Risk of preterm birth after prior term cesarean

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Objective To determine the risk of overall preterm birth (PTB) and spontaneous PTB in a pregnancy after a caesarean section (CS) at term.

Design Longitudinal linked national cohort study.

Setting The Dutch Perinatal Registry (1999–2009).

Population 268 495 women with two subsequent singleton pregnancies were identified.

Methods A cohort study based on linked registered data from two subsequent pregnancies in the Netherlands.

Main outcome measures The incidence of overall PTB and spontaneous PTB with subgroup analysis on gestational age at first delivery and type of CS (planned or unplanned).

Results Of 268 495 women with a singleton first pregnancy who delivered at term, 15.76% (n = 42 328) had a CS. The incidence of PTB in the second pregnancy was 2.79% (n = 1182) in women with a previous CS versus 2.46% (n = 5570) in women with a previous vaginal delivery (adjusted odds ratio [aOR] 1.14, 95% confidence interval [CI] 1.07–1.21). This increased risk is mainly driven by an increased risk of spontaneous PTB after previous CS at term (aOR 1.50, 95% CI 1.38–1.70). Analysis for type of CS compared with vaginal delivery showed an aOR on spontaneous PTB of 1.86 (95% CI 1.58–2.18) for planned CS and an aOR of 1.40 (95% CI 1.24–1.58) for unplanned CS.

Conclusions CS at term is associated with a marginally increased risk of spontaneous PTB in a subsequent pregnancy.

Keywords Caesarean section, mode of delivery, preterm birth, risk factor, spontaneous preterm birth.

Tweetable abstract Caesarean section at term is associated with a marginally increased risk of spontaneous PTB in a subsequent pregnancy.

Linked article This article is commented on by ML Urquia, p. 618 in this issue. To view this mini commentary visit https://doi.org/10.1111/1471-0528.16099.

Introduction

Preterm birth is a global health concern, and a leading cause of perinatal mortality and paediatric morbidity.[1–3] The aetiology of preterm birth (PTB) remains, despite many publications on the subject, largely indefinite.[4] Although the main significant risk factor for PTB is prior PTB,[4] in some cases PTB occurs after a previous birth at term. In this population, specific risk factors have been suggested.[5] Factors associated with an increased risk of PTB in a subsequent pregnancy are an inter-pregnancy interval of less than 18 months (odds ratio [OR] 1.37, 95% confidence interval [CI] 1.21–1.55) and tobacco use started after

first delivery (OR 2.33, 95% CI 1.61–3.38).[5] Other factors in the obstetrical history do not seem to create an increased risk: prolonged second stage of labour, induction of labour or operative vaginal delivery.[6,7] Recently, an association has been suggested between preterm birth and an history of CS.[4,5,8,9] A large multicentre cohort study observed an association between a history of CS and risk of overall PTB (OR 1.2, 95% CI 1.1–1.3). Subgroup analysis showed a significantly higher risk of spontaneous but not of iatrogenic PTB.[4] A case-control study by Wong et al. also found that women with a history of a CS had an increased risk of PTB in the subsequent pregnancy (OR 2.20, 95% CI 1.57–3.08).[5] That study, however, did not make a distinction between spontaneous or iatrogenic PTB. With rising CS

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rates and persistent high PTB rates, a possible association between the two requires further evaluation.[1,2,10,11] The presence of a caesarean scar contributes to increased risk of complications in a subsequent pregnancy such as placenta praevia, abnormal adhesive placenta and placental abruption in a subsequent pregnancy[12]. The uterine scar might also develop a scar defect ('niche') with stasis of fluid or blood. It is unclear if this might attribute to the risk of PTB in a subsequent pregnancy.[13] The objective of this study is to evaluate the risk on both overall PTB and spontaneous PTB after a previous CS at term.

Material and methods

Patients

We used data from the Netherlands Perinatal Registry (Perined). This registry contains information on mothers and children regarding pregnancy and delivery (>22 weeks of gestational age) with a follow up until 28 days after the delivery. Approximately 96% of all deliveries are recorded in the Perined registry. The Perined database is an assemblage of three different registries, obtained by a validated linkage: the midwifery registry, the obstetrics registry and the neonatology registry of hospital admissions of newborn neonates.[14,15] The Netherlands Perinatal Registry processes patient's data anonymously, therefore patients' consent is not required. Data in the registry are recorded at child's level, therefore the structure of the registry does not provide follow up on outcomes of subsequent pregnancies in the same mother. To create a cohort with data on first and second delivery of the same mother, a longitudinal probabilistic linkage procedure was performed. Details on the first longitudinal linkage study (2000–2007) by Schaaf et al. have been published elsewhere.[16,17] In the second longitudinal linkage study (birth dates between 1 January 1999 until 31 December 2009) more linkage variables have been added; resulting in seven linkage varables.[16,17] The Perined registry approved use of the data for this study (Approval no. 2017.22). Patients have not been involved in the development of this research. From the longitudinal database, we identified all women who delivered their first and second child in The Netherlands between 1 January 1999 until 31 December 2009. We excluded all multiple gestations, women with a first delivery at a gestational age >43.6 weeks or <37.0 weeks, as well as women with one pregnancy or both pregnancies complicated by congenital anomalies and antenatal deaths. We also excluded women with either hypertensive disorders of pregnancy (HD) or small-for-gestational-age (SGA) neonates in the first pregnancy, as there might be a common pathway leading to HD, SGA and PTB, possibly through an abnormal angiogenic profile leading to placental insufficiency.[18] SGA was defined as a birthweight below the 10th percentile according to the

birthweight data of the Perined registry.[19] We evaluated demographic and obstetrical baseline characteristics including ethnicity, socio-economic status, maternal age, and mean gestational age at delivery in first pregnancy and spontaneous or iatrogenic onset of delivery in first pregnancy. The socio-economic status score was based on national data from 2010 collected by the Netherlands Institute of Social Research (mean income level, the percentage of households with a low income, the percentage of inhabitants without a paid job and the percentage of households with, on average, low education level) in a 4-digit postal code area and is expressed as percentage of women with a low economic socio-economic status score (≤25th percentile).

Comparison

We compared perinatal outcomes between women with a vaginal birth and a CS. The main outcome and secondary outcomes were analysed for both groups. Secondly, women with a prior CS were divided in subgroups based on mode of delivery in first pregnancy: unplanned or planned CS.

Outcome measures

Our main outcome measure was PTB rate in the second pregnancy. The ratios of total PTB and spontaneous PTB in subsequent pregnancy were evaluated. Beside this, the gestational age (GA) at delivery in the second pregnancy after a CS versus a vaginal delivery was evaluated. The Perined Registry contains fixed outcome measures, therefore the core outcome sets which are internationally recommended and used in clinical trials on this topic could not be used.[20]

Spontaneous preterm birth was defined as having spontaneous onset of labour and/or spontaneous rupture of the membranes in the preterm period (<37.0 weeks of pregnancy). Preterm birth without spontaneous onset of labour or spontaneous rupture of the membranes was considered to be iatrogenic. A planned CS is defined as a CS planned during pregnancy independently of the onset of labour. An unplanned CS is defined as childbirth with the patients' and obstetricians' intention to deliver vaginally but which ended up with a caesarean section due to intrapartum complications. Unfortunately, the indications for planned or unplanned CS are not reported consistently in the registry and were therefore left out of the analysis.

Analysis

To assess specifically the impact of spontaneous PTB after prior CS at term, we performed a sensitivity analysis in which we excluded women with HD and SGA (<p10) neonates in the first pregnancy. The outcome of the second pregnancy was compared between women with a prior vaginal birth and CS. We first compared the duration of

pregnancy between those groups and then analysed the time to iatrogenic delivery and time to spontaneous delivery using competing endpoints techniques in Kaplan–Meier analysis. Subsequently, outcome of second pregnancy was analysed for women with prior unplanned or planned CS at term.

Data were analysed with the SAS statistical software package, version 9.3. We performed univariate analyses with the Student t-test for the continuous variables and the χ^2 test for the categories variables to compare baseline characteristics. If the continuous variables were normally distributed, the equal variance test was used and for skewed distributions the unequal variance test was used.

PTB rates in the second pregnancy were adjusted for maternal age at first delivery, ethnicity, socio-economic status, recurrent HD, inter-pregnancy interval, and recurrent SGA in a multivariable logistic regression analysis. All statistical tests were 2-sided; we chose a probability value of 0.005 as the threshold to indicate statistical significance.

Results

A total of 391 026 women delivered twice between 1 January 1999 and 31 December 2009. We applied the following general exclusion criteria: multiple gestations ($n = 11\ 038$), gestational age in first pregnancy >43.6 weeks or <37.0 weeks ($n = 26\ 807$), pregnancies with congenital anomalies ($n = 18\ 091$) and cases with antenatal death ($n = 3215$). After exclusion of all women with HD ($n = 32\ 962$) and SGA neonates ($n = 30\ 454$) in the first pregnancy, 268 495 singleton pregnancies remained in the analysis. Figure 1 shows the selection process. In the first pregnancies, 226 167 (84.24%) children were born vaginally and 42 328 (15.76%) children were born through CS. Table 1 shows the baseline characteristics for both groups.

Table 2a shows an overall incidence of PTB of 2.79% ($n = 1182$) in women with a previous CS versus 2.46% ($n = 5570$) in women with a previous vaginal delivery. A marginally increased risk of PTB was observed after prior CS at term (adjusted odds ratio [aOR] 1.14, 95% CI 1.07–1.21) compared to prior vaginal delivery at term. This higher risk of PTB in a subsequent pregnancy was observed for women with a history of both unplanned and planned CS when compared with women with a previous vaginal delivery (aOR 1.11, 95% CI 1.03–1.20 versus aOR 1.22, 95% CI 1.09–1.36, respectively). Table 2b shows the analysis on spontaneous PTB. The incidence of spontaneous PTB is higher in women with prior CS (1.15%) than women with prior vaginal delivery (0.75%, aOR 1.50, 95% CI 1.38–1.70). We observed this effect after both unplanned and planned CS when compared with vaginal delivery (aOR 1.40, 95% CI 1.24–1.58 versus aOR 1.86, 95% CI

1.58–2.18, respectively). Table 3 illustrates GA at delivery in the second pregnancy and shows that if women deliver preterm after prior birth at term, most women deliver in the late preterm period (between 34–37 weeks of gestational age). Survival analysis (Figure 2) validates these results. We evaluated the risk of having iatrogenic PTB in the subsequent pregnancy after CS compared with after vaginal delivery and did not observe an increased risk (aOR 1.03, 95% CI 0.95–1.12) in this cohort of women.

Discussion

Main findings

We studied the association between a first CS at term and the risk of spontaneous PTB in the second pregnancy. We observed a small increased risk of spontaneous PTB in the second pregnancy in women with a history of CS at term.

Strengths and limitations

This study is based on national data from a population-based perinatal registry that contains 96% of all pregnancy and birth characteristics in The Netherlands, as well as information on the subsequent pregnancy. The missing data are mainly due to non-reporting by general practitioners and midwifes. The registration by obstetricians was nearly complete (>99%). All women with a CS or a history of a CS in our study delivered in the hospital; therefore, we did not miss many cases due to non-reporting. The prevalence of CS in our cohort corresponds with epidemiological data in previous publications.[21]

There are some limitations of the study. First, not all variables with potential effect on the primary outcome were available in the National Perinatal Registry, such as body mass index (BMI) and smoking. Moreover, not all details concerning the first delivery were available. For instance, no distinction can be made between first and second stage of labour in the Perined registry. Therefore, we cannot evaluate the influence of prolonged stage of labour on the risk of PTB in the second pregnancy. Secondly, of particular importance is the exact calculation of gestational age. The way the expected date of delivery of the studied pregnancies used in the Perined database was calculated is not reported on an individual level and could either be based on the first day of the last menstrual period and/or early ultrasound; where there was a difference of 1 week, dating by ultrasound prevailed. Thirdly, regarding the primary outcome, the indication of iatrogenic preterm birth was not registered, as it is not an obligatory field in the registry.

Interpretation

Due to an increasing rate of CS, complications following a CS have been studied extensively because of the
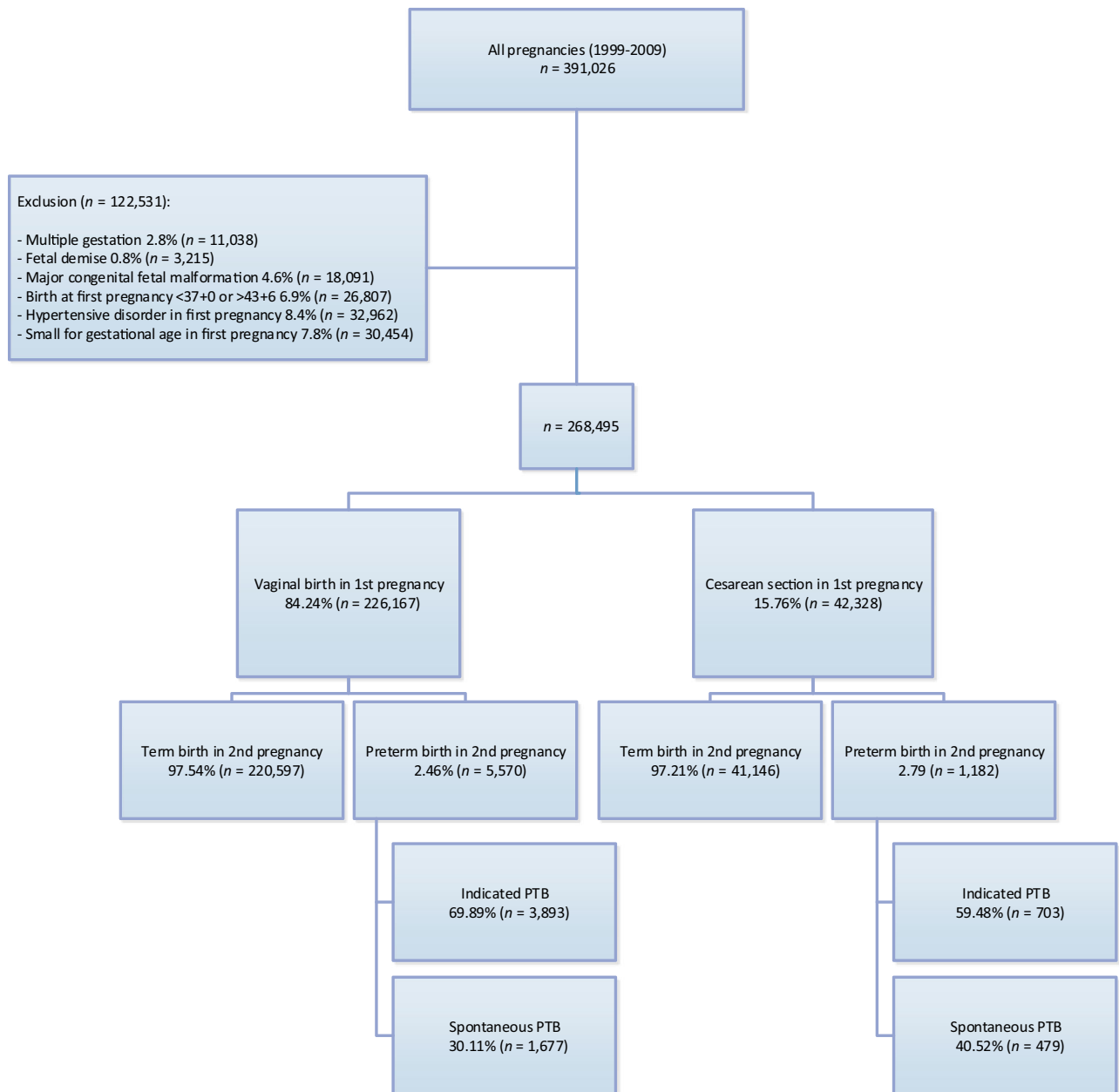
Figure 1. Flowchart: mode of delivery in first pregnancy and type of preterm birth in second pregnancy

possible clinical implications for subsequent pregnancies. Increased risk of several obstetrical adverse outcomes for women with a history of CS have been reported, such as a higher risk of haemorrhage, placenta praevia, uterine rupture, repeat CS, but also HD and stillbirth.[5,22–24] It has proven to be difficult in these studies to isolate the attributable effect of a CS on the risk of adverse outcome in a subsequent pregnancy from other (obstetrical) characteristics. It seems that women who undergo a CS have a higher *a priori* risk of adverse outcome compared

with women who deliver vaginally. In our study, this was also reflected in the difference in the baseline characteristics. The higher prevalence of total and spontaneous PTB in women with a history of a planned CS might be illustrating the higher *a priori* risk of obstetrical complications in women with an indication for a planned CS. Certain confounding factors increase the risk of both a planned CS and PTB, such as HD, fetal growth restriction, and maternal obesity and maternal diseases.[25–28] We observed this in this cohort of women

Table 1. Baseline demographics and clinical characteristics of women in their first and second pregnancy

Characteristics	Mode of delivery 1st pregnancy		P-value
	Vaginal delivery (*n* = 226 167)	CS (*n* = 42 328)	
Non white race, *n* (%)	26 638 (11.78)	4552 (10.75)	<0.0001
Low socio-economic status, *n* (%)	47 305 (26.45)	8242 (19.47)	<0.0001
1st pregnancy			
Maternal age, years, mean (± SD)	28.39 (4.21)	29.36 (4.09)	<0.001
GA at delivery, weeks, mean (± SD)	39.70 (1.27)	39.69 (1.44)	0.25
Spontaneous onset of labour, *n* (%)	152 992 (67.65)	11 094 (26.21)	<0.001
2nd pregnancy			
Maternal age, years, mean (± SD)	31.01 (4.20)	32.07 (4.07)	<0.001
Hypertensive disorders, *n* (%)	5716 (2.53)	1541 (3.64)	<0.001
SGA < p10, *n* (%)	13 895 (6.14)	2625 (6.20)	0.65
Spontaneous onset of labour, *n* (%)	174 540 (77.17)	18 214 (43.03)	<0.001
Macrosomia (>4500 g), *n* (%)	9575 (4.23)	1911 (4.51)	0.009
Inter-pregnancy interval, months, mean (± SD)	23.76 (15.78)	23.28 (14.35)	<0.001

GA, gestational age; SGA, small for gestational age; HD, hypertensive disorders of pregnancy; SD, standard deviation.

Table 2a. Total of preterm births in second pregnancy related to mode of delivery in first pregnancy

Mode of delivery in 1st pregnancy	*n*	Primary outcome in 2nd pregnancy		
		Preterm birth, *n* (%)	Term birth, *n* (%)	aOR (95%CI)[*]
Vaginal delivery	226 167	5570 (2.46)	220 597 (97.54)	–
All CS	42 328	1182 (2.79)	41 146 (97.21)	1.14 (1.07–1.21)
Unplanned CS	30 213	824 (2.73)	29 389 (97.27)	1.11 (1.03–1.20)
Planned CS	12 115	358 (2.96)	11 757 (97.04)	1.22 (1.09–1.36)

aOR, adjusted odds ratio; CI, confidence interval; CS, caesarean section.
*Adjusted for: maternal age at first delivery, ethnicity, socio-economic status, recurrent HD, inter-pregnancy interval and recurrent SGA.

Table 2b. Spontaneous preterm birth in second pregnancy related to mode of delivery in first pregnancy**

Mode of delivery in 1st pregnancy	*n*	Primary outcome in 2nd pregnancy		
		Spontaneous preterm birth, *n* (%)	Term birth, *n* (%)	aOR (95% CI)*
Vaginal delivery	222 274	1677 (0.75)	220 597 (99.25)	–
All CS	41 625	479 (1.15)	41 146 (98.85)	1.50 (1.38–1.70)
Unplanned CS	29 702	313 (1.05)	29 389 (98.95)	1.40 (1.24–1.58)
Planned CS	11 923	166 (1.39)	11 757 (98.61)	1.86 (1.58–2.18)

aOR, adjusted odds ratio; CI, confidence interval; CS, caesarean section.
*Adjusted for: maternal age at first delivery, ethnicity, socio-economic status, recurrent HD, inter-pregnancy interval and recurrent SGA.
**Women with indicated PTB in second pregnancy were excluded from this analysis.

as well. In several studies concerning the effect of CS on adverse outcome in a subsequent pregnancy, a proportion of these confounding factors have not been taken into account. Wood et al. observed an association between CS and stillbirth in the subsequent pregnancy in the first instance. However, after re-analysis (including multivariate analysis for confounding factors) this association disappeared.[23,24] In our analysis, we evaluated a low-risk population and corrected for maternal age, race and socio-economic status.

Table 3. Gestational age at delivery in second pregnancy after previous vaginal delivery at term versus planned or unplanned caesarean at term

GA at delivery in 2nd pregnancy	Mode of delivery in 1st pregnancy		
	Vaginal (*n* = 226 167)	Caesarean	
		Planned (*n* = 12 115)	Unplanned (*n* = 30 213)
<28 weeks GA, *n* (%)	197 (0.09)	11 (0.09)	33 (0.11)
28–32 weeks GA, *n* (%)	380 (0.17)	20 (0.17)	53 (0.18)
32–34 weeks GA, *n* (%)	549 (0.24)	28 (0.23)	90 (0.30)
34–37 weeks GA, *n* (%)	4444 (1.96)	299 (2.47)	648 (2.14)
37–42 weeks GA, *n* (%)	220 597 (97.54)	11 757 (97.04)	29 389 (97.27)

GA, gestational age.

1 Planned cesarean 2 Unplanned cesarean 3 Vaginal delivery
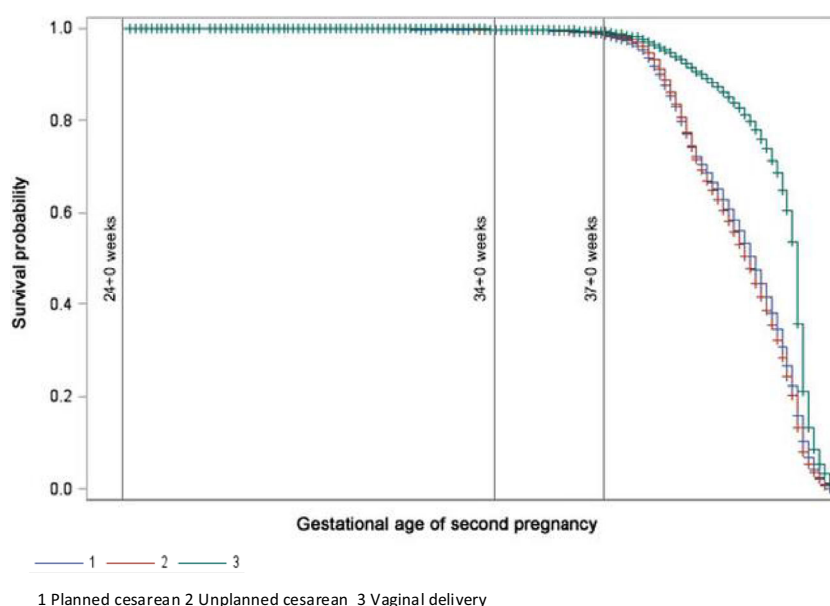
Figure 2. Time to birth in second pregnancy after caesarean versus vaginal delivery in first pregnancy

Previous publications on the association between a CS in the first and PTB in the second pregnancy also show an increased risk of PTB after a term CS.[4,5,29–31] Nevertheless, the effect size is not concordant between studies. In a large nationwide individual patient-level analysis, an odds ratio of 1.2 (95% CI 1.1–1.4) for overall PTB in the second pregnancy and odds ratios of 1.4–1.9 for spontaneous PTB were reported,[4] which is in line with our results. This study illustrates individual and population attributable risk factors for PTB and shows that a previous CS is associated with an increased risk of PTB when corrected for prior PTB.[4] Another study by Wong et al. showed a more than twofold increased risk of PTB after term CS in a case-control study of 38 215 women. Comparable to our data, most preterm deliveries in second pregnancy were late preterm (34–37 weeks). However, there was no distinction made between spontaneous and iatrogenic PTB in this cohort, which might be an explanation for the greater effect size of this study.[5] A recently published systematic review shows results similar to ours, concluding that prior CS (both for elective and emergency indications) shows an increased risk of subsequent PTB >32 weeks of pregnancy.[30] Another very recent publication of an American cohort study with a comparable design to our study shows higher incidence of spontaneous PTB and iatrogenic PTB after CS at term; however, none of those results was statistically significant after adjustment for confounding factors such as the indication for the prior CS.[29]

However, despite these observations, the pathophysiological pathway towards preterm birth after prior CS remains

largely unclear. The increased risk of spontaneous PTB might be attributable to the presence of the caesarean scar. Possible pathways include abnormal placental implantation, changed uterine microenvironment with or without increased inflammation, disruption or dehiscence of tissue, affected cervical function due to cervical damage during the prior CS or stasis of fluid or blood in the lower uterine segment that might induce the cascade leading to preterm birth.[13,30–32] For instance, in women with prior CS the incidence of a scar dehiscence (in the absence of uterine scar rupture) has been reported to be 3.2% and is associated with preterm birth in a subsequent pregnancy.[33]

Conclusion

Women with one previous CS at term have a slightly increased risk of having spontaneous PTB in a subsequent pregnancy. Yet it is unknown whether there is a causal relationship or an association due residual to confounding.

Recommendations

Obstetricians need to be aware of the association between a previous (planned or unplanned) CS at term and an increased risk of spontaneous PTB in the subsequent pregnancy. However, the overall increase in risk of PTB is modest, as the absolute risk of having PTB after a previous birth at term is low (2.5% according our data).

Our findings support the need for further research on the association between CS and PTB. PTB remains a major health issue. Also, rising CS rates are a current health concern. The World Health Organization (WHO) recommends the CS rates should not to rise above 15%.[34] Their systematic review shows that CS rates up to 10–15% are associated with decreases in maternal, neonatal and infant mortality, and rates above 15% do not attribute to a further decrease in mortality.[35]

So, the increasing CS rates have several consequences on perinatal morbidity and mortality and might also attribute to the PTB rates. We recommend that further research focuses on reduction of CS rates.

Disclosure of interests

The authors report no conflicts of interests. Completed disclosure of interests forms are available to view online as supporting information.

Contribution to authorship

LV, MdB and BM were involved in the conception and design of the study. Analysis was conducted by BK, LV and CS. LV and CS drafted the manuscript. MdB, MO, CdG, BK, BM and AR contributed to the interpretation of the analysis and writing of the manuscript. All authors approved the final manuscript.

Details of ethics approval

The data in the perinatal registry are anonymous and therefore ethical approval was not needed. The Netherlands Perinatal Registry (Perined, https://www.perined.nl/) gave their approval for the use of their data for this study (approval no. 2017.22).

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article. ∎

References

1 Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. *Lancet* 2012;379:2162–72.

2 Lee AC, Blencowe H, Lawn JE. Small babies, big numbers: global estimates of preterm birth. *Lancet Glob Health* 2019;7:e2–3.

3 Chawanpaiboon S, Vogel JP, Moller AB, Lumbiganon P, Petzold M, Hogan D, et al. Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. *Lancet Glob Health* 2019;7:e37–46.

4 Ferrero DM, Larson J, Jacobsson B, Di Renzo GC, Norman JE, Martin JN Jr, et al. Cross-country individual participant analysis of 4.1 million singleton births in 5 countries with very high human development index confirms known associations but provides no biologic explanation for 2/3 of all preterm births. *PLoS ONE* 2016;11:e0162506.

5 Wong LF, Wilkes J, Korgenski K, Varner MW, Manuck TA. Risk factors associated with preterm birth after a prior term delivery. *BJOG* 2016;123:1772–8.

6 Levine LD, Bogner HR, Hirshberg A, Elovitz MA, Sammel MD, Srinivas SK. Term induction of labor and subsequent preterm birth. *Am J Obstet Gynecol* 2014;210:e1–8.

7 Levine LD, Srinivas SK. Length of second stage of labor and preterm birth in a subsequent pregnancy. *Am J Obstet Gynecol* 2016;214: e1–4.

8 Cong A, de Vries B, Ludlow J. Does previous caesarean section at full dilatation increase the likelihood of subsequent spontaneous preterm birth? *Aust N Z J Obstet Gynaecol* 2018;58:267–73.

9 Levine LD, Sammel MD, Hirshberg A, Elovitz MA, Srinivas SK. Does stage of labor at time of caesarean delivery affect risk of subsequent preterm birth? *Am J Obstet Gynecol* 2015;212:e1–7.

10 Blanchette H. The rising caesarean delivery rate in America: what are the consequences? *Obstet Gynecol* 2011;118:687–90.

11 O'Leary CM, de Klerk N, Keogh J, Pennell C, de Groot J, York L, et al. Trends in mode of delivery during 1984–2003: can they be explained by pregnancy and delivery complications? *BJOG* 2007;114:855–64.

12 Getahun D, Oyelese Y, Salihu HM, Ananth CV. Previous caesarean delivery and risks of placenta previa and placental abruption. *Obstet Gynecol* 2006;107:771–8.

13 Vervoort AJ, Uittenbogaard LB, Hehenkamp WJ, Brolmann HA, Mol BW, Huirne JA. Why do niches develop in Caesarean uterine scars? Hypotheses on the aetiology of niche development. *Hum Reprod* 2015;30:2695–702.

14 Meray N, Reitsma JB, Ravelli AC, Bonsel GJ. Probabilistic record linkage is a valid and transparent tool to combine databases without a patient identification number. *J Clin Epidemiol.* 2007;60:883–91.

15 Tromp M, Ravelli AC, Meray N, Reitsma JB, Bonsel GJ. An efficient validation method of probabilistic record linkage including readmissions and twins. *Methods Inf Med* 2008;47:356–63.

16 Schaaf JM, Hof MH, Mol BW, Abu-Hanna A, Ravelli AC. Recurrence risk of preterm birth in subsequent singleton pregnancy after preterm twin delivery. *Am J Obstet Gynecol.* 2012;207:e1–7.

17 Schaaf JM, Hof MH, Mol BW, Abu-Hanna A, Ravelli AC. Recurrence risk of preterm birth in subsequent twin pregnancy after preterm singleton delivery. *BJOG* 2012;119:1624–9.

18 Romero R, Dey SK, Fisher SJ. Preterm labor: one syndrome, many causes. *Science* 2014;345:760–5.

19 Visser GH, Eilers PH, Elferink-Stinkens PM, Merkus HM, Wit JM. New Dutch reference curves for birthweight by gestational age. *Early Hum Dev* 2009;85:737–44.

20 van 't Hooft J. A core outcome set for evaluation of interventions to prevent preterm birth: summary for CROWN. *BJOG* 2016;123(Suppl 3):107.

21 Betran AP, Ye J, Moller AB, Zhang J, Gulmezoglu AM, Torloni MR. The increasing trend in caesarean section rates: global, regional and national estimates: 1990–2014. *PLoS ONE* 2016;11:e0148343.

22 Cho GJ, Kim LY, Min KJ, Sung YN, Hong SC, Oh MJ, et al. Prior caesarean section is associated with increased preeclampsia risk in a subsequent pregnancy. *BMC Pregnancy Childbirth* 2015;15:24.

23 Wood SL, Chen S, Ross S, Sauve R. The risk of unexplained antepartum stillbirth in second pregnancies following caesarean section in the first pregnancy. *BJOG* 2008;115:726–31.

24 Wood S, Ross S, Sauve R. Cesarean section and subsequent stillbirth, is confounding by indication responsible for the apparent association? An updated cohort analysis of a large perinatal database. *PLoS ONE* 2015;10:e0136272.

25 Johansson S, Villamor E, Altman M, Bonamy AK, Granath F, Cnattingius S. Maternal overweight and obesity in early pregnancy and risk of infant mortality: a population based cohort study in Sweden. *BMJ* 2014;349:g6572.

26 MacInnis N, Woolcott CG, McDonald S, Kuhle S. Population attributable risk fractions of maternal overweight and obesity for adverse perinatal outcomes. *Sci Rep* 2016;6:22895.

27 Shen M, Smith GN, Rodger M, White RR, Walker MC, Wen SW. Comparison of risk factors and outcomes of gestational hypertension and pre-eclampsia. *PLoS ONE* 2017;12:e0175914.

28 Wei YM, Yang HX, Zhu WW, Liu XY, Meng WY, Wang YQ, et al. Risk of adverse pregnancy outcomes stratified for pre-pregnancy body mass index. *J Matern Fetal Neonatal Med* 2016;29:2205–9.

29 Vahanian SA, Hoffman MK, Ananth CV, Croft DJ, Duzyj C, Fuchs KM, et al. Term caesarean delivery in the first pregnancy is not associated with an increased risk for preterm delivery in the subsequent pregnancy. *Am J Obstet Gynecol* 2019;221:61.e1–7.

30 Zhang Y, Zhou J, Ma Y, Liu L, Xia Q, Fan D, et al. Mode of delivery and preterm birth in subsequent births: a systematic review and meta-analysis. *PLoS ONE* 2019;14:e0213784.

31 Yasseen Iii AS, Bassil K, Sprague A, Urquia M, Maguire JL. Late preterm birth and previous caesarean section: a population-based cohort study. *J Matern Fetal Neonatal Med* 2019;32:2400–7.

32 Klar M, Michels KB. Cesarean section and placental disorders in subsequent pregnancies–a meta-analysis. *J Perinat Med* 2014;42:571–83.

33 Baron J, Weintraub AY, Eshkoli T, Hershkovitz R, Sheiner E. The consequences of previous uterine scar dehiscence and caesarean delivery on subsequent births. *Int J Gynaecol Obstet* 2014;126:120–2.

34 Betran AP, Torloni MR, Zhang JJ, Gülmezoglu AM, WHO Working Group on Caesarean Section. WHO statement on caesarean section rates. *BJOG* 2016;123:667–70.

35 Betran AP, Torloni MR, Zhang J, Ye J, Mikolajczyk R, Deneux-Tharaux C, et al. What is the optimal rate of caesarean section at population level? A systematic review of ecologic studies. *Reprod Health* 2015;12:57.

Is the association between previous caesarean section and preterm delivery causal?

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To determine whether a caesarean section is a risk factor for preterm delivery in a subsequent pregnancy is challenging. As an experimental approach raises ethical and feasibility concerns, any clarification on the issue relies on observational studies. In this issue of the journal, Visser et al. (*BJOG* 2020;127;610–7) tackle this question using a national administrative cohort of Dutch women who delivered at term in their first singleton pregnancy and had a subsequent birth. Overall and spontaneous preterm delivery rates in the second pregnancy were compared between those who delivered by caesarean section or vaginally in the first pregnancy. An adjusted odds ratio of 1.14 in overall preterm birth was observed in the caesarean section group. The magnitude of the association is similar to that of a recent meta-analysis of cohort studies by Zhang et al. (*PLoS ONE* 2019;14: e0213784). Previous studies have attributed the association to cervical damage and formation of a uterine scar that may affect uterine function in future pregnancies. It is also possible that unmeasured characteristics of women who are selected or self-selected for a caesarean section are associated with increased risk of subsequent preterm delivery, such as mode of delivery in the second pregnancy, body mass index, advanced maternal age, diabetes, hypertension, other pregnancy complications, stress, and a myriad of social and behavioural factors. Existing studies have accounted for some of these potential confounders but none has convincingly ruled out residual confounding. Although meta-analyses provide more robust evidence than single studies, meta-analyses of observational studies may carry biases that are shared by the included studies. A modest increase of <15% in risk is likely to disappear after accounting for unmeasured confounders.

Additionally, both the exposure and the outcome are heterogeneous. Studying the broad association of any type of caesarean section and any type of preterm delivery may mask specific pathways and dilute effects. Subgroup analyses may provide clues to identify where the action is and where it is not. For example, Visser et al. found that the overall association was actually driven by spontaneous (adjusted odds ratio [AOR]: 1.50) but not iatrogenic preterm birth, although the ability of the study to detect associations with iatrogenic preterm birth lessened after excluding women with pregnancy hypertension and large neonates. Going a step further, Visser et al. also found that the association with spontaneous preterm birth was stronger among women who had a planned caesarean section in the first pregnancy (AOR: 1.86) than among those who had an unplanned caesarean section (AOR: 1.40). The magnitude of these associations warrants further scrutiny of preterm birth and caesarean section typologies. Studies to date have had a limited ability fully to use longitudinal information spanning a woman's repeated pregnancies. As obstetric practice and the timing of delivery in subsequent pregnancies are conditioned by the context and outcome of the first pregnancy, future studies would benefit from collecting detailed information on the clinical profiles, mode of delivery and potential confounders across repeated pregnancies of the same women. Such detailed longitudinal information may be more informative if assembled in well-designed studies testing specific pathways.

Disclosure of interests

None declared. Completed disclosure of interests form is available to view online as supporting information. ■