Induction of labour : Foley catheter revisited

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THE RISK OF CAESAREAN DELIVERY IN TERM NULLIPAROUS WOMEN WITH AN UNFAVOURABLE CERVIX AT START OF INDUCTION OF LABOUR; A CLINICAL PREDICTION MODEL

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Submitted

ABSTRACT

Objective: To develop a clinical prediction model to assess the risk of caesarean section at the start of labour induction in term nulliparous women with an unfavourable cervix, using clinical parameters known before induction of labour.

Methods: We performed a secondary analysis of the PROBAAT trials (NTR 1646), conducted between February 2009 and May 2010. In nulliparous women undergoing induction of labour with an unfavourable cervix at term we prospectively evaluated which combination of maternal age, height, BMI, gestational age at induction, indication for induction of labour, cervical ripening method, and Bishop score with its five components predicts the risk for caesarean section best. After predictors were found to be associated with caesarean section in univariable analysis ($p<0.50$) the predictors of the multivariable logistic regression model were identified using backward selection. Model performance was evaluated by area under the receiver operating curve and a calibration plot. To correct for potential overfitting, the model was internally validated with bootstrapping.

Results: We studied 766 nulliparous women, of whom 217 (28%) underwent a caesarean section. BMI, maternal height, maternal age, and gestational age were independent predictors for caesarean section. The model showed good calibration and moderate discrimination with an area under the ROC-curve of 0.68 (95% CI 0.64-0.73).

Conclusion: The risk of caesarean section can be reasonably predicted by BMI, maternal height, maternal age, and gestational age in term nulliparous women undergoing induction of labour with an unfavourable cervix. This model could aid us in counselling of patients and decision making at the start of induction.

INTRODUCTION

Induction of labour is a common intervention in obstetrics, comprising 20-30% of all births.[1,2] The risk of caesarean section after induction of labour, especially in nulliparous women with an unfavourable cervix, is increased.[3,4] In the Netherlands, 15% of all pregnant women deliver by caesarean section. Approximately 25% of women in whom labour is induced will undergo an emergency caesarean section.[2] Emergency caesarean section carries a greater risk of maternal and neonatal morbidity than a planned caesarean section or vaginal birth.[5-7] Therefore it would be helpful to identify women at high risk for emergency caesarean section prior to induction of labour. In women with a very high risk, it would be useful to re-evaluate the indication for induction. Furthermore, a model identifying these women could aid us in counselling regarding the risk of emergency caesarean delivery. Several factors that increase the risk of caesarean section have been identified in earlier studies, such as nulliparity, low Bishop score, short stature, higher maternal weight, BMI, and maternal age. [8-11] However, currently no model is available that validly predicts the risk of a caesarean birth after induction of labour, using clinical parameters known before induction of labour. Therefore, the objective of this study was to develop a clinical prediction model to assess the risk of caesarean section in nulliparous women with an unfavourable cervix at the start of induction of labour.

METHODS

This was a secondary analysis of the randomised controlled PROBAAT trials,[12-14] in which term and post term pregnant women with an unfavourable cervix, with intact membranes and a viable fetus in cephalic presentation were randomised to induction of labour with either a transcervical Foley catheter or vaginal prostaglandins. Women with a history of caesarean birth were excluded. The primary outcome of the trials was caesarean section rate. Maternal history, pregnancy and antenatal characteristics were noted prospectively. Intra- and postpartum outcomes were extracted from the charts.

Patients

In the original trials 1176 women were randomised, of whom 776 were nulliparous. We analyzed nulliparous women only, as the risk of caesarean section is much higher in these than in parous women and this was the majority of women induced with an unfavourable cervix.

Predictors under study

We selected candidate predictors for caesarean section based on clinical reasoning and earlier studies.[8-11,15] Only predictors known before start of induction were included because the aim of this study was to predict caesarean section risk before the start of induction of labour. Candidate predictors were maternal age

(years), maternal height (centimeters), BMI categorised in <20, 20-25 (reference category, largest group), 25-30, 30-35, 35-40 and >40, gestational age at the start of induction (days), the Bishop score and its five components (consistency, dilation, effacement, and position of the cervix, and engagement of the presenting fetal presenting part)[16] product actually used for cervical ripening (Foley catheter, Prostaglandin E2 gel (reference category, advised method in the Netherlands), Prostaglandin E2 insert, misoprostol, more than one method) and the reason for induction of labour, categorised as hypertensive disorders, post term pregnancy, IUGR, oligohydramnios, decreased fetal movements, diabetes, other maternal disease, other/elective indication (reference category, lowest risk). We included BMI as categories based on the -2 Log Likelihood values. As we included women with an unfavourable cervix, and only 1% had >2 cm dilation at start of induction, we categorised dilation to any versus no dilation (reference category, largest group).

Statistical methods

There were missing values for the predictors maternal weight, maternal height, and indication for induction of labour. To avoid generating biased results by analyzing incomplete data sets, we used multiple imputation. In multiple imputation, several datasets are created to take into account the imprecision caused by the fact that the distribution of the variables with missing values is estimated. We created ten imputed datasets from the original dataset.

Univariable regression analysis was used to identify factors associated with caesarean section ($p<0.50$). Maternal age and gestational age were analyzed as continuous variables. Linearity of their association with the outcome was assessed using cubic splines.[17] Using backward selection in a multivariable model predictors independently associated with caesarean birth were selected, using Akaike's Information Criterion ($p<0.157$).[18] To account for differences between imputation sets predictors were then selected in each imputed dataset separately. To select the predictors for the final multivariable model we used the majority method, in which predictors are included in the final model if selected in at least five out of ten imputation sets.[19] To come to the final prediction model, the regression coefficients and standard errors of the final predictors were calculated in each imputation set separately, and combined using Rubin's rules.[20]

The performance of the model was assessed by discrimination and calibration. The ability of the model to discriminate between women with and without a caesarean section was studied with the area under the Receiver Operating Curve (ROC) curve. Calibration indicates the agreement between the predicted probabilities and the observed frequencies of caesarean section and was assessed using a calibration plot. In general, a model performs worse when it is applied to a population other than in which the model was developed. This is especially true when the number of events per variable is relatively low, which gives the chance of finding spurious predictors and overestimated regression coefficient (overfitting). To adjust for

this we internally validated the model using bootstrapping. The original dataset was resampled with replacement, to create 100 datasets of equal size as the original set. Within each bootstrap sample the multivariable modelling process described above was repeated. This yielded a shrinkage factor which was used to perform uniform shrinkage of the regression coefficients to adjust for optimism.[17] All analyses were performed using R version 5.2.

RESULTS

Between February 2009 and May 2010, 1176 women were randomised, of whom 776 were nulliparous. Ten women were excluded from this analysis, as they did not receive any induction agent. Five women had a favourable cervix at induction, three women withdrew their consent after randomization, one women had a gestational age <37 weeks, and one women was lost to follow-up. For all 766 women analyzed, complete data for the primary outcome were available. For potentially predictive factors for the current model, in 7% of cases maternal weight, in 8% maternal height, in 1% indication for induction of labour was missing. Data were complete for the remaining potential predictors. Of all nulliparous women, 28% [217/766] had a caesarean delivery. Descriptive characteristics of the population are presented in Table 1, overall and for the subgroups vaginal and caesarean delivery.

Factors associated with caesarean section in univariable analysis were maternal age, height, BMI, gestational age at the start of induction, consistency of the cervix (stiff vs. soft), dilation (any vs. none), engagement of the fetal head (Hodge 1 vs. Hodge 2), and reason for induction of labour (Table 2). In multivariable analysis maternal age, height, BMI, and gestational age were independent predictors for caesarean section (Table 2.). The prediction model had an area under the ROC-curve of 0.68 (95% CI 0.64-0.73). The predicted probabilities for this model ranged from 6 % to 68 %. The model showed a good agreement between the predicted risk and observed proportion of caesarean delivery (Figure 1).

DISCUSSION

We identified factors predicting caesarean section in nulliparous women in whom labour is induced at term with an unfavourable cervix. We found that maternal age, height, BMI, and gestational age can independently predict caesarean section, yielding a prediction model with a moderate discriminative ability and good calibration.

Although multiple research groups have studied different maternal and neonatal characteristics as predictors of caesarean birth after induction of labour in women with an unfavourable cervix, this is one of the few studying them in a large prospective trial. Due to the large number of women included, we were able to study all factors known at the start of induction that could influence the risk of caesarean delivery, leading to a robust result, in contrast to previous studies. [8-10,21,22]

Table 1. Baseline Characteristics

	Nulliparous women with unfavourable cervix (n=766)	Vaginal delivery (n=549)	Caesarean delivery (n=217)
Maternal age (years)	30.1 (21.6-38.9)	29.5 (4.9)***	31.5 (5.0)***
BMI			
<20	70 (9%)	59 (11%)	11 (5%)
20-25	332 (43%)	250 (46%)	83 (38%)
25-30	223 (29%)	154 (28%)	69 (32%)
30-35	80 (10%)	52 (9%)	28 (13%)
≥35	61 (8%)	35 (6%)	26 (12%)
Maternal height (cm)	169 (158-180)*	170 (6.8)***	167 (6.9)***
Gestational age (weeks)	39.9 (38.4-41.4)**	39.9 (38.2-41.3)**	40.2 (38.6-41.6)**
Bishop score			
0	111 (14%)	79 (14%)	32 (15%)
1	185 (24%)	128 (23%)	57 (26%)
2	194 (25%)	139 (25%)	55 (25%)
3	144 (19%)	104 (19%)	40 (18%)
4	101 (13%)	78 (14%)	23 (11%)
5	31 (4%)	21 (4%)	10 (5%)
Dilation			
none	423 (55%)	206 (54%)	127 (59%)
any	343 (45%)	243 (46%)	90 (41%)
Effacement			
0%	452 (59%)	318 (58%)	134 (62%)
25%	233 (30%)	174 (32%)	59 (27%)
50%	69 (9%)	49 (9%)	20 (9%)
75%	12 (2%)	8 (1%)	4 (2%)
Fully effaced	0	0	0
Consistency			
Stiff	232 (30%)	167 (30%)	65 (30%)
Moderately soft	504 (66%)	360 (66%)	144 (60%)
Soft	30 (4%)	22 (4%)	8 (4%)
Engagement			
Hodge 1	741 (97%)	531 (97%)	210 (93%)
Hodge 2	25 (3%)	18 (3%)	7 (3%)
Hodge 3	0	0	0
Position cervix			
Posterior	567 (74%)	405 (74%)	162 (75%)
Median	176 (23%)	127 (23%)	49 (23%)
Anterior	23 (3%)	17 (3%)	6 (3%)
Indications for induction of labour			
Elective	56 (7%)	38 (7%)	18 (8%)
Hypertensive disorders	286 (37%)	213 (39%)	73 (34%)
Oligohydramnios	25 (3%)	15 (3%)	10 (5%)
IUGR	57 (7%)	50 (9%)	7 (3%)
Decreased fetal movements	17 (2%)	14 (3%)	3 (1%)
Maternal disease	25 (3%)	18 (3%)	7 (3%)
Post term pregnancy	255 (33%)	185 (32%)	80 (37%)
Diabetes	41 (5%)	24 (4%)	17 (8%)
Other	3 (1%)	1 (0%)	2 (1%)

Table 1. *Continued*

	Nulliparous women with unfavourable cervix (n=766)	Vaginal delivery (n=549)	Caesarean delivery (n=217)
Method of induction (actually given)			
PGE2 gel	265 (35%)	194 (35%)	71 (33%)
Foley catheter	343 (45%)	243 (44%)	100 (46%)
PGE1 tablet	41 (5%)	32 (6%)	9 (4%)
PGE2 insert	82 (11%)	59 (11%)	23 (11%)
More than one method	35 (5%)	21 (4%)	14 (6%)

*mean +95% CI, **median+ IQR, ***mean+SD

In distinction with a recently published model by Frederiks et al,[9] we did not use any intra- and postpartum factors to create our model. However, in the current model we used exclusively candidate predictors that are readily available for every women before the start of induction of labour, which makes this model applicable to any women in whom labour is to be induced in a setting comparable to ours. As it is not standard practice to perform ultrasound before induction of labour in the Netherlands, we did not add factors that would require additional examinations such as estimating the fetal weight by ultrasound or sonographic measurement of the cervix. Although this choice potentially lowers the predictive capability of our model, it also makes this model easy to use in every clinical setting.

As was found in previous studies, maternal age, height, BMI, and gestational age were predictive of caesarean section.[8] Although earlier studies already point out that Bishop score is a poor predictor for caesarean delivery,[23] it surprisingly had

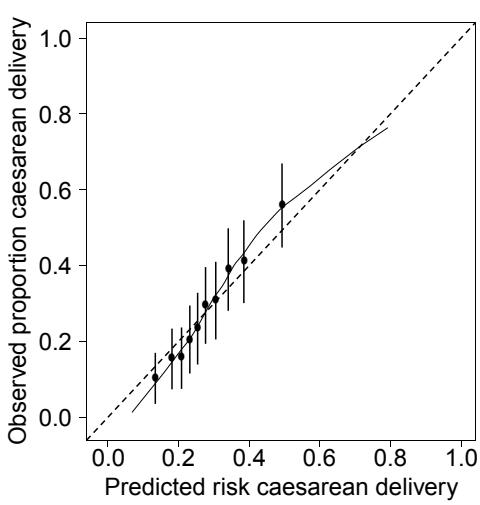

Figure 1. Calibration plot of the observed proportion against the predicted risk of caesarean delivery. The circles indicate deciles of women with similar predict risk and its 95% CI

Table 2. Univariable and multivariable analysis

	Univariable analysis OR (95% CI)	Multivariable analysis OR (95% CI)**[coefficient]
Intercept	Not applicable	1.085
Maternal age (years)*	1.08 (1.05-1.12)	1.06 (1.03-1.10) [0.061]
BMI*		
<20	0.57 (0.28-1.20)	0.69 (0.33-1.44) [-0.37)
20-25	1	1
25-30	1.35 (0.91-2.01)	1.36 (0.90-2.04) [0.31)
30-35	1.66 (0.95-2.89)	1.60 (0.90-2.85) [0.47]
>35	2.20 (1.28-4.13)	1.93 (1.06-3.51) [0.66]
Maternal height (cm)	0.94 (0.92-0.96)	0.95 (0.93-0.98) [-0.05]
Gestational age (weeks)*	1.11 (1.00-1.22)	1.12(1.01-1.24) [0.11]
Bishop score		
0	1	Not selected
1	1.10 (0.66-1.84)	
2	0.98 (0.58-1.64)	
3	0.95 (0.55-1.64)	
4	0.73 (0.39-1.35)	
5	1.18 (0.50-2.77)	
Dilation		
0	1	Not selected
1-2	0.82 (0.60-1.14)	
Effacement*		
0%	1	Not selected
25%	0.81 (0.56-1.15)	
50%	0.97 (0.56-1.69)	
75%	1.19 (0.35-4.01)	
Consistency		
Stiff	1	Not selected
Moderately soft	1.01 (0.71-1.42)	
Soft	0.93 (0.40-2.20)	
Engagement		
Hodge 1	1	Not selected
Hodge 2	0.99 (0.41-2.39)	
Position cervix		
Posterior	1	Not selected
Median	0.97 (0.66-1.41)	
Anterior	0.88 (0.34-2.28)	
Indications for induction of labour*		
Elective	1	Not selected
Hypertensive disorders	0.72 (0.39-1.35)	
Oligohydramnios	1.40 (0.53-3.73)	
IUGR	0.29 (0.11-0.77)	
Decreased fetal movements	0.45 (0.11-1.76)	
Maternal disease	0.81 (0.29-2.27)	
Post term pregnancy	0.96 (0.51-1.78)	
Diabetes	1.50 (0.65-3.48)	
Other	3.93 (0.33-46.5)	
Method of induction*		
PGE2 gel	1	Not selected
Foley catheter	1.12 (0.79-1.61)	
PGE1 tablet	0.77 (0.35-1.69)	
PGE2 insert	1.07 (0.61-1.85)	
More than one method	1.82 (0.88-3.78)	

*p<0.50, **Mean shrinkage 0.83

no additional value to the current model, nor did any of the separate components of the Bishop score, of which especially dilation has previously been found to be a predictive factor.[8,24] It is, however, to be noted that all women in the current study had an unfavourable Bishop score, and most other studies compared unfavourable versus favourable Bishop score.[4,9,23] BMI, height and weight have also previously been identified as factors influencing the risk of caesarean delivery,[8-10,15] all studies showing a lower caesarean section rate in taller women with a lower weight and BMI. Maternal age has also been found to be associated with caesarean section rates, in favour of younger women, as was shown in the current study.[4,15]

The area under the curve of the current model was 0.68. This means that the model has moderate discriminatory capability. In medical practice, multiple models are in use with a comparable area under the receiver operating characteristic curve, as for instance the model used in fertility medicine to predict spontaneous pregnancy in couples with unexplained subfertility.[25] The rationale behind the widespread use of this model, is that it is the best model available. To our knowledge, there are no other clinical models for prediction of caesarean birth in women that have comparable ease of usability in any women undergoing induction of labour with an unfavourable cervix as the current model. We therefore think it could be useful for clinical practice, despite the moderate discriminatory capability. When using the model, however, the limitations should be taken into account.

The predicted probabilities of the model were between 6 and 68%, meaning that the model can detect very low risk of caesarean birth, up to a risk of 68%, which is substantially higher than the overall 28% in our study population and higher than the 25% in the Netherlands. The goal of every induction is a safe and uncomplicated delivery for mother and child, but also a safe and uncomplicated pregnancy and delivery in future gestations. The overall likelihood of caesarean delivery is higher after induction than after spontaneous labour, especially in nulliparous women with an unfavourable cervix. A caesarean delivery not only poses risks for the index pregnancy, it also has implications for future pregnancies, such as abnormal placentation, or uterine rupture. It is therefore valuable to prevent caesarean deliveries in nulliparous women.[26] The main considerations in induction of labour should be the decision for induction, this should be made independent of the condition of the cervix. If then the decision for induction is made based on specific medical indications, we could use our model to adapt the information we give to individual patients to their personal situation. For example, in a situation where the predicted risk of caesarean delivery is very high, this could be important information when planning the induction, making sure that all the necessary means are available in case an emergency caesarean section will have to take place. Even more important, when the indication for induction is not very urgent, we could better explain why we need to await the occurrence of spontaneous labour, or postpone induction until the cervix would be favourable in case of a very high predicted risk of caesarean section. On the other hand, we should be very cautious when we find a very low predicted risk, avoiding

induction of labour with elective indications and falsely reassuring ourselves and our patients about the risk of caesarean delivery.

Despite our internal validation of the model, in order to investigate the applicability of the model in a different population, this model needs to be validated in an external cohort of induced women. This is planned to be done in the population of the PROBAAT 2 trial, which is currently including term women with an unfavourable cervix with indicated induction of labour in the Netherlands.[27]

In conclusion, we found that the risk of caesarean section can be predicted with moderate discriminatory capability by BMI, maternal height, maternal age, and gestational age in term nulliparous women undergoing induction of labour with an unfavourable cervix. Because of the right of every woman to be fully informed about the risks and benefits of induction of labour, we created a model that is clinically useful at the start of every induction. After external validation this model could be used to help patients and their care providers to be better informed about the risk of caesarean delivery when induction of labour is considered in term pregnant nulliparous women with an unfavourable cervix. We should however be cautious with the use of this model in decision making in labour induction, and keep in mind that induction should only be started in nulliparous women with an unfavourable cervix when there is an urgent medical indication, bearing in mind that preventing the first caesarean is of utmost importance.

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