

Effect of Induction of Labor on Maternal and Perinatal Outcomes in Low-Risk Singleton Pregnancies: A Retrospective Case-Control Study

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Abstract

Background: To investigate the effect of induction of labor on maternal and fetal outcomes.

Methods: This retrospective case-control study included 4386 pregnant women with low-risk singleton pregnancies who underwent regular prenatal examination and successful vaginal delivery at ≥ 41 weeks and 0 days of gestation in Fujian Maternal and Child Health Hospital between January 2014 and December 2018. Clinical data were reviewed according to the mode of labor initiation; the women were divided into an induction of labor group (2007 cases) and a spontaneous onset of labor group (2361 cases). Two-sample independent t-test and χ^2 tests were used to analyze the differences in clinical characteristics such as maternal age and parity between the two groups.

Results: The induction of labor group had a significantly longer total duration of labor (9.37 ± 5.37 vs. 8.82 ± 5.13 h; $P < 0.001$), was associated with more postpartum blood loss (219.18 ± 188.32 vs. 199.95 ± 124.69 mL; $P = 0.01$), and had a significantly higher incidence of severe postpartum hemorrhage (PPH) (0.8% [16/2007] vs. 0.33% [8/2361]; $P = 0.041$) than the spontaneous onset of labor group. However, no significant difference was found in the neonatal outcomes. After adjusting for age, induction of labor in nulliparous women was more likely to lead to PPH than spontaneous onset of labor (2.74% [55/2007] vs. 1.65% [39/2361]; odds ratio=1.557; 95% confidence interval: 1.039–2.332; $P < 0.05$).

Conclusion: Induction of labor increases postpartum blood loss, especially in primary parturients, leading to an increased risk of PPH, which may be related to the prolongation of the total duration of labor. Therefore, low-risk nulliparous women should try to avoid induction of labor without medical indications.

Background

Induction of labor (IOL) means that before the spontaneous onset of labor, the labor process is initiated by human stimulation of uterine contraction to achieve the purpose of delivery, often when the risks of continuing pregnancy outweigh the benefits. As a routine obstetrical operation, the proportion of IOL is approximately 4–12% in developing states; it is more common in developed countries, including 26% in Australia and 23.3% in the United Kingdom. The proportion of IOL in Queensland in 2014 was reported to be 24.9% [1]. The risk to mothers and fetuses increases in the third trimester of pregnancy; therefore, as one of the most important methods of pregnancy termination, IOL should be used rationally to optimize pregnancy outcomes.

Pregnancies that progressed to 41 weeks of gestation had an increased risk of adverse pregnancy outcomes, with worse outcomes after 42 weeks of gestation. It is recommended that the gestational age at delivery should be < 42 weeks [2]. Women with low-risk pregnancies are advised to terminate the pregnancy between 41 and 42 weeks of gestation, suggesting that women at > 41 weeks of gestation without spontaneous parturition should undergo IOL [3].

A large multicenter randomized controlled study conducted between 2014 and 2017 found that low-risk primigravida with IOL after 39 weeks of gestation could avoid one cesarean section for every 28 induced deliveries and IOL had a lower risk of perinatal death and severe neonatal complications than continued expectant management [4]. Based on that study, the Society of Maternal-Fetal Medicine recommends that it is reasonable to offer elective IOL to low-risk nulliparous women after 39 weeks of gestation who check the gestational age accurately [2]. Spontaneous onset of labor is not a clinical “decision;” during the process of waiting for spontaneous onset of labor, complications may occur and reduce the possibility of vaginal delivery. Therefore, it is inappropriate to compare waiting for spontaneous onset of labor with IOL.

To decide whether it is safe to relax the indication of IOL, it is necessary to investigate if IOL will pose an additional risk to the mother and fetus. Currently, the effect of IOL on pregnancy outcomes in low-risk pregnant women remains controversial. The present study retrospectively reviewed the clinical data from low-risk, later than term pregnant women with successful vaginal delivery, and discussed the influence of IOL on pregnancy outcomes of women with low-risk pregnancies.

Methods

Study design and data source

This retrospective cohort study included a total of 4386 pregnant women with low-risk singleton pregnancies who underwent regular prenatal examination and successful vaginal delivery at ≥ 41 weeks' gestation between January 2014 and December 2018 in Fujian Maternal and Child Health Hospital, which is affiliated to Fujian Medical University. According to the mode of labor initiation, the women were divided into the IOL group (any method) and the spontaneous onset of labor group. The study was approved by the Ethics Committee of the Fujian Provincial Maternity and Children's Hospital and was conducted in accordance with Chinese law and the Guidelines of the National Human Biomedical Research Policies. Written informed consent was not required because the data were anonymous and did not affect the patient's treatment.

Study selection and data extraction

Women who were aged between 18 and 45 years and had a vaginal birth after 41 weeks of gestation, with reliable dating and no obstetric or medical complications were eligible, regardless of the availability of cervical examination. Women were excluded if they had a scarred uterus and were transferred to undergo cesarean section; those with missing data on gestational age and the volume of vaginal bleeding at the time of delivery were also excluded.

Potential confounders and other variables of interest

A pregnant woman is considered “full term” if she gives birth anytime from 37 to 42 weeks' gestation. The gestational age (in weeks' gestation) is further divided as follows: early term, 37–38; full term, 39–40; late

term, >41; and post term, >42. The gestational age was determined by the crown rump length measured on ultrasound during early pregnancy. If the estimated gestational week difference is >5 days when the gestational age is <9 weeks or >7 days between 9 and 14 weeks' gestation, the gestational week determined on ultrasound should be considered; a volume of vaginal bleeding of ≥ 500 mL within 24 h after vaginal birth is considered postpartum hemorrhage (PPH) and that of >1000 mL is considered severe postpartum hemorrhage (sPPH). Parity and assisted conception pregnancies were self-reported.

Statistical analyses

The normally distributed measurement data were expressed as $x \pm s$, using two-sample independent t -tests. The countable data were described as percentages, and the χ^2 test was used to analyze the differences between the two groups. The outcomes were reported as mean differences for continuous outcomes or odds ratios (ORs) for binary outcomes, with their accompanying 95% confidence intervals (CIs). The difference was considered statistically significant at $P < 0.05$.

Results

A total of 48,719 pregnant women underwent pregnancy examinations. Women who did not meet our study criteria ($n=44,020$) and those who had obstetric or medical complications ($n=331$) were excluded. Finally, 4386 pregnant women with low-risk singleton pregnancies who had successful vaginal delivery at ≥ 41 weeks of gestation were included in the analysis. They were divided into the IOL group (2007 cases) and the spontaneous onset of labor group (2361 cases) (Fig. 1).

Baseline characteristics

Most women aged between 18 and 34 years, with a median maternal age of 28.5 years. There was no significant difference in the average age and distribution of each age range between the two groups ($P > 0.05$). The IOL group had a significantly greater number of nulliparous women (71.0% vs. 66.6%) and a longer gestational age (289.26 ± 1.54 vs. 288.33 ± 1.62 days) than the spontaneous onset of labor group ($P < 0.05$). Table 1 shows the additional baseline characteristics of all study participants.

IOL with a longer duration of labor

The total duration of labor and the duration of each stage of labor in the IOL group were longer than those in the spontaneous onset of labor group. The duration of the first (8.62 ± 5.12 vs. 8.17 ± 4.88 h) and second (0.65 ± 0.78 vs. 0.55 ± 0.69 h) stages of labor and the total duration of labor (9.37 ± 5.37 vs. 8.82 ± 5.13 h) were significantly different between the IOL and spontaneous onset of labor groups ($P < 0.05$). Additional characteristics of the duration of labor are presented in Table 2.

The total duration of labor in the nulliparous group was the longest. The average length of time was 11.07 ± 5.12 h, and the time shortened with an increase in the number of parturitions. The total duration of labor in multipara women was mostly within 8 h (Table 3).

IOL increases postpartum blood loss

The IOL group was associated with more postpartum blood loss (219.18 ± 188.32 vs. 199.95 ± 124.69 mL; $P=0.01$) and a significantly increased risk of sPPH (0.8% [16/2007] vs. 0.33% [8/2361]; $P=0.041$) compared with the spontaneous onset of labor group; however, no significant difference was found in the incidence of PPH (3.8% [77/2007] vs. 2.8% [66/2361]; $P=0.054$).

The volume of vaginal bleeding increased with the prolongation of the total duration of labor and increased significantly when the total duration of labor was >20 h (Fig. 2). IOL increased the risk of PPH compared with spontaneous onset of labor (2.74% vs. 1.65%; OR: 1.557, 95% CI: 1.039–2.332) in nulliparous women, but there was no significant difference in multipara women (Table 4).

IOL and secondary pregnancy outcomes

The incidence of chorioamnionitis and rate of operative vaginal birth were significantly higher in the IOL group than in the spontaneous onset of labor group (4.33% vs. 2.33%; $P<0.05$ and 3.5% vs. 5.0%; $P<0.05$, respectively). However, there was no significant difference in the incidence of third-degree amniotic fluid contamination (15.5% vs. 14.7%; $P>0.05$) and placental abruption (4.48% vs. 2.96%; $P>0.05$) between the IOL and spontaneous onset of labor groups.

The neonatal intensive care unit (NICU) admission rate of newborns was significantly higher in the IOL group than in the spontaneous onset of labor group (3.74% vs. 2.16%; $P<0.05$). However, there was no significant difference between the two groups in terms of birth weight and its distribution, sex of the newborn, incidence of neonatal brain injury, incidence of neonatal intraventricular hemorrhage, perinatal death, neonatal hyperbilirubinemia, neonatal septicemia, neonatal pneumonia, and Apgar score ≤ 7 at birth ($P>0.05$).

Discussion

Our study showed that IOL increases postpartum blood loss, leading to an increased risk of PPH, which is possibly caused by prolonged labor. Therefore, we suggest that low-risk nulliparous women should avoid IOL without medical indications.

The maternal and fetal risk increases in the third trimester of pregnancy. IOL is an important measure to terminate a pregnancy when the benefits of pregnancy termination are greater than those of pregnancy continuation; therefore, correctly identifying the timing of IOL can optimize the pregnancy outcomes to the maximum extent. Currently, the effect of IOL on pregnancy outcomes in low-risk pregnant women remains controversial. This retrospective case-control study selected women with low-risk delayed pregnancy and vaginal delivery and compared and analyzed the pregnancy outcomes between the IOL and spontaneous onset of labor groups, which yielded more objective results.

Vahratian et al. [5] showed that the labor process in pregnant women with IOL was significantly longer than that in those with a spontaneous onset of labor, which is consistent with our findings. In our study,

the increase in the duration of labor in the IOL group was predominantly in the first stage of labor, extended by nearly 0.5 h. Further stratified analysis of parity showed that the total duration of labor in the IOL group was shortened with an increase in parity, with the duration being the longest in nulliparous women with IOL (11.07 ± 5.12 h); the duration was usually <8 h in multipara women. The proportion of multipara women in the spontaneous onset of labor group was higher than that in the IOL group, which suggested that multipara women were more likely to start labor spontaneously and their duration of labor was shorter.

Cheng et al. [6] found that the extension of the first stage of labor increases the prolongation of the second stage of labor and is associated with an increased risk of PPH [7,8]. We showed that the IOL group had more postpartum blood loss than the spontaneous onset of labor group (219.18 ± 188.32 vs. 199.95 ± 124.69 mL). The average postpartum blood loss increased with the prolongation of the total stages of labor, which led to an increase in the risk of PPH and even sPPH, especially when the total stages of labor was ≥ 20 h. Compared with the spontaneous onset of labor group with the same total duration of labor, the IOL group had a higher volume of vaginal bleeding with more postpartum blood loss, suggesting that prolonged labor is not the only reason. IOL can lead to an increase in postpartum blood loss, with the peak of postpartum blood loss moving forward (Fig. 2).

Because the significantly longer total duration of labor in nulliparous women is associated with a higher incidence of PPH and IOL can lead to an increase in postpartum blood loss, attention should be paid to avoid selective IOL in nulliparous women without medical indication as far as possible.

This study showed a higher incidence of operative vaginal birth and chorioamnionitis in the IOL group, which was related to a higher risk of admission to the NICU and did not lead to an increase in other adverse maternal and perinatal outcomes, which is consistent with the results of some previous studies [9,10]. In this study, low-risk, later than term pregnant women with successful vaginal delivery but without obstetric or medical complications were selected to eliminate the influence of confounding factors to the maximum extent, the study population differ from previous studies [11,12]. These steps eliminate the influence of confounding factors has helped better explain the impact of IOL on perinatal outcomes.

Limitations of our study are the missing data about the use of oxytocin for labor augmentation during delivery and the way of IOL which was associated with a longer total duration of labour and greater frequency of adverse outcomes. However, in contrast to the existing randomized controlled trials, our study design was eliminated the influence of some confounding factors in the transition to a cesarean section, and developed to assess postpartum blood loss rather than the success rate of the IOL.

Conclusions

IOL prolongs the total duration of labor and increases postpartum blood loss; therefore, the clinical decision-making of IOL without medical indications for low-risk nulliparous women needs to be more prudent. Low-risk pregnant women should try to avoid IOL without medical indications.

Abbreviations

IOL=induction of labor; PPH=postpartum hemorrhage; sPPH=severe postpartum hemorrhage;
NICU=neonatal intensive care unit

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Fujian Provincial Maternity and Children's Hospital and was conducted in accordance with Chinese law and the Guidelines of the National Human Biomedical Research Policies. Informed consent was not required owing to the retrospective study design. Permission to access anonymized (non-identified) data was granted by the Fujian Provincial Maternity and Children's Hospital Database steering committee.

Consent for publication

Not applicable.

Data availability statement

Data were anonymized and no patient identifying information was included for preserve patient confidentiality. All data to evaluate the conclusions in the paper available for scientific purposes if needed.

Competing interests

The authors declare that they have no competing interests.

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Author contribution statement

Zhang Qinjian and Chen Siwen designed the analyses, and Zhang Qinjian drafted the manuscript. Yan Jianying conceptualized the study; and Xu Xia and Zhang Huale contributed to data acquisition. All authors have revised the manuscript for important intellectual content.

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Tables

Table 1. Baseline characteristics and main pregnancy outcomes

Baseline characteristics	Spontaneous onset of labor (n=2,361)	Induction of labor (n=2,007)	P value
	n (%)	n (%)	
Maternal age at delivery year, no. (%)	28.59 (28.59±3.87)	28.55 (28.55±3.80)	0.732
<18	5 (0.2%)	5 (0.2%)	NC
18–34	2188 (92.7%)	1853 (92.3%)	NC
35–39	147 (6.2%)	130 (6.5%)	NC
≥40	21 (0.9%)	19 (0.9%)	NC
Mean gestational age (days)	288.33±1.62	289.26±1.54	0
Nulliparous, no. (%)[‡]	1573 (66.6%)	1425 (71.0%)	0.002
Maternal outcomes, no. (%)			
Operative vaginal birth, no. (%) [‡]	82 (3.5%)	101 (5.0%)	0.01
Chorioamnionitis, no. (%) [‡]	55 (2.33%)	87 (4.33%)	0.0002
Placental abruption, no. (%)	7 (2.96%)	9 (4.48%)	0.408
Amniotic fluid contamination, no. (%)	348 (14.7%)	291 (14.5%)	0.823
Postpartum blood loss (mL) [‡]	199.95±124.69	219.18±188.32	0.01
Postpartum hemorrhage, no. (%)	66 (2.8%)	77 (3.8%)	0.054
Severe postpartum hemorrhage, no. (%) [‡]	8 (0.33%)	16 (0.8%)	0.041
Neonatal outcomes, no. (%)			
Apgar score at 1 min (4–7)	3 (0.1%)	8 (0.4%)	0.074
Apgar score at 1 min (<4)	1 (0)	0 (0)	0.357
Hyperbilirubinemia	628 (26.6%)	583 (29.05%)	0.072
Perinatal death	0	0	NC
Neonatal sepsis	21 (0.89%)	16 (0.8%)	0.74
Neonatal pneumonia	22 (0.93%)	16	0.633
Neonatal brain injury	1 (0)	0 (0)	0.357
Neonatal intracranial	2 (0.09%)	1 (0.05%)	0.66

hemorrhage			
NICU admission [‡]	51 (2.16%)	75 (3.74%)	0.002
Sex of the newborn, no. (%)			
Male	1098 (46.51%)	950 (47.33%)	0.584
Female	1263 (53.49%)	1057 (52.67%)	0.584
Birth weight (g), no. (%)			
≤2500	3 (0.1%)	3 (0.1%)	0.21
2501–3999	2169 (91.9%)	1864 (92.9%)	0.20
≥4000	189 (8.0%)	140 (7.0%)	

[‡]P values were <0.05.

Abbreviations: NC: not calculate; NICU: neonatal intensive care unit

Table 2. Correlation between the duration of labor and induction of labor

	Spontaneous onset of labor (n=2361) n (%)	Induction of labor (n=2007) n (%)	P value
Duration of labor (h)			
First stage of labor [‡]	8.17±4.88	8.62±5.12	0.003
Second stage of labor [‡]	0.55±0.69	0.65±0.78	<0.001
Third stage of labor	0.11±0.11	0.12±0.12	0.314
Total stages of labor [‡]	8.82±5.13	9.37±5.37	0.001

The total duration of labor and the duration of each stage of labor in the induction of labor group were longer than those in the spontaneous onset of labor group, and there were significant differences between the two groups in the first and second stages of labor and the total duration of labor. [‡]P<0.05.

Table 3. Induction of labor in nulliparous women with a longer duration of labor

	Parity			
	1	2	3	>3
Total duration of labor (h)	11.07±5.12	5.29±3.32	4.29±2.82	4.18±0.77
<i>P</i>	<0.001			

Nulliparous women had the longest total duration of labor, and the time shortened with an increase in the number of parturitions.

Table 4. Induction of labor and postpartum hemorrhage in nulliparous women

Group	Cases	Parity			
		1	2	3	>3
Spontaneous onset of labor group	2361	39 (1.65%)	25 (1.06%)	2 (0.08%)	0
Induction of labor group	2007	55 (2.74%)	3 (0.15%)	1 (0.05%)	0
OR (95% CI)	-	1.557 (1.039–2.332)	1.103 (0.635–1.917)		
<i>P</i>	-	0.03	0.671	0.794	NC

Induction of labor in nulliparous women increased the risk of postpartum hemorrhage, but there was no significant difference in multipara women.

OR: odds ratio; CI: confidence interval; NC: not calculate.

Figures

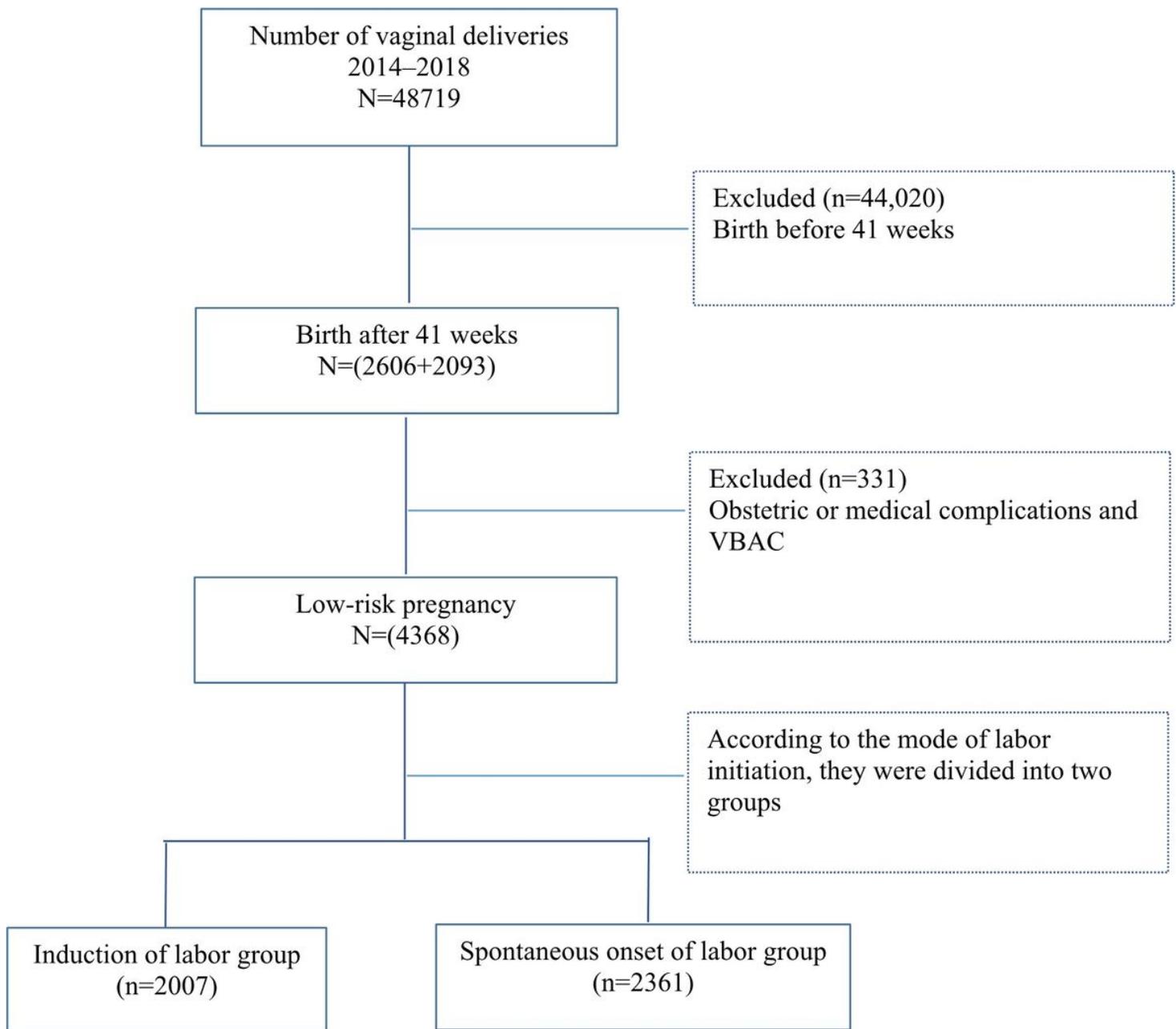


Figure 1

Flowchart of subject selection. VBAC=vaginal birth after cesarean section

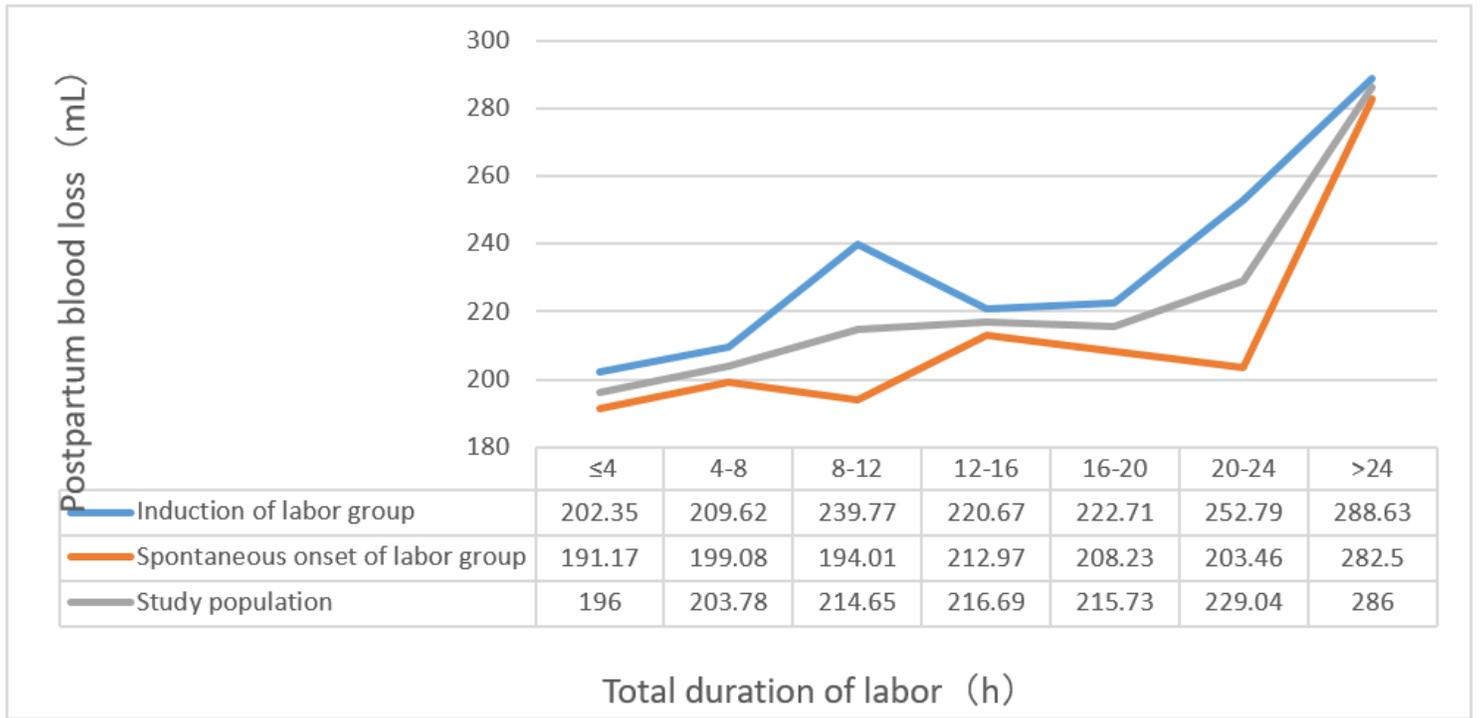


Figure 2

Relationship between the total duration of labor and postpartum blood loss. Postpartum blood loss increases with the prolongation of the total duration of labor. Moreover, the induction of labor group had higher postpartum blood loss than the spontaneous onset of labor group for the same total duration of labor.