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## Induction of labor in late-term pregnancy: amniotomy plus early oxytocin perfusion versus amniotomy plus oxytocin perfusion delayed by 24 h

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### Abstract

**Objective:** To assess the maternal and fetal benefits of delaying oxytocin perfusion by 24 h following labor induction by amniotomy after 41 weeks of gestation (WG).

**Methods:** We performed a retrospective review including all women with a vertex presentation fetus who had an indication for labor induction by amniotomy with or without oxytocin after 41 WG between 2015 and 2022. Patients who underwent an IOL by amniotomy followed by oxytocin perfusion within 0 to 4 hours (early oxytocin group: EO group) were compared with patients who underwent an IOL by amniotomy alone or followed by an oxytocin perfusion after an expectant period for up to 24 hours in the absence of a spontaneous onset of labor (delayed oxytocin group: DO group). The primary outcome was the rate of vaginal delivery (natural or operative). The secondary outcomes were maternal and neonatal complications.

**Results:** We included 363 patients: 103 patients in the EO group and 260 in the DO group. Only 47 of the women in the DO group (18%) required oxytocin. The proportion of vaginal deliveries was significantly higher in the DO group (248 patients, 95.4%) than in the EO group (85 patients, 82.55%) ( $p<0.01$ ). Maternal morbidity did not differ significantly between groups. Fewer babies displayed severe newborn acidemia or required transfer to the neonatal intensive care unit in the DO group ( $p<0.05$ ).

**Conclusion:** Delaying oxytocin administration by 24 hours after amniotomy was associated with a significantly higher rate of vaginal delivery. These results required confirmation in prospective randomized studies.

### **Keywords**

Induction of labor, late-term pregnancy, amniotomy, oxytocin

### **Introduction**

The induction of labor (IOL) in late-term pregnancy is a crucial intervention in obstetric care, accounting for 28.7% of IOL indications [1]. Several studies have demonstrated that the IOL after 41 weeks of gestation (WG) significantly decreases perinatal morbidity and mortality [2].

Amniotomy with intravenous (IV) oxytocin is the preferred method of IOL in patients with a mature cervix [3]. However, due to the lack of existing evidence, the ideal interval between amniotomy and oxytocin perfusion remains unclear and is not specified by French guidelines. Instead, this timing of the oxytocin perfusion is left to the discretion of the maternity units. The small number of trials investigated different intervals found no differences in terms of rates of caesarean delivery or fetal morbidity. However, in most of these studies, the interval considered was no more than four hours, which may be too short a time span for a difference to be detectable [4].

Seller et al. demonstrated that amniotomy resulted in high levels of prostaglandins, which are known to contribute to the pathogenesis of inflammatory processes and myometrial contractility, thereby initiating the onset of labor [5, 6]. However, we hypothesize that this action may begin later in some patients. Indeed, in an analogous situation, in the TERMPROM study, a spontaneous onset of labor was observed within 15 hours of membrane rupture in only 15% of patients experiencing a prelabor rupture of the membrane (PROM) at term, whereas labor began spontaneously within 24 hours of membrane rupture in 64% [7]. No increase in fetal morbidity was observed, but the rate of maternal infection increased after 15-20 hours [8]. National Institute for Health and Care Evidence (NICE) guidelines suggest an expectant period for up to 24 hours [9].

Given that oxytocin perfusion may be unnecessary after amniotomy in 19-68% of women [10, 11], an expectant approach could potentially decrease the use of oxytocin and associated adverse effects, including postpartum hemorrhage, uterine hyperstimulation, high levels of pain, tachycardia, bradycardia, headaches, and nausea [12, 13].

We therefore decided, in 2018, to allow an interval of 24 hours between amniotomy and intravenous oxytocin perfusion in late-term pregnancy if patients did not go into labor spontaneously. The objective of this study was to assess the outcomes of delaying the injection of oxytocin after amniotomy, in terms of its effects on the mode of delivery, and on maternal and neonatal morbidity.

## **Methods**

### **Patient selection**

Following institutional IRB approval (No. 24.30) of the study, we reviewed all consecutive births between 41 and 41+6 WG from 2015 to 2022, identified with the P08 and P82 codes of the International Classification of Diseases. Five hundred medical records collected before 2018 could not be accessed for evaluation.

The inclusion criteria were deliveries of babies in a vertex presentation in women undergoing an IOL by amniotomy at 41 and 41+6 weeks of gestation. The exclusion criteria included a history of cesarean section, spontaneous prelabor membrane rupture and oxytocin administration between 4 and 24 hours after amniotomy without the onset of labor.

### **Monitoring of late-term pregnancy and protocol for the IOL**

Late-term pregnancy monitoring consisted of one visit every two days from 41+1 to 41+5 WG. During the first two visits, the following procedures were conducted: fetal cardiotocography (CTG), ultrasound assessment of amniotic fluid volume, urine analysis, and a recording of hemodynamic parameters. An IOL was proposed in cases of oligoamnios, decreases in fetal movement, metrorrhagia, high blood pressure, proteinuria and an absence of spontaneous labor onset by 41+5 WG.

Before 2018, oxytocin was administered immediately after amniotomy, or within a few hours of amniotomy, at various intervals. Since 2018, a protocol has been followed in which oxytocin is administered only after 24 hours of expectant management following amniotomy, if labor does not begin spontaneously. The IOL by amniotomy was considered in all patients in whom amniotomy was feasible, regardless of Bishop score, and without epidural anesthesia. Patients were transferred to the high-risk patient unit after two hours of observation following amniotomy for the expectant period.

Before 2017, oxytocin perfusion was started at a rate of 2.5 mIU/min, with an increase in the dose every 30 minutes up to a maximum of 20 mIU/min or until three or four uterine contractions per 10 minutes were observed. In 2017, the starting rate was decreased to 2 mIU/min in accordance with French National College of Obstetricians and Gynaecologists (CNGOF) guidelines [16]. For patients going into labor spontaneously after amniotomy, oxytocin was administered if cervical dilation stopped or if it was deemed necessary to accelerate labor. Labor arrest was defined as the absence of progression for 4 hours, at a cervical dilation of between 5 and 7 cm, or the absence of progression for 2 hours after reaching a diameter of 7 cm [16]. A cesarean section was considered if no change in cervical dilation was observed during the latent phase and no fetal distress was observed after 12-18 hours of oxytocin infusion. Antibiotic prophylaxis was administered 12 hours after the amniotomy [3].

### Data collection

Data were collected from medical records. The demographics included age, body mass index (BMI), parity, presence of *Streptococcus B*, gestational diabetes and Bishop score. The labor-related parameters considered were the duration of the latent phase, the time between IOL and birth, the total duration of oxytocin exposure, the mean maximum rate of oxytocin administration, antibiotic use, epidural anesthesia use, mode of delivery (natural vaginal delivery, operative vaginal delivery or cesarean delivery) and the occurrence of a high risk of acidosis and premortal fetal heart CTG abnormalities as defined by the CNGOF classification [17].

The maternal complications considered were hyperthermia ( $T^{\circ} > 38^{\circ}\text{C}$  confirmed at one-hour intervals) and post-partum hemorrhage (PPH), defined as the loss of more than 500 ml blood. The neonatal parameters collected were newborn weight, macrosomia (weight  $> 4$  kg), pH and lactate levels at birth, Apgar score [18], neonatal hospitalization, ventilation, and early neonatal bacterial infections. In accordance with European Association of Perinatal Medicine recommendations, severe newborn acidemia was defined as a pH below 7.1 and metabolic acidosis was defined as a pH lower than 7 together with a lactate concentration  $> 12$  mmol [19].

### Analysis strategy and outcomes

We assessed the effect of delaying oxytocin administration by comparing patients who underwent an IOL by amniotomy followed by oxytocin perfusion within 0 to 4 hours (early oxytocin group: EO group) with patients who underwent an IOL by amniotomy alone or followed by an oxytocin perfusion after an expectant period for up to 24 hours in the absence of a spontaneous onset of labor (delayed oxytocin group: DO group). The four-hour cutoff point was selected for the definition of the EO group in accordance with the results of two trials demonstrating an absence of significant difference between the immediate administration of intravenous oxytocin and administration after four hours [14, 15].

We first determined the demographics and labor progress characteristics of the two groups. We then compared the following outcomes between the two groups: the primary outcome was the rate of vaginal delivery (spontaneous and operative) and the secondary outcomes were maternal fever during labor and postpartum hemorrhage as maternal complications, and Apgar score  $\leq 7$  at 5 minutes,

lactate concentration  $\geq 5$  mmol/l, metabolic acidosis, severe acidemia, mask ventilation, early neonatal bacterial infection and transfer to the neonatal intensive care unit (NICU) as neonatal complications.

Finally, we assessed the robustness of our findings by performing several sensitivity analyses in which the sample was divided into subgroups. We first compared nulliparous and multiparous subjects. We then compared patients with Bishop scores of less than 6 with those with Bishop scores of 6 or above. We then compared the indication of no onset of labor at 41+5 weeks with other indications, including metrorrhagia, decrease in fetal movement, oligoamnios, and non-severe CTG abnormalities. Finally, a before-and-after analysis was conducted, comparing patients who underwent IOL before the protocol change (2015-2017) with those who underwent IOL after the protocol change (2018-2022).

## Statistics

Descriptive statistics are reported, with the median and interquartile range (IQR) for continuous variables, and frequencies and percentages for categorical variables. Mann-Whitney tests were used to compare continuous variables between the two groups. For categorical variables, Fisher's exact test or  $\chi^2$  tests were performed, depending on the expected number of patients in each category. Time to delivery was plotted on a Kaplan-Meier curve, and comparisons were performed with log-rank tests. Statistical analyses were performed in R software (R version 4.1.3, <http://www.r-project.org/>). All tests were two-tailed with  $P$  values  $<0.05$  considered significant.

## Results

### Demographics

In total, 480 of the 1413 late-term pregnancies met the inclusion criteria. The remaining patients were excluded due to a previous caesarean section in 55, prelabor membrane rupture in 42, and oxytocin administration within 4 to 24 hours after amniotomy without the induction of labor in 21. Ultimately, 363 patients were included in the study: 103 patients in the EO group and 260 in the DO group (see Figure 1).

The median age of the patients was 31 years (IQR: 27-35 years) in the EO group and 32 years (28-35 years) in the DO group ( $p=0.9$ ). The median BMI, gestational diabetes rates, and median Bishop scores did not differ significantly between the two groups ( $p>0.05$ ). However, the EO group included a significantly higher percentage of nulliparous women than the DO group: 36.9% (38 women) versus 23.8% (62 women) ( $p<0.01$ ). *Streptococcus* B colonization was detected in 13 patients (12.6%) from the EO group and 36 patients (13.9%) from the DO group ( $p=0.9$ ).

Over 70% of the patients in each group underwent induction at 41+5 WG due to absence of spontaneous labor, and the distribution of indications did not differ significantly between groups ( $p=0.08$ ). The demographics and indications for IOL are shown in Table 1.

### Description of labor progress

Labor characteristics are presented in Table 2. Labor was significantly shorter in the EO group, with a median duration of 7.3 hours (4.5-9.3 hours) versus 9.3 hours (6-14.1 hours) in the DO group ( $p<0.01$ ). Time to delivery is shown in Figure 2.

Oxytocin was administered to all women in the EO group, but only 18% of women in the DO group received any oxytocin ( $p<0.01$ ). Abnormal fetal CTG recordings were obtained for 50 fetuses (48.5%) in the EO group and 85 (32.7%) in the DO group ( $p<0.01$ ).

Rates of epidural anesthesia were similar in with the two groups, at 90.3% for the EO group and 82.9% for the DO group ( $p=0.1$ ). Antibiotics were administered more frequently in the DO group (39.2%) than in the EO group (19.4%) ( $p<0.01$ ).

### Maternal parameters

In total, 85 patients (82.55%) in the EO group and 248 patients (95.4%) in the DO group had a vaginal delivery ( $p<0.01$ ), this delivery being operative in 18 patients (17.5%) in the EO group and 39 (15%) in the DO group ( $p=0.6$ ) (Table 3). The Kiwi Omnicup Vacuum® was the instrument most frequently used, in 14 cases (77.8%) in the EO group and 36 (92.3%) in the DO group ( $p=0.18$ ).

The primary indication for cesarean section was labor arrest, in 8 patients (44.5%) in the EO group and 6 patients (50%) in the DO group. Abnormal CTG was the secondary indication in 8 patients in the EO group and 3 in the DO group ( $p=0.66$ ).

Six patients (5.8%) in the EO group and 29 (11.2%) in the DO group experienced fever during labor ( $p=0.17$ ). In addition, PPH occurred in 20 patients (19.4%) in the EO group and 32 (12.3%) in the DO group ( $p=0.09$ ).

### Newborn parameters

The median weight of newborns was 3715 g (3360-4050 g) in the EO group and 3712 g (3516-4017 g) in the DO group ( $p=0.22$ ). Macrosomia was detected in 26% of the newborns in each group. There was no difference between the groups for Apgar scores, rates of lactate concentration above 5mmol/l, metabolic acidosis and number of newborns requiring mask ventilation ( $p>0.05$ , Table 4). Early neonatal bacterial infection occurred in three newborns: one in the EO group (0.4%) and two in the DO group (2%) ( $p=0.19$ ). However, the proportion of newborns with severe acidemia was higher in the EO group (8.4%) than in the DO group (3.2%) ( $p=0.048$ ). Five newborns (4.9%) from the EO group were transferred to a neonatal care unit, versus only three (1.2%) in the DO group ( $p=0.04$ ).

### Stratified analysis

The sensitivity analyses for parity, Bishop score, and IOL indications are provided in the supplementary files (Tables S1, S2, and S3, respectively). The direction and intensity of the associations were similar in the two groups. A non-significant trend towards a higher rate of vaginal delivery was observed in the DO group for nulliparous patients (28/38, 73.7% in the EO group versus 55/62, 88.7% in the DO group,  $p=0.07$ ) and for patients with a Bishop score below 6 (24/28, 85.7% in the EO group versus 96/100, 96% in the DO group,  $p=0.07$ ).

The before-and-after study showed that the DO protocol was not used in 45 of 304 patients (14.8%) after 2018, whereas the EO strategy was used in 58 of 59 patients before 2018. The rate of vaginal delivery was higher among patients from the 2018-2022 period, with 287 vaginal deliveries (94.4%) versus only 46 (78%) before 2018 ( $p<0.01$ ).

### Discussion

In recent years, it has been shown that IOL is not necessarily more risky than spontaneous labor, leading to an increase in the number of patients undergoing IOL [20, 21]. Immediate oxytocin infusion is supported by most studies, but our results suggest that most women go into labor without oxytocin less than 24 hours after amniotomy (82%). We found that waiting 24 hours after amniotomy before initiating oxytocin administration significantly increased the rate of vaginal delivery. The benefits may be greater in multiparous women and patients with a Bishop score  $\geq 6$ .

Only a few trials have studied long intervals between amniotomy and oxytocin perfusion for IOL. The largest observational and retrospective series of cases of IOL by amniotomy without oxytocin for 24 hours was that studied by Cooley et al, which included 3,586 women and reported a spontaneous labor rate of 90%, consistent with our findings [22]. In a randomized trial, Titulaer et al. compared amniotomy plus immediate oxytocin perfusion with amniotomy plus oxytocin perfusion 12 hours later. No significant difference in mode of delivery was observed but this study included only 64 patients [11]. In the randomized trial performed by Moldin et al. and including 196 patients, amniotomy plus immediate oxytocin perfusion was compared with amniotomy with oxytocin perfusion delayed by 24 h. This trial also reported no significant difference in the mode of delivery [10]. Contrary to our study, both these studies included patients who had undergone prior cervical ripening or IOL from 36 to 37 weeks of gestation onwards. Given the increase in amniotic fluid prostaglandin levels throughout pregnancy, with a peak just before the onset of labor, the DO method might be expected to be more effective in our population of late-term pregnancies [21].

We observed a higher incidence of high-risk CTG abnormalities in the EO group, potentially due to the mechanism of uterine hyperstimulation induced by oxytocin [23]. Indeed, in a study of a cohort of 430 women, Johnsson et al. found that the occurrence of  $\geq 6$  uterine contractions in 10 minutes was associated with a higher risk of umbilical cord pH  $< 7.05$  [24]. However, the incidence of severe acidemia and NICU transfer in our cohort were too low for any firm conclusions to be drawn. The smaller number of cases of PPH in multiparous women provides further evidence in favor of limiting the use of oxytocin whenever possible, especially in women with a favorable cervix. Indeed, if Bishop score was below 6, no significant difference was observed, although there was a trend towards higher rates of vaginal delivery in the DO group.

The DO strategy may be challenging for maternity units to implement, given its association with prolonged labor. One potential strategy for managing the flow of patients would be to transfer patients to an antenatal care unit after an observation period of two hours. This organizational approach was found to increase the time spent in the delivery room by only one hour in the study conducted by Moldin et al. [10]. However, it nevertheless requires additional beds and health professionals dedicated to these patients, which may not be possible in many institutions, although this requirement can be offset by the decrease in cesarean deliveries. This management was also possible because amniotomy was not performed under epidural anesthesia. The patients could therefore move around and walk, but this entails a risk of umbilical cord injury and emergency cesarean delivery. However, no such events occurred in our study. The incidence of these complications was low, and our patients had low levels of exposure to the known risk factors, including abnormal fetal presentation, multiparity, low birth weight, prematurity, polyhydramnios and spontaneous membrane rupture, especially in patients with high Bishop scores [25].

This study was a contemporary analysis in real-life conditions, the second such investigation since 1996 to explore the benefits of a 24-hour observation period following amniotomy for IOL at late term [10].

The DO strategy aimed to reduce the use of oxytocin and its adverse effects. It may also be more in line with the birth plans of patients who wish to avoid epidural anesthesia because endogenous oxytocin is known to increase feelings of calm and to reduce pain, whereas synthetic oxytocin does not cross the blood-brain barrier in sufficient quantities to have such effects [26]. Further studies are needed to assess patient satisfaction, which has often been reported to decrease with increasing duration of labor [14].

This study is subject to several limitations. First, the number of patients in each group was unbalanced due to the lack of availability of 25% of the medical records before 2018 and because three years were included in the EO group versus five years in the DO group, potentially leading to a selection bias and an overrepresentation of caesarean sections. The introduction of the DO protocol coincided with the revised definition of normal labor and changes in oxytocin use. Some of the results obtained may reflect the use of this different protocol but Ahmadi et al. showed that the change in oxytocin use did not reduce the number of cesarean deliveries [25]. Finally, the cohort was divided according to the method used rather than the time period, due to the heterogeneity of protocol application. Maternal or fetal conditions may have led some obstetricians to initiate oxytocin administration immediately. However, the sensitivity analysis based on indication gave similar results and the before-and-after analysis showed a higher rate of vaginal delivery after the protocol change.

In conclusion, delaying oxytocin perfusion until 24 h after amniotomy may reduce the rate of cesarean deliveries, especially in multiparous women. However, further studies — including clinical trials — are warranted to replicate these findings and to assess the impact on maternal satisfaction.

**Declaration of interest:** None

**Ethics approval:** This study was approved by the ethics committee of Rennes University Hospital (no. 24.30).

**Findings:** None

## References

1. Blanc-Petitjean P, Salomé M, Dupont C, et al (2019) [Overview of induction of labor practices in France]. *Gynecol Obstet Fertil Senol* 47:555–561. <https://doi.org/10.1016/j.gofs.2019.05.002>
2. Hussain AA, Yakoob MY, Imdad A, Bhutta ZA (2011) Elective induction for pregnancies at or beyond 41 weeks of gestation and its impact on stillbirths: a systematic review with meta-analysis. In: Database of Abstracts of Reviews of Effects (DARE): Quality-assessed Reviews [Internet]. Centre for Reviews and Dissemination (UK)
3. Sénat M-V, Schmitz T, Bouchghoul H, et al (2022) Term prelabor rupture of membranes: guidelines for clinical practice from the French College of Gynaecologists and Obstetricians (CNGOF). *J Matern Fetal Neonatal Med* 35:3105–3109. <https://doi.org/10.1080/14767058.2020.1810230>

4. Pergialiotis V, Bellos I, Vrachnis N, et al (2022) Early versus delayed oxytocin infusion following amniotomy for induction of labor: a meta-analysis of randomized controlled trials. *J Matern Fetal Neonatal Med* 35:4889–4896. <https://doi.org/10.1080/14767058.2021.1872535>
5. Sellers SM, Mitchell MD, Anderson ABM, Turnbull AC (1981) The Relation Between the Release of Prostaglandins at Amniotomy and the Subsequent Onset of Labor. *BJOG: An International Journal of Obstetrics & Gynaecology* 88:1211–1216. <https://doi.org/10.1111/j.1471-0528.1981.tb01199.x>
6. Bakker R, Pierce S, Myers D (2017) The role of prostaglandins E1 and E2, dinoprostone, and misoprostol in cervical ripening and the induction of labor: a mechanistic approach. *Arch Gynecol Obstet* 296:167–179. <https://doi.org/10.1007/s00404-017-4418-5>
7. Melamed N, Berghella V, Ananth CV, et al (2023) Optimal timing of labor induction after prelabor rupture of membranes at term: a secondary analysis of the TERMPROM study. *Am J Obstet Gynecol* 228:326.e1-326.e13. <https://doi.org/10.1016/j.ajog.2022.09.018>
8. Hannah ME, Ohlsson A, Farine D, et al (1996) Induction of labor compared with expectant management for prelabor rupture of the membranes at term. TERMPROM Study Group. *N Engl J Med* 334:1005–1010. <https://doi.org/10.1056/NEJM199604183341601>
9. (2021) Recommendations | Inducing labor | Guidance | NICE. <https://www.nice.org.uk/guidance/ng207/chapter/Recommendations#induction-of-labor-in-specific-circumstances>. Accessed 22 Dec 2023
10. Moldin PG, Sundell G (1996) Induction of labor: a randomised clinical trial of amniotomy versus amniotomy with oxytocin infusion. *Br J Obstet Gynaecol* 103:306–312. <https://doi.org/10.1111/j.1471-0528.1996.tb09733.x>
11. Titulaer LML, de Wolf GS, Bakkum EA, Moll E (2019) Delayed versus immediate oxytocin infusion after amniotomy for induction of labor: A randomised controlled pilot trial. *Eur J Obstet Gynecol Reprod Biol* 240:357–363. <https://doi.org/10.1016/j.ejogrb.2019.07.036>
12. Wei S-Q, Luo Z-C, Xu H, Fraser WD (2009) The effect of early oxytocin augmentation in labor: a meta-analysis. *Obstet Gynecol* 114:641–649. <https://doi.org/10.1097/AOG.0b013e3181b11cb8>
13. Rousseau A, Burguet A (2017) Oxytocin administration during spontaneous labor: Guidelines for clinical practice. Chapter 5: Maternal risk and adverse effects of using oxytocin augmentation during spontaneous labor. *J Gynecol Obstet Hum Reprod* 46:509–521. <https://doi.org/10.1016/j.jogoh.2017.04.009>
14. Selo-Ojeme DO, Pisal P, Lawal O, et al (2009) A randomised controlled trial of amniotomy and immediate oxytocin infusion versus amniotomy and delayed oxytocin infusion for induction of labor at term. *Arch Gynecol Obstet* 279:813–820. <https://doi.org/10.1007/s00404-008-0818-x>
15. Tan PC, Soe MZ, Sulaiman S, Omar SZ (2013) Immediate compared with delayed oxytocin after amniotomy labor induction in parous women: a randomized controlled trial. *Obstet Gynecol* 121:253–259. <https://doi.org/10.1097/AOG.0b013e31827e7fd9>
16. Gaucher L, Le Ray C (2017) Oxytocin administration during spontaneous labor: Guidelines for clinical practice. Chapter 2: Indications of oxytocin according the first and second stages of

spontaneous labor. *J Gynecol Obstet Hum Reprod* 46:479–487.

<https://doi.org/10.1016/j.jogoh.2017.04.007>

17. Masson E Classification CNGOF du rythme cardiaque fœtal : obstétriciens et sages-femmes au tableau ! In: *EM-Consulte*. <https://www.em-consulte.com/article/840391/classification-cngof-du-rythme-cardiaque-f?tal-ob>. Accessed 23 Dec 2023

18. AMERICAN ACADEMY OF PEDIATRICS COMMITTEE ON FETUS AND NEWBORN, AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS COMMITTEE ON OBSTETRIC PRACTICE, Watterberg KL, et al (2015) The Apgar Score. *Pediatrics* 136:819–822. <https://doi.org/10.1542/peds.2015-2651>

19. Vayssière C, Yli B, Ayres-de-Campos D, et al (2024) EUROPEAN ASSOCIATION OF PERINATAL MEDICINE (EAPM) Position statement: Use of appropriate terminology for situations related to inadequate fetal oxygenation in labor. *European Journal of Obstetrics and Gynecology and Reproductive Biology* 294:55–57. <https://doi.org/10.1016/j.ejogrb.2024.01.006>

20. Grobman WA, Rice MM, Reddy UM, et al (2018) Labor Induction versus Expectant Management in Low-Risk Nulliparous Women. *N Engl J Med* 379:513–523. <https://doi.org/10.1056/NEJMoa1800566>

21. Wood R, Freret TS, Clapp M, Little S (2023) Rates of Induction of Labor at 39 Weeks and Cesarean Delivery Following Publication of the ARRIVE Trial. *JAMA Netw Open* 6:e2328274. <https://doi.org/10.1001/jamanetworkopen.2023.28274>

22. Cooley SM, Geary MP, O’Connell MP, et al (2010) How effective is amniotomy as a means of induction of labor? *Ir J Med Sci* 179:381–383. <https://doi.org/10.1007/s11845-010-0502-6>

23. Parer JT, King T, Flanders S, et al (2006) Fetal acidemia and electronic fetal heart rate patterns: Is there evidence of an association? *The Journal of Maternal-Fetal & Neonatal Medicine* 19:289–294. <https://doi.org/10.1080/14767050500526172>

24. Jonsson M, Nordén-Lindeberg S, Östlund I, Hanson U (2008) Acidemia at birth, related to obstetric characteristics and to oxytocin use, during the last two hours of labor. *Acta Obstetrica et Gynecologica Scandinavica* 87:745–750. <https://doi.org/10.1080/00016340802220352>

25. Dilbaz B, Ozturkoglu E, Dilbaz S, et al (2006) Risk factors and perinatal outcomes associated with umbilical cord prolapse. *Arch Gynecol Obstet* 274:104–107. <https://doi.org/10.1007/s00404-006-0142-2>

26. Bonapace J, Gagné G-P, Chaillet N, et al (2018) N° 355-Fondements physiologiques de la douleur pendant le travail et l’accouchement: approche de soulagement basée sur les données probantes. *Journal of Obstetrics and Gynaecology Canada* 40:246–266. <https://doi.org/10.1016/j.jogc.2017.11.022>

## Figures

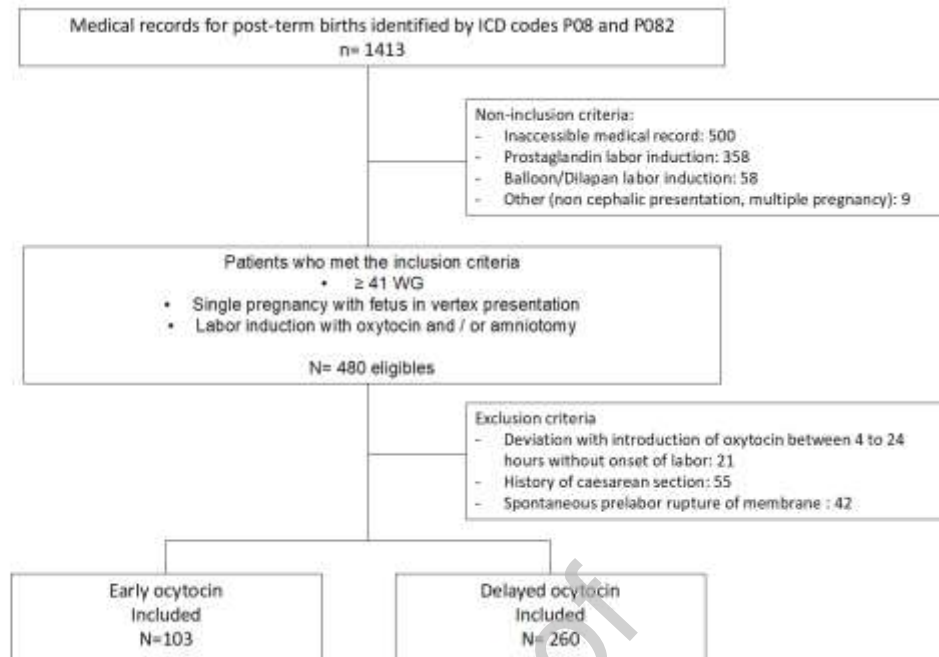


Figure 1: Flow chart

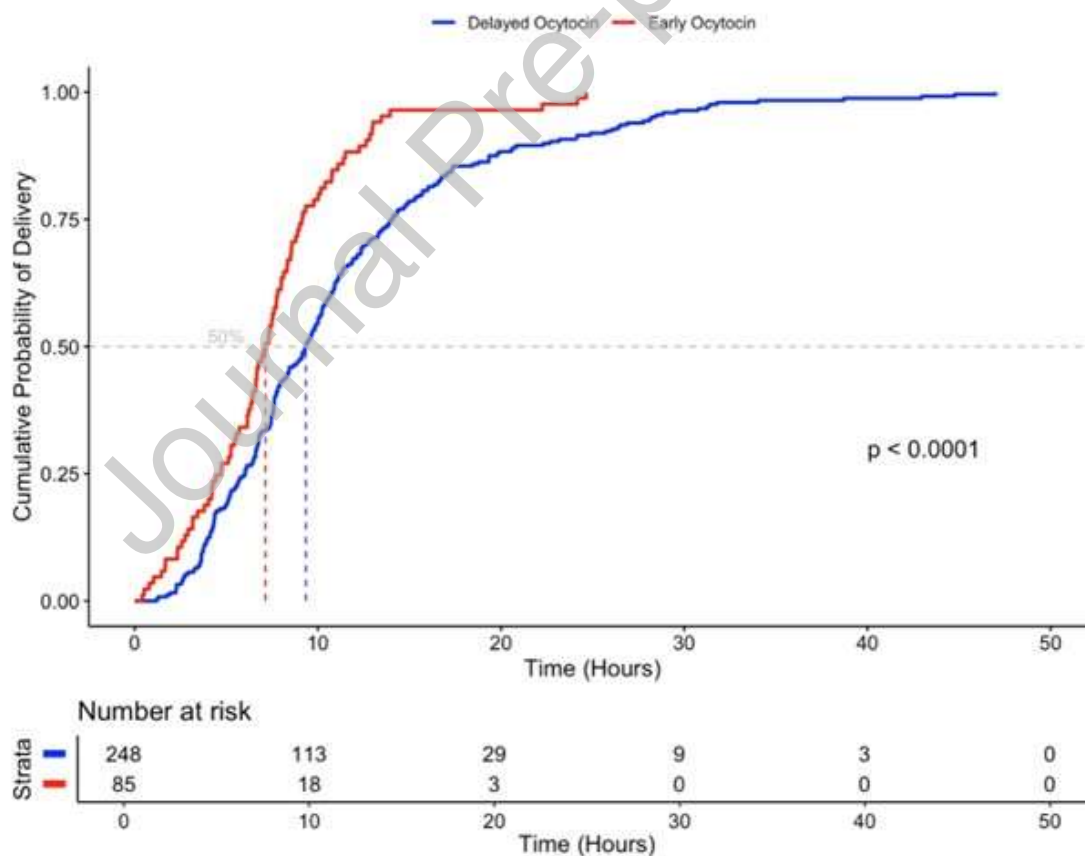


Figure 2: IOL-to-delivery time, by IOL method

**Tables**

Table 1: Characteristics of the patients and induction of labor

Table 2: Labor progress parameters

Table 3: Mode of delivery

Table 4: Newborn parameters

**Supplementary material**

Supplementary table 1: Subgroup analysis by parity: nulliparous versus multiparous women

Supplementary table 2: Subgroup analysis by Bishop score

Supplementary table 3: Subgroup analysis by indication for labor induction

Supplementary table 4: Before/after change of protocol subgroup analysis

**Tables****Table 1: Demographics and IOL indications**

Demographics and IOL indications	Early oxytocin group (EO group)		Delayed oxytocin group (DO group)		<i>p</i>
	N= 103		N= 260		
<b>Maternal age, in years: median (IQR)</b>	31	(27-35)	32	(28-35)	0.9
<b>BMI, in kg/m<sup>2</sup>: median (IQR)</b>	25	(22.1-28.7)	24.7	(22.4-29.1)	0.8
<b>Nulliparity: <i>n</i> (%)</b>	38	(36.9%)	62	(23.8%)	<b>&lt;0.01</b>
<b>Gestational diabetes: <i>n</i> (%)</b>	10	(9.7%)	29	11.1%	0.9
<b><i>Streptococcus</i> B colonization: <i>n</i> (%)</b>	13	(12.6%)	36	13.9%	0.9
<b>Bishop score: median (IQR)</b>	6	(5-7)	6	(5-7)	0.07
<b>Indication for labor induction <i>n</i> (%)</b>					0.08
Late term (41WG+5d)	74	(71.8%)	182	(70%)	
Oligohydramnios	13	(12.6%)	22	(8.5%)	
Decreased fetal movements	3	(7.2%)	23	(8.9%)	
Metrorrhagia	5	(4.9%)	5	(1.9%)	
Others	8	(9.9%)	28	(10.8%)	

**Table 2: Labor progress parameters**

Labor progress parameters	EO group		DO group		<i>p</i>
	<i>N</i> = 103		<i>N</i> = 260		
Oxytocin use: <i>n</i> (%)	103	(100%)	47	(18%)	<b>&lt;0.01</b>
Duration of oxytocin use, in hour: median (IQR)	6.5	(4.5-9.5)	4.5	(2-7)	<b>&lt;0.01</b>
Peridural anesthesia use: <i>n</i> (%)	93	(90.3%)	214	(82.9%)	0.1
Cervical dilation at the onset of epidural anesthesia, in cm: median (IQR)	3	(2-4)	4	(3-5)	<b>&lt;0.01</b>
Fetal cardiotocography abnormalities: <i>n</i> (%)	50	(48.5%)	85	(32.7%)	<b>&lt;0.01</b>
Antibiotic use: <i>n</i> (%)	20	(19.4%)	102	(39.2%)	<b>&lt;0.01</b>
Duration, in hours: median (IQR)					
Latency phase of the 1 <sup>st</sup> stage	3.8	(1.7-6.2)	5.1	(3-9.1)	<b>&lt;0.01</b>
Active phase of the 1 <sup>st</sup> stage	1.5	(1-3)	2	(1-3.1)	0.4
Complete dilation	1	(0.1-2)	1	(0.1-2)	0.9
Induction to birth	10.2	(6.6-18.6)	13.1	(8.4-19.2)	<b>&lt;0.01</b>

Table 3: Mode of delivery

Mode of delivery	EO group		DO group		<i>p</i>
	<i>N</i> = 103		<i>N</i> = 260		
Vaginal delivery	85	(82.5%)	248	(95.4%)	<b>&lt;0.01</b>
Spontaneous delivery	67	(65%)	209	(80.4%)	<b>&lt;0.01</b>
Operative delivery	18	(17.5%)	39	(15%)	0.6
Cesarean delivery	18	(17.5%)	12	(4.6%)	<b>0.01</b>

Table 4: Newborn parameters

Newborn parameters	EO group		DO group		<i>p</i>
	<i>N</i> = 103		<i>N</i> = 260		
Apgar score ≤ 7 at 5 min*	1	(1%)	5	(1.9%)	1
Severe newborn acidemia (pH<7.10)	8	(8.4%)	8	(3.2%)	<b>0.048</b>
Metabolic acidosis*	0	(0%)	2	(0.8%)	1
Lactates > 5 mmol.l <sup>-1</sup>	38	(38,8%)	76	(30%)	0,13
Mask ventilation	14	(13.6%)	21	(8.1%)	0.12
Transfer to neonatal unit*	5	(4.9%)	3	(1.2%)	<b>0.04</b>
Early neonatal bacterial infection*	1	(1%)	2	(3%)	0.19

*\*Fisher's test used*

**Declaration of interest:** None

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