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Cesarean scar defect: A prospective study on risk factors

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Condensation

This large prospective study shows for the first time that both maternal overweight and gestational diabetes increase the risk for isthmocele development. Moreover, the risk is strenghtened by increasing number of previous cesarean deliveries. These findings are important since the prevalence of obesity and gestational diabetes is increasing dramatically and both conditions could be subjected to early management and interventions.

Short version of the article title: Risk factors for post-cesarean isthmocele

A. As the rate of cesarean deliveries is increasing, we wanted to evaluate the risk factors related to isthmocele in a large prospective cohort study.

B. Gestational diabetes, obesity and multiple cesarean deliveries increase the risk of isthmocele.

C. The identification of obesity and gestational diabetes as risk factors for isthmocele is a novel finding. Thus, the results reported here are significant because there has been a dramatic increase worldwide in the prevalence of obesity and diabetes in women of childbearing age.

Abstract

Background Cesarean scar defect (isthmocele) is a known complication after cesarean delivery. It has become more common due to a rising cesarean delivery rate. Isthmocele has been associated with various gynecological and obstetric problems such as uterine rupture, cesarean scar pregnancy and bleeding disorders.

Objective To prospectively investigate factors associated with the risk for isthmocele assessed by sonohysterography.

Study design A prospective observational cohort study was conducted in 401 non-pregnant women who were recruited within three days of cesarean delivery. Women were evaluated with sonohysterography six months after cesarean delivery in order to detect a possible isthmocele. The ultrasonographer was blinded to any clinical information. The main outcome measure was the presence of isthmocele. Type of surgery (elective versus emergency), maternal background variables, and factors related to pregnancy, labor and post-operative recovery were analyzed in relation to isthmocele. A logistic regression model was used to assess independent risk factors from univariate analysis.

Results Three hundred and seventy-one women were examined with sonohysterography resulting in a follow-up rate of 92.5%. The prevalence of isthmocele was 45.6%. Independent risk factors for isthmocele development were a history of gestational diabetes (OR 1.73 [95% CI 1.02–2.92]; P=0.042), previous cesarean delivery (OR 3.14 [95% CI 1.90–5.17]; P <0.001) and advanced maternal BMI (OR 1.06 [95% CI 1.01–1.11]; P =0.012). Every additional unit of BMI increased the risk of isthmocele by 6%. In the subgroup of emergency cesarean delivery, longer duration of active labor increased the risk for isthmocele (OR 1.06 [1.01–1.11]; P=0.032). There was no statistically significant difference in prevalence between the groups of elective and emergency cesarean delivery (p=0.898).

Conclusion Based on sonohysterographic examination, maternal body mass index, gestational diabetes and previous cesarean deliveries are associated with an increased risk for incomplete healing of the uterine incision.

Keywords cesarean scar defect, cesarean delivery, isthmocele, sonohysterography. ultrasonography.

Introduction

Cesarean delivery (CD) is potentially a life-saving procedure if performed for the right indications.[1] The World Health Organization has stated that CD rates at up to 10-15% at the population level are associated with decreases in maternal, neonatal and infant mortality. Above this level, the increasing rate of CD is no longer associated with reduced mortality.[2] However, rates up to 50% have been reported, which consequently can lead to a growing number of complications.[3,4] One of these complications, cesarean scar defect, has been shown to be associated with various gynecological and obstetric problems. Uterine rupture and ectopic cesarean scar pregnancy are fairly rare complicatios of cesarean scar defect yet with potentially catastrophic consequences.[5,6] However, postmenstrual spotting, dysmenorrhea, dyspareunia or chronic pelvic pain are frequently described in relation to cesarean scar defect. [7–11] Additionally, cesarean scar defect may increase the risk for complications in gynecological procedures such as IUD placement, evacuation and embryo transfer.[11,12]

Therefore, in the past several years, numerous studies have been published concerning the scar defect (also called 'isthmocele' or 'niche'). The isthmocele represents an inadequate healing of the myometrium at the site of cesarean incision. Its prevalence varies substantially, between 6.9-69%, depending on the study population and the methodology used.[13,7] Appropriate diagnosis of isthmocele is made with contrast-enhanced ultrasonography.[14] A history of multiple CDs is generally considered to be a major potential risk factor for isthmocele. Additionally, advanced stage of labor and uterine retroflexion have been associated with isthmocele.[13,15] However, prospective studies on this subject are scarce and quite heterogeneous. Most of them include a small sample size or are performed in selected populations of symptomatic women. To develop preventive strategies for reducing the risk for isthmocele and thus overcoming possible adverse outcomes, it is essential

to identify related risk factors. The aim of this study was to investigate factors that increase the risk of isthmocele in a large prospectively collected and unselected population.

Materials and Methods

This prospective observational cohort study was designed to assess the prevalence, risk factors and clinical outcome of cesarean scar defect. The results of risk factor analysis are reported here, while the clinical outcome will be published after a sufficient follow-up of the participants. The study was carried out at Tampere University Hospital, Tampere, Finland. The date of the trial registration (ClincalTrials.gov: Identifier: NCT02717312, ID: R15104) of this study was March 9, 2016. The study protocol was approved by the institutional review board of Tampere University Hospital, Finland (ETL code R15104).

Women who delivered by CD at Tampere University Hospital between January 2016 and January 2017 were asked to participate. They were recruited either before the CD in the case of elective surgery or within three days after the operation in the case of emergency CD. All participants provided written informed consent before enrollment. Exclusion criteria included a known uterine anomaly, lack of common language and age under 18. Clinical information concerning pregnancy, operation technique and recovery time were obtained from the electronic medical database. Six months after the CD, participants were invited to the gynecologic outpatient clinic for ultrasound examination. Transvaginal ultrasonography (TVUS) and sonohysterography (SHG) were performed using the Samsung WS80 Elite (Samsung Medison CO., Ltd, Gangwon-do, Republic of Korea).

Women without contraception were examined during the follicular phase of the menstrual cycle to avoid an eventual early pregnancy. Otherwise, a random phase of the menstrual cycle was accepted. Women who were pregnant at the time of ultrasound (US) were excluded. All TVUS and SHG procedures were performed by the first author, who was blinded to the clinical information. Women were examined in the lithotomy position with an empty bladder. The uterus was examined in a standardized way, with TVUS performed first.[16] Isthmocele was defined as an anechoic defect in the anterior wall of the lower uterine segment, communicating with the endometrial cavity. If an

isthmocele was detected, the depth and width of the isthmocele, the residual myometrial thickness (RMT) overlying the isthmocele and the adjacent myometrial thickness (AMT) fundal to the isthmocele were measured in the midsagittal plane. The length of the isthmocele was measured in the transverse plane (Figure 1).[8] The uterine position was classified as anteverted or retroverted. For the diagnosis of isthmocele, we used a predetermined definition of a defect at least 2.0 mm deep.[10] In case more than one defect was found, the largest one was measured. To assess a low RMT, we used the cut-off point of 3.0 mm because it is regarded as the minimum RMT for hysteroscopic treatment for symptomatic patients.[17] Women without isthmocele were included in the group of RMT of ≥3.0 mm because it is presumable that without isthmocele, the myometrium thickness remains unchanged. Moreover, isthmocele was considered large if the ratio between the depth of the isthmocele and the AMT was ≥0.50. Immediately after the TVUS, SHG was performed. A small catheter (Insemination cannula standard, Laboratoire CCD, Paris, France) was inserted into the uterus, and sterile saline was flushed until the site of cesarean scar was visualized. The same measurements as mentioned above were performed. The volume of flushed saline was measured.

Statistical analyses

This prospective study was designed to investigate the prevalence, risk factors and clinical outcome of isthmocele. The primary outcome measure of the entire study was the prevalence of isthmocele. The study was designed to assess the effect of isthmocele on the incidence of bleeding disorders (i.e., postmenstrual spotting defined as ≥2 days of brownish discharge at the end of menstruation with total bleeding days of ≥7 or non-cyclic bleeding not related to menstruation). The detection of a two-fold difference in the prevalence of bleeding disorder between the isthmocele and non-isthmocele groups was the aim of the analyses. The sample size calculations were based on the following assumptions: the prevalence of bleeding disorders among women with isthmocele is 30%,

and the prevalence of isthmocele was estimated to be approximately 50% according to previous data.[9] To achieve 80% power with a two-sided alpha of 0.05, we needed to enroll 266 women in the study. Considering the drop-out rate, which we anticipated to be up to 30%, we planned to recruit 400 women. This number was supposed to be sufficient also for the present study on risk factors, where the primary objective was the association of elective versus emergency CD with the risk of isthmocele when the prevalence of elective CD corresponded to 44% out of the total number of CDs at our hospital.

Data were analyzed using SPSS version 22.0 (IBM Corp, Armonk, NY). Associations between categorical variables and the formation of isthmocele were compared with chi-square tests and between continuous variables and isthmocele with binary logistic regression. A logistic regression model was used for the multivariate analysis assessing the effect of statistically significant risk factors from univariate analysis. Two-tailed p-values of <0.05 were considered statistically significant.

The isthmocele detected by SHG was defined as the outcome of interest in the statistical analyses because SHG is considered as a method of choice when evaluating isthmocele.[8,18]

Results

Four hundred and one women gave their informed consent. Later, twenty-six women refused to continue the study. Three women were excluded because of detected pregnancy at the time of examination, and one was excluded because of severe vulvodynia, which made it impossible to perform SHG. Finally, we examined three hundred and seventy-one women successfully by both TVUS and SHG resulting in a follow-up rate of 92.5% (Figure 2). The examinations were performed, on average, 6.7 months after the CDs (range 4.5-10.0 months). Demographic background variables testing for their predictive ability are shown in Table 1. The mean age of all participants was 32.5 years. The gestational age at CD varied from 24 to 42 weeks, with a mean value of 39+2 weeks. A total of 215 (58%) participants had no previous deliveries. Fifty-eight (16%) women had at least one previous vaginal delivery (range 1-6 deliveries), while 117 (32%) had a history of previous CD (range 1-3 CDs). One hundred fifty-five women (41.8%) underwent elective CD, and 216 women (58.2%) underwent an emergency CD. This distribution corresponds to the rate upon which the statistical power calculations were based. Of the emergency CDs, twelve (3.2%) were emergent-crash (i.e., requiring immediate intervention). The most common reasons for elective CD were fear of childbirth (32.9%), breech presentation (22.6%) and previous CD (20.0%). For emergency CD the most common reasons were prolonged labor (44.0%) and fetal asphyxia (32.4%). Intrapartum or post-operative infection was diagnosed in fifty-nine out of 371 women (15.9%). Diagnosed infections included chorioamnionitis, postpartum wound infections and endometritis. The diagnostic criteria for chorioamnionitis included intrapartum fever and elevated infection parameters (CRP, leucocyte count) with maternal or fetal tachycardia. There were no differences regarding the rate of primary or emergency cesarean section, age, gestational diabetes (GDM), body mass index (BMI) or parity between women who participated in the present study and those who also delivered by CD during the study period but did not participate in the study.

Eighty-three isthmocele cases were detected by TVUS and 169 by SHG. Thus 86 women had a normal TVUS inspite of an isthmocele diagnosed by SHG. The prevalence of isthmocele was 22.4% with TVUS and 45.6% with SHG. Most of the isthmoceles were triangular in shape (92%), while the rest were round (3.9%), oval (2.5%) and total defect (1.8%). The prevalence of isthmocele detected by SHG was defined as the outcome of interest in the statistical analyses (Figure 3). There was no significant difference in the presence of isthmocele between the groups of elective and emergency CD (p=0.898). Parity was also a significant risk factor for isthmocele (p<0.001). However, prior vaginal deliveries did not increase the isthmocele risk (p=0.327), but a history of previous CD had a significant influence on isthmocele formation (p<0.001). Women without previous CD had a 35% chance of having isthmocele, while after one, two or three CDs, the risk was 63%, 76% and 88%, respectively. Similarly, parity increased the risk of isthmocele (p<0.001).

Women with isthmocele had higher BMIs both before pregnancy and at the time of CD than women without isthmocele (p=0.001 and p=0.002, respectively). Every additional unit of BMI raised the risk by 6%. However, the absolute change in maternal weight during pregnancy was not associated with the risk of isthmocele. Women with GDM were more likely to have isthmocele (p=0.002). However, type I diabetes did not increase the risk. A retroverted position of the uterus at US examination was associated with an increased risk for isthmocele (p=0.049). The method of wound closure (single vs. double layer sutures) could not be analyzed because in all but one woman, the uterine incision was closed in double layer with continuous unlocked sutures using polyglactin (Vicryl®), which represents the standard way of uterine wound closure at our hospital. The remaining one woman had single layer, continuous unlocked sutures. In a subgroup of women with emergency CD, the duration of active labor (i.e., number of hours with regular contractions) was longer in women who developed isthmocele, with a mean duration of 16.3 vs. 13.9 hours (p=0.039). Previous CD (P=0.001), maternal age (P=0.032), peripartal infections (P=0.035) and GDM

(P=0.046) were also associated with the development of isthmocele. Cervical dilatation or station of the presenting fetal part, induction of labor, multiple pregnancy, and unsuccessful vacuum delivery prior to CD did not influence the risk of developing isthmocele.

We entered the significant risk factors from the univariate analysis into the multivariate analysis. Additionally, maternal age was included in the multivariate analysis. Because BMI at CD is dependent on BMI before pregnancy, we decided to enter BMI at the time of CD in the multivariate analysis. The results of the multivariate logistic regression analysis are shown in Table 2. Independent risk factors for isthmocele were previous CDs, maternal BMI and GDM (OR 3.14 [95% CI 1.90–5.17]; P<0.001; OR 1.06 [95% CI 1.01–1.11]; P=0.012; OR 1.73 [95% CI 1.02–2.92]; P=0.042, respectively).

We also performed the multivariate analysis of the subcohort of patients undergoing an emergency CD (n=216). Factors showing statistically significant associations with isthmocele in the univariate analysis were entered into the multivariate analysis (i.e., previous CD, parity, maternal age, peripartal infections, duration of labor and GDM). The independent risk factor for isthmocele in this subgroup was the duration of labor (OR 1.06 [95% CI 1.01–1.11]; P=0.032). The results of the multivariate logistic regression in this subcohort are shown in Table 3.

RMT was measured in 282 women. A total of 73 (19.7%) of participants had RMT<3.0 mm. Risk factors for reduced RMT (< 3.0 mm) were peripartal infection (p=0.008) and advanced cervical dilatation (p=0.045). Parity and the number of previous CDs were associated with large isthmocele defects (p=0.033 and p=0.002, respectively).

Comment

In this prospective observational cohort study, we show that advanced maternal BMI, a history of GDM and previous CD are independent risk factors for isthmocele development, regardless of the type of CD. In the subgroup of emergency CD, longer duration of active labor appears to increase the risk for isthmocele. We also report here that peripartal infections and advanced cervical opening raise the risk for low RMT values.

The strength of our study is that it represents, to our knowledge, the largest study performed to date in which isthmocele was evaluated with contrast-enhanced sonography in relation to the defined risk factors. As far as we know, only one previous study included a larger sample size in the assessment of isthmocele risk factors.[19] However, they used only unenhanced TVUS to diagnose isthmocele. Currently, contrast-enhanced ultrasonography is considered to be the gold standard in isthmocele diagnostics.[8]

Another strength of our study is the prospective observational cohort study design, in which participants were recruited as early as within three days of CD, thus avoiding possible selection bias. Only few previous prospective studies have been published, mainly recruiting participants a few months after CD, which may cause selection bias since symptomatic women may be more willing to participate. We found two previous studies that recruited participants close to CD.[10,20] However, in those studies, the US examination was performed as early as 6-12 weeks after CD. We decided to perform the examinations six months after CD because it has been suggested that the cesarean wound healing process will take at least six months. On the other hand, we wanted to minimize the risk of a new pregnancy at the time of US, which would have prevented the performance of SHG. However, it is possible that the healing process will continue beyond six months. Thus, doing the measurements at a later time point might have revealed different results, which has to be taken into account when interpreting the results.

It is a limitation of our study that 370 out of 371 women received a double-layer closure of the uterine incision. Therefore, we could not study the influence of closure technique on the risk of isthmocele. Another limitation of our study is that RMT was measured only if there was any visible indentation at the site of the CD scar. Therefore, in 89 (24.0%) women, RMT remained unmeasured. However, in that group, almost all women had no history of previous CD (n=78/89; 88%). Low RMT values have been associated with the number of previous CDs, and a strong association between low RMT values and the presence of isthmocele has been shown.[19] Therefore, we found it reasonable to include women without isthmocele in the group with RMT≥3.0 when we assessed the risk factors for low RMT.

Our results concerning the impact of obesity and GDM are novel. Maternal BMI and diabetes have not been regarded as risk factors for isthmocele in previous trials.[13,21,22] This may be due to a relatively small sample size in these studies; thus, the number of women was too small for significant associations. Additionally, the diagnostics and treatment of GDM may vary in different countries. In Finland, there is a population-wide maternity health care system and clear indications for glucose tolerance testing during pregnancy, ensuring that almost all cases of GDM become diagnosed. Obesity has been associated with impaired cutaneous wound healing in general and total wound failure after surgical procedures.[23] Consistently, diabetes mellitus has a negative effect on wound healing by various mechanisms.[23,24] We think that it is reasonable to presume that obesity and diabetes affect also the healing of uterine incision and the negative effect may be true for gestational diabetes as well. Both obesity and diabetes have various systemic consequences. Chronic, low-grade inflammation, insulin-resistance and hyperglycemia are some of the factors associated with impaired wound healing related to these conditions.[24,25]

A relationship between multiple CDs and isthmocele has been reported previously.[7,15,26,27] A pre-existing CD scar has been shown to negatively influence the healing of a new cesarean uterine incision. The results from our study support these data. The risk for isthmocele increased considerably with the number of previously performed CDs. The proposed pathophysiology is that repeated trauma to the isthmic wall disrupts the normal healing process. Additionally, vascular perfusion may be reduced in the scar tissue.[7,15]

In the subcohort of women who attempted a trial of labor, the duration of active labor increased the risk for isthmocele. As far as we know, there are no previous studies in which a subgroup of emergency CD is evaluated for the risk factors. In univariate analysis, the results obtained from the subgroup analysis were similar compared to the whole cohort with respect to parity, GDM and obesity. In multivariate analysis, only the duration of labor remained as a significant risk factor for isthmocele. This may be attributable to smaller sample size in the subgroup analysis. It is possible that in active labor the healing circumstances are unique because the lower uterine segment is more stretched, which may specifically affect the healing properties of myometrium.

We found that advanced cervical dilatation raises the risk for low RMT values. This finding is in agreement with previous data[13]. Osser et al found that cervical dilatation raises the risk for large isthmocele, which was defined by RMT $\leq$ 2.5 mm. In contrast to our results, they also found that the station of the presenting fetal part at CD was associated with the risk for large isthmocele. This difference may have arisen because our study included only a few women with presenting fetal part below the pelvic inlet. Moreover, the estimate of the height of the presenting part is quite subjective and thus sensitive to mistakes and hardly repeatable.

The development of isthmocele seems to depend on various patient-related and pregnancy-related, as well as operative, factors. We have shown here for the first time that both maternal obesity and gestational diabetes raise the risk for isthmocele. These findings are important since obesity and GDM are conditions that could be affected by early management and interventions. In the future, this association may become even more important because there has been a dramatic increase worldwide in the prevalence of obesity and GDM in women of childbearing age.[28] We want to emphasize that our results reflect the quantitative healing of the uterine scar. The clinical outcome of isthmocele will be ascertained only in the course of follow-up of our prospective study cohort. Nevertheless, more prospective high-quality studies are needed to ascertain the clinical significance of isthmocele in order to facilitate the definition of clinical guidelines for the possible prevention and management of isthmocele.

Acknowledgements

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Table 1

Demographic background data and the results of univariate logistic regression analysis

	Without isthmocele n=202 (54.4%)	With isthmocele n=169 (45.6%)	OR	95% CI	p-value
Maternal age, mean (SD), y	32.1 (5.6)	33.1 (4.9)	1.04	1.00-1.08	0.074
Gestational age, mean (SD), weeks+days	39+2 (2.5)	39+2 (2.2)	1	0.92-1.09	0.947
Parity, mean (range)	0 (0–6)	1 (0–5)	1.54	1.22-1.93	0.001
Prior vaginal delivery, n (%)	35 (17.3)	23 (13.6)	0.75	0.43-1.33	0.327
Prior CD, n (%)	38 (18.8)	79 (46.7)	3.69	2.38-6.03	<0.001
Indication for CD, n (%)					
Elective	85 (42.1)	70 (41.4)			0.898
Emergency	117 (57.9)	99 (58.6)	1.03	0.68-1.56	
Birth weight, mean (SD), g*	3532 (705)	3595 (610)	1.02	0.98-1.05	0.375
Smoking during pregnancy, n (%)	9 (4.5)	6 (3.6)	0.79	0.28-2.26	0.660
Gestational diabetes, n (%)	49 (24.3)	66 (39.1)	2.00	1.28-3.12	0.002
Diabetes mellitus, n (%)	6 (3.0)	6 (3.6)	1.20	0.38-3.80	0.753
BMI before pregnancy, mean (SD), kg/m²	25.1 (5.3)	27.1 (6.1)	1.07	1.03-1.11	0.001
BMI at CD, mean (SD), kg/m²	30.4 (5.3)	32.3 (5.9)	1.06	1.02-1.10	0.002
Change in maternal weight, mean (SD), kg	14.3 (6.2)	13.4 (6.0)	0.98	0.94-1.01	0.159
Uterine position at ultrasound, n (%)					
Anteversion	149 (73.8)	108 (64.3)			0.049
Retroversion	53 (26.2)	60 (35.7)	1.56	1.00-2.44	
Cervical dilatation at CD, n (%), cm					
0	95 (47.0)	82 (48.5)			0.071
1-4	62 (30.7)	36 (21.3)	0.67	0.41-1.12	0.125

≥5	45 (22.3)	51 (30.2)	1.31	0.80-2.16	0.284
Intrapartum or post-operative infection, n (%)	26 (12.9)	33 (19.5)	1.64	0.94-2.88	0.083
Experience of an operator, n (%)					
Resident	133 (65.8)	110 (65.1)			0.879
Specialist	69 (34.2)	59 (34.9)	1.03	0.67-1.59	
Induction of labor, n (%) **	59 (29.2)	38 (22.5)	0.63	0.37-1.10	0.103
Multiple pregnancy, n (%)	12 (5.9)	8 (4.7)	0.79	0.31-1.97	0.609
Pre-eclampsia, n (%)	15 (7.4)	8 (4.7)	0.62	0.26-1.50	0.288
Antenatal corticosteroid, n (%)	16 (7.9)	10 (5.9)	0.73	0.32-1.66	0.453
Duration of labor, mean (SD), hours **	13.9 (6.7)	16.2 (7.6)	1.05	1.00-1.10	0.039
Oxytocin augmentation during labor, n (%) **	70 (59.8)	68 (68.7)	1.00	0.99-1.01	0.530
Unsuccessful vacuum delivery prior to CD, n (%) **	8 (6.8)	5 (5.1)	0.73	0.23-2.29	0.584
Station of presenting part, n (%) **					
At or above pelvic inlet	105 (48.8)	85 (39.5)			0.494
Below pelvic inlet	12 (5.6)	13 (6.0)	1.34	0.58-3.09	

CD, cesarean delivery; BMI, body mass index.

* twin pregnancies excluded; ** in the subgroup of emergency CD

Table 2

Results of multivariate logistic regression analysis in the study cohort (N=371)

Parameter	Odds ratio	95% CI	p-value
Maternal age, y	1.00	0.95-1.04	0.846
Parity	0.90	0.64-1.27	0.558
Previous CD	3.14	1.90-5.17	<0.001
Gestational diabetes	1.73	1.02-2.92	0.042
BMI at CD	1.06	1.01-1.11	0.012
Uterine position at ultrasound	1.60	0.98-2.60	0.058

CD, cesarean delivery; BMI, body mass index.

Table 3

Results of multivariate analysis in the subcohort of emergency cesarean delivery (N=216)

Parameter	Odds ratio	95% CI	p-value
Maternal age, y	1.02	0.95-1.09	0.670
Parity	1.28	0.65-2.51	0.472
Previous CD	2.64	0.90-7.73	0.076
Gestational diabetes	1.81	0.86-3.79	0.118
Intrapartum or post-operative infection	2.05	0.95-4.42	0.068
Duration of labor, h	1.06	1.01-1.11	0.032

CD, cesarean delivery.

Figure 1

Figure title:

Schematic presentation of isthmocele measurements.

Figure legend:

In longitudinal plane: a. Depth of isthmocele, b. Width of isthmocele, c. Thickness of adjacent myometrium, d. Thickness of residual myometrium. In transverse plane: e. Length of isthmocele.

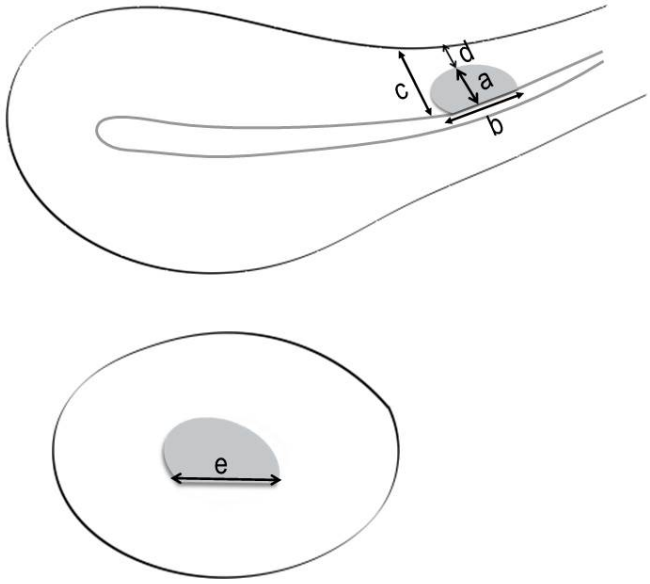

Figure 2

Figure title: Flow chart of the study

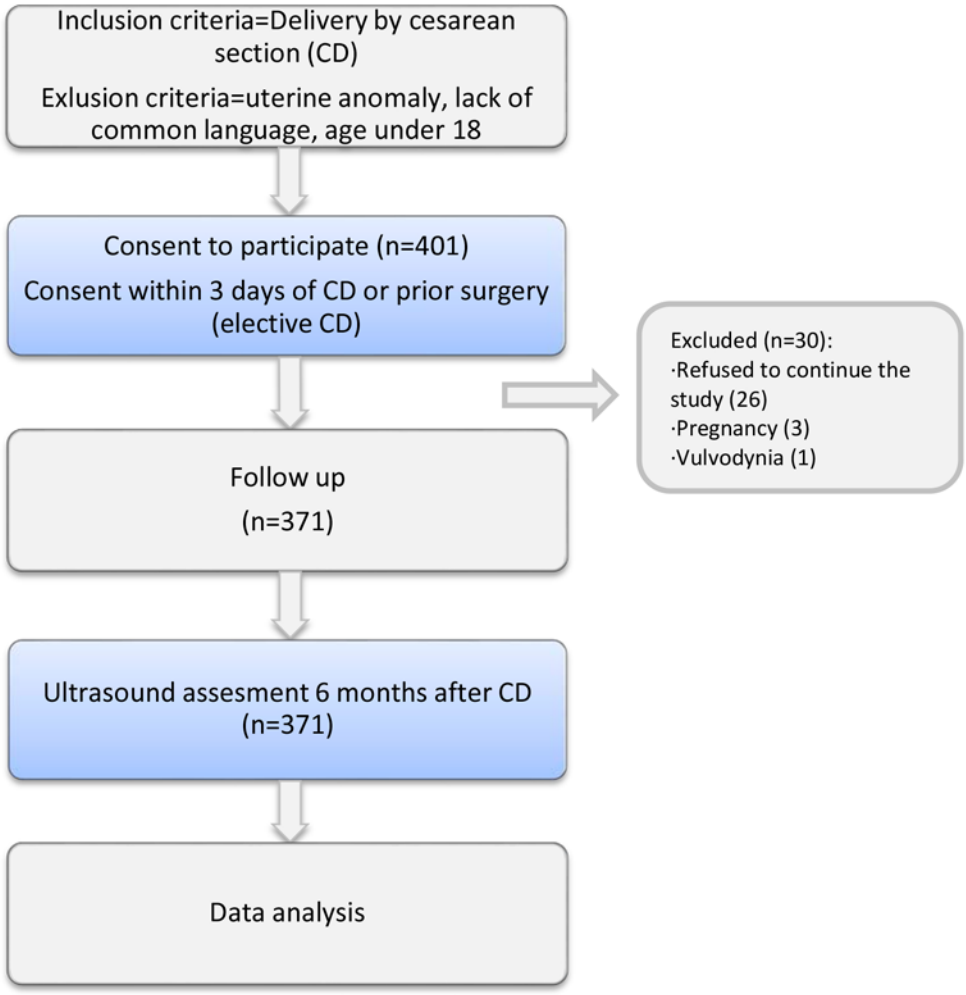

Figure 3

Figure title: Sonohysterographic image of a triangular shaped isthmocele. Hypoechogenic defect is marked by an asterisk.