General introduction
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Breech presentation at term occurs in 3% to 4% of the term pregnancies. It is found in around 6,000 women annually in the Netherlands. Even if there is no underlying fetal or maternal abnormality, both mother and fetus face an increased risk of a complicated delivery. Secondary prevention of breech presentation is possible by attempting external cephalic version (ECV), which in about 40% of the cases solves a possible obstetrical treatment dilemma; the choice between “vaginal breech or planned caesarean delivery”.

ECV is an obstetrical intervention that has been proven to reduce the number of breech presentations. It has probably been practiced since the time of Aristotle (384 to 322 B.C.). Justus Heinrich Wigand, a German gynaecologist, was the first to describe it in 1907. ECV was mostly practiced before term and became routine obstetrical practice on the basis of personal experience, as well as promising results from non-randomised studies. However, ECV eventually fell out of favour as a result of reports on high rates of spontaneous reversion if performed before 36 weeks of gestation, fetal complications, and the perception of caesarean delivery as a safer option than ECV.

The revival of the use of ECV came in the early 1980s, when the first randomised controlled trials on the subject appeared. Since then ECV has been subjected to five randomised controlled trials assessing its effectiveness. A Cochrane review published first in 1996 demonstrated a significant reduction of the risk of caesarean delivery (OR 0.55, 95% CI 0.33 to 0.91) when ECV was performed after 36 weeks. Still, safety of the procedure remained an issue until two reviews appeared. The most recent review by Collaris et al. showed that complications as they had been reported in studies around 1970 nowadays seem to be far less frequent. ECV is a safe manoeuvre with a risk of an emergency caesarean delivery of 0.43%.

Unfortunately there is no uniformity in the eligibility of patients for the procedure. Three national guidelines on contra-indications for ECV (RCOG, ACOG and the NVOG) all advocate different contra-indications for ECV. Most contra-indications are relative and the evidence level is low (level IV). There are however some obvious contra-indications mentioned in all guidelines, such as a contra-indication to vaginal delivery, ruptured membranes and multiple pregnancy.
Several methods to improve ECV such as uterine relaxation, vibro-acoustic stimulation, epidural or spinal analgesia, and amnioinfusion have been proposed. Of these methods, uterine relaxation was the only method that showed effectiveness. The majority of studies that evaluated the effectiveness of uterine relaxation for ECV have used β-agonists\textsuperscript{12}. These studies reported a beneficial effect of the use of β-agonists over placebo in ECV from 40% to 57% (relative risk 0.74 95% CI 0.64 to 0.87). However, β-agonists have known adverse maternal cardiovascular side effects in terms of flushing, chest pain and palpitations\textsuperscript{13;14}, and as a result the implementation of routine uterine relaxation is low. A Dutch survey on ECV showed that only 35% of the gynaecologists performing ECV used uterine relaxants\textsuperscript{15}. In view of this issue, there is considerable interest in the evaluation of alternative uterine relaxants in ECV.

The calcium antagonist nifedipine has relaxant effects on isolated, non labor human myometrium, and is therefore used for tocolysis in obstetrics\textsuperscript{16;17}. In women with threatened preterm labor, it is more effective in delaying delivery, and it has considerably fewer side effects than β-agonists\textsuperscript{18}. Moreover, long-term neonatal follow-up showed no adverse effects\textsuperscript{19}. To our knowledge, there are no randomised controlled trials assessing the effectiveness of nifedipine in ECV until now.

Despite the effectiveness of ECV in preventing breech presentation and thus lowering the risk of a caesarean delivery, acceptance for both women and doctors to enter an ECV attempt vary. Reported rates of maternal refusal of an ECV attempt range from 18% to 76\%\textsuperscript{20-22}. Conversely, the number of women potentially suitable for ECV who were not offered an attempt range from 4% to 33\%\textsuperscript{20;23;24}. Although there is no formal survey on factors that influence the decision to enter an ECV attempt, uncertainty about success of an ECV attempt might explain this reluctance. In 1987 it was reported that multiparity as well as some ultrasound factors like amniotic fluid volume, fetal abdominal circumference, type of breech, etc. were predictors of success\textsuperscript{25}. This study was followed by several other studies reporting on factors that predict the outcome of an ECV attempt\textsuperscript{18;26-42}. However, systematic knowledge of these factors is lacking. Thus far, five studies have assessed the prognostic value of these indicators in a multivariable approach\textsuperscript{27;33;38;42;43}. Two of these studies used prognostic indicators to develop a scoring system\textsuperscript{38;42}. Both studies have some methodological flaws and a reliable prediction of the outcome of an ECV attempt is still not possible. Accurate prediction of the outcome of an ECV attempt may help in convincing both women and doctors to undergo an ECV attempt. This is an important issue since caesarean delivery rates for the at term breech presentation are high.
Until 2000, two small randomised controlled trials concerning mode of delivery for term breech presentation had been published. Meta-analysis of these trials indicated that there was insufficient evidence for a policy of planned caesarean delivery for breech presentation. Guidelines on the subject, such as the National Consensus Conference on Aspects of Caesarean Birth, stated that planned vaginal birth should be recommended for either frank or complete breech presentation at term. In spite of this recommendation, caesarean delivery rates increased and seemed to be the preferred method of delivery.

In 2000 the results of the Term Breech Trial, in which planned vaginal delivery was compared to a planned caesarean delivery, were published. After interim analysis revealed a strong improvement in neonatal outcome at one month after birth in the elective caesarean group the trial was stopped. The overall risk of perinatal and neonatal mortality in the planned caesarean group was reduced (RR 0.23, 95% CI 0.07 to 0.8; \( P < 0.01 \)). A composite neonatal outcome of mortality and serious neonatal morbidity was similarly reduced (RR 0.33, 95% CI 0.19 to 0.56; \( P < 0.0001 \)). This corresponds with a number needed to treat of 14, i.e. 14 caesarean sections would be performed to prevent one case of bad neonatal outcome.

The results of this study seemed to confirm the presumption that an elective caesarean delivery would reduce morbidity and mortality among children in breech presentation, accordingly the results of this trial had a major impact on the management of the term breech. The caesarean delivery rate in women with a fetus in breech presentation in the Netherlands has increased from 45% to around 80%. This change was accompanied by a substantial decrease in perinatal mortality from breech pregnancies. This beneficial effect might have a drawback as caesarean deliveries are associated with increased maternal morbidity, longer hospital admission and consequences for future pregnancies, such as an increased risk of abnormal placental implantation, uterine rupture and, ultimately, fetal death due to uterine rupture.

Both maternal and infant outcomes were assessed in follow-up studies of the Term Breech Trial. At two years of age, there was no difference in risk of death or neurodevelopmental abnormality between planned vaginal delivery and planned caesarean delivery (RR 1.09, 95% CI 0.52 to 2.30; \( P = .85 \)). However, follow-up was incomplete as neonatal outcome was only known in 80%. Independent of the choice for vaginal or caesarean delivery, prevention of breech presentation at term remains an important matter.
Aim of the thesis

The aim of this thesis was to answer the following questions:

- Which clinical factors influence the probability of success of ECV as estimated by clinicians?
- Which clinical and ultrasound factors can predict a successful outcome of an ECV attempt?
- What are the complications of ECV and are they associated with fetal position after ECV?
- What is the effectiveness of nifedipine as a uterine relaxant for ECV compared to placebo?
- Can the outcome of ECV be predicted?
- What is the preference of expectant parents for mode of delivery in case of term breech position, and what is their judgment of neonatal short- and long-term risks as well as the maternal risks?
Outline of the thesis

In chapter 2 we report the results of a survey among Dutch gynaecologists. We evaluate their ability to predict ECV outcome in fictive patient cases. Potential prognostic factors that varied between the cases were parity, maternal body mass index, engagement of the fetus, amniotic fluid, fetal growth, fetal presentation and placental localisation. Firstly, we evaluate the concordance between the gynaecologists with respect to predictions on ECV outcome with and without uterine relaxation. Secondly, we evaluate the concordance between the gynaecologists with respect to their subsequent treatment decisions.

In chapter 3 we systematically review the medical literature reporting on potential clinical prognosticators for the outcome of ECV. We performed a meta-analysis to identify and quantify clinical factors that can predict a successful outcome of an ECV attempt. We identified 53 primary articles reporting on 10,149 women.

In chapter 4 we describe the results of a meta-analysis that was performed to identify and quantify ultrasound factors that can predict a successful outcome of an ECV attempt. We identified 37 primary articles reporting on 7,709 women.

In chapter 5 we focus on the safety of the ECV manoeuvre. We report on the complications of 12,955 ECV attempts. We report on the incidence of general complications, serious complications, and ECV related emergency deliveries. Furthermore, we report on the association of complications with fetal position after ECV.

In chapter 6 we describe a randomised controlled trial assessing the effectiveness of nifedipine as a uterine relaxant for ECV compared to placebo. Women with a singleton fetus in breech presentation and a gestational age of 36 weeks or more were randomised between ECV after two doses of nifedipine 10 mg or placebo, 30 and 15 minutes before the ECV attempt. The primary outcome was the fetus being in cephalic position immediately after the procedure.

In chapter 7 we present a model for the prediction of successful ECV. The outcome of ECV is dependent on several variables. In this study we built a prediction model by analysing the influence of several variables on successful ECV. We did this by multivariable logistic regression in 310 ECV attempts.
In **chapter 8** we explore patient’s preferences concerning delivery in case of persisting breech presentation. Eighty women (40 with a fetus in breech presentation and 40 with a fetus in cephalic presentation) with a gestational age from 36 weeks onwards were offered scenarios of vaginal and caesarean breech delivery in which one-month and two-year neonatal and maternal complication rates were varied. The complication rates were increased until women switched their preference to a different mode of delivery.

In **chapter 9** we summarise the results of the studies presented in this thesis and give clinical implications and implications for future research in this field.
References


