Efficacy and safety of induction of labour in case of pregnancy termination or intrauterine fetal death in patients with a scarred uterus: a retrospective cohort study

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Abstract

Objective: Assess efficacy and safety of labour induction in women with one or more previous caesarean deliveries during second and third trimester pregnancy termination or intrauterine fetal death. Design: Retrospective single-centre study between 2007 and 2018. Setting: Lille, France Population: 136 women with history of previous caesarean deliveries (CD) (study group) and 272 controls undergoing labour induction for pregnancy termination or intrauterine fetal death. Methods: Before 32 weeks, misoprostol 400 µg was given orally every 3 hours up to a maximum of five doses in 24 hours. Study group received half doses. After 32 weeks, oxytocin infusion, misoprostol (PGE1) or PGE2 (dinoprostone) were used according to the Bishop score. Main outcome measures: Vaginal delivery within the 24 hours after induction without uterine rupture or severe post-partum haemorrhage defined as blood loss > 1 litre (PPH). Results: Vaginal delivery within the 24 hours after induction without uterine rupture or PPH was 83.5% in the study group versus 92.6% in the control group (p=0.005). 5 (3.7%) uterine ruptures occurred in the study group, 1.7% in case of one previous CD and 15.8% in case of 2 or more previous CD. There were more severe PPH in the study group (6.7% versus 2.2% p=0.03), but no difference was found between women with one or more previous CD. Conclusions: Women with 2 or more prior CD should be informed that they are at higher risk of complications such as uterine rupture and severe post-partum haemorrhage.

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Short title: Termination of pregnancy in patients with a scarred uterus

FULL ABSTRACT

Objective: Assess efficacy and safety of labour induction in women with one or more previous caesarean deliveries during second and third trimester pregnancy termination or intrauterine fetal death.

Design: Retrospective single-centre study between 2007 and 2018.

Setting : Lille, France

Population : 136 women with history of previous caesarean deliveries (CD) (study group) and 272 controls undergoing labour induction for pregnancy termination or intrauterine fetal death.

Methods : Before 32 weeks, misoprostol 400 μg was given orally every 3 hours up to a maximum of five doses in 24 hours. Study group received half doses. After 32 weeks, oxytocin infusion, misoprostol (PGE1) or PGE2 (dinoprostone) were used according to the Bishop score.

Main outcome measures : Vaginal delivery within the 24 hours after induction without uterine rupture or severe post-partum haemorrhage defined as blood loss $>$ 1 litre (PPH).

Results: Vaginal delivery within the 24 hours after induction without uterine rupture or PPH was 83.5% in the study group versus 92.6% in the control group (p =0.005). 5 (3.7%) uterine ruptures occurred in the study group, 1.7% in case of one previous CD and 15.8% in case of 2 or more previous CD. There were more severe PPH in the study group (6.7% versus 2.2% p =0.03), but no difference was found between women with one or more previous CD.

Conclusions : Women with 2 or more prior CD should be informed that they are at higher risk of complications such as uterine rupture and severe post-partum haemorrhage.

Keywords

Misoprostol, scarred uterus, uterine rupture, labour induction, pregnancy termination, intrauterine fetal death

TWEETABLE ABSTRACT

Second and third trimester pregnancy terminations in women with 2 or more caesarean scars are at risk of uterine rupture

ABBREVIATIONS

ARM: Artificial rupture of membranes

CD: Caesarean delivery

IUFD: Intrauterine fetal death

PPH: postpartum haemorrhage

TOP: termination of pregnancy

INTRODUCTION

In case of intrauterine fetal death (IUFD) or termination of pregnancy (TOP), induction of labour can be necessary. With the evolution of caesarean delivery (CD) rates in the past decade, the number of patients with a history of CD who require induction of labour in the second or third trimester of pregnancy has increased (1).

Different methods of cervical ripening have been proposed including synthetic prostaglandins and mechanical methods such as dilatation using laminaria tents or Foley catheter (2–4). Misoprostol is one of the most

common drugs used for termination of pregnancy (5). Most studies on labour induction in case of IUFD or TOP focus on the second trimester only, due to different national abortion policies (5–8). Efficacy and safety profile of misoprostol use in late gestation or in women with previous CD remain a controversial subject. Chapman et al. reported a high risk of uterine rupture and haemorrhage with this drug in women with caesarean scars, whereas other authors, more recently, have shown it to be relatively safe (9–11). These conflicting reports lead to suggest that the safety of misoprostol is yet to be clearly established for women with a scarred uterus (12). A recent review provided evidence that the use of prostaglandins in the second trimester is associated with greater efficacy and is safe for women with only 1 previous CD, but at higher risk of uterine rupture for women with 2 or more previous CD (5). Furthermore, FIGO recommendations concluded that there is insufficient evidence available to recommend a regimen of misoprostol for use at more than 26 weeks' gestation in women who have had a previous caesarean or a transmural uterine scar (13).

Therefore, the purpose of this study was to assess the efficacy and safety of induction of labour in women with previous CD during both second and third trimester termination of pregnancy.

METHODS

It was a comparative, retrospective, monocentric (Lille, France) cohort between 2007 and 2018 of all patients requiring induction of labour for TOP or IUFD between 15 and 41 weeks of gestation. Exclusion criteria were multiple gestation, premature rupture of membranes, indication of CD for maternal reasons, and spontaneous labour.

The protocol in our centre was the same for IUFD and TOP management. All patients received 600 μg of mifepristone prior to induction. The patients were examined 24 hours after induction. If artificial rupture of membrane (ARM) was not possible, laminaria tents were used as adjuncts to labour induction. Before 32 weeks, misoprostol 400 μg was given orally every 3 hours up to a maximum of five doses in 24 hours. A new course of misoprostol was started the next day if delivery had not occurred. As recommended by national guidelines, half doses of misoprostol were applied for a scarred uterus (14,15). After 32 weeks, oxytocin infusion, misoprostol (PGE1) or dinoprostone (PGE2) were used according to the Bishop score and at the appreciation of the senior obstetrician. In case of failure of two courses of misoprostol or PGE2, a Foley catheter (CH 18, filled with 60 ml of saline) was placed. If still unsuccessful, management was individualized to patient's choice (continuation or CD). Above 22 weeks of gestation and in case of TOP, feticide was proposed to patients and performed prior to the administration of abortifacients.

The primary outcome was a composite endpoint of patients achieving vaginal delivery within the 24 hours of induction, without uterine rupture or severe post-partum haemorrhage (blood loss $>$ 1000ml). The following complications were noted: uterine rupture, post-partum haemorrhage (PPH) defined as blood loss more than 500 ml, need for manual removal of placenta or surgical procedures for retention, hyperthermia, endometritis and phlebitis.

Statistics

Two groups were defined. The study group included patients with a history of previous CD. The control group consisted of randomly matched women with no history of CD and undergoing induction of labour for TOP or IUFD between 15 and 41 weeks during the same timeline. Participants were matched for gestational age ($\pm$ 2 weeks) and indication of labour induction (TOP or IUFD) using the global optimal matching algorithm. Subgroups were formed according to the number of previous caesarean sections (one or $\geq$ 2).

Categorical variables were expressed in frequencies (percentages), and the quantitative variables in median [interquartile range (IQR)]. Normality of distribution was checked graphically by using the Shapiro-Wilk test. Comparisons between groups were made using linear and logistic mixed regression models, including groups (case/control status) as fixed effect, and matched sets as random effects to take into account the matched design. For linear mixed models, normality of model residuals was checked. For subgroups analyses, cases were compared with their matched control. Comparisons between women with one previous CD and those with 2 or more previous CD were made using Chi-square test or Fisher exact test for categorical variables

and using Mann-Whitney U test for quantitative variables. Statistical testing was done at 2-tailed α level of 0.05 using the SAS software (SAS Institute version 9.4, Cary, NC, USA).

Ethical Approval

This study was approved by the French National Commission on Informatics and Liberty (DEC16-223) and by the Obstetrics and Gynaecology Research Ethics Committee (CEROG 2020-OBS-0103).

RESULTS

Four hundred and eight patients were included during the study period (Figure 1): 272 controls and 136 patients with a history of CD whom 117 had 1 previous CD and 19 had 2 or more previous CD (15 with 2 previous CD and 4 with more than 2 CD).

Table 1 describes demographic and clinical characteristics of patients included in the study. Two patients had a history of myomectomy and were considered as a scarred uterus, one of them was nulliparous at the time of the study. In the group of patients with a history of previous CD, 118 (86.8%) had a low transverse scar and 3 (2.2%) had a corporeal incision. 54 patients (39.2 %) had a previous successful vaginal delivery, half of which occurred after their history of CD. Median time since last CD was 47 months (24; 72). The reason of induction was IUFD in 23% of cases and TOP for fetal or maternal reasons in 77% of cases. 64% of patients were induced after 24 weeks of gestation and 39.2% after 28 weeks.

Labour induction methods are described in table 2. Immediate ARM was possible for 33 patients (24.3 %) with a scarred uterus and for 103 (37.8%) of the controls. It allowed 3 vaginal deliveries without the use of additional abortifacients. Among the remaining patients, 119 (95.2%) received misoprostol, 75 (63%) in association with laminar tents. 10 women (7.4%) with a scarred uterus required a second line of induction. Misoprostol was also the most frequently used drug in the control group (n = 258, 98.1%).

Primary endpoint

The rate of successful vaginal delivery within the first 24 hours of induction without severe PPH or uterine rupture was significantly lower in the case of history of CD compared to controls (83.5% versus 92.6%,$p = 0.005$) (Table 3). There was no difference between women with one previous CD and those with 2 or more previous CD ($p = 0.08$).

Secondary endpoint

Two women (0.7%) with an unscarred uterus required CD because of failure to achieve vaginal delivery, whereas 5 (3.7%) in the study group needed CD, 3 for failure of induction and 2 for suspicion of uterine rupture. In total, 5 (3.7%) uterine rupture occurred. All cases were in the study group, 2 (1.7%) in the subgroup of one previous CD and 3 (15.8%) in the subgroup of 2 or more CD. Among these uterine ruptures, 2 were symptomatic with patients reporting acute abdominal pain during induction leading to an emergency CD. Both suffered severe PPH and required blood transfusion and a hysterectomy was necessary for one patient. Two ruptures with no clinical signs were diagnosed during surgical procedures after failure to achieve vaginal delivery. The fifth patient reported abdominal pain 3 days after TOP with vaginal delivery at 27 weeks and uterine rupture was diagnosed on the computed tomography scan. All cases are summarized in table S1.

The median induction-to-delivery interval was higher in the study group compared to controls (9 (6;14.2) versus 7 (5;11), $p = 0.0004$), and also in all subgroups compared to controls. Median blood loss was not different between study and control groups, but severe PPH was more frequent in the study group (6.7% versus 2.2%, $p = 0.03$). There was no difference between women with history of previous CD compared to controls for manual removal of placenta, revision of uterine cavity, curettage, endometritis or phlebitis.

DISCUSSION

Main findings

The prevalence of women with uterine scars has increased in the past decades due to higher rates of CD worldwide (1). Various protocols have been described for induction of labour in case of IUFD or TOP in women with uterine scars. In our study, vaginal delivery was achieved in 96.3% of cases in the group of patients with history of previous CD with 83.5% of the patients delivering in less than 24 hours without uterine rupture or severe PPH. Misoprostol was the most frequently used abortifacient. The incidence of uterine rupture was overall 3.7% in our study group, 1.7% in case of one previous CD and 15.8% in case of 2 or more previous CD.

Interpretation

Misoprostol is a synthetic analogue of prostaglandin E1 used both orally and vaginally for its effectiveness and low cost (16,17). FIGO's recommendations concluded that misoprostol could be used for TOP or IUFD in women with previous cesarean or other uterine scars throughout 13–26 weeks (13). However, caution is required, and a half dose regimen is recommended, regardless of gestational age (14,15,17).

Our results indicate its efficacy in women with a history of previous CD. We observed 96.3% vaginal deliveries. This is in accordance with the latest review on cervical ripening agents in women with a scarred uterus (5). A metanalysis conducted by Andrikopolou et al. included 17 descriptive studies (563 patients) and 21 comparative studies between patients with previous CD and those with no uterine scar (8419 patients) before 28 weeks of gestation. It provided evidence that patients with a scarred uterus who used PGE1 had higher risk of uterine rupture (RR 6.57; 95% CI 2.21-19.52). However, this risk was statistically significant only for women with 2 or more previous CD.

Several authors have shown interest in labour induction for TOP or IUFD in women with a scarred uterus, especially before 28 weeks. Some reported more than 90% vaginal delivery rates and no increased likelihood of uterine rupture when using vaginal misoprostol 200μg every 4 to 6 hours in women with only 1 previous CD (10,18–20). This regimen appears less effective when patients with 2 or more previous CD were included (21). Fawzy et al., in an evaluation of TOP before 26 weeks in 31 women with 3 prior CD, concluded that misoprostol was less effective compared to patients with an unscarred uterus (90.3% vaginal deliveries vs 100%, $p = 0.01$) (22). In another study including 193 patients and 86 patients with a scarred uterus, 60 with 1 previous CD and 26 with 2 or more previous CD, Güleç et al. reported a lower vaginal delivery rate in patients with 2 or more previous CD compared to patients with only 1 previous CD but the difference was not statistically significant ($p = 0.06$) (23). They also reported the highest rate of uterine rupture (11.5%) in patients with 2 or more CD.

To date, only 3 authors have included patients with a scarred uterus after 28 weeks using mifepristone followed by 400 μg oral misoprostol every 3 hours until delivery, a regimen similar to our local protocol (3,24,25). In a study of 67 patients with a scarred uterus (50 with 1 previous CD, 13 with 2 previous CD and 4 with 3 or more previous CD) undergoing induction of labour for TOP or IUFD between 14-37 weeks, Cayrac et al. reported 95.5 % of vaginal deliveries, 4.8% of uterine rupture and 3% of severe PPH (25). When compared to 202 unscarred uterus, Mazouni et al. found 4 % of uterine rupture in a retrospective cohort of 50 scarred uterus between 15-35 weeks, but no significant difference for vaginal delivery rates, median induction to abortion time or severe PPH (3).

In our cohort, we observed 5 uterine ruptures, all women had a scarred uterus but were at different gestational age, had different induction to abortion time intervals and time since last CD ranged from 5 months to 5 years. Two patients had severe bleeding that required blood transfusion and one hysterectomy was necessary. Recently, in a study of 339 patients with a scarred uterus, Daniel et al. reported 7 uterine rupture (2.1%) but they limited their study under 23 weeks of gestation (26). Uterine rupture is the most serious complication of labour induction and a history of previous CD is an important contributing factor (26). The reported incidence ranges from 0% to 0.5% in patients with a scar-free uterus (26). Daskalalis et al. reported a case of uterine rupture in a patient with no history of CD or uterine surgery after using misoprostol, leading to think there might be other factors that may increase the risk of uterine rupture among patients undergoing labour induction for TOP or IUFD (2). It has been suggested that prostaglandins could induce biochemical

modifications of scars that may play a role and Peng et al. demonstrated that a thinner lower uterine segment was associated with a higher risk of uterine rupture in patients undergoing TOP before 28 weeks (27,28). Association of misoprostol with other cervical ripening methods also increases the risk (6). Also, it is unclear if the dose of abortifacients is a contributing factor for uterine rupture and cases of uterine rupture have been described with low doses of misoprostol (29). The median dose of misoprostol necessary to induce abortion was lower in our scarred uterus group, and it significantly impacted time to delivery interval, especially in the subgroup of 2 or more previous CD. This is particularly relevant since a prolonged induction of labour of more than 24 hours is associated with a higher risk of uterine rupture (30).

The other major contributing factor is gestational age. All of our ruptures occurred at 24 weeks or beyond and 39.2% of inductions occurred after 28 weeks. This is related to morphological scans performed around 22 weeks of gestation in France. In the event of prenatal diagnosis of any "serious illness recognized as incurable at the time of diagnosis", TOP is allowed regardless of gestational age, after a review by a multidisciplinary committee (31). These findings could explain our higher rates of uterine rupture.

Strengths and Limitations

This study on labour induction in the case of TOP or IUFD included patients up until 41 weeks of gestation, regardless of the number of previous CD and the type of scar. Overall, uterine rupture is rare even over our long period of study. A larger subgroup of women with history of 2 or more CD would have allowed more analysis. The external validity of this study as well as of all those previously cited is questionable as protocols and abortion laws vary worldwide. Comparison with other studies is made difficult by methodological heterogenicity regarding use of mifepristone or not, differences in misoprostol doses, route of administration, use of other abortifacients and gestational age.

CONCLUSION

Misoprostol, in association with mifepristone, is an effective and safe drug to induce labour for TOP or IUFD in women with history of one previous CD. Patients should be informed of the higher risk of uterine rupture and severe PPH in case of 2 or more previous CD. Induction of labour should be decided on a case-by-case basis, considering local protocol, number of previous CD, time from last CD and gestational age.

DISCLOSURE OF INTEREST

The authors have no conflicts of interest

CONTRIBUTION OF AUTHORSHIP

Y.H collected data from patient files. She wrote the manuscript with assistance of C.G. E.D conducted all the statistical analysis and wrote the statistic methodology. L.G, D.S, V.H-D and E.C reviewed and corrected the manuscript.

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	Total	**Controls**	**Study Group**		
			All Scarred Uterus	1 previous CD	$\geq$ 2 previou
	n = 408	n = 272	n = 136	n = 117	n = 19
Maternal age (years)	31 (27 ; 35)	30 (26 ; 34)	34 (30 ; 37)	34 (29 ; 37)	36 (31 ; 38)
BMI	23.7 (20.8 ; 27.5)	23 (20.4 ; 26)	24.8 (21.3 ; 29.1)	24.6 (21.3 ; 29.1)	26 (23.2 ; 2
Multiparous	285 (69.9)	150 (55.1)	135 (99.3)	116 (99.1)	19 (100)
Medical history					
Myomectomy	2 (0.5)	0	2 (1.5)	2 (1.7)	0
Vaginal Delivery	204 (50)	150 (55.1)	54 (39.2)	52 (44.4)	2 (10.6)
Indication of previous CD					
- Before labour		NA	61 (50)	53 (49.5)	8 (53.3)
Hysterotomy		NA			
- Low transverse scar			118 (97.5)	102 (87.2)	16 (84.2)
- Corporeal scar			3 (2.5)	3 (2.5)	0

	Total	Controls	Study Group		
- Unknow			15 (11)	12 (10.3)	3 (15.8)
Time since last CD (months)		NA	47 (24-72)	48 (28-72)	36 (21-69)
Indication of induction					
IUFD	94 (23)	62 (22.8)	32 (23.5)	23 (19.7)	9 (47.4)
TOP	314 (77)	210 (77.2)	104 (76.5)	94 (80.3)	10 (52.6)
Fetal Anomaly	300 (95.5)	198 (95.2)	102 (96.2)	92 (95.8)	10 (100)
Maternal cause	14 (4.5)	10 (4.8)	4 (3.8)	4 (4.2)	0
Feticide	211 (67.2)	142 (67.6)	69 (66.3)	63 (67)	6 (60)
Gestation (weeks)					
Median	25.5 (22.7 ; 32)	25.6 (22.9 ; 32)	25 (22.2 ; 32)	25 (22 ; 32)	25 (22.3 ; 3
≥ 24	262 (64.2)	181 (66.5)	81 (59.6)	71 (60.7)	10 (52.6)
> 28	160 (39.2)	108 (39.7)	52 (38.2)	47 (40.2)	5 (26.3)
Fetal presentation					
Cephalic	202 (64.1)	136 (65.4)	66 (61.7)	59 (64.1)	7 (46.7)
Breech	113 (35.9)	72 (34.6)	41 (38.32)	33 (35.9)	8 (53.3)
Fetal weight (g)	830 (400 ; 1670)	850 (400 ; 1665)	795 (410 ; 1690)	837.5 (410 ; 1730)	705 (360 ; 1

Table 1. Demographic and clinical characteristics of patients

BMI = body mass index; CD = cesarean delivery; IUFD = intrauterine fetal death; NA = not applicable; TOP = Termination of pregnancy

Values are presented as n (%) or median (IQR1; IQR3)

	Total	Controls	Study Group		
			All Scarred Uterus	1 previous CD	≥ 2 previous CD
	n = 408	n = 272	n = 136	n = 117	n = 19
Immediate ARM	136 (33.4)	103 (37.8)	33 (24.3)	32 (27.4)	1 (5.3)
Spontaneous labour	3 (0.7)	0	3 (2.2)	3 (2.6)	0
First course needed	405 (99.3)	272 (100)	133 (97.8)	114 (97.4)	19 (100)
Prostaglandins	388 (95.6)	263 (96.7)	125 (93.9)	109 (95.6)	16 (84.2)
Misoprostol	377 (92.9)	258 (98.1)	119 (95.2)	103 (94.5)	16 (100)
- With laminar tents	208 (51.7)	133 (51.5)	75 (63)	59 (57.3)	16 (100)
Dinoprostone	11 (2.7)	5 (1.9)	6 (4.8)	6 (5.5)	0
Oxytocin	8 (2)	6 (2.2)	2 (1.5)	1 (0.8)	1 (5.3)
Transcervical balloon	9 (2.2)	3 (1.1)	6 (4.5)	4 (3.5)	2 (10.5)
Second course needed	22 (5.4)	12 (4.4)	10 (7.4)	7 (6)	3 (15.8)
Prostaglandins	8 (36.4)	7 (58.3)	1 (10)	1 (14.2)	0
Oxytocin	4 (18.2)	0	4 (40)	3 (42.9)	1 (33.3)
Transcervical balloon	10 (45.4)	5 (41.7)	5 (50)	3 (42.9)	3 (66.7)

Table 2. Cervical ripening methods for labour induction

ARM = artificial rupture of membranes

Values are presented as n (%)

	All Scarred Uterus	All Scarred Uterus	1 previous CD	1 previous CD	≥ 2 previous
	Controls	Cases	Controls	Cases	Controls

	All Scarred Uterus	All Scarred Uterus	1 previous CD	1 previous CD	≥ 2 previous
	n = 272	n = 136	n = 234	n = 117	n = 38
Primary outcome	251 (92.6)	111 (83.5) *	214 (91.8)	98 (85.9)	37 (97.4)
Secondary outcomes					
Vaginal delivery	270 (99.3)	131 (96.3)	233 (99.6)	115 (98.3)	37 (97.4)
Hysterotomy	2 (0.7)	5 (3.7)	1 (0.4)	2 (1.7)	1 (2.6)
Uterine rupture	0	5 (3.7)	0	2 (1.7)	0
Abortion > 24 hours	12 (4.4)	9 (6.7)	12 (5.2)	9 (7.8)	0
Manual removal of placenta	39 (14.3)	17 (12.7)	29 (12.4)	16 (13.7)	10 (26.3)
Revision of uterine cavity	69 (25.4)	34 (25.6)	53 (22.6)	32 (27.6)	16 (42.1)
Curettage	12 (4.4)	2 (1.5)	12 (5.1)	2 (1.7)	0
Blood loss					
- Volume	100 (50; 200)	100 (50; 300)	100 (50; 200)	100 (50; 300)	100 (50; 200)
- ≥ 500 mL	21 (7.7)	17 (12.7)	20 (8.5)	14 (12.2)	1 (2.6)
- ≥ 1000 mL	6 (2.2)	9 (6.7) *	6 (2.6)	7 (6.1)	0
Time intervals					
- Induction to abortion	7 (5; 11)	9 (6; 14.2) *	7.5 (5;11)	9 (6; 13.8) §	6.5 (4; 9)
- Induction to ARM	3 (0; 5)	4.5 (0.5; 6.2) *	3.5 (0; 5)	4.3 (0; 6) §	4 (0; 4.5)
- ARM to abortion	4.4 (2.7; 7)	5.5 (3; 8.1)	4.5 (3.7)	5.1 (2.8; 8)	3.3 (2; 5)
Misoprostol dose (μg)	800 (400; 1200)	600 (400; 800) *	800 (600; 1200)	600 (400; 800) §	800 (400; 1200
Hyperthermia	12 (5.4)	10 (9.4)	9 (4.9)	6 (6.4) ¥	3 (7.9)
Endometritis	6 (2.7)	7 (6.5)	5 (2.7)	5 (5.4)	1 (2.7)
Phlebitis	1 (0.5)	2 (1.9)	0	1 (1.1)	1 (2.7)

Table 3. Outcomes of induction of labour

ARM = artificial rupture of membranes, CD = cesarean delivery. Values are presented as n (%) or median (IQR1; IQR3)

* p<0.05 Comparison between all controls and all scarred uterus; § p<0.05 Comparison between controls and 1 previous CD; # p<0.05 Comparison between controls and ≥ 2 previous CD. Cases were compared with their matched control (2:1) using linear and logistic regression models.

¥ p<0.05 Comparison between 1 previous CD and ≥ 2 previous CD using Chi-square test or Fisher exact test for categorical variables and using Mann-Whitney U test for quantitative variables.

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`Figure 1. Flowchart.docx` available at https://authorea.com/users/315659/articles/445984-efficacy-and-safety-of-induction-of-labour-in-case-of-pregnancy-termination-or-intrauterine-fetal-death-in-patients-with-a-scarred-uterus-a-retrospective-cohort-study