Time matters—a Swedish cohort study of labor duration and risk of uterine rupture

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Abstract

Introduction: Uterine rupture is an obstetric emergency associated with maternal and neonatal morbidity. The main risk factor is a prior cesarean section, with rupture occurring in subsequent labor. The aim of this study was to assess the risk of uterine rupture by labor duration and labor management.

Material and methods: This is a Swedish register-based cohort study of women who underwent labor in 2013–2018 after a primary cesarean section (n = 20 046). Duration of labor was the main exposure, calculated from onset of regular labor contractions and birth; both timepoints were retrieved from electronic medical records for 12 583 labors, 63% of the study population. Uterine rupture was calculated as events per 1000 births at different timepoints during labor. Risk estimates for uterine rupture by labor duration, induction of labor, use of oxytocin and epidural analgesia were calculated using Poisson regression, adjusted for maternal and birth characteristics. Estimates were presented as adjusted rate ratios (ARR) with 95% confidence intervals (CI).

Results: The prevalence of uterine rupture was 1.4% (282/20 046 deliveries). Labor duration was 9.88 hours (95% CI 8.93–10.83) for women with uterine rupture, 8.20 hours (95% CI 8.10–8.31) for women with vaginal delivery, and 10.71 hours (95% CI 10.46–10.97) for women with cesarean section without uterine rupture. Few women (1.0/1000) experienced uterine rupture during the first 3 hours of labor. Uterine rupture occurred in 15.6/1000 births with labor duration over 12 hours. The highest risk for uterine rupture per hour compared with vaginal delivery was observed at 6 hours (ARR 1.20, 95% CI 1.11–1.30). Induction of labor was associated with uterine rupture (ARR 1.54, 95% CI 1.19–1.99), with a particular high risk seen in those induced with prostaglandins and no risk observed with cervical catheter (ARR 1.19, 95% CI 0.83–1.71). Labor augmentation with oxytocin (ARR 1.60, 95% CI 1.25–2.05) and epidural analgesia (ARR 1.63, 95% CI 1.27–2.10) were also associated with uterine rupture.

Abbreviations: ARR, adjusted rate ratio; CI, confidence interval; CS, cesarean section; ICD-10, the 10th revision of the International Classification of Diseases.

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Conclusions: Labor duration is an independent factor for uterine rupture among women attempting vaginal delivery after cesarean section. Medical induction and augmentation of labor increase the risk, regardless of maternal and birth characteristics.

Keywords: augmentation of labor, cesarean section, induction of labor, labor duration, morbidity, oxytocin, TOLAC, uterine rupture, uterine scar

1 | INTRODUCTION

Uterine rupture is an obstetric emergency, globally associated with maternal and neonatal morbidity and mortality.1–4 The main risk factor in medium- and high-resource settings is a previous cesarean section (CS); rupture usually occurs in subsequent labor after onset of contractions.2–4 The rate of uterine rupture in women attempting a trial of labor after one previous low transverse CS has been estimated at between 0.2% and 1.5%, reflecting that selection for and management of trial of labor differ between healthcare settings and countries.1,2,5–8,9,13 Efforts to improve safety of vaginal delivery after CS have focused on the identification of risk factors for uterine rupture, but few studies have examined the actual course of labor.10–12 Recognition of clinical signs of uterine rupture is challenging due to the lack of specific symptoms; moreover, most signs do not precede, but follow, uterine rupture. Induction of labor has been identified as a risk factor for uterine rupture,1,2 but findings are suggested to be confounded by factors such as an unfavorable cervix and longer duration of labor.13 Dystocia is commonly reported in cases with uterine rupture11 and augmentation with oxytocin poses a risk,8,10,12,14 but these features are also frequently present in labor without rupture. In a nested case–control study of women with prior CS, labor patterns and duration at early dilations were similar among women with uterine rupture, intrapartum CS and vaginal delivery. However, in the later stage of labor, women with uterine rupture progressed slower than women with a successful trial of labor, but at a similar rate as women with a failed trial of labor.10

Induction of labor and management of dystocia are modifiable factors in women undergoing a trial of labor after CS.10,11,15 Information on labor patterns may aid in identification of women at risk of uterine rupture and improve practice to prevent adverse maternal and neonatal outcomes.16

The aim of this study was to evaluate labor duration with respect to uterine rupture in a first trial of labor after one CS. Furthermore, we aimed to explore modifiable risk factors including induction and management of labor, particularly the use of prostaglandins, oxytocin and epidural analgesia.

2 | MATERIAL AND METHODS

This was a population-based register study of women (n = 31,409) having their second child after one prior CS, between 2013 and 2018, encompassing 17 counties in Sweden. The primary dataset was retrieved from the Swedish pregnancy register in September 2019.17 Women with a multi-fetal pregnancy (n = 764), pre-labor CS (n = 10,594) and duplicates in the register (n = 5) were excluded; thus, 20,046 women undergoing a trial of labor after CS were included (Figure 1). Information about onset of labor was available for 12,583 labors, representing 63% of the study population. Information on maternal demographics and characteristics, including maternal age at delivery, height, weight and body mass index at first antenatal visit, was provided by electronic antenatal birth records. Manually entered antenatal information in the register included maternal country of birth (classified as Sweden/other Nordic country, other European country or outside Europe) and interpreter needed (yes/no) during antenatal/healthcare appointments.

Labor characteristics were retrieved from electronic birth records and included gestational week of delivery (completed weeks), preterm birth (<37 gestational weeks), post-term birth (>42 gestational weeks) and fetal heart rate at admission, recorded as normal or abnormal. Induction of labor was retrieved based on midwife-reported onset of labor in electronic birth records or diagnostic codes in the 10th revision of the International Classification of Diseases (ICD-10), retrieved from labor records at discharge. Mechanical induction was by either cervical catheter or primary amniotomy. For medical induction and augmentation of labor, use of prostaglandins or oxytocin was identified based on procedure codes (Table S1).

Labor records further provided information on epidural analgesia (combined with procedure codes), fetal presentation at birth (occiput anterior, occiput posterior, breech), mode of delivery categorized as spontaneous vaginal, operative vaginal (vacuum extraction or forceps) or CS. Neonatal data included Apgar score at birth, umbilical pH and birthweight (in grams).

Duration of labor was the main exposure and was calculated through subtracting patient self-reported or midwife-observed time of onset of regular contractions from time of birth. Information on
time of birth (day-hour-minute) was retrieved from data filled out by the midwife in the electronic birth record. Two different timepoints for start of labor are recorded in electronic birth records, one for the start of contractions and the other for the start of regular (established) contractions. In this study, the latter was used to define onset of labor. The distribution of times was checked visually; values below the 0.10th or above the 99.9th percentile were considered invalid and were excluded (n = 15). Labor duration ranged from 0.12 to 51.5 hours. Secondary exposures were induction of labor, augmentation of labor and epidural analgesia.

Cases with uterine rupture were identified based on the diagnosis codes O710 (n = 10) and O711 (n = 272) from the ICD-10.

2.1 | Statistical analyses

Characteristics of the population, grouped by cases of uterine rupture and non-rupture, were described and compared using bivariate analysis with Pearson’s chi-square test for categorical variables and Student’s t test for continuous variables. Mean duration of labor with 95% confidence interval (95% CI) was calculated for women with uterine rupture, vaginal birth and intrapartum CS without rupture, and the groups were compared using one-way independent analysis of variance. Dunnett’s post-hoc test was used for pairwise comparisons between cases of non-rupture and uterine rupture. The association between labor duration and uterine rupture was calculated based on events (uterine ruptures) per 1000 births among women at risk, at different timepoints within 3-hour intervals (0–2, 3–5, 6–8, 9–11 and ≥12 hours). The rate ratio of uterine rupture per vaginal delivery was further assessed using a Poisson regression on time-split data. Follow-up time for each individual was split into intervals of 1 hour, where the rate was assumed to be constant and was modeled as a cubic regression spline within the framework of generalized additive models. The model was adjusted for maternal age (years), height (cm) and induction of labor (yes or no). The associations with uterine rupture at different times during labor were presented as adjusted rate ratios (ARR) with 95% CI, using vaginal delivery without rupture as a reference group. Birth unit was included as a random factor to account for clustering and different management of labor between birth units. Confounders were identified through a theoretical framework and a directed acyclic graph (Figures S1–S2) (www.dagitty.net) for investigating the total effect of labor duration and risk of uterine rupture.

Statistical analyses were performed using SPSS software for Mac, version 25 (IBM Corp., Armonk, NY, USA) and R version 3.6.3.

2.2 | Ethical approval

The Regional Ethics Board at Uppsala University approved the study on 15 August 2018, with an amendment approved on 7 November 2018 (Dnr 2018/287/1).

3 | RESULTS

There were 282 uterine ruptures among 20046 women undergoing a trial of labor after one CS (1.4%). Women with uterine rupture were older, shorter and more often required an interpreter during pregnancy, compared with women without rupture (Table 1). One-third of women with uterine rupture underwent induction of labor vs 23% of women without rupture (<0.001). Among 121 cases of uterine rupture, there was no time of onset of regular contractions reported, meaning that 161 cases (63%) of uterine rupture could be analyzed regarding duration of labor. Missing data on time were more common among older
women, women born outside Europe, those with induced labor and those delivered by CS, and the incidence of uterine rupture was 1.6% among cases without information on labor duration (Table S2). Mean hours of labor duration was 9.88 (95% CI 8.93–10.83) for women with uterine rupture, 8.20 hours (95% CI 8.10–8.31) for women with vaginal delivery, and 10.71 hours (95% CI 10.46–10.97) for women with intrapartum CS without rupture (Figure 2). Uterine rupture occurred in 1.0/1000 births during the first 3 hours and increased to 15.6/1000 births after 12 hours of labor. The rate ratio of uterine rupture within one additional hour of labor at different timepoints of labor revealed a bell-shaped curve with the highest adjusted rate ratio after 6 hours of regular contractions (ARR 1.20, 95% CI 1.11–1.30) (Figure 3, Table 2).

Induction of labor increased the risk of uterine rupture (ARR 1.54, 95% CI, 1.19–1.99), with the highest risk observed with prostaglandins (ARR 1.96, 95% CI, 1.40–2.75). Labor augmentation with oxytocin and epidural analgesia were also associated with uterine rupture (Table 3). Labor characteristics stratified by onset of labor are presented in Table S3. Apgar score <7 at 5 minutes was recorded in 59/280 (21.1%) of neonates following uterine rupture compared with 479/19764 (2.4%) without uterine rupture (p < 0.001). Neonatal umbilical pH (arterial or venous) was analyzed in 65% of all newborns, and a pH <7.00 was recorded in 23% after uterine rupture compared with 1.7% without rupture (p < 0.001) (results not presented in Table).

### DISCUSSION

Women with uterine rupture had longer duration of labor than women with vaginal delivery, but not when compared with women with intrapartum CS. Few women experienced a uterine rupture

| Age, years, mean (SD) | Uterine rupture | No uterine rupture | p |
|----------------------|----------------|-------------------|---|
| Missing %            | n = 282 | %                  | n = 19764 | %                  | p  |
| 32.7 (4.9)           | 31.9 (4.7) | 0.005             |

| Country of birth | Gestational length, weeks, mean (SD) | Preterm | Post-term | Abnormal FHR at admission | Induction of labor | Epidural | Fetal presentation | Mode of delivery | Birthweight, grams, mean (SD) |
|------------------|--------------------------------------|---------|-----------|---------------------------|-------------------|----------|-------------------|-----------------|--------------------------|
| Nordic           | 163 69.1 12294 69.6                  | 12 4.3 1235 6.2 | 36 12.8 1433 7.3 | 170 18 7.8 1199 7.3 | 93 33.0 4484 22.7 | 181 64.2 9865 49.9 | 8.0  | 188 89.1 16771 92.0 | 0.4 3680 (547) | 3680 (547)               |
| Other Europe     | 14 5.9 1304 7.4                     |         |           |                           |                   |          |                   |                 | 3680 (547)               |
| Outside Europe   | 59 25.0 4065 23.0                   |         |           |                           |                   |          |                   |                 | 3680 (547)               |
| Interpreter needed | 16.6 34 15.9 1770 10.7               |         |           |                           |                   |          |                   |                 | 3680 (547)               |

Data presented as absolute (n) and relative (%) frequencies or means with standard deviation. The p values were calculated using Pearson’s chi-square test and Student’s t test. Abbreviations: BMI, body mass index; FHR, fetal heartrate; SD, standard deviation.

### TABLE 1 Maternal and labor characteristics among cases with and without uterine rupture (n = 20046)
during the first 3 hours of labor; the highest rate ratio for uterine rupture within one additional hour compared with vaginal delivery was observed after 6 hours of labor. Induction and augmentation of labor and epidural analgesia increased the risk of uterine rupture, with maternal and birth characteristics taken into account.

An important strength of the study was the national cohort design with a large sample size based on a register with reliable information on pregnancy and labor characteristics. Information was collected prospectively, which limits recall bias. Confounders were established through a theoretical framework including directed acyclic graphs. The Poisson regression analysis revealed a non-linear association between time and uterine rupture and allowed for assessing risk estimates at different timepoints during labor, taking important confounding factors into account. Furthermore, to evaluate any clustering effect on reporting of labor onset and duration between birth units, birth unit was included in the model.

Identification of cases with uterine rupture was based on diagnostic codes in the register; the accuracy of coding and severity of rupture (complete or partial) was not checked against medical records. In prior register-based studies, complete ruptures have been reported to account for about two-thirds of cases, with an increasing trend of both partial and complete ruptures over time. Compared with a recent multi-country population-based study, the rate of uterine rupture in our study was higher, indicating that partial ruptures were included in our study. Underreporting of uterine ruptures by diagnostic codes in registers might also influence the results but, if non-differential, it would bias the effect towards the null effect. Duration of labor was based on information collected independently of the diagnosis of uterine rupture precluding recall bias, but coding of prostaglandins and oxytocin might be different among cases and non-cases. Information on cervical ripeness, dilation and station of fetal presenting part at induction of labor and during labor was not available, thus the uterine rupture could not be assessed at different stages of labor. The timepoint of onset of labor was based on self-reported or midwife-reported onset of regular labor contractions, available in 63% of women attempting labor after a previous CS. We noticed a selection bias in the available data on timepoint of onset of labor, with a higher proportion among younger women of Nordic origin, spontaneous onset of labor and vaginal deliveries. Self-reported onset of labor has in other settings been reported to be in agreement with midwife assessment of onset of labor in less than one-third of cases, which could result in a skewed distribution of estimated labor duration between women with spontaneous labor onset and those with induced onset in our study. Longer duration of labor was reported in women with spontaneous onset compared with induced onset in our study.

Our results are in line with those of Harper et al., who found that the risk of uterine rupture increased at a later stage of labor. Another study examining labor patterns in women with trial of labor reported a slower progress at both the first and second stage of labor among 90 cases with uterine rupture compared with 260 controls, concluding that prolonged labor
in women with prior CS is a warning sign.\textsuperscript{12} In a cohort study of women attempting vaginal birth after CS (n = 4579), uterine rupture increased with a prolonged second stage of labor, from 0.7% at <1 hour to 3.1% among women with a second stage lasting ≥3 hours.\textsuperscript{24} In our study, the Poisson regression analysis revealed a non-linear association between time and uterine rupture and allowed for assessment of risk estimates at different timepoints during labor. No increased risk was seen at an early stage of regular contractions, indicating that the risk of uterine rupture either increases at the acceleration phase of labor or with augmentation with oxytocin. Labor augmentation with oxytocin and induction with prostaglandins have been associated with a 2- to 6-fold increased risk of rupture compared with spontaneous onset of labor.\textsuperscript{1,3,6,8,14} and clinical guidelines advise restrictive use of medical induction and cautious use of oxytocin during labor if the woman has a history of CS. A Swedish retrospective cohort study of 910 induced women with one prior CS found no increased rate of uterine rupture among women if prostaglandins were administered orally in low doses (2.0%), compared with among women induced with a cervical catheter (2.1%). However, the rate of uterine rupture was 5.0% among women induced with vaginally administered prostaglandins.\textsuperscript{25} We found that induction of labor with prostaglandins doubled the risk of uterine rupture, and augmentation of labor with oxytocin increased the risk by 60%. In 2016, a Swedish national guideline on induction of labor was published by the Swedish Society for Obstetrics and Gynecology. The guideline proposed a restrictive use of prostaglandins in the case of prior CS. In our study, 7.5% of women with prior CS were induced with prostaglandins during 2013–2018 and the rate did not decline after 2016 (result not presented). In concordance to prior reports,\textsuperscript{9,26} we also found that women induced with a cervical catheter had

| Duration of labor (h) | At risk (n) | Cumulative events (n) | UR /1000 women at risk | UR/VD rate ARR\textsuperscript{a} | 95% CI |
|-----------------------|-------------|-----------------------|------------------------|----------------------------------|-------|
| ≥0-2                  | 12583       | 13 150 1265           | 1.0                    | 0.99                             | 0.82–1.20 |
| ≥3-5                  | 11155       | 41 525 4208           | 2.5                    | 1.09                             | 0.95–1.23 |
| ≥6-8                  | 7809        | 87 959 6602           | 5.9                    | 1.20                             | 1.11–1.30 |
| ≥9-11                 | 4935        | 117 1388 8272         | 6.1                    | 1.08                             | 1.00–1.17 |
| ≥12                   | 2806        | 161 2201 10221        | 15.7                   | 0.94                             | 0.86–1.08 |

Abbreviations: ARR, adjusted rate ratio; CI, confidence interval; CS, cesarean section without UR; UR, uterine rupture; VD, vaginal delivery without UR.

\textsuperscript{a}Adjusted rate ratio of uterine rupture within the next hour compared with vaginal delivery, estimated using Poisson regression adjusted for maternal age at delivery, maternal height and induction of labor.

### TABLE 2

| Duration of labor (h) | At risk (n) | Cumulative events (n) | UR /1000 women at risk | UR/VD rate ARR\textsuperscript{a} | 95% CI |
|-----------------------|-------------|-----------------------|------------------------|----------------------------------|-------|
| ≥0-2                  | 12583       | 13 150 1265           | 1.0                    | 0.99                             | 0.82–1.20 |
| ≥3-5                  | 11155       | 41 525 4208           | 2.5                    | 1.09                             | 0.95–1.23 |
| ≥6-8                  | 7809        | 87 959 6602           | 5.9                    | 1.20                             | 1.11–1.30 |
| ≥9-11                 | 4935        | 117 1388 8272         | 6.1                    | 1.08                             | 1.00–1.17 |
| ≥12                   | 2806        | 161 2201 10221        | 15.7                   | 0.94                             | 0.86–1.08 |

### TABLE 3

| Study population | Uterine rupture | Risk estimates |
|------------------|----------------|---------------|
| n = 20046        | Rate (%)       | RR 95% CI     |
| Induction of labor | 4577 22.8 | 93 33.0 | 1.66 1.30–2.13 |
| Mechanical induction\textsuperscript{a} | 2510 12.5 | 44 15.6 | 1.29 0.94–1.78 |
| Cervical catheter | 1931 9.6 | 34 12.1 | 1.29 0.90–1.84 |
| Amniotomy | 602 3.0 | 8 2.8 | 0.94 0.47–1.91 |
| Medical induction\textsuperscript{b} | 2004 10.0 | 49 17.4 | 1.89 1.39–2.58 |
| Prostaglandins | 1494 7.5 | 41 14.5 | 2.11 1.52–2.94 |
| Oxytocin | 9594 47.9 | 175 62.1 | 1.78 1.40–2.27 |
| Epidural | 10 046 50.1 | 181 64.2 | 1.78 1.40–2.28 |

Relative risks presented as rate ratios with 95% confidence intervals estimated using Poisson regression, in which uterine rupture was the outcome; the explanatory factor is stated in the table.

Adjusted rate ratios (ARR): adjusted for maternal age, height, gestational length as continuous covariates and the explanatory factor stated in the table included in the model (\textsuperscript{*} included in analysis, n = 19569).

Abbreviations: ARR, adjusted rate ratio; CI, confidence interval; ICD-10, 10th revision of the International Classification of Diseases; RR, rate ratio.

\textsuperscript{a}ICD-10 code O61.1. Unspecified or combined methods may have been used.

\textsuperscript{b}ICD-10 code O61.0. Unspecified or combined methods may have been used.
no increased risk of uterine rupture. A systematic review of eight randomized controlled trials encompassing 707 women induced after a prior CS concluded that the studies were underpowered to detect clinically important outcomes such as uterine rupture and there was no clear evidence on the most efficient or safe method of induction in women with a prior CS.27

We found a higher proportion of use of epidural analgesia among women with uterine rupture in our study. Dystocia, augmentation of labor and epidural analgesia are closely interlinked, but the observed association is not necessarily attributed to longer duration of labor. Uterine rupture has been associated with frequent epidural dosing, indicating that a persistent pain should be acknowledged as a potential sub-clinical uterine rupture.28

A population-based study demonstrated an increasing trend of uterine rupture in Norway from 1967 to 2008.21 In Denmark, an increased rate of uterine rupture has been observed in post-term pregnancies in 2000–2012.29 Our observed rate of uterine rupture of 1.4% was slightly higher than rates from other settings and time periods in Sweden but could also be attributed to our case definition of uterine rupture.5,7,22

5 | CONCLUSION

Risk factors for uterine rupture, including advanced maternal age, short stature and induction of labor, are also associated with dystocia and prolonged labor. However, after adjusting for these factors, labor duration predicts uterine rupture in women attempting vaginal delivery after CS. Modifiable risk factors for uterine rupture include induction and augmentation of labor, and cautious use of oxytocin is, therefore, advocated. Our finding highlights that time matters and that, to decrease the risk for uterine rupture, careful assessment of progress and management of labor is crucial in women with prior CS.

CONFLICT OF INTEREST

Dr. Hesselman reported receiving personal fees from Baxter Medical AB for serving on an advisory board. The other authors have stated explicitly that there are no conflicts of interest in connection with this article.

AUTHOR CONTRIBUTIONS

SH, MJ and A-KW conceived the study. SH and EL managed the data and performed the statistical analysis. SH wrote the first draft. All authors contributed with critical input on analysis, interpretation of data and the final manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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