12 $\pm$ 1.05	4.05 $\pm$ 1.12	0.378	0.706
Post-placement Bishop score (score, $\bar{x} \pm s$)*	7.35 $\pm$ 1.42	6.58 $\pm$ 1.65	2.913	0.004
Improvement of Bishop score (score, $\bar{x} \pm s$)	3.23 $\pm$ 1.15	2.53 $\pm$ 1.38	3.185	0.002
Neonatal birth weight (g, $\bar{x} \pm s$)	3198.08 $\pm$ 364.24	3208.20 $\pm$ 391.00	0.210	0.834
Neonatal body length (cm, $\bar{x} \pm s$)	50.45 $\pm$ 1.72	50.20 $\pm$ 1.89	-0.607	0.544

*Note: The post-placement Bishop score was assessed after balloon removal and prior to subsequent obstetric interventions.

Table 3

Comparison of the duration of labor and key process indicators between two groups of vaginal delivery parturients

Index	Research group 1 (n = 73)	Research group 2 (n = 61)	z	P
Time from balloon placement to spontaneous detachment or manual removal (h)	10.5 ± 2.8	14.2 ± 3.5	-6.734	< 0.001
Time from labor induction to labor onset* (h)	3.5 ± 1.8	5.2 ± 2.4	-4.541	< 0.001
Duration of the first stage of labor (min)	325.48 ± 246.75	421.72 ± 272.42	2.264	0.024
Duration of the second stage of labor (min)	91.34 ± 114.36	68.56 ± 72.65	-1.305	0.192
Duration of the third stage of labor (min)	9.34 ± 6.69	11.85 ± 11.11	0.660	0.509
Duration of the total stage of labor (min)	455.79 ± 284.14	550.49 ± 337.77	1.725	0.085

*Time from induction to labor onset: defined as the time interval from the initiation of subsequent labor interventions (such as artificial rupture of membranes or oxytocin administration) after balloon removal to the onset of regular uterine contractions.

Table 4

Comparison of pregnancy outcomes and intervention measures between the two groups of women with vaginal delivery

Index	Research group 1 (n = 73)	Research group 2 (n = 61)	z/χ ²	P
Oxytocin administration [n (%)]	54 (74.0%)	39 (63.9%)	1.577	0.209
No oxytocin administration [n (%)]	19 (26.0%)	22(36.1%)		
Volume of postpartum hemorrhage (ml)	318.90 ± 108.92	329.43 ± 148.30	-0.460	0.646
Volume of postpartum hemorrhage >500ml [n (%)]	4 (5.5%)	10 (16.4%)	4.231	0.040
Neonatal Apgar score in 1 minute	9.82 ± 0.59	9.85 ± 0.48	0.404	0.686
Neonatal Apgar score in 5 minute	9.99 ± 0.12	10.00 ± 0.00	0.914	0.361
Neonatal Apgar score in 10 minute	10.00 ± 0.00	10.00 ± 0.00	-	1.000
Neonatal umbilical artery PH	7.29 ± 0.06	7.28 ± 0.06	0.971	0.334

Discussion

The results of this study indicate that placing the cervical balloon in the morning (before 12:00) can significantly shorten the balloon indwelling time, the time from induction to onset of labor, and the duration of the first stage of labor, while reducing the incidence of postpartum hemorrhage (> 500 ml), without significant effects on the second stage of labor, the third stage of labor, total labor duration, oxytocin usage rate, and neonatal outcomes. This finding supports the clinical importance of the circadian rhythm of childbirth in cervical balloon induction, suggesting that optimizing the timing of balloon placement is an effective strategy to improve delivery outcomes.

In this study, the duration of the first stage of labor in the morning balloon placement group (325.48 ± 246.75 min) was significantly shorter than that in the afternoon and night placement group (421.72 ± 272.42 min), with a statistically significant difference ($P = 0.024$). This result is consistent with a large-scale retrospective cohort study by Cataldo et al², which included 3286 full-term pregnant women undergoing labor induction and found that the labor duration was the shortest when induction was initiated in the early morning (05:00–09:00, mean 14.5 h) and significantly prolonged when initiated at night (mean 20.8 h). In addition, the time from balloon placement to detachment/removal (10.5 ± 2.8 h) and the time from induction to onset of labor (3.5 ± 1.8 h) in the morning balloon placement group were also significantly shorter than those in the control group (14.2 ± 3.5 h and 5.2 ± 2.4 h, respectively), indicating that morning balloon placement not only accelerated the process of cervical ripening but also shortened the subsequent time interval to the onset of labor. The possible mechanism is that the responsiveness of the uterus to mechanical stimulation and endogenous uterine contraction signals exhibits a circadian rhythm. A retrospective analysis of more than 550,000 singleton deliveries by Moškon et al¹ revealed that the peak of spontaneous labor (onset of uterine contractions) occurs at 6–7 a.m., while the peak in the induced labor group (as a control) is around 10 a.m. This time window highly overlaps with the morning balloon placement period (before 12:00) in this study, suggesting that morning balloon placement may conform to the endogenous labor rhythm, coupling the subsequent labor progression with the peak of physiological uterine contractions, thereby shortening the first stage of labor. A study by Duong et al. further confirmed that the expression of uterine oxytocin receptor (Oxtr) mRNA exhibits circadian rhythm changes, and the responsiveness of the uterus to oxytocin is regulated by the circadian rhythm, providing a direct molecular basis for the above phenomenon³.

It is worth noting that the Bishop score after placement and the improvement value of the Bishop score in the morning balloon placement group were significantly higher than those in the afternoon and night groups ($P < 0.01$), but there was no difference in the Bishop score before placement between the two groups. This indicates that morning balloon placement itself may be more conducive to promoting cervical ripening. Collagen metabolism and matrix metalloproteinase activity in cervical connective tissue are also regulated by the biological clock. Using DNA microarray and RNA interference techniques, Tasaki et al⁵ confirmed that multiple clock genes such as Bmal1, Per, and Cry are rhythmically expressed in rat endometrial stromal cells, and can regulate genes closely related to uterine stromal decidualization and cervical ripening, such as insulin-like growth factor 1 (Igf1), providing direct

experimental evidence for the existence of an intrinsic biological clock in uterine tissue and the regulation of cervical remodeling by local rhythms. In addition, melatonin, a hormone secreted at night, not only regulates the sleep-wake cycle but also participates in the regulation of cervical ripening and uterine contraction coordination⁶. Although the balloon is a mechanical ripening method, the synergistic effect of endogenous melatonin and oxytocin may be more efficient in the morning, thereby accelerating cervical softening and cervical dilation.

The incidence of postpartum hemorrhage (> 500 ml) was significantly lower in the morning placement group than in the afternoon and night groups (5.5% vs. 16.4%, $P = 0.040$), although there was no statistically significant difference in the average postpartum blood loss between the two groups. This finding has important clinical significance. Postpartum hemorrhage is closely related to uterine atony, and the circadian rhythm of uterine contractions has been reported. Olcese et al⁶. proposed that melatonin enhances oxytocin-induced contractions by binding to MT1/MT2 receptors on uterine smooth muscle, and this effect may still retain a certain effect in the early morning near the end of melatonin secretion. In addition, the shortening of the first stage of labor may reduce the fatigue of uterine smooth muscle, thereby reducing the risk of postpartum uterine atony. Although there was no difference in the oxytocin usage rate between the two groups in this study, the morning placement group may have a more coordinated response of the uterus to oxytocin due to the advantage of the endogenous uterine contraction rhythm, thereby reducing postpartum hemorrhage^{4,7}.

No significant differences were found between the two groups in total labor duration, cesarean section rate, and neonatal outcomes. Although the total labor duration tended to be shorter in the morning group (455.79 vs. 550.49 min, $P = 0.085$), it did not reach statistical significance, which may be related to the limited sample size or large variation in the second and third stages of labor. The lack of difference in the cesarean section rate may be related to the diversity of cesarean section indications (such as fetal distress, labor arrest, etc.). The cesarean section rates in the two groups in this study were 34.8% and 24.7%, respectively. Although there was no statistical difference ($P = 0.132$), the numerical difference is worthy of attention, and the sample size needs to be expanded for further verification. There were no differences in neonatal Apgar scores and umbilical artery blood pH values between the two groups, suggesting that different placement times do not affect short-term neonatal outcomes, which is consistent with previous studies [3,8]. A current systematic review comprehensively evaluated the effects of mechanical and pharmacological cervical ripening methods, pointing out that different induction regimens have their own advantages and disadvantages, and individualized selection should be made according to clinical conditions⁹. Another study compared the effects of outpatient and inpatient mechanical cervical ripening, suggesting that medical settings and placement timing may affect resource utilization and patient satisfaction¹⁰.

It is worth noting that the balloon indwelling time itself is also an important variable affecting the outcome of labor induction. Bleicher et al¹¹. conducted a large-scale historical controlled study ($n = 1704$) comparing the outcomes of labor induction after 6 hours and 12 hours of balloon placement. The

results showed that the cesarean section rate (22.5% vs. 28.6%) and instrumental delivery rate (6.2% vs. 12.0%) in the 6-hour group were significantly lower, and the vaginal delivery rate within 24 hours was higher. This study indicates that shortening the balloon indwelling time (6 hours instead of 12 hours) can lead to better delivery outcomes. The balloon indwelling time in the morning placement group in this study (10.5 ± 2.8 h) was significantly shorter than that in the afternoon and night groups (14.2 ± 3.5 h). This difference echoes the findings of Bleicher et al¹³.—a shorter balloon indwelling time may partially explain the benefits of shorter first stage of labor and reduced postpartum hemorrhage in the morning group. However, there is currently a lack of studies exploring the interaction between placement time and indwelling duration. In the future, randomized controlled trials can be designed to clarify the independent and interactive effects of the two.

However, the existing evidence is inconsistent regarding the optimal timing of balloon placement. Kehl et al¹².conducted a multicenter retrospective cohort study, including 415 full-term pregnant women with immature cervix undergoing labor induction, using a sequential induction regimen of double-balloon catheter combined with oral misoprostol, and compared the outcomes between the morning group (balloon placement at 02:00–15:00) and the evening group (balloon placement at 15:00–02:00). The results found that the evening balloon placement group had a lower induction failure rate in primiparas (4% vs. 12%, $P = 0.043$), a shorter interval from induction to delivery in multiparas (1349 vs. 1756 min, $P = 0.046$), and a higher delivery rate within 24 hours (56% vs. 35%, $P = 0.016$). This conclusion is significantly different from this study. Possible reasons for the differences include: (1) Differences in induction regimens: Kehl et al. used a combination of balloon and misoprostol (a prostaglandin drug), while in this study, artificial rupture of membranes and oxytocin were mainly used after balloon removal, and prostaglandins were not routinely used. The pharmacokinetics and uterine responsiveness of prostaglandins also have circadian rhythm characteristics, and their interaction with the balloon may change the window of optimal placement time. (2) Differences in study population and grouping cut-off values: Kehl et al. used 02:00 and 15:00 as grouping cut-off values, and the morning group had a time span of 13 hours, while this study used 12:00 as a single cut-off value, and the time distribution of the two groups was more concentrated. (3) Differences in the focus of outcome indicators: Kehl et al. mainly focused on the cesarean section rate and induction failure (no vaginal delivery within 72 hours), while in this study, the differences in the duration of the first stage of labor and the postpartum hemorrhage rate were more significant. These differences suggest that the optimal balloon placement time may vary depending on the subsequent induction regimen (oxytocin vs. prostaglandin) and population characteristics (primiparas vs. multiparas). Currently, several clinical practice guidelines emphasize that the selection of induction timing should comprehensively consider cervical conditions, gestational age, maternal-fetal status, and circadian rhythm factors^{13,14}, but no clear recommendation has been given on the specific time window for balloon placement. In addition, the latest clinical practice guideline of ACOG has systematically updated the cervical ripening methods, emphasizing individualized decision-making¹⁵. In the future, targeted randomized controlled trials are needed to clarify the optimal placement time under different induction regimens.

This study has certain limitations. First, it was a retrospective observational design. Although the baseline data of the two groups were comparable, selection bias could not be completely excluded. Second, the balloon placement time was not randomly assigned, which may be affected by factors such as the time of the parturient's admission and the ward work arrangement. Third, the levels of hormones such as melatonin and cortisol in the parturients were not monitored, and the rhythm mechanism could not be directly verified. In the future, prospective randomized controlled trials can be adopted, and biological samples can be collected at specific time points to clarify the molecular mechanism. In addition, the research idea of Yogamoorthy et al⁸. can be used to explore the interaction between different balloon indwelling durations and placement times to further optimize the induction regimen.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Beijing Tongren Hospital, Capital Medical University. All procedures were performed in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments. Due to the retrospective design and the use of anonymized, routinely collected clinical data, the requirement for individual informed consent was waived by the Ethics Committee of Beijing Tongren Hospital, Capital Medical University.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Author Contribution

Tian Xingyue and Wang Wenwen conceived and designed the study. Tian Xingyue performed data collection and Wang Wenwen statistical analysis. Tian Xingyue drafted the manuscript. Wang Wenwen and Zhou Li critically reviewed and revised the manuscript. All the authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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