Management of preterm delivery in women with abnormal fetal presentation
Bergenhenegouwen, Lester

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
Vaginal delivery versus caesarean section in preterm breech delivery: a systematic review

L.A. Bergenhenegouwen
L.J.E. Meertens
J. Schaaf
J.G. Nijhuis
B.W. Mol
M. Kok
H.C. Scheepers

Abstract

There is controversy on the preferred mode of delivery (vaginal delivery (VD) versus caesarean section (CS)) in preterm breech delivery in relation to neonatal outcome. While CS is supposed to be more safe for the fetus, arguments against CS can be the increased risk of maternal morbidity, risks for future pregnancies and costs. Moreover, neonatal respiratory distress syndrome occurs more frequently after CS compared to VD.

In the past, several RCT’s have been started on this subject, but they were all preliminary stopped due to recruitment difficulties. As the Cochrane review of these RCT’s reported on 116 women only, knowledge on the effectiveness of CS and VD can at present only be obtained from non-randomised studies.

We performed a systematic review and meta-analysis of non-randomised studies that assesses the association between mode of delivery and neonatal mortality in women with preterm breech presentation. We therefore searched Pubmed, Embase and The Cochrane library for articles comparing neonatal mortality after VD versus CS in preterm breech presentation (gestational age 25+0 till 36+6 weeks). The weighted risk of neonatal mortality was 3.8% in the CS group and 11.5% in the VD group. (Pooled RR 0.63 (95% CI 0.48 to 0.81)). We conclude that cohort studies indicate that CS reduces neonatal mortality as compared to VD.

Introduction

Preterm delivery, defined as delivery before 37 weeks of gestation, is associated with a high prevalence of breech presentation. Nearly 25-30% of the fetuses present in breech presentation at 28 weeks of gestation. This percentage decreases to 4% in term pregnancies.1,2

Since publication of the Term Breech Trial in the year 2000, planned Caesarean Section (CS) is the preferred mode of delivery for term breech presentation in most countries.3,4 In the Netherlands CS rates in term breech presentation increased from 50% to over 80% after publication of this trial.5

In preterm breech presentation, the mode of delivery is controversial. In many countries, CS is applied for preterm breech presentation. In the Netherlands, women with preterm labour and a child in breech position deliver more often vaginally as compared to other developed countries.6

While CS is supposed to be the safer route for the fetus, arguments against CS can be the increased risk of maternal morbidity, risks for future pregnancies and costs.5 Moreover, neonatal respiratory distress syndrome occurs more frequently after CS compared to VD.7

A final argument is that in women with threatened preterm delivery the exact moment of delivery is sometimes difficult to predict, thus implicating that a CS is sometimes performed to early, an event that is not the case for vaginal delivery.

In the past, several randomized controlled trials (RCT’s) have been started on this subject, but they were all preliminary stopped due to recruitment difficulties.8,9,10 The Cochrane review on these RCT’s, published by Alferivic et al in 2012, could therefore only report on a total of 116 women from six trials with a sample size varying between 12 and 38. The difference between the two groups with regard to perinatal deaths was not significant (0.29, 95% CI 0.07 to 1.14; three trials, 89 women), as were the reports on neonatal morbidity. The conclusion of this review was therefore that there is not enough evidence to evaluate the use of a policy of planned immediate caesarean section for preterm babies. In the absence of RCT’s with a large number of women included, evidence should be obtained from observational studies. We performed a systematic review and meta-analysis of these non-randomised studies to investigate the association between the mode of delivery and perinatal mortality in preterm breech presentation.
Methods

Searching and selection
We searched the electronic databases Pubmed (Medline), Embase and The Cochrane Library from inception until 1st September 2011. The medical literature was searched for RCT’s and cohort studies studying the effect of the mode of delivery on neonatal mortality in preterm breech presentation. The following terms were used: ((“Breech Presentation”[Mesh]) OR (breech)) AND ((“Obstetric Labor, Premature”[Mesh]) OR (“Premature Birth”[Mesh]) OR (preterm) OR (premature)) AND ((vaginal delivery) OR (cesarean) OR (abdominal delivery) OR (“Cesarean Section”[Mesh])) AND (“Mortality”[Mesh]) OR (mortality) OR (death)) AND (Humans[Mesh])). We also performed a manual search of reference lists from the retrieved studies.

Publication date restriction was imposed on studies published before 1980, since perinatal care and interventions have greatly improved over the years. Language restrictions were not applied. Two authors (LB and LM) independently performed the search and screened the abstracts of identified studies. Disagreement between reviewers was resolved by consensus, and if needed the judgement of a third author was decisive.

Study population and eligibility criteria
All studies that compared the relation between the mode of delivery and neonatal mortality in preterm breech presentation were eligible. Preterm delivery was defined as delivery between a gestational age between 25+0 and 36+6 weeks. Studies that solely used low-birth-weights as inclusion criterion were excluded from this review. Primary outcome was neonatal mortality. Secondary outcomes were neonatal morbidity (low Apgar scores, respiratory distress syndrome, ventilatory support, low umbilical artery pH, cerebral haemorrhage, infection, bronchopulmonary dysplasia and survival without disability), and maternal morbidity (duration of hospital recording and puerperal fever). Two reviewers independently performed eligibility assessment.

Quality assessment and data extraction
Data extraction was independently completed by LB and LM using a prespecified data extraction form. The following data were extracted from the selected studies: (1) methods of study (including study design, data collection and time-period of the study); (2) characteristics of trial participants (including number of participants, setting and country) and the inclusion and exclusion criteria; (3) type of intervention (VD versus CS); (4) type of outcome measures (perinatal and/or neonatal mortality, secondary outcomes); (5) statistical methods.

To ascertain the validity of eligible observational studies, the reviewers independently determined the adequacy of inclusion and exclusion criteria, characteristics of study participants, inception cohort, selection bias, interventions and co-interventions, outcome measurement, confounders, subgroup analyses and follow-up.

To explore the heterogeneity in study results the following hypothesis was specified before conducting the analysis. The reviewers hypothesized that the intention for the individual interventions (CS or VD) may differ in the studies leading to confounding by indication.

Data analysis
We constructed two by two tables comparing the mode of delivery and neonatal mortality in women preterm delivering a child in breech presentation. Relative risks (RR’s) and their 95% confidence intervals were calculated for the outcome neonatal mortality and total mortality (intrapartum and neonatal death). Overall estimates of effect were calculated with the Mantel-Haenszel method.

The random-effects model was used in advance, as this method takes into account the variation between studies. Heterogeneity was tested with the chi-squared (P= 0.10) and Tau test. Inconsistency (I²) was measured, because this method does not inherently depend on the number of studies and is accompanied by an uncertainty interval. A subgroup analysis was performed to address whether the summary effects vary in relation to gestational age. RR’s and their 95% confidence intervals were also calculated for the secondary outcomes where possible. Statistical analysis was carried out using Review Manager software (RevMan version 5.0, The Cochrane Collaboration).

Results

Selected studies
Our search strategy identified 723 studies (Figure 1). Of these studies, 706 were discarded after screening the abstracts and titles, because they did not meet the eligibility criteria. Three studies could not be included because their full text was not available online or in the university depot and the authors e-mail addresses were unknown. The full texts of the remaining 14 studies were assessed in detail. Seven studies did not meet the eligibility criteria: three did not define the gestational age period12-14, two studies were performed before 198015-16, one study was terminated because of insufficient patient recruitment17 and one study included both preterm and low birth weight infants.17 References of the 14 full text studies revealed no new relevant papers. Finally, seven studies met the eligibility criteria and were included in this systematic review.18-24
Description of studies

The seven selected studies involved a total of 3557 women (range 88-2674 women per study) delivering preterm of a fetus in breech presentation. All studies were retrospective studies published in English. Detailed information on the characteristics of the included studies is provided in Figure 2.

The data sources of five of the seven included studies were maternal and neonatal charts,18, 20, 21, 22, 23, the other two studies used hospital databases.19, 22 All participants were recruited in a hospital setting, mostly tertiary care centres. The main inclusion criteria entailed women who delivered preterm singleton fetuses in breech presentation. The gestational age was different in the selected studies, varying from 25+0 weeks as lower limit to 36+6 weeks as the upper limit. All studies excluded cases of antepartum death and lethal congenital malformations. Three studies had more narrow exclusion criteria.18, 19, 22 Four studies were single centre, 18, 20, 23, 24 two studies were
multicentre\textsuperscript{19, 22} and one study was nationwide.\textsuperscript{21} All studies compared CS and VD. The sample size of almost all studies was relatively small, except for the study performed by Herbst et al.\textsuperscript{21}, which included 2674 women.

Neonatal mortality

Neonatal mortality was defined differently in the studies: neonatal mortality in the first 7 days after birth, neonatal mortality in first 28 days after birth and neonatal mortality in the period from birth till discharge from the hospital. Two studies, Malhotra et al.\textsuperscript{23} and Herbst et al.\textsuperscript{21}, reported a significant lower neonatal mortality after CS (RR 0.52 (95% CI 0.32-0.84) and RR 0.50 (95% CI 0.31-0.81)). The other studies showed a trend favouring CS, except for the study of Wolf et al.\textsuperscript{20}, which was the only study that showed a non-significant trend favouring VD, RR 1.3 (95% CI 0.64-2.6).

The pooled analysis showed that CS reduced the risk of neonatal mortality by 37% (pooled RR 0.63 (95% CI 0.48-0.81) compared to VD (Figure 3). The absolute risks were 3.8% for CS and 11.5% for VD respectively, corresponding with a number needed to treat to prevent one neonatal death in the overall group of 13.

Total perinatal mortality, i.e. intrapartum and neonatal mortality, was reported in six of the seven studies. Total perinatal mortality was significantly different in two studies favouring CS, RR 0.49 (95% CI 0.30-0.80) and RR 0.50 (95% CI 0.27-0.96). The other studies, except the study of Wolf et al.\textsuperscript{19}, showed a non-significant trend favouring CS. The pooled analysis for total mortality indicated a RR of 0.63 (95% CI 0.44-0.92) favouring CS (Figure 4).

Only two of seven studies explicitly mentioned intention to treat analysis\textsuperscript{19, 22}. The study of Kayem et al.\textsuperscript{22} showed a non-significant trend in favour of CS for the outcome neonatal mortality, RR 0.85 (95% CI 0.30-2.42) and for total mortality, RR 0.66 (95% CI 0.25-1.77).

Figure 3 Comparison of CS versus VD for preterm breech presentation, Outcome Neonatal mortality

In this study, in the planned VD group 49% delivered by CS, whereas in the planned CS group 5.9% delivered vaginally. The study of Wolf et al.\textsuperscript{19} was also analysed according intention to treat, and showed a non-significant trend in favour of vaginal delivery for the outcome neonatal mortality, RR 1.29 (95% CI 0.64-2.60), and for total mortality, RR 1.27 (95% CI 0.66-2.45). This study however only included women with gestational age 26-32 weeks. The other five included studies did not use an intention to treat analysis, these studies described the number of VD compared to the number of CS.

A subgroup analysis for neonatal mortality according to gestational age and mode of delivery was also performed. Outcomes in different gestational age groups were reported in two of the seven studies.\textsuperscript{21, 22} Herbst et al.\textsuperscript{21} showed a significant difference for neonatal mortality in gestational age 25-28 weeks favouring CS, RR 0.30 (95% CI 0.18-0.49) and there was a non-significant trend favouring CS for gestational age 28-33 weeks and 34-37 weeks (Figure 5). The study of Warke et al.\textsuperscript{20} showed a non-significant trend towards VD for gestational age 30-34 weeks, (RR 1.1; 95% CI 0.32-3.8) and a non-significant trend favouring CS for 34-37 weeks of gestation (RR 0.67; 95% CI 0.19-2.4). Data stratified for gestational age could not be pooled since the studies did not analyse the same subgroups of gestational age. The study of Kayem et al.\textsuperscript{22} was limited to preterm breech deliveries between 26-29.6 weeks of gestation. This study showed a non-significant trend favouring CS for the outcome neonatal mortality (RR 0.85; 95% CI 0.30-2.4) and total mortality (RR 0.66; 95% CI 0.25-1.8).

Neonatal morbidity

Neonatal morbidity was reported in all studies, but analysis was hampered since the included studies used different morbidity outcomes. The Apgar scores were variably
reported as low 1-min and 5-min Apgar scores. A low 1-min Apgar score was significantly different favouring CS in the study of Herbst et al.21 (44, RR 0.7; 95% CI 0.53-0.94) and in Malhotra et al.23 (0.3, RR 0.68; 95% CI 0.47-0.97). The low 1-min Apgar score was similar between the two groups as reported in Malhotra et al.21 (66, RR 0.80; 95% CI 0.64-1.01), Van Eyk et al. 24 (66, RR 0.98; 95% CI 0.53-1.82) and Ziadeh et al. 18 (66, RR 0.9595% CI 0.73-1.23).

The incidence of a low 5-min Apgar scores occurred significantly more frequent in the VD Group, as published by Herbst et al.21 (5, RR 0.50; 95% CI 0.31-0.81), Kayem et al.22, (66, RR 0.33; 95% CI 0.16-0.69) and Malhotra et al. 23 (66, RR 0.62; 95% CI 0.41-0.92). The low 5-min Apgar scores were similar between the two groups as reported by Ziadeh et al.18 (66, RR 0.88; 95% CI 0.52-1.50) and Malhotra et al.23 (4.6, RR 0.63; 95% CI 0.36-1.09). In the study of Warke et al.20 infants above 30 weeks of gestation had statistically lower 5-min-Apgar scores in the VD group as compared to the CS group (≤6, RR 0.88; 95% CI 0.53-1.47) performing a CS as compared to VD in preterm infants, short term morbidity is not always correlated to a long-term adverse outcome.

Neonatal mortality was chosen as main outcome for this review since this outcome is relevant and easy to measure, and therefore often reliably reported. Morbidity, although also important, is much more difficult to define. For neonatal morbidity, the included studies used different types of neonatal outcomes whereby it was impossible to pool these data and to draw valid conclusions. Besides, especially in preterm infants, short term morbidity is not always correlated to a long-term adverse outcome. The data on maternal morbidity had insufficient power to draw valid conclusions.

This systematic review assesses the mode of delivery for women preterm (gestational age ≥25+6 to ≥36+6 weeks) delivering a fetus in breech presentation. We retrieved no randomized studies and seven non-randomized studies. The absolute risk for neonatal mortality was 3.8% in the CS group and 11.5% in the VD group. The pooled RR was 0.63 (95% CI 0.48 to 0.81) for neonatal mortality after CS compared to VD.

Neonatal mortality was chosen as main outcome for this review since this outcome is relevant and easy to measure, and therefore often reliably reported. Morbidity, although also important, is much more difficult to define. For neonatal morbidity, the included studies used different types of neonatal outcomes whereby it was impossible to pool these data and to draw valid conclusions. Besides, especially in preterm infants, short term morbidity is not always correlated to a long-term adverse outcome.

The duration of hospital stay was significantly longer in the CS group (mean 8.4 days versus mean 6.3 days). The incidence of puerperal fever was not different (CS 9% versus VD 3%; RR 2.93; 95% CI 0.68-12.5). No major maternal complications were described in the studies.

**Discussion**

This systematic review demonstrates that neonatal mortality is significantly reduced by 37% (pooled RR 0.63 95% CI 0.48 to 0.81) performing a CS as compared to VD in preterm breech presentation in gestational age ≥25+6 till 36+6 weeks. As these data originate from non-randomised studies, some comments have to be highlighted. An important issue in studies on this subject is that the intention of the mode of delivery often is not clearly described. Consequently, in most studies there is only a description of the number of women who delivered vaginally and the number of women that delivered by CS. This is also the case in studies identified for this review, as only two of seven studies clearly described the intention of the mode of delivery and used intention to treat analysis.19,22 Not analysing according to intention to treat...
analysis implicates that in women with expected adverse outcome (severe growth restriction or a “non intervention” policy) or rapid progress of labour a VD possibly is more common. On the other hand, emergency CS are included in the CS group and the outcome of the infants who were “intended” to deliver vaginally may be worse, suggesting an even better outcome in planned CS. Planning a CS in the preterm period is however also not without risks. If an incorrect diagnosis of unavoidable preterm birth is made, the fetus might be delivered at an earlier gestational age than necessary. However, the impact of CS is so strong that we do not expect that the individual women, who would have delivered later if VD would be awaited, will compensate for this difference.

Another problem of this review is that the included studies had different subgroups of gestational age, whereby we were unable to pool these data and conclude which subgroup of gestational age has the most benefit by delivering by CS. Obviously, in neonates born very preterm the baseline risk of neonatal mortality will be higher than in neonates born late preterm. Consequently, the relative benefit of a CS will be stronger in neonates born late preterm.

Ideally, of course, an RCT would reveal the best management for preterm breech presentation, taking gestational age in account as a treatment prediction marker.

Although several attempts have been made for a RCT, including women into such a trial is very difficult and all RCT’s were stopped before reaching the calculated sample size due to recruitment difficulties. The Cochrane review on this subject could include only 116 women, the authors concluded that there is not enough evidence to evaluate the use of a policy of planned immediate caesarean delivery for preterm babies. Further studies are needed in this area, but adequate recruitment has proven to be difficult. Therefore evidence should be obtained from a review of cohort studies: on this subject the best available evidence. Although this is a very important topic, we believe that it is very unlikely that a new large RCT on preterm breech presentation, the mode of delivery and neonatal mortality will be performed in the near future.

Conclusion

We found no large randomised controlled studies addressing the optimal mode of delivery in women delivering a fetus in breech presentation preterm. The available cohort studies indicate that CS reduces neonatal mortality by 37% as compared to VD in preterm breech delivery. This conclusion should carefully be interpreted, concerning the lack of intention to treat analysis and other bias that is inevitably in cohort studies. However, we have summarized the best available data on the subject. Further studies on this subject are necessary, but a large randomized controlled trial is unlikely to be performed in the near future.

Acknowledgements
No specific acknowledgements have to be listed in the article.

Disclosure of interests
No relevant financial, personal, political, intellectual or religious interests were disclosed.

Contribution to authorship
LB is the first and main author of the manuscript. LM was the second reviewer; she independently screened titles and abstracts of identified studies and independently performed the data extraction using the data extraction form and contributed an essential part to the writing of the manuscript. HS participated as the third independent reviewer when disagreement occurred and contributed to the writing of the manuscript. JS, JN and BM contributed to the writing of the manuscript and to the methodology and statistical co-analysis.

Funding
There was no funding by a commercial company, charity or government department for writing this systematic review.
References


5. LVR data (nationwide perinatal databank in The Netherlands)


