Epidural analgesia during labor and its optimal initiation time-points

A real-world study on 400 Chinese nulliparas

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Abstract

Recent research has suggested that 6 cm of cervical dilation should be the threshold for the active labor phase, and it has confirmed that epidural analgesia (EA) is a safe method of pain relief during labor. However, the evidence provided for these findings comes mainly from randomized controlled clinical trials (RCTs), which suffer from the limitation of real-world generalizability.

To test the generalizability of the conclusions from these previous RCTs, we conducted a prospective cohort, real-world study (RWS) on 400 Chinese term nulliparas. A total of 200 of the participants (the EA group) received EA upon request. The participants in the EA group were further subdivided as follows according to their cervical dilation when the EA administration was initiated (CDE): [EA1 group (CDE < 3 cm), EA2 group (3 cm < CDE < 6 cm), and EA3 group (CDE ≥ 6 cm)]. We compared the labor duration of the EA group versus the non-EA (NEA) group, and the NEA group versus the 3 EA subgroups. We also compared delivery outcomes between the EA and NEA groups.

The median total labor duration for the EA group [676 (511–923) minutes] was significantly longer than that of the NEA group [514 (373–721) minutes] (P < 0.001). The median durations of both the first- and second-stages of labor for the EA group [600 (405–855) minutes, 68 (49–97) minutes] were longer than those of the NEA group [420 (300–630) minutes, 50 (32–85) minutes] (P < .001, P < .001). In addition, the median total labor durations in both the EA1 [720 (548–958) minutes] and EA2 groups [688 (534–926) minutes] were longer than in the NEA group (P < .001 and P < .001, respectively), and the first- and second-stage labor durations of these subgroups were similar to their total labor durations. A Cox regression analysis showed that EA was associated with longer first-stage labor [hazard ratio (HR) 0.55, 95% confidence interval (CI) 0.42–0.71, P < .001] and longer second-stage labor (HR 0.66, 95%CI 0.51–0.85, P = .001). The delivery modes and neonatal outcomes between the EA and NEA groups were not statistically different, however.

Our findings suggest that EA administered before a cervical dilation of 6 cm may be associated with longer total, first-, and second-stage labor durations compared with no EA, while later EA administration is not. In addition, though EA prolongs labor duration, it does not impact delivery outcomes. These results confirm the significance of a 6 cm cervical dilation threshold in real-world labor settings.

Abbreviations: ACOG/SMFM = American Congress of Obstetricians and Gynecologists and Society for Maternal-Fetal Medicine, BMI = maternal body mass index, BPD = biparietal diameter, CDE = cervical dilation when initiating epidural, CI = confidence interval, EA = epidural analgesia, HR = Hazard Ratio, NEA = non-epidural analgesia, PROM = premature rupture of membranes, RCT = randomized controlled trial, RWS = real-world study, VAS = visual analog scale.

Keywords: analgesia, cervical dilation, labor pain, labor stage, real-world study
1. Introduction

In the past 2 decades, an increase in the cesarean delivery rate has caused great concern about its overuse.\(^1\) Many women are choosing cesarean delivery for various medical reasons, such as labor arrest and non-reassuring fetal tracing, as well as some non-medical reasons, such as simple maternal preference and the fear of labor pain.\(^2,3\) The assurance of adequate pain management is important if unnecessary cesarean deliveries are to be reduced.\(^4\) Epidural analgesia (EA) is well-accepted for labor pain relief,\(^5,6\) however, there is still a debate regarding the in

Many factors influence labor duration, with labor practice being the primary concern.\(^12,13\) Zhang et al reported that contemporary labor practices differ significantly from the traditional Friedman curve.\(^14\) In nulliparas, the active labor phase may not even start until the cervical dilation is greater than 3 cm.\(^15,16\) On the basis of studies by Zhang, the American Congress of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine (ACOG/SMFM) jointly developed new labor guidelines in 2014.\(^1,17\) In these new guidelines, which have greatly impacted labor practices since their inception, it is recommended that a cervical dilation of 6 cm should be considered the threshold for the active labor phase.\(^18–20\) This recommendation affects the use of EA in the delivery room, as EA and the timing of its administration influence labor duration.\(^21\) Studies on the effects of EA under the new ACOG/SMFM guidelines are limited, however.

The studies on EA and the new labor guidelines that have been conducted are mainly randomized controlled trials (RCTs), which have long been regarded as the “gold standard” for evaluating the efficacy of interventions. However, RCTs have well-known limitations regarding their generalizability.\(^22\) Recently, real-world studies (RWS) have garnered increased interest, as they generate more realistic and generalizable evidence.\(^23,24\) With this in mind, we designed a large prospective cohort RWS to test the generalizability of the conclusions from the previous RCTs in a more authentic setting. We followed the new ACOG/SMFM labor recommendations and investigated the best EA initiation timing, as well as the possible impacts of EA on delivery outcomes. We hypothesized that initiating EA administration after 6 cm of cervical dilation does not prolong the duration of labor, and that EA administration does not have a negative impact on delivery outcomes.

2. Materials and methods

2.1. Ethical approval

We conducted this study between May and October of 2018 at Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology (Wuhan, Hubei). The institutional review board of Tongji Hospital approved the study (ID: TJ-IRB20180513; Date: May 23, 2018). Although not a clinical trial,\(^25\) according to the policies of clinicaltrials.gov, and given the significance of cohort studies,\(^26\) this cohort study was registered at www.clinicaltrials.gov (ID: NCT03381495; Date: July 11, 2018). Written informed consent was obtained from all participants. During the study period, the overall epidural labor analgesia rate at our institution was approximately 53.1%.\(^27\)

2.2. Participants and procedures

We recruited 400 healthy nulliparas at term (vertex presentation, singleton pregnancy) with planned vaginal deliveries when they were sent to the delivery room, and their cervical dilations were at least 0.5 cm. Those who requested and received EA before full cervical dilation were included in the EA group, while the remaining participants, who refused and did not receive EA during labor, were included in the non-epidural (NEA) group. The exclusion criteria were contraindications to neuraxial techniques (e.g., coagulopathy, increased intracranial pressure), scarred uterus, placenta previa, cephalopelvic disproportion, severe obstetric comorbidities or complications (e.g., severe heart defects, severe hepatitis, idiopathic thrombocytopenic purpura, severe preclampsia, and eclampsia). All the participants were inpatient women, and no one was lost to follow-up.

Upon a patient’s request for EA, the obstetrician and anesthetist performed a pre-procedural comprehensive assessment. If no contraindications existed, formal consent was obtained from the patient. Two junior anesthetists were on 24-hour duty in the delivery room, and 1 senior anesthetist was on 24-hour call. The time to initiate the EA administration depended on the timing of the patient’s request. Before the EA puncture, senior midwives or obstetricians examined and recorded the dilation of the patient’s cervix. We divided the EA group into the following 3 subgroups according to the women’s cervical dilation at the initiation of the EA administration (CDE): the EA1 group (CDE < 3 cm), the EA2 group (3 cm ≤ CDE < 6 cm), and the EA3 group (CDE ≥ 6 cm) (Fig. 1). We chose the CDE cut-offs for each of the subgroups based on the threshold of the active labor phase in the traditional Friedman curve\(^14\) and the contemporary labor curve.\(^1,15,16\)

We administered the EA in the left lateral position at the L2–3 or L3–4 interspace for the parturients who requested it. This involved placing a 19-G epidural catheter (Arrow International, Reading, PA) through a 16-G epidural needle (SCW Medical, Shenzhen, China) into the epidural space. The catheter was used to administer the drugs into the epidural space during labor. First, we injected a test dose of 5 mL of 1% lidocaine to observe if the mother had any side effects (e.g., perioral numbness, ringing in the ears, or a metallic taste in the mouth). If no adverse effects were observed 10 minutes after the test dose, we then administered a bolus injection of a mixture of 0.075% ropivacaine and 0.2 μg/mL sufentanil (initial dose: 8–10 mL). Afterward, we connected the epidural catheter to a patient-controlled EA pump, and the ropivacaine and sufentanil mixture was administered through the pump (bolus: 5 mL; lock out time: 10 minutes) into the catheter to optimize pain relief until the neonate was delivered. After the delivery, we injected a dose of 10 mL 0.2% ropivacaine to keep the patient comfortable during the third stage of labor and the process of laceration repair. We removed the catheter after the laceration repair was complete.

Because most Chinese parturients refuse to receive systematic analgesia, such as opioids, intramuscularly or intravenously because of a concern for the influence of the drugs on the neonate, we offered nonpharmacological analgesic methods (i.e., Doula accompaniment in combination with Lamaze breathing) for the parturients who refused the EA. A Doula midwife provided psychological and physical care, as well as mental and spiritual support, during the entire labor process. Those who refused EA and received nonpharmacological analgesic methods during labor were included in the NEA group. We also offered these nonpharmacological analgesic methods to the parturients in the EA group before initiating the EA administration.

All the parturients who desired a vaginal delivery were sent to the delivery room with a cervical dilation of at least 0.5 cm and regular uterine contractions at least every 5 minutes. We combined the new labor recommendations\(^1,28\) and the standard...
procedures in the Obstetrics and Gynecology Guidelines published by the People’s Medical Press to guide labor management for all the participants. The onset of labor was defined as the time in which there were regular uterine contractions, cervical effacement, and a descending fetus. We chose a cervical dilation of 6 cm as the threshold for the active labor phase based on studies by Zhang et al[15,16] and the ACOG/SMFM[1,17] labor recommendations. Active-phase arrest in the first stage of labor was defined as >6 cm of cervical dilation with ruptured membranes, plus one of the following criteria: ≥4 hours of adequate uterine contractions; or ≥6 hours of inadequate contractions and no cervical change. Arrest of the second stage was performed after at least 3 hours of pushing in the nulliparas without EA, and 4 hours of pushing in the nulliparas with EA. Midwives and obstetricians performed cervical examinations for the parturients at intervals of less than 2 hours, and when necessary, infused oxytocin to augment the labor progress according to the clinical guidelines. We asked all the parturients to push early at the beginning of full cervical dilation. The first-stage labor duration was defined as the time from the onset of labor to full cervical dilation. Postpartum hemorrhaging was defined as blood loss exceeding 500 mL during a vaginal delivery, or greater than 1000 mL during a cesarean delivery.[29,30]

2.3. Outcome measures
The primary outcome was labor duration, including the total labor duration and the durations of the 3 stages of labor. The secondary outcomes were the delivery outcomes, including the mode of delivery, rate of oxytocin infusion during labor, episiotomy rate, degree of pain, and muscle strength. We used a visual analog scale (VAS), ranging from 0 to 10 (a 10 cm line with endpoints labeled “no pain” and “worst imaginable pain”), to measure pain during the latent and active phases, full cervical dilation, crowning of the head, and laceration repair. To measure patient muscle strength at the same time points, we used a modified Bromage score, which had 4 categories: 0 - no motor paralysis; 1 - inability to raise an extended leg, but able to move the knee and foot; 2 - inability to raise an extended leg and move the knee, but able to move the foot; and 3 - inability to raise an extended leg or move the knee and foot.[31] We also recorded neonatal outcomes, including 1-minute and 5-minute Apgar scores, the neonatology department admission rate, and a blood gas analysis of the umbilical artery.[32]

2.4. Sample size estimation and power analysis
As this was an RWS, instead of an RCT, we did not implement a sample size estimation. Utilizing the G*Power software package (http://www.gpower.hhu.de/), version 3.1.9.2, we instead performed a post-hoc power analysis based on our results.

2.5. Statistical analysis
The statistical analyses were performed using SPSS version 23.0 (IBM). Depending on the distribution, we compared continuous
variables using the 2-tailed Student t test or the Mann–Whitney U test for 2 groups and a 1-way analysis of variance (ANOVA) or the Kruskal–Wallis test for 3 or more groups. Categorical variables were compared using the χ² or Fisher exact tests. Continuous variables were described as mean ± SD when normally distributed or median (interquartile range) when non-normally distributed, and categorical variables were described as numbers (percentages). For single comparisons, a Bonferroni corrections to multiple comparisons. For the primary outcome variable (labor duration), we constructed and compared Kaplan–Meier curves with log rank tests. In addition, we used a Cox regression to examine the association between predictors and prolonged labor duration. We included the following predictors: EA, maternal age, maternal body mass index (BMI), gestational age, gravidity, gestational diabetes mellitus, premature rupture of membranes (PROM), induction of labor, and biparietal diameter (BPD) measured in the last fetal Doppler color ultrasonic treatment.[33]

3. Results

3.1. Demographic characteristics

In total, 400 parturients participated in our study, of which 200 were administered EA during labor, while the others received nonpharmacological analgesic methods. A flow-process diagram of this study is presented in Figure 1. The demographic and obstetrical characteristics of the participants are summarized in Table 1. There were no statistically significant differences between the 2 groups.

3.2. EA and labor duration

The median total labor duration in the EA group was significantly longer than that of the NEA group [676 (511–923) vs 514 (373–721) minutes, \( P < .001 \)]. Among the 3 stages of labor duration, we found that the median first-stage labor duration in the EA group was longer compared to the NEA group [600 (403–855) vs 420 (300–630) minutes, \( P < .001 \)]. We found the same for the median second-stage labor duration [68 (49–97) vs 50 (32–85) minutes, \( P < .001 \)]. However, there was no statistical difference in the median third-stage labor durations between the 2 groups [7

| Table 1  |
| --- |
| **Demographic and obstetrical characteristics.** |
| Characteristics | NEA group | EA group | \( P \) |
| --- | --- | --- | --- |
| Maternal age, year | 28 (26, 30) | 28 (26, 30) | .830 |
| Pregnancy BMI, kg/m² | 26.1 ± 3.2 | 26.4 ± 3.0 | .361 |
| Gravidity | 1 (1–2) | 1 (1–1) | .132 |
| Gestational age, week | 40 (39, 40) | 40 (39, 40) | .748 |
| Premature rupture of membranes | 49 (24.5) | 52 (26.0) | .730 |
| Gestational diabetes mellitus | 31 (15.5) | 28 (14.0) | .672 |
| Cervical ripening/Labor induction | Cook balloon | 1 (0.5) | 1 (0.5) | >.999 |
| | Dinoprostone | 31 (15.5) | 28 (14.0) | .672 |
| | Oxytocin | 1 (0.5) | 2 (1.5) | .623 |

Values are given as mean ± standard deviation, median (interquartile range) or number (percentage), unless indicated otherwise. BMI = body mass index, EA = epidural analgesia, NEA = nonepidural analgesia.

(5–10) vs 6 (5–10) minutes, \( P = .200 \). These differences are graphically displayed in Figure 2 using Kaplan–Meier curves.

3.3. Initiation timing of EA and labor duration

The relationship between the initiation timing of the EA administration and labor duration is summarized in Table 2. The median total labor duration was significantly different between the NEA and EA1 groups (\( P < .001 \)), as well as between the NEA and EA2 groups (\( P < .001 \)) (Fig. 3A). The median first- and second-stage labor durations were significantly different between the groups as well (1st stage: EA1 vs NEA, \( P < .001 \); EA2 vs NEA, \( P < .001 \)) (Fig. 3B,C). However, the labor durations were not significantly different between the NEA and EA3 groups (\( P > .05 \)) or the EA1 and EA2 groups (\( P > .05 \)).

The post-hoc power analyses comparing the total labor durations of the NEA and EA3 groups showed that, given the observed results shown in Table 2 (resulting in an effect size of 0.08), the power to detect this difference was only 8%. On the contrary, in order to detect this effect at 80% power, we needed 6134 patients in the NEA group and 1534 patients in the EA3 group. These large sample sizes are not practical. In addition, an effect size of 0.08 is negligible.

![Figure 2](image-url)
Table 2
Comparison of labor duration in NEA group and 3 epidural subgroups.

| Labor duration , min | NEA group (N = 191) | EA1 group (N = 95) | P (EA1/NEA) | EA2 group (N = 47) | P (EA2/NEA) | EA3 group (N = 46) | P (EA3/NEA) | P (EA1/EA2) |
|----------------------|---------------------|-------------------|--------------|-------------------|--------------|-------------------|--------------|-------------|
| The total labor      | 514 (373, 721)      | 720 (548, 958)    | < .001†      | 688 (534, 926)    | < .001†      | 532 (377, 740)    | .751         | .387        |
| The first stage of labor | 420 (300, 630)    | 675 (450, 900)    | < .001†      | 600 (413, 840)    | < .001†      | 465 (289, 710)    | .456         | .295        |
| The second stage of labor | 50 (32, 85)        | 69 (49, 96)       | .001†        | 79 (63, 121)      | < .001†      | 64 (59, 88)       | .123         | .118        |
| The third stage of labor | 6 (5, 10)          | 6 (5, 10)         | .591         | 7 (5, 10)         | .437         | 7 (5, 10)         | .091         | .741        |

Values are given as median (interquartile range).
EA = epidural analgesia, NEA = nonepidural analgesia.
† Parturients of cesarean delivery were excluded.
* Statistically significant.

3.4. EA and delivery outcomes

As summarized in Table 3, no statistical differences were observed in the delivery modes between the EA and NEA groups (P > .05). However, the EA group had higher rates of oxytocin infusion (49.5% vs 29.0%, respectively, P < .001) and episiotomy (41.5% vs 29.4%, respectively, P = .013) during labor than the NEA group. No parturients in the EA and NEA groups had second to fourth degree perineal tears.

The median VAS (Fig. 4A) and modified Bromage scores (Fig. 4B) of the EA and NEA parturients were graphed at 5 time points (latent phase, active phase, full dilation of the cervix, crowning of the head, and laceration repair) during the entirety of labor. The figure shows progressive changes in the degree of pain and muscle strength during labor in the two groups, as the parturients administered EA exhibited a significant decrease in the VAS compared with those without EA (all P < .001). There was no significant difference in the modified Bromage scores (P > .05) between the groups, however.

Neonatal outcomes were not significantly different between the EA and NEA groups, and the blood gas analysis of the umbilical cord arteries also showed no significant differences in the pH and base excess extracellular fluid (BE-ecf) (P > .05).

3.5. Cox regression analysis: first- and second-stage labor duration

The Cox regression results are summarized in Table 4. The results show that EA administration was associated with a longer first-stage labor duration [hazard ratio (HR) 0.55, 95% confidence interval (CI) 0.42–0.71, P < .001]. We also found that other factors, including gestational age and PROM, influenced first-stage labor duration. EA administration was also significantly associated with a longer second-stage labor duration (HR 0.66, 95% CI 0.51–0.85, P = .001), with maternal age being a possible contributor.

4. Discussion

In Eastern cultures, there is great importance placed on childbirth being a natural process, and the use of EA for the management of labor pain has received little interest. In addition, misconceptions regarding the safety of EA have contributed to the lack of widespread EA use in many Eastern countries.

Our results demonstrate that parturients administered EA exhibited a significant decrease in the VAS, which show the effectiveness of EA in labor pain relief. And we also find that the EA group presented higher VAS compared with the NEA group in the latent phase, which may attribute to the fact that women feeling more pain in the early first stage of labor has more tendency to ask for EA. EA administration during labor does not have an adverse effect on maternal muscle strength, delivery modes, and neonatal outcomes. However, the timing of EA administration initiation is associated with labor duration.

Our results show that EA may be associated with prolonged labor duration. The first- and second-stage labor duration was longer in the EA1 (CDE < 3 cm) and EA2 (3 cm ≤ CDE < 6 cm) groups than in the NEA group. However, EA administration did not have an adverse influence on labor duration in the EA3 (CDE < 6 cm) groups.

Figure 3. Kaplan–Meier curves for the labor durations of parturients in the 3 EA Subgroups and the NEA group. CDE = cervical dilation when the epidural analgesia administration was initiated, EA = epidural analgesia, NEA = nonepidural analgesia.
≥6 cm) group. These results show that initiating EA administration at a cervical dilation of ≥6 cm does not prolong first- and second-stage labor, compared with those without EA administration, whereas earlier EA administration does. Furthermore, the labor duration did not differ significantly between the EA1 and EA2 groups, which indicates that initiating EA administration before the cervical dilation is 3 cm or delaying administration until it is 3 to 6 cm has no significant effect on labor duration. These findings are consistent with the ACOG/SMFM guidelines indicating that a cervical dilation of ≥6 cm should be considered the threshold for active labor. Because the cervix dilates more rapidly during the active labor phase and is rarely affected by outside factors,[29,30] it is unsurprising that initiating EA at a cervical dilation of ≥6 cm is not associated with prolonged labor duration.

Considering that most parturients suffer severe pain during the latent phase, initiating EA after a cervical dilation of 6 cm seems too late to offer a satisfactory delivery experience for the mother. As no significant differences were found in the duration of labor between the EA1 and EA2 groups, it is not necessary to delay EA initiation when the cervical dilation is less than 3 cm. The ACOG guidelines for obstetric analgesia and anesthesia suggest that maternal request is a sufficient medical indication for alleviating labor pain when there is no medical contraindication, therefore, every parturient who asks for EA during labor should not be deprived of this service,[34] regardless of cervical dilation.

Table 3
Comparison of delivery outcomes between EA group and NEA group.

| Delivery outcomes                  | NEA group (N = 200) | EA group (N = 200) | P   |
|-----------------------------------|---------------------|-------------------|-----|
| Mode of delivery:                 |                     |                   |     |
| Spontaneous vaginal delivery      | 191 (95.5)          | 187 (93.5)        | .380|
| Instrumental delivery             | 0 (0)               | 1 (0.5)           | >.999|
| Cesarean delivery                 | 9 (4.5)             | 12 (6.0)          | .494|
| Indication for cesarean           |                     |                   |     |
| Labor arrest                      | 3 (1.5)             | 4 (2.0)           | .724|
| Nonreassuring fetal status        | 2 (1.0)             | 5 (2.5)           | .449|
| Nonreassuring fetal tracing       | 3 (1.5)             | 2 (1.0)           | >.999|
| Maternal request                  | 1 (0.5)             | 1 (0.5)           | >.999|
| Episiotomy                       | 57 (28.4)           | 78 (41.5)         | .013†|
| Oxytocin infusion during labor    | 58 (29.0)           | 99 (49.5)         | <0.001†|
| Postpartum hemorrhage             | 7 (3.5)             | 9 (4.5)           | .610|
| Neonatal outcomes:                |                     |                   |     |
| Birth weight, kg                  | 3.3 (3.0, 3.5)      | 3.3 (3.1, 3.6)    | .616|
| 1 min Apgar score < 7             | 5 (2.5)             | 10 (5.0)          | .188|
| 5 min Apgar score < 7             | 1 (0.5)             | 1 (0.5)           | >.999|
| Admission to neonatology department | 34 (17.0)       | 33 (16.5)         | .893|
| Blood gas analysis of umbilical artery |               |                   |     |
| PH                               | 7.27 ±0.09          | 7.24 ±0.08        | .226|
| BE-ecf, mmol/L                   | −6.25 ±3.26         | −6.34 ±3.15       | .799|

Values are given as mean ± standard deviation, median (interquartile range) or number (percentage), unless indicated otherwise.

BE-ecf = base excess extracellular fluid, EA = epidural analgesia, NEA = non-epidural analgesia, PH = a solution indicates how acid or alkaline the solution is.

† Parturients of cesarean delivery were excluded from the percentage.

‡ Statistically significant.

Figure 4. The Visual Analog Scale (VAS) and Modified Bromage Scores between EA and NEA Groups. Black arrows: initiation time of EA. Only parturients who initiate epidural at the latent phase (<6 cm) were included. All P values of VAS between the two groups were less than .01. All P values of Modified Bromage Scores between 2 groups were larger than .05. EA = epidural analgesia, NEA = non-epidural analgesia.
et al.[7] and Ohel et al.[8] reported that early EA administration was associated with longer labor duration, however. Furthermore, initiating EA administration before a cervical dilation of 6cm may be associated with longer first- and second-stage labor durations compared with those who do not initiate EA administration. Later EA administration is not associated with longer labor duration, however. Moreover, initiating EA administration before a cervical dilation of 3cm or delaying it until the cervical dilation is 3 to 6cm does not have a statistically significant effect on labor duration. Therefore, when a woman requests EA after the onset of labor, it is appropriate to initiate administration regardless of the cervical dilation. Although EA administration may have a prolonging effect on labor duration, depending on when it is administered, it does not have an adverse effect on the delivery modes and neonatal outcomes.

### 5. Conclusion

In a real-world setting, nulliparas who initiate EA administration before a cervical dilation of 6cm may be associated with longer first- and second-stage labor durations compared with those who do not initiate EA administration. Later EA administration is not associated with longer labor duration, however. Furthermore, initiating EA administration before a cervical dilation of 3cm or delaying it until the cervical dilation is 3 to 6cm does not have a statistically significant effect on labor duration. Therefore, when a woman requests EA after the onset of labor, it is appropriate to initiate administration regardless of the cervical dilation. Although EA administration may have a prolonging effect on labor duration, depending on when it is administered, it does not have an adverse effect on the delivery modes and neonatal outcomes.

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### Table 4

Cox regression analysis: the first- and second-stage labor duration.

| Variables                             | The first-stage labor duration | P       | The second-stage labor duration | Hazard ratio (95% CI) | P       |
|---------------------------------------|--------------------------------|---------|---------------------------------|-----------------------|---------|
| Epidural analgesia                    | 0.55 (0.42–0.71)               | <.001†  | 0.66 (0.51–0.85)                | **.001†**             |         |
| Maternal age, year                    | 1.00 (0.97–1.04)               | .938    | 0.96 (0.93–1.00)                | .024†                 |         |
| Pregnancy BMI, kg/m²                  | 0.99 (0.94–1.03)               | .533    | 0.97 (0.93–1.01)                | .118                  |         |
| Gravidity                             | 1.02 (0.92–1.28)               | .830    | 1.15 (0.92–1.44)                | .255                  |         |
| Gestational age, week                 | 0.87 (0.77–0.99)               | .034†   | 1.02 (0.89–1.16)                | .837                  |         |
| Gestational diabetes mellitus         | 1.17 (0.81–1.71)               | .402    | 0.94 (0.66–1.34)                | .719                  |         |
| Premature rupture of membranes        | 1.53 (1.14–2.06)               | .005†   | 1.10 (0.82–1.45)                | .546                  |         |
| Cervical ripening/Labor induction      | 1.34 (0.93–1.92)               | .115    | 1.02 (0.71–1.47)                | .980                  |         |
| Biparietal diameter of fetal, cm      | 1.45 (0.99–2.12)               | .055    | 0.99 (0.69–1.43)                | .991                  |         |

BM = body mass index, CI = confidence interval.
† Biparietal diameter measured in the last fetal Doppler color ultrasonic.
∗ Statistically significant.
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