Prediction of successful ECV

We performed an external validation of a prediction model for the chance of successful external cephalic version (ECV) (Chapter 2). External validation is a vital step before a model can be implemented in clinical practice. So far this is the first prediction model on ECV that has been externally validated. With the model we were able to make a good distinction between women with a poor probability of successful ECV and a good probability of successful ECV. However, the model made a slight underestimation of the probability of success in all women. We made a score chart that can be used in daily practice to help individualize the counselling for women with a fetus in breech presentation at term. The most important and disputed question is whether one should withhold women an ECV attempt when a poor chance of success is predicted. ECV is cost-effective when the probability of success will be greater than 32%. It is questionable whether this 32% should be a threshold for offering women an ECV. External cephalic version is considered a safe procedure with few contraindications and low reported complication rates. A meta-analysis on 12,955 ECV attempts showed a pooled complication rate of 0.24% (95% CI 0.17-0.34%) for serious complications, including stillbirth and placental abruption. However, it is unknown whether complication rates are similar for all women, or that complications are more frequent in women with a lower predicted success. Future research should focus on identifying possible risk factors associated with the occurrence of complications. Which might provide new insights and an answer to whether or not an ECV attempt should be withheld from subgroups of women with a poor predicted chance of success. For now, we believe that even when the predicted chance of a successful ECV is low an attempt should be offered to all eligible women. Shared decision making has become an important part of obstetric care. It is a process in which patients and clinicians collaborate together to make decisions about health care. Women should be informed with unbiased nondirective information on the advantages, disadvantages and expected risks and outcomes of an ECV attempt, and be facilitated in developing informed preferences based on their values and health goals, after which they can make a balanced decision.

Increased risk for instrumental delivery after successful ECV

ECV has proven to be a successful procedure in the reduction of non-cephalic birth (RR 0.46 (95% CI 0.31-0.66)). The ultimate goal of a successful ECV is to achieve a vaginal delivery of a fetus in cephalic presentation. In chapter 3 we described a meta-analysis of 11 studies in which we found that women who have their fetus in cephalic position after ECV are at
increased risk for a caesarean section (OR 2.2, 95% CI 1.7-2.8), as well as instrumental vaginal delivery (OR 1.4, 95% CI 1.1-1.7), compared to women with a spontaneous cephalic presenting fetus. This increased risk was due to both dystocia (OR 2.2, 95% CI 1.6-3.0) and suspected fetal distress (OR 2.2, 95% CI 1.6-2.9). The reason why women after successful ECV have an increased risk for operative delivery is not clearly understood, and several hypotheses have been posed in an attempt to explain this difference. One of the theories is that there is a biological difference between breech and cephalic presenting fetuses, with smaller head circumferences, lower birthweight and lower fetal-placental ratio in breech presenting fetuses. Differences in fetal behavioural status between breech and cephalic presenting fetuses have also been described, with more behavioural state transitions in breech presentation and different heart rate patterns. These findings could suggest that breech fetuses might be less tolerant to labor and show earlier signs of fetal distress. Secondly, known risk factors for breech presentation such as uterine anomalies and different maternal pelvic configuration could explain a higher risk of dystocia during labor. A third explanation could be that after successful ECV the fetal head has less time to adjust to the maternal pelvis and women are more likely to have an unengaged cephalic presenting fetus with an unmoulded head, a head in asynclitic position, or a combination of these.

Identification of those women that are at increased risk for operative delivery would be beneficial in optimizing intra-partum care for women after successful ECV. In an attempt to find factors associated with this increased risk we conducted a cohort study (Chapter 4). In a cohort of 301 women with a cephalic presenting fetus after successful ECV, we tried to identify factors that could be predictive for an operative delivery. However, the results of the study did not enable us to make a proper selection of those women who are especially at increased risk. Nulliparity was the only factor that we found to be associated with an increased risk for caesarean section (OR 2.7, 95% CI 1.2-6.1), and operative delivery (OR 4.2 (95% CI 2.1-8.6)). Operative delivery was the combined outcome of caesarean delivery and instrumental vaginal delivery. Three previous studies have also identified nulliparity as a factor associated with the risk of caesarean section after successful ECV. Other factors that have been reported in association with an increased risk for caesarean section after successful ECV are a higher birth weight, advanced maternal age, higher gestational age, epidural use, a time interval below 96 hours between ECV and delivery, induction of labour, occiput posterior position of the fetal head during labour, flexed breech position and an amniotic fluid index below 13 cm prior to ECV. Most factors are also described in association with the risk of caesarean section in spontaneous cephalic presenting fetuses. It might be that the answer can be found in factors that are different prior to ECV. In our study we were limited in the parameters we were able to examine since our data came from a larger study on the implementation of ECV. Larger observational studies are necessary to be able to make a proper selection of those women who are especially at increased risk.
for caesarean section after successful ECV. So that we can select those women who might benefit from starting labour in a unit where facilities for emergency caesarean section are available.

At this moment, in the Netherlands, women after a successful ECV receive identical care compared to women with a primary cephalic presentation. The Dutch obstetric care system is characterised by a, well-defined, distribution of primary and secondary care. Low risk pregnancies are under surveillance of midwives or general practitioners, so called primary care. In contrary to women with a presumed high-risk pregnancy who are under the care of obstetric professionals, working in hospitals, so called secondary care. The indications for referral from primary to secondary care, have been formulated and are based on consensus reached by the professionals involved, and are documented in an obstetric indication list.\textsuperscript{16} Risk selection remains a continuous process during pregnancy and delivery. One of the reasons for referral of women with a low risk pregnancy, from primary care to secondary care, is breech presentation. After successful ECV this referral will be reversed from secondary to primary care. This means that after successful ECV women with a low risk pregnancy have the option for a home delivery under the care of a midwife. For some women the reason to undergo an ECV attempt is the fact that after a successful ECV they are able to have a home birth. In 2013, 7.4\% of all term pregnancies in The Netherlands ended in an intra-partum CS.\textsuperscript{17} In our cohort we found an intra-partum CS rate of 13\%. Women should be informed about this increased risk to enable them to make a balanced decision. Regardless of the increased risk we found for operative delivery after successful ECV, we still advise women with an uncomplicated breech presentation at term to undergo an ECV attempt. Especially since it is a relatively safe procedure with a low complication rate.\textsuperscript{3} Increasing caesarean delivery rates are a major topic of concern in current obstetric practice and breech presentation contributes considerably to these numbers. In the Netherlands in 2013, 31\% of the elective caesarean sections, for term singleton pregnancies, were due to breech presentation.\textsuperscript{17} We estimated that with every three versions one caesarean delivery could be prevented (Chapter 3).

The relation between successful ECV and DDH

A number of fetal and maternal factors are widely accepted as being associated with a higher risk of DDH, among which female gender, breech presentation and family history of DDH are the most consistent ones, both in case-control and observational cohort studies.\textsuperscript{18-20} We found breech presentation to be the strongest predictor with an OR 5.7 (95\% CI 4.4-7.4) (Chapter 5).
It is thought that the mechanical strengths that are placed on the neonatal hip by its position in utero causes the increased risk of DDH in breech presentation, especially during the last weeks of gestation when the breech will be engaged in the maternal pelvis. There are studies that showed a strong increase of the incidence of DDH after vaginal delivery in breech presentation. After successful ECV, the fetus will not be exposed to the mechanical forces in the last weeks of gestation and during delivery. With this theory, it can be expected that neonates born in cephalic presentation after successful ECV have a lower incidence of DDH. We found, in a cohort of 498 women with a breech presentation, that the incidence of neonates treated for DDH born in cephalic presentation after successful ECV (2.8%) was significantly lower than the incidence of neonates treated for DDH born in breech presentation after unsuccessful ECV (9.3%), (OR 0.29, 95% CI 0.09-0.95) (Chapter 6). Women with a positive family history of DDH and known congenital abnormalities of the fetus were excluded and in multivariate analysis we corrected for confounding factors. There is only one other study that examined the risk of DDH in neonates born in cephalic presentation after successful ECV. In a cohort of 257 women with a child in breech presentation the incidence of neonates treated for DDH after successful ECV was 3.2%, compared to 1.0% in neonates born in persistent breech presentation. This difference was not statistically significant and no correction for confounding factors was undertaken. In this study the incidence of DDH in neonates with a spontaneous cephalic presentation was 0.1%. Our study did not include a control group of women with a spontaneous cephalic presenting fetus. Reported incidences of DDH in the literature vary significantly, ranging from 1.4 to 35 per 1000 live births. This large range in incidence has probably more to do with how the disorder is defined, the diagnostic method and timing of evaluation, than the real population variance. The main problem is that an exact definition of DDH in the international literature is missing. One study performed in The Netherlands, in an unselected population, found an incidence of DDH in 3.7%, but also in this study no clear definition of DDH was given. Which makes it difficult to answer the question whether the risk of DDH after successful ECV is increased compared to fetuses with a spontaneous cephalic presentation. What we can conclude from our data is that the risk of DDH decreases after successful ECV. However, after combining the data of both studies in a meta-analysis the difference in the incidence of DDH in neonates born in cephalic presentation after successful ECV compared to neonates born after persistent breech presentation was not significant (OR 0.81 (95% CI 0.08-8.7)) (Chapter 7). The decreased incidence of DDH after successful ECV in our study might reflect a beneficial effect of ECV, but it can also be reversed, that it is a reflection of a fetus that can be easier to turn. One observational study found different fetal leg position between breech and cephalic fetuses already early in the third trimester. In this phase of the pregnancy the breech will not be engaged in the maternal pelvis in the majority of cases, and movement restrictions are thought not to be significant. These observations could lead to the hypothesis that DHH
is one of the causes of breech presentation, in which malfunction of the hip is the reason for these fetuses to remain in breech presentation. In this case the question remains, why a fetus with DDH is more difficult to turn. Observational studies on spontaneous version of breech presentation to cephalic presentation showed an importance of flexion of the knee joints.\textsuperscript{26-28} Possibly, flexion of the knee joints is also an important factor for the success of ECV, and that fetuses with DDH are less able to perform this flexion.

**Screening for DDH**

There are several screening strategies for detecting DDH in infants, which involve clinical examination, ultrasound examination (universal, or targeted to high risk groups) or a combination of both. Recommendations for screening strategies vary by country. In Germany, Austria and Switzerland universal ultrasound screening is currently applied. In many other countries, including Australia, North America and European countries a selective screening is adopted.\textsuperscript{29,30} Unfortunately neither of these strategies have shown to improve clinical outcomes including late diagnosed DDH and the need for surgery.\textsuperscript{31} Most studies are underpowered to detect significant differences in the uncommon events of late diagnosed DDH and the need for surgery. Second, there are no studies available that compare the outcome of unscreened neonates with screened neonates in an experimental or observational study.\textsuperscript{31} This provides us with a good example of how early acceptance of an intervention or technology can inhibit or even prevent good quality research, resulting in possibly permanent uncertainty. However so far none of the countries have abandoned their established screening programme, although some have decided not to add universal ultrasound screening.\textsuperscript{23}

In the Netherlands we adopted a selective screening programme, performed by child health centres, in which all children are screened by physical examination and in the presence of risk factors by additional ultrasound evaluation at three months age. One of the considered risk factors is breech presentation in the last trimester of pregnancy. This includes all neonates born in breech presentation, term and preterm, from single and multiple gestations and children born in cephalic presentation after successful ECV.\textsuperscript{24,32} We tried to explore whether this increased risk for DDH was equal for all breech presenting fetus and whether screening of all neonates born in breech presentation is justified.

We found only a limited amount of studies that examined different aspects of breech presentation in relation to DDH (Chapter 7). In the literature twin pregnancy is frequently reported as a risk factor for DDH. Some selective screening strategies also consider twin pregnancies a risk factor. We found breech presentation in multiple gestation pregnancies not to be associated with an increased risk for DDH, in contrary to breech presentation in
singletons. And there is no evidence that selective ultrasound screening in these neonates should be advised. This decreased incidence of DDH might be explained by the type of breech presentation in multiple gestation pregnancies, with more often complete breech presentation and the leg position more resembling that of a cephalic presenting fetus. There is currently only one study that reports on the incidence of DDH in premature neonates. This study found a similar incidence of DDH in term and preterm neonates born in breech presentation. Although, of the three affected preterm neonates in this study, two were born at a gestational age of 36 weeks and only one before a gestational age of 32 weeks. Since the incidence of breech presentation increases with a decrease in gestational age, a high percentage of premature neonates is born in breech presentation. Apparently, the factors that are associated with breech that lead to DDH at term, do not play a role at earlier gestational ages, when the prevalence of breech presentation is much higher. Longitudinal studies that answer whether the duration of breech presentation or the moment in gestation that a fetus is in breech presentation is of influence on the incidence of DDH are not available. There seems to be limited evidence for selective ultrasound screening in premature neonates born in breech presentation, and further research is necessary to determine from which gestational age on this increased risk is present.

As mentioned earlier, we found no significant difference in the incidence of DDH in neonates born in cephalic presentation after successful ECV compared to neonates born after persistent breech presentation in a meta-analysis of two studies (Chapter 7). A larger cohort with a primary cephalic control group is necessary to establish the definite nature of this relation. Until then, we believe that these neonates should be screened accordingly to the current screening protocol for DDH, in which breech presentation in the last trimester is considered a risk factor and an indication for selective ultrasound screening.

Since all neonates in breech presentation are delivered in the hospital, clinical hip examination and referral for ultrasound evaluation of the hips, is often arranged during hospital admission. In a survey among hospitals in the Netherlands, we inquired the current policy of obstetric professionals with regard to screening for DDH of breech presenting neonates (Chapter 8). We demonstrated a large practice variance between hospitals, with clinical hip examination, after birth in breech presentation, being performed in 47% of the hospitals, and in 19% of the hospitals after successful ECV. 87% of the hospitals referred neonates born in breech presentation for ultrasound evaluation of the hips and 27% of the hospitals arranged this referral for children born in cephalic presentation after successful ECV. Apparently, awareness of the increased risk for DDH after successful ECV is missing.

There are many health care professionals involved in the screening for DDH, obstetricians, midwives, paediatricians, orthopaedists and professionals of child health centres. In our survey we only inquired the policy of obstetric professionals, and we acknowledge that it would be interesting to expand this survey to all health care professionals involved in the
screening for DDH. We suggest the development of a multidisciplinary, national guideline for all involved departments in which the role of the obstetrician and midwife needs to be determined. The only national guideline currently available for the screening of DDH is developed by the child health service and does not incorporate guidance for the role of the obstetrician. With our studies we tried to provide evidence for optimizing the current screening programme for DDH in breech presenting neonates. Although, we do acknowledge that screening strategies should be analysed first before proper guidelines can be developed.

Clinical implications

COUNSELLING OF WOMEN WITH A BREECH PRESENTATION AT TERM

The studies presented in this thesis, provides information that can be used to counsel women with a fetus in breech presentation. First, we externally validated a prediction model for the chance of successful ECV and developed a score chart that can be used in clinical practice when counselling women with a breech presentation at term. Engaging women in shared decision-making has become an important part of obstetric care. This individualized counselling can be beneficial in the counselling of women and help guide their expectations before an ECV attempt. Furthermore, once an ECV is performed, women with a successful outcome should be counselled that they are at increased risk of a caesarean and instrumental delivery. Although, we do not believe that a change of care for these women from for instance primary care to secondary care is needed. In 2013, 7.4% of all term pregnancies in the Netherlands ended in an intra-partum caesarean section. Even if this percentage is doubled women still have a high chance of spontaneous vaginal delivery. Second, we found that the increased risk of operative delivery was caused by both dystocia as well as suspected fetal distress. If this increased risk consisted only of women with suspected fetal distress this advice would be different. As mentioned earlier, engaging women in shared decision making has become an important part of obstetric care. We believe that the care for women after successful ECV should involve counselling of this increased risk. For instance, for some women this could involve the decision to start labour in a unit where facilities for emergency caesarean section are available. Furthermore, this information can be used in the counselling of women prior to an ECV attempt. Nevertheless, we should warrant that this information does not change the attitude of obstetricians toward these women, by not offering an ECV or lowering their threshold to perform an intra-partum caesarean section after successful ECV.
OPTIMIZING SCREENING STRATEGIES FOR DDH

Currently, the best screenings strategy for DDH still needs to be established. The studies presented in this thesis, provides information that can be used in the optimisation of existing and the development of new screening programmes for DDH. For now, we believe that neonates born in cephalic presentation after successful ECV should be screened according to the current screening protocol for DDH in which breech presentation in the last trimester is considered a risk factor. However, we found no evidence that neonates born in breech presentation from multiple gestations are at increased risk for DDH, and it seems that additional ultrasound evaluation of the hips in these neonates could be abandoned. More research seems necessary to determine whether preterm neonates born in breech presentation, especially extreme premature neonates, are at increased risk.

We found that the current practice of screening for DDH in hospitals in the Netherlands varies considerably. Based on the work presented in this thesis we recommend that the role of the obstetrician and midwife, in the screening for DDH, should be incorporated in a national guideline to ameliorate the identification of neonates at risk for DDH. Until then, we should follow the current screening strategy developed by child health centres.

Future research implications

The work presented in this thesis introduces some directions for future research.

COMPLICATIONS OF ECV

Future research should focus on identifying possible risk factors associated with the occurrence of complications in ECV. These studies might provide new insights and an answer to whether or not an ECV attempt should be withheld from subgroups of women with a poor predicted chance of success.

PREDICTION FOR CAESAREAN SECTION AFTER SUCCESSFUL ECV

Larger observational studies are necessary to be able to make a proper selection of those women who are especially at increased risk for caesarean section after successful ECV. So that we can select those women who might benefit from starting labour in a unit where facilities for emergency caesarean section are available. These studies should incorporate fetal and maternal characteristics prior to ECV, so that it might be possible to construct a
model to predict vaginal delivery before an ECV attempt. Which in turn will be useful in the counselling of women prior to an ECV attempt.

**AETIOLOGY OF DDH**

The exact nature of the relation between breech presentation and DDH is still not clarified. Therefore, we propose longitudinal studies that examine whether the duration of breech presentation, or the moment in gestation that a fetus is in breech is of influence on the incidence of DDH. These studies will also provide the evidence, whether premature neonates born in breech presentation should be considered to be at risk for DDH. And could answer the question whether for instance, early ECV could be beneficial in reducing the incidence of DDH. Insight in the aetiology of DDH is essential to improve the screening for DDH in breech presenting neonates. However, this should be preceded by a clear, international definition of DDH.

**SCREENING FOR DDH**

Currently, there is no evidence for the best screenings strategy for the detection of DDH. It is unclear whether clinical screening alone is sufficient, or in combination with selective or universal ultrasound assessment. There are no studies that compare a screened to a non-screened population with measurements of functional outcomes after an adequate period of follow-up. Large randomized trials are necessary to evaluate the additional value of screening for DDH, and if so which screenings strategy is superior. Although, we believe that medico legal concerns, combined with the beliefs about effectiveness of screening will prevent the participation needed for a large randomised trial.
References


