Predictive factors of labour onset using ultrasonography

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Abstract

We analysed the effectiveness of transvaginal ultrasonographic and foetal/maternal pulse Doppler findings as predictors of labour onset within 1 week. We included 22 single normal pregnancies and evaluated the one-point and short- and long-term differences in uterine artery pulsatility index (PI), umbilical artery PI, middle cerebral artery PI (MCA-PI), peak systolic velocity, and cervical length (CL). Presence of funnelling and membrane separation over the internal cervical os was evaluated. Significant changes were observed in the one-point measurement of and short-term and long-term differences in CL, the one-point measurement of and long-term difference in MCA-PI, and the presence of membrane separation (Grade 2). In multivariate analysis, the significant predictors were short-term differences in CL (odds ratio [OR]: 5.27), long-term differences in MCA-PI (OR: 13.3), and presence of membrane separation (Grade 2) (OR: 5.38). Transvaginal ultrasonographic and foetal pulse Doppler findings were effective predictors of labour onset within 1 week.

Keywords: pulse Doppler; membrane separation; predictive factor; labour onset; ultrasonography

Impact statement

- **What is already known on this subject?**

Parameters reported to predict labour onset include the Bishop score, cervical length, decreased long-term cervical length, funnelling of the internal cervical os, and adrenal gland volume.

- **What do the results of this study add?**

Short-term changes in cervical length, long-term changes in middle cerebral artery pulsatility index, and the presence of membrane separation Grade 2 were found to be useful predictive factors of labour onset in this study.

・**What are the implications of these findings for clinical practice and/or further research?**

The prediction of labour onset enables clinicians to properly manage pregnancy and delivery considering maternal and foetal conditions.

Introduction

Time of delivery is the greatest concern in pregnant women in the third trimester. If they have knowledge about this, they can prepare for delivery. Furthermore, clinicians can properly manage pregnancies and deliveries and judge the time of intervention considering maternal and foetal conditions. Parameters reported to predict labour onset include the Bishop score (Rozenberg *et al*. 2000), cervical length (CL) (Rozenberg *et al*. 2000, Miura *et al*. 2010, Giyahi *et al*. 2018), decreased long-term CL (Miura *et al*. 2010), funnelling of the internal cervical os (Miura *et al*. 2010), and adrenal gland volume (Bhat *et al*. 2019). However, useful predictive factors of labour onset have not been established yet.

Regarding pulse Doppler findings, the umbilical artery pulsatility index (UA-PI) decreases depending on fetoplacental vascular system expansion throughout pregnancy (Maulik 1989). Similarly, the middle cerebral artery PI (MCA-PI) decreases and peak systolic velocity (MCA-PSV) increases throughout pregnancy (Van den *et al*. 1989). Before labour onset, although no significant changes could be confirmed in the UA-resistance index (RI), a significant decrease was confirmed in the MCA-RI (Morales-Roselló *et al*. 2014). Additionally, the uterine artery PI (UtA-PI) is associated with the strength of uterine contractions, and the PI of contractions might be effective for detecting preterm birth (Olgan and Celiloglu 2016). Chorioamniotic membrane separation has been shown to be a risk factor for the preterm premature rupture of membranes and premature delivery (Lewi *et al*. 2004), and membrane separation over the internal cervical os is associated with membrane ruptures (Devlieger *et al*. 2003, Patel *et al*. 2014). However, the relationship between the UtA-PI and membrane separation and labour onset remains unclear.

We aimed to evaluate the effectiveness of the UtA-PI and membrane separation over the internal cervical os in addition to the UA-PI, MCA-PI, MCA-PSV, and funnelling of the internal cervical os as the predictive factors of labour onset within 1 week.

Materials and methods

Patients

We included single pregnancies managed at the Department of Obstetrics and Gynaecology, Takashima Municipal Hospital, between August 2019 and January 2020. Informed consent was obtained from all patients. This study protocol was approved by the Institutional Review Board of Takashima Municipal Hospital (IRB numbers: 4). Pregnancies with major structural anomalies, hypertensive disorders, foetal growth restriction, labour induction, and planned caesarean section were excluded. According to the Japanese policy, pregnant women received prenatal care biweekly after 24 weeks of gestation and weekly after 36 weeks of gestation. We examined and evaluated the UtA-PI, UA-PI, MCA-PI and PSV, CL, and presence of funnelling and membrane separation over the internal cervical os biweekly after 32 weeks and weekly after 36 weeks of gestation. Spontaneous labour was defined as regular uterine contractions within 10 minutes of cervical changes leading to admission for delivery. According to the institutional policy, we performed labour induction as the indication of post-term pregnancy at 41 weeks of gestation.

Measurement data

All pulse Doppler measurements were recorded by a single experienced operator using the Voluson S8 ultrasound system (GE Healthcare, Tokyo, Japan), with a wall motion filter of 60 Hz and a gate size fitting within the blood vessels, evaluating five or more consecutive waveforms. For the UtA-PI, we identified the iliac arteries and UtAs using Doppler colour-flow mapping, recorded at an angle of <30° on the UtA just cranial to the crossing with the external iliac artery; we measured the PI on the placental and non-placental sides, and obtained the average of both values. The UA was evaluated by the abdominal insertion of the umbilical cord to the foetal pelvis to avoid changes in UA-PI depending on the measurement position, because the UA-PI is significantly higher at the foetal end of the cord than at the placental end (Maulik *et al*. 1990). The MCA was evaluated in the direction of the blood flow at <10° to obtain accurate blood flow velocity values. Transvaginal ultrasonography was performed by a single experienced operator for the assessment of CL and the funnelling of and membrane separation over the internal cervical os with the Voluson P8 ultrasound system equipped with a 5-MHz transvaginal transducer (GE Healthcare, Tokyo, Japan). Pregnant women with an empty bladder were placed in the dorsal lithotomy position for the examination. The ultrasound probe was placed at the anterior vaginal fornix and withdrawn until a sagittal view of the cervix was obtained without cervical distortion due to pressure from the probe. CL was measured as the distance from the internal to the external os along the cervical canal. Cervical funnelling was recorded when the depth of the funnel was at least 3 mm in length (Iams *et al*. 1996). Membrane separation over the internal cervical os was defined as a single hyperechoic line, representing the chorioamniotic membrane, separated away from and noncontiguous with the cervix, lower uterine segment, or both (Devlieger *et al*. 2003, Patel *et al*. 2014). Membrane separations were classified into separation over the internal cervical os only (Grade 1 [G1]; Figure 1-A) and beyond (Grade 2 [G2]; Figure 1-B) based on a previous report (Patel *et al*. 2014). All Doppler measurements and ultrasonographic findings were obtained after confirming by palpation that there were no uterine contractions.

We collected data on maternal characteristics and perinatal outcomes including maternal age, parity, body mass index, gestational age (GA) at delivery, mode of delivery, birthweight, and umbilical artery pH.

Regarding the UtA-PI, UA-PI, MCA-PI and PSV, and CL, we evaluated not only the one-point measurement but also the short- and long-term differences considering individual differences in these measurements as reported previously (Miura *et al*. 2010). The short-term difference was defined as the difference between the values at 1 week, and the long-term difference was defined as the difference between the values at 1 month. We calculated the percentage difference between the first and second measurements as 100% at the first measurement.

Statistical analyses

Among the data measured biweekly after 32 weeks and weekly after 36 weeks of gestation, we compared between the data measured within 1 week before labour onset and other data using the Mann–Whitney U-test and Fisher's exact test. Receiver operating characteristic (ROC) curves were constructed to portray the relationship between the sensitivity and the false positive rate (1–specificity) for the UtA-PI, UA-PI, MCA-PI and PSV, and CL. The optimal cut-off point was considered to be the point corresponding to the highest sensitivity in relation to the highest specificity. Regarding funnelling and membrane separation, the probability of spontaneous labour onset within 1 week was assessed using the odds ratio (OR) and 95% confidence intervals (CIs). P-values <0.05 were considered statistically significant. Statistical analyses were performed using the Easy R software (EZR, R Foundation for Statistical Computing, Vienna, Austria) for Windows (Kanda 2013).

Results

Overall, 22 single pregnancies were analysed. Demographic data, characteristics, and clinical outcomes are shown in Table 1.

We performed univariate analysis for the UtA-PI, UA-PI, MCA-PI and PSV, CL, and presence of funnelling and membrane separation. No significant changes were observed in the UtA-PI, UA-PI, short-term differences in MCA-PI and MCA-PSV, and presence of funnelling and membrane separation G1. However, significant changes were observed in the one-point measurement of and short-term and long-term differences in CL, the one-point measurement of and long-term difference in MCA-PI, and the presence of membrane separation G2 (Table 2).

The ROC curve of the one-point measurement of and short-term and long-term differences in CL for predicting labour onset within 1 week was created. The area under the curve (AUC) and optimal cut-off values of the one-point measurement of and short-term and long-term differences in CL were 0.717 and 21 mm (OR: 6.32 [95% CI: 3.43–11.66]), 0.759 and -9.483% (OR: 10.0 [95% CI: 5.23–19.0]), and 0.809 and 43.243% shortening (OR: 12.0 [95% CI: 6.08–23.9]), respectively.

The ROC curve of the one-point measurement of and long-term difference in MCA-PI for predicting labour onset within 1 week was created. The AUC and optimal cut-off values of the one-point measurement of and long-term difference in MCA-PI were 0.77 and 1.32 (OR: 10.7 [95% CI: 5.52–21.0]) and 0.751 and 10.938% shortening (OR: 4.10 [95% CI: 2.19–7.67]), respectively.

Funnelling and membrane separation G1 and G2 were observed in 4.9% (4/81), 20.9% (17/81), and 20.9% (17/81) of measurements, respectively. There was a significant relationship between the presence of membrane separation G2 and labour onset within 1 week (sensitivity: 59.1%; specificity: 93.2%; OR: 19.8 [95% CI: 5.46-71.4]).

We performed multivariate analysis using the logistic regression model for the one-point measurement of and short-term and long-term differences in CL, one-point measurement of and long-term difference in MCA-PI, and presence of membrane separation G2. The ROC curves of multivariate analysis for these variables for predicting labour onset within 1 week are presented in Figure 2. The AUC was 0.941. The cut-off values for CL and MCA-PI were evaluated. The significant predictive factors were the short-term difference in CL, long-term difference in MCA-PI, and presence of membrane separation G2 (Table 3).

The equation for the days remaining to labour, developed using multiple regression, is shown below (P = 0.019, Multiple R-squared; 0.2435):

Days remaining to labour = 14.23 -0.11*[(the short-term differences of CL) +(the long-term differences of MCA-PI)]-1.73*(membrane separation G2).

Discussion

Short-term changes in CL, long-term changes in MCA-PI, and the presence of membrane separation G2 were found to be useful predictive factors of labour onset in this study.

Membrane separation over the internal os is caused by uterine contractions, membrane sweeping, or stretching of the foetal membrane owing to the descending foetal head (Devlieger *et al*. 2003, Patel *et al*. 2014), which increases phospholipase A2 activity and the prostaglandin F2 alpha concentration and might lead to labour onset (McColgin *et al*. 1993). In our study, all cases of membrane separation were spontaneous. A significant relationship between data within 1 week before labour onset and other data was not observed for membrane separation G1 but was observed for membrane separation G2. In the multivariate analysis, there was a significant relationship between the presence of membrane separation G2 and labour onset within 1 week. Membrane separation was shown to be associated with the rupture of membranes (Devlieger *et al*. 2003, Patel *et al*. 2014). In the 14 cases with membrane separation G2 within 1 week before labour onset, 12 cases involved labour onset and 2 involved a rupture of membranes followed by labour onset.

Although the presence of funnelling has been reported to be useful as a predictive factor of labour onset (Miura *et al*. 2010, Bayramoglu *et al*. 2005), another study contradicts such a finding (Brieger *et al*. 1997). Our study does not suggest a relationship between the presence of funnelling and labour onset within 1 week. It might be difficult to predict labour onset in all pregnant women based only on the presence of funnelling, which is a frequent observation in the third trimester of normal pregnancies (Brieger *et al*. 1997).

CL is a predictive factor of labour onset (Rozenberg *et al*. 2000, Miura *et al*. 2010, Bayramoglu *et al*. 2005), and long-term changes in CL have been reported (Miura *et al*. 2010, Meijer-Hoogeveen *et al*. 2008). In our study, a significant relationship between data within 1 week before labour onset and other data was observed for the one-point measurement of and short-term and long-term differences in CL. In the multivariate analysis, although the one-point measurement of and long-term difference in CL were not identified as predictive factors, the short-term difference in CL was a useful predictive factor. Contrastingly, there are reports that CL is not a useful predictor of labour onset (Grotegut *et al*. 2011, Mukherji *et al*. 2017). The measurements for changes in CL before labour onset were classified into unchanged CL, decline in CL in the last 2 weeks, and gradual changes in CL starting before the last 2 weeks (Meijer Hoogeveen *et al*. 2008). Therefore, as with funnelling, it might be difficult to predict labour onset in all pregnant women based only on CL assessment. However, our study suggested that the short-term change of CL was a useful predictive factor as it might reflect changes in the last 2 weeks before labour onset.

A previous report showed a significant reduction in the foetal MCA Doppler impedance before labour onset (Morales-Roselló *et al*. 2014). The pressure associated with a descending foetal head might affect MCA pulse Doppler findings; however, in these cases, MCA-PI has been shown to increase (Măluțan *et al*. 2019). Hypoxia associated with placental insufficiency during pregnancy might affect foetal pulse Doppler findings as that seen owing to the brain-sparing mechanism during foetal growth restriction; however, in such cases, MCA-PI and UA-PI have been shown to decrease and increase, respectively (Cheema *et al*. 2006). Our study suggested that the UA-PI remained unchanged, although the one-point measurement of and long-term difference in MCA-PI decreased significantly, and the long-term difference in MCA-PI was found to be a useful predictive factor. The changes in foetal blood flow might suggest foetal preparation to adapt to intrapartum hypoxia (Morales-Roselló *et al*. 2014) because uterine contractions during labour cause significant reduction in placental perfusion and might lead to foetal hypoxia (Sinding *et al*. 2016). Such changes may also be caused by the labour onset-associated increase in the levels of corticotrophin-releasing hormone (Kamel 2010), which causes nitrous oxide release in the placental circulation and a vasodilatory response (Clifton *et al*. 1995).

Additionally, we developed an equation for calculating the days to labour using multiple regression analysis. Although the equation had the ability to predict the days to labour, it had insufficient accuracy. A previous study reported a model for predicting the delivery date using CL and the MCA-RI; however, this model also had insufficient accuracy (Morales-Roselló *et al*. 2013). As mentioned in that report, new parameters, such as cervical elastography, for predicting cervical ripening (Peralta *et al*. 2017) can be included to increase accuracy. This aspect should be investigated in a future study.

This study has a few limitations. First, the sample size was small. Therefore, further prospective studies are needed to clarify the effectiveness of transvaginal ultrasonographic findings and foetal and maternal pulse Doppler measurements as predictive factors of labour onset. Second, although UtA-PI measurements during uterine contraction might be effective for detecting preterm birth (Olgan and Celiloglu, 2016), we could not assess this issue in this study. Therefore, the relation between the UtA-PI during uterine contraction and labour onset within 1 week should be evaluated to clarify the effectiveness of UtA-PI as a predictive factor of labour onset.

Conclusion

We speculate that there are individual differences during pregnancy before labour onset. The prediction of labour onset enables clinicians to properly manage pregnancy and delivery considering maternal and foetal conditions; hence, establishing effective predictors of labour onset is of the utmost importance. Although transvaginal ultrasonographic and foetal pulse Doppler findings were shown to be effective predictive factors of labour onset within 1 week, these findings need to be further evaluated comprehensively considering time-related changes.

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Data availability statement

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

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Table 1. Demographic data and patient characteristics

Characteristics	Total group
Patients	22
Age (years)[a]	31.9 (19–42)
BMI (kg/m^2)[a]	20.1 (17.0–24.2)
Primipara (%)	50.0 (11/22)
Vaginal delivery (%)	100 (22/22)
GA at delivery (weeks)[a]	39.4 (38.3–40.4)
Birth weight (g)[a]	3056.5 (2314–3574)
Umbilical artery pH[a]	7.29 (7.19–7.39)

[a]Mean (range)

BMI, body mass indices; GA, gestational age.

Table 2. One-point measurement of and short-term and long-term differences in CL, UtA-PI, UA-PI, MCA-PI, and PSV in univariable analysis (n = 22)

Data comparison		Data within 1 week before labour onset	Other data	P value
CL [a]	One-point (cm)	19.0 (3.0–37.0)	29.3 (9.6–50.0)	0.003
	Short-term (%)	15.4 (-5.8–75.2)	0.14 (-27.7–50.1)	< 0.001
	Long-term (%)	44.8 (0.0–89.3)	3.1 (-17.2–57.2)	< 0.001
UtA-PI[a]	One-point	0.63 (0.43–0.85)	0.59 (0.40–1.17)	0.701
	Short-term (%)	-1.49 (-66.6–15.8)	0 (-59.1–28.3)	0.126
	Long-term (%)	-13.4 (-35.8–27.4)	0 (-57.8–22.5)	0.897
UA-PI[a]	One-point	0.80 (0.60–1.19)	0.83 (0.54–1.15)	0.883
	Short-term (%)	-0.58 (-48.1–32.6)	3.49 (-59.7–38.6)	0.103
	Long-term (%)	6.75 (-42.6–30.3)	13.6 (-40.2–52.6)	0.276
MCA-PI[a]	One-point	1.21 (0.86–1.78)	1.53 (0.82–1.92)	< 0.001
	Short-term (%)	15.1 (-59.7–44.1)	4.2 (-43.9–53.4)	0.202

	Long-term (%)	29.5 (0–52.6)	10.6 (37.1–61.1)	0.011
MCA-PSV[a]	One-point	52.0 (33.2–68.8)	48.8 (26.3–83.4)	0.5
	Short-term (%)	-5.77 (-112.2–39.2)	-2.89 (-65.1–50.3)	0.457
	Long-term (%)	-23.9 (-85.9–34.1)	-21.8 (-75.0–30.8)	0.826
Funnelling[b] (%)		9.0 (2/22)	3.3 (2/59)	0.297
Membrane separation[b] (%)	Grade 1	31.8 (7/22)	16.9 (10/59)	0.218
	Grade 2	59.0 (13/22)	6.7 (4/59)	< 0.001

"Other data" implies all data except data within 1 week before labour onset that were measured biweekly after 32 weeks and weekly after 36 weeks of gestation.

[a] Mann–Whitney U-test was used to compare data between groups. Data are expressed as median (range).

[b] Fisher`s exact test was used to compare data between groups.

CL, cervical length; UtA-PI, uterine artery pulsatility index; PI, pulsatility index; UA, umbilical artery; MCA, middle cerebral artery; PSV, peak systolic velocity.

Table 3. One-point measurement of and short-term and long-term differences in CL, one-point measurement of and long-term difference in MCA-PI, and the presence of membrane separation G2 in multivariable logistic regression analysis

Data comparison		OR (95% CI)	P value
CL	One-point	0.84 (0.15–4.53)	0.843
	Short-term	5.27 (1.13–24.6)	0.034
	Long-term	2.86 (0.32–25.2)	0.345
MCA-PI	One-point	2.62 (0.65–10.6)	0.176
	Long-term	13.3 (2.27–78.5)	0.004
Membrane separation	Grade 2	5.38 (1.16–25.0)	0.032

CL, cervical length; MCA-PI, middle cerebral artery pulsatility index; OR, odds ratio; CI, confidence interval.

Figure legends

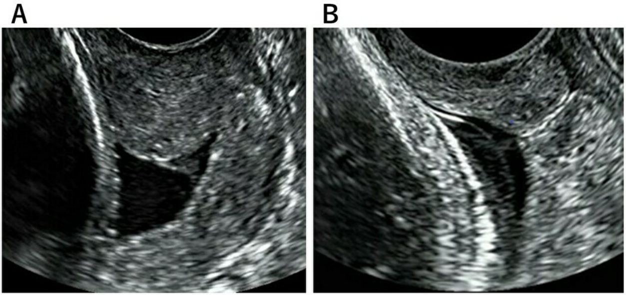
Figure 1. Ultrasonographic findings

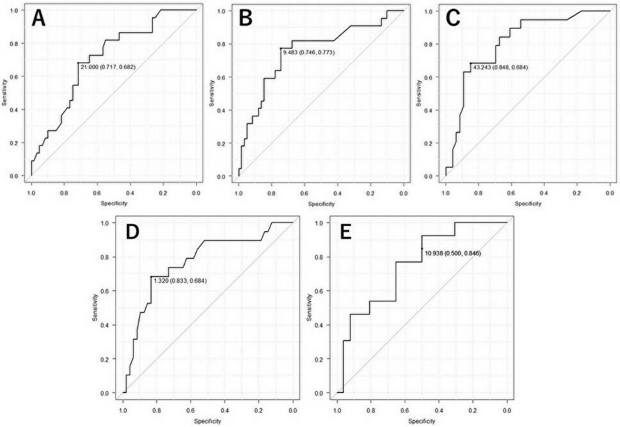
A: Grade 1: Membrane separation over the internal cervical os only.

B: Grade 2: Membrane separation over the internal cervical os and beyond.

Figure 2.

Likelihood of labour onset within 1 week. Receiver operating characteristic curves of multivariate analysis for the short-term difference in cervical length, the long-term difference in middle cerebral artery pulsatility index, and the presence of membrane separation Grade 2.


A
B


A
21.000 (0.717, 0.682)
B
9.483 (0.746, 0.773)
C
43.243 (0.848, 0.684)
D
1.320 (0.833, 0.684)
E
10.938 (0.500, 0.846)
Sensitivity
Specificity