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Development and internal validation of a clinical prediction model for external cephalic version

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ABSTRACT

Objective: To develop a prediction model for the chance of successful external cephalic version (ECV).
Study design: This is a secondary analysis of a multicenter, open-label randomized controlled trial that assessed the effectiveness of atosiban compared to fenoterol as uterine relaxant during ECV in women with a singleton fetus in breech presentation with a gestational age of 36 weeks or more. Potential predictors included maternal, pregnancy, fetal, and treatment characteristics and were recorded in all participants. Multivariable logistic regression analysis with a stepwise backward selection procedure was used to construct a prediction model for the occurrence of successful ECV. Model performance was assessed using calibration and discrimination.
Results: We included a total of 818 women with an overall ECV success rate of 37%. Ten predictive factors were identified with the stepwise selection procedure to be associated with a successful ECV: fenoterol as uterine relaxant, nulliparity, Caucasian ethnicity, gestational age at ECV, Amniotic Fluid Index, type of breech presentation, placental location, breech engagement, possibility to palpate the head and relaxation of the uterus. Our model showed good calibration and a good discriminative ability with a c-statistic of 0.78 (95% CI 0.75 to 0.81).
Conclusion: Prediction of success of ECV seems feasible with a model showing good performance. This can be used in clinical practice after external validation.

Introduction

Breech presentation occurs in 3 to 4% of all term pregnancies [1,2]. Vaginal delivery of a fetus in breech position is associated with higher rates of neonatal morbidity and mortality compared to a planned caesarean delivery [3]. Consequently, the global rate of term vaginal breech deliveries has declined substantially, while the rate of planned caesarean deliveries increased for fetuses in breech position [4,5]. However, caesarean delivery is associated with short and long-term consequences for maternal and neonatal health [6,7]. External cephalic version (ECV) is a safe and effective procedure to reduce the number of breech presentations at term and consequently the caesarean delivery rate for this indication [8–12]. Considering the global rise in caesarean deliveries in the last decade from approximately 23 to 34%, of which malpresentation is the third indication (approximately 17%) [13], ECV is an important intervention that can contribute to put a hold on this. Even as the complication rate is very low (a pooled risk on fetal death is 0.19% [8]), it is important to weigh these risks of complications with the alternatives to an ECV, namely the risk of perinatal mortality in planned vaginal breech birth (2.0/1000) and planned caesarean delivery (0.5/1000) and with caesarean section and in future pregnancies (1.0/1000) [14]. Therefore, ECV is recommended to all women with an uncomplicated breech pregnancy near term [13].

The success rate of ECV varies from approximately 35% up to 86% with an average of 50–60% [4,15]. Therefore, a more reliable and individualized prediction of successful ECV would be useful to counsel women for an ECV attempt and to improve individualized care and shared decision making. Recently, a systematic review including six prediction models for successful ECV was published [16]. They concluded that one prediction model was validated in an external cohort and had acceptable predictive performance.

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However, none of the models incorporated all important variables in their analysis determined in literature [17,18], thereby potentially limiting the performance of the models. Therefore, the aim of this study was to identify which combination of all important variables in daily clinical practice best predicts the success of ECV.

Materials and methods

The current manuscript was reported according to the TRIPOD reporting guideline [19], and is based on data that had been prospectively collected as part of a multicenter, open-label randomized controlled trial in one academic and seven teaching hospitals in the Netherlands [20]. This study assessed the effectiveness of atosiban compared to fenoterol as uterine relaxant during ECV. Atosiban was associated with a lower success rate (RR 0.73 (95% CI 0.55 to 0.93)). The study was approved by the research ethics committee of the Academic Medical Center in Amsterdam (reference number MEC 08–364) and by the board of directors of each of the participating hospitals. The study was registered in the Dutch Trial register (NTR 1877). In this randomized controlled trial, all women presenting between August 2009 and May 2014 with a singleton fetus in breech position who were scheduled for ECV were eligible for the study. Exclusion criteria were maternal age less than 18 years old, gestational age below 34 weeks, any contra-indication to vaginal birth (e.g. placenta praevia), any contraindication for ECV (scarred uterus other than transverse in the lower segment, known uterine anomalies, placental abruption in history or signs of placental abruption, severe preeclampsia or HELLP syndrome, third trimester blood loss or seven days prior to ECV, ruptured membranes), any known contra-indication to one of the two drugs, suspected intrauterine growth restriction (defined as estimated fetal weight < P5 for gestational age assessed by ultrasonography), severe oligohydramnios (deepest pool < 2 cm), fetal anomalies or non-reassuring fetal heart rate monitoring. Women were randomly assigned to receive atosiban or fenoterol. Fifteen minutes before starting ECV, the participating woman received an intravenous bolus of atosiban (6.75 mg in 0.9 ml (7.5 mg/ml)) or fenoterol (40 μg in 0.8 ml (0.5 mg/10 ml)) administered by a physician.

Experienced obstetricians and midwives performed the ECV procedure, and the procedure was successful if the fetus was still in cephalic position 30 min after the ECV attempt.

Candidate predictors

Based on literature [17,18] and clinical reasoning, we selected candidate predictors that are available in clinical practice. Candidate predictors were: parity, maternal age, body mass index (BMI), ethnicity, gestational age, placental location, fetal position, estimated fetal weight (EFW), amniotic fluid index in cm (AFI), position of the fetal spine, breech engagement, symphysis fundal height defined in weeks, possibility of palpation of the fetal head, and relaxation of the uterus all assessed by the clinician performing the ECV. Ethnicity initially consisted of six different groups, but ethnicity was recorded as Caucasian or non-Caucasian, based on a review on ethnicity. It showed a negative effect of Caucasian race on successful ECV. EFW was calculated with the Hadlock formula [21]. Fetal position was defined as frank breech (reference), non-frank breech, incomplete breech or transvers lie. Placental location was defined as anterior (reference), posterior, fundal or lateral position. Breech engagement was defined as non-engaged (reference), descent into pelvis or fixed in pelvis. Palpation of the fetal head was defined as easy (reference), difficult or unremarkable which is defined as not easy nor difficult to palpate the head of the baby. Relaxation of uterus was defined as relaxed (reference), unremarkable or non-relaxed.

Data analysis

We used successful ECV at 30 min after the attempt as the end point of the study. Various candidate predictors had missing values (Table 1). Because these are often selectively missing, deleting them would lead to a loss of statistical power in multivariable analysis and it is well documented that a complete case analysis probably yields biased results [22]. Hence, we used multiple imputation (ten times) to handle missing values. The imputation model included all potential predictors and the outcome.

Baseline characteristics were analyzed using descriptive statistics and presented as mean with standard deviation (SD) or median with interquartile range (IQR) for continuous variables as appropriate, and as numbers and percentages of the whole population for categorical and dichotomous variables.

To assess potential non-linearity of the association between the continuous variables maternal age, gestational age, BMI, and EFW, and the outcome (i.e. successful ECV) multivariable fractional polynomials were used, and continuous variables were transformed accordingly [23].

First, the univariable associations were assessed for each individual variable with the outcome using logistic regression, resulting in odds ratios (ORs) with 95% confidence intervals (CIs), and corresponding p values. Since selection based on univariable statistics might result in unstable prediction models we chose not to perform any preselection and to include all candidate predictors in the multivariable analyses [24,25]. Subsequently, multivariable logistic regression analysis with a stepwise backward selection procedure was used to construct a prediction model for the occurrence of successful ECV. Selection of variables was based on Akaike's Information Criterion. Since results may differ between imputation sets variable selection was repeated within each imputation set. Afterwards the final model was determined based on the majority rule, meaning that variables that were selected in 5 or more imputation sets were included in the final model [26]. Afterwards, the final model was fitted within each imputation set separately and intercept and regression coefficients were pooled using Rubin's rules [27].

With each model development there is a chance of overfitting, meaning that the model is too strongly fit to the data on which it was developed and consequently may perform poorly when externally validated. To assess the degree of overfitting or optimism, we internally validated the model using bootstrapping techniques. One hundred bootstrap samples of equal size to the original data (n = 818) were drawn from the original data set with replacement, allowing for multiple sampling of the same individual. Within each sample the entire modelling process described above was repeated. This yields a shrinkage factor, with which the regression coefficients of the predictors are multiplied (uniformly shrunken) to correct the model for optimism and overfitting [24].

Model performance will be assessed using discrimination and calibration. The discriminative ability of the models, being the ability to distinguish between those with and without a successful ECV, was assessed with the c-statistic [24]. Calibration was assessed graphically using calibration plots.

Furthermore, the following accuracy measures are assessed: sensitivity (or true positive rate), specificity, positive predictive value, negative predictive value, and false positive rate. As no clear relevant cut-off value exists, these measures were presented for different cut-off values based on the deciles of the predicted probabilities.