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Vikhareva, Olga

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PO Box 117
221 00 Lund
+46 46-222 00 00

Ultrasound Studies of Caesarean Hysterotomy Scars



Olga Vikhareva Osser

2010

**Institution of Clinical Sciences Malmö, Lund University
Department of Obstetrics and Gynaecology,
Skåne University Hospital, Malmö, Sweden**

“Man is a mystery: if you spend your entire life trying to puzzle it out, then do not say that you have wasted your time. I occupy myself with this mystery, because I want to be a man.”

Fyodor Dostoevsky

*To the memory of my
grandmother Julia*

Preface

During my career as an obstetrician, I have encountered severe complications such as placenta accreta, with life-threatening bleeding and uterine rupture, resulting in dramatic consequences for both mother and child. Almost all these patients had previously undergone a caesarean delivery. These complications led to extremely difficult and stressful situations in which decisions about treatment had to be made within seconds. Massive blood transfusions, coagulopathy, injury to other organs requiring further surgery, renal insufficiency and respiratory distress are potentially devastating consequences associated with these conditions. These situations were very difficult for all those involved – the medical team, the patient and her family. When reviewing these cases retrospectively, I often wondered if it could be possible to predict, and perhaps prevent, these complications. Life-threatening bleeding and uterine rupture are still very uncommon, but the frequency of caesarean deliveries is increasing worldwide, and this may be accompanied by an increase in the complication rate.

In recent years I and my experienced colleagues at the Ultrasound Department have observed an increased frequency of defects in hysterotomy scars after caesarean deliveries. The clinical importance of large scar defects detected by ultrasound in non-pregnant women is yet not known, but scar defects are likely to reflect incomplete healing of the uterine wall. The work presented in this thesis was, therefore, carried out in an attempt to prevent disastrous complications by determining the prevalence of caesarean scar defects in the uterine wall by ultrasound, and identifying the factors that increase the risk of large caesarean scar defects. Furthermore, I investigated whether, and how, ultrasound could be used to predict the risk of such severe complications as uterine rupture or uterine dehiscence in subsequent pregnancies after caesarean delivery.

Original papers

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals. The papers are appended at the end of the thesis.

- I. Vikhareva Osser O, Jokubkiene L, Valentin L. High prevalence of defects in Cesarean section scars at transvaginal ultrasound examination.
Ultrasound Obstet Gynecol. 2009;34: 90-7.
- II. Vikhareva Osser O, Jokubkiene L, Valentin L. Cesarean section scar defects: agreement between transvaginal sonographic findings with and without saline contrast enhancement.
Ultrasound Obstet Gynecol. 2010; 35: 75-83.
- III. Vikhareva Osser O, Valentin L. Risk factors for incomplete healing of the uterine incision after caesarean.
BJOG 2010; 117: 1119-26.
- IV. Vikhareva Osser O, Valentin L. Association between the appearance of hysterotomy scars at transvaginal ultrasound examination of non-pregnant women and the outcome of subsequent pregnancies and deliveries.
Submitted 2010

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Background

Ultrasonography is a valuable method for the diagnosis of various obstetrical conditions in all three trimesters of pregnancy. It is a good diagnostic tool in the management of conditions such as scar pregnancy and placenta praevia, and may contribute to the diagnosis of placenta accreta/increta/percreta. Despite the fact that uterine rupture is a major problem among patients with a scarred uterus, leading to life-threatening complications for the mother and asphyxia in the infant, the number of publications on this complication is very limited. A few groups have attempted to investigate the possibility of using ultrasound to predict a uterine defect due to a hysterotomy scar resulting from a previous caesarean delivery before the current caesarean, but the numbers of cases included in these studies were small [Araki and Inooka, 1982; Brown et al., 1986; Michaels et al., 1988; Tanik et al., 1996]. In a study on a larger group, the risk of an anatomical defect in the anterior uterine wall during subsequent labour was estimated to be directly correlated to the degree of lower uterine segment thinning measured at 36-38 weeks of gestation in women having previously undergone a caesarean delivery [Rozenberg et al., 1996]. It was confirmed that women with a scarred uterus where the thickness of the lower uterine segment measured 3.5 mm or more had a very low risk of uterine rupture during a subsequent trial of labour. In a following study it was suggested that ultrasound findings should encourage obstetricians commonly performing repeat caesareans to suggest a trial of labour in women when the lower segment was at least 3.5 mm [Rozenberg et al., 1999]. This had little effect on the total rate of caesarean deliveries, but the proportion of elective versus acute caesarean deliveries changed in favour of elective operation. Rozenberg et al. concluded that ultrasound examination of the lower uterine segment could increase the safety of vaginal birth after caesarean delivery when evaluating the risk of uterine rupture.

It has been reported that transvaginal ultrasound can accurately detect caesarean scars in non-pregnant women [Monteagudo et al., 2001; Regnard et al., 2004]. However, different definitions have been used to describe hysterotomy scars after caesarean, making it difficult to compare the results from different studies and to employ ultrasound findings in the clinical situation.

The infusion of saline into the uterine cavity prior to ultrasound scanning (hydrosonography) was first described by Parson and Lense in 1993. Hydrosonography has been shown to be useful in assessing the uterine cavity, in particular for the detection and evaluation of intrauterine focal lesions [Dueholm et al., 1999; Epstein et al., 2001]. According to Monteagudo et al. [2001] hydrosonography is indispensable when evaluating caesarean scar defects. However, to the best of my knowledge, no comparisons of ultrasonic findings with and without hydrosonography regarding caesarean scar defects have been reported. Neither could any studies be found on the factors affecting the appearance of hysterotomy scars at ultrasound examination. Furthermore, there appear to be no studies on whether defects in caesarean scars, visible at transvaginal ultrasound examination of non-pregnant

women, are associated with a higher risk of complications such as uterine rupture or dehiscence than apparently intact scars, or whether large defects are associated with a higher risk of complication than small defects.

The predictors of the risk of failed vaginal birth and uterine rupture after previous caesarean delivery are extensively described in the literature [Hamilton et al., 2001; Smith et al., 2005; Macones et al., 2006; Spong et al., 2007; Grobman et al., 2008; Al-Zirqi et al. 2010]. However, transvaginal ultrasound examination of non-pregnant women could provide a better means of assessing caesarean scars in the uterine wall, with the aim of predicting, and possibly reducing, the risk of severe complications in subsequent pregnancies.

Caesarean delivery

The rate of caesarean delivery has increased markedly during recent decades. In the USA the reported rate in 2005 was 30% and in Europe 25% [Hamilton et al., 2007; Althabe et al., 2006]. .Caesarean delivery was relatively rare in Sweden up to the 1950s. After the introduction of electronic foetal surveillance during the 1970s the rate of caesarean deliveries increased significantly due to the ability to diagnose acute foetal distress. During the same period, more knowledge was gained on new antibiotics, and regional anaesthesia, e.g. spinal/epidural, was developed. The risk of surgical and anaesthesiological complications has decreased in general over recent decades. This has led to a more liberal interpretation of the indications for caesarean delivery. According to data from the Swedish National Board of Health and Welfare, the rate of caesarean deliveries in Sweden was 17% in 2005, compared with 12% in 1993 and 5% in 1973. Interestingly, in the period between 1983 and 1990 the rate of caesarean deliveries in Sweden decreased steadily from 12.3% to 10.8%. During this period, perinatal mortality was halved and the number of newborns with a low Apgar score decreased, indicating that it is possible to reduce the rate of caesarean deliveries without increasing the risk of adverse outcome for newborns [Nielsen at al., 1994]. As can be seen in Figure 1, the rate of caesarean delivery in Malmö is around 14%, and has been stable since 1999 (the information is taken from the official annual rapports of Malmö Hospital).

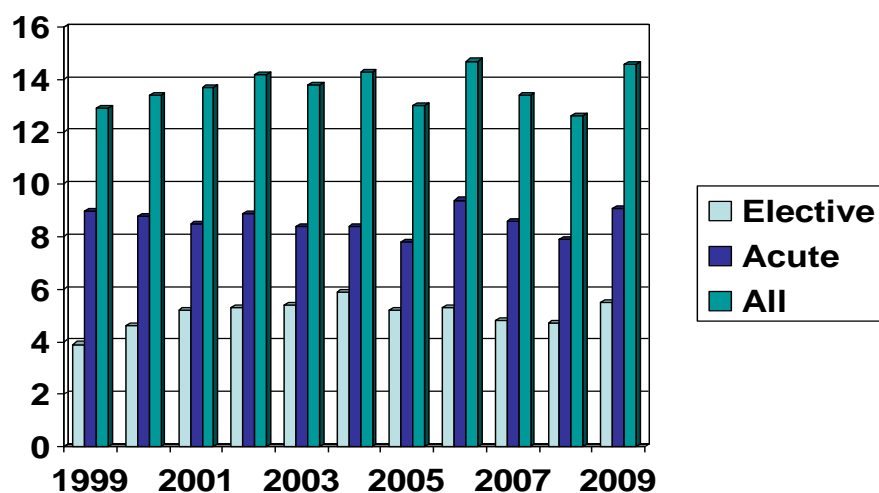


Figure 1. Rate of caesarean delivery in Malmö from 1999-2009.

Reasons for the increase in caesarean deliveries are due to changes in the population, for example, women are having children later in life, and obesity has become more common [Cunningham et al., 1995; Ogden et al., 2006]. Both these factors lead to higher risks of complications during pregnancy leading to the need for caesarean deliveries [Ecker et al., 2001; Chu et al., 2007]. Furthermore, women are now demanding more control over the kind of delivery. Maternal request for a caesarean delivery is a relatively new indication, but has become common during the last decade [Declercq et al., 2005].

The increased rate of caesarean deliveries has led to a decrease in the experience and skills in practical obstetrics, i.e. vaginal delivery in breech presentation, internal podalic version of the second twin in transverse lie, and operative vaginal delivery, such as by forceps. The skill required to correctly select cases suitable for vaginal delivery in these situations is also decreasing.

The number of obstetricians being reported for malpractice has increased in recent years [Savage et al., 1993; Pearlman 2006], which had led to the common belief that one will never be accused of malpractice if one performs a caesarean. During the period 1975 to 2000, the cost of medical malpractice for obstetricians and gynaecologists rose by nearly four times more than that of other medical costs. It is thus not unusual for obstetricians to perform caesarean deliveries to protect themselves against malpractice claims [Pearlman 2006]. This leads to a vicious circle increasing the rate of caesarean deliveries.

Repeat caesarean delivery

An increasing rate of caesarean deliveries will lead to an increase in the population of pregnant women with a scarred uterus, thus leading to a higher risk of the need for caesarean delivery in following pregnancies, i.e. one caesarean leads to another [Kolås et al., 2003]. Despite several reports of a successful outcome in a high proportion of cases of vaginal birth following caesarean delivery, the rate of trial of labour after caesarean delivery has decreased during the past ten years [Caughey, 2008]. A repeat caesarean delivery rate of 64% was reported in the UK in 2001 [Royal College of Obstetricians and Gynaecologists. The National Sentinel Caesarean Audit Report 2001].

In 2009, 223 women with a scarred uterus resulting from a caesarean delivery were delivered at the Department of Obstetrics and Gynaecology in Malmö; 176 of these having undergone one previous caesarean. Only 16.1% (36/223) of the women with a scarred uterus were delivered vaginally. The repeat caesarean delivery rate was 83.9%, confirming the common belief that once a caesarean delivery has been performed, the risk of a caesarean in the next pregnancy is high.

Caesarean deliveries are associated with serious obstetric complications in subsequent pregnancies, such as caesarean-scar pregnancy, uterine rupture, uterine dehiscence and placenta praevia/accreta.

Caesarean-scar pregnancy

This is a form of ectopic pregnancy located on a deficient caesarean scar. A viable caesarean-scar pregnancy can lead to severe complications in the late term, such as placenta accreta/percreta and uterine rupture with life-threatening bleeding leading to emergency hysterectomy [Ben-Nagi et al., 2005]. The number of cases of caesarean-scar pregnancy has increased in recent years. The incidence has been reported to vary between 1/1800 and 1/2216 pregnancies [Jurkovic et al., 2003; Seow et al., 2004]. These figures can be explained by the increase in the number of caesarean deliveries and improvements in ultrasound diagnostics in early pregnancy.

Uterine rupture

This is defined as a full-thickness separation of the uterine wall and the overlying serosa. It is a rare but potentially catastrophic event during childbirth, with high rates of perinatal morbidity and mortality. A uterine scar from a previous caesarean delivery is the most common risk factor. According to Kennare et al. [2007] women who have previously undergone caesarean delivery had an increased risk of uterine rupture in their next delivery (odds ratio 84.4, 95% confidence interval 14.64-∞). Contractions are a significant risk factor for uterine rupture. In a recent Norwegian study it was reported that women who had previously undergone caesarean delivery, had about eight times higher risk of uterine rupture after trial of labour than at repeat elective caesarean [Al-Zirqi et al., 2010]. After intensive attempts to develop models to predict the occurrence of uterine rupture, investigators have concluded that uterine rupture cannot be predicted by antepartum or early intrapartum factors [Grobman et al., 2008; Macones et al., 2006].

Uterine dehiscence

Uterine dehiscence is the incomplete separation of the myometrium at the site of a uterine scar, usually resulting from a previous caesarean delivery. This condition has not been associated with significant maternal or perinatal mortality, but during active labour it may lead to complete uterine rupture with disastrous consequences. The reported prevalence is 0.02-0.04% of all deliveries, and after one or two caesarean deliveries the risk increased with odds ratio of 9.9 [Diaz et al., 2002].

Asakura et al. [2000] found that 4.7% of women with previous caesarean deliveries had uterine dehiscence. The International Classification of Diseases coding does not include incomplete uterine rupture (dehiscence) as a separate diagnosis. In a study of coding practice of intrapartum ruptures at Oslo University Hospital in 2003 it was found that in all cases of dehiscence a code was used that did not differentiate the condition (Medical Birth Registry of Norway) [Al-Zirqi et al., 2010]. According to Suzuki et al. [2000] uterine dehiscence could not be predicted by clinical symptoms, but the ultrasonographic finding of a thin lower uterine segment at 36 weeks gestation was associated with dehiscence at the caesarean delivery.

Placenta praevia/accreta

These placental complications are serious and are associated with increased maternal morbidity. They are the most frequent indications for emergency hysterectomy [Shellhaas et al., 2009]. Each additional caesarean delivery is associated with an increased risk of placenta praevia/accreta in a subsequent pregnancy [Silver et al., 2006]. The risk of placenta accreta in a patient with placenta praevia is approximately 4% in women with no prior caesarean deliveries. The risk increases to approximately 25% with one prior caesarean delivery and to 40% with two prior caesarean deliveries [Clark et al., 1985]. According to Grobman et al. [2007], more than 50% of women with placenta praevia and two prior caesarean deliveries will have a significant adverse outcome; among women with placenta praevia and three or more prior caesarean deliveries, fewer than one in five will be spared serious maternal complications.

Factors possibly affecting hysterotomy healing after caesarean

Uterine incision

Low transverse (Kerr) hysterotomy

This method was introduced by Kerr [1926]. The advantage of this incision is its location on a more passive part of the uterus, allowing better wound healing and less stretching of the scar during subsequent pregnancies. A low transverse incision is made in more than 90% of caesarean deliveries [Joy et al., 2010]. The incision is made 1-2 cm above the original upper margin of the bladder. The rate of uterine rupture after Kerr hysterotomy reported in several large retrospective cohort studies is 0.3-1% [Flamm et al., 1997; Landon et al., 2004]. Rates of 0.5-1% are commonly used when counselling patients with no other additional risk factors [Caughey et al., 2008].

Low vertical (Krönig) hysterotomy

A vertical incision may be used in certain obstetrical situations. The results of cohort studies have shown that the risk of uterine rupture is no greater in patients who have had a vertical incision in the lower uterine segment than in those with a transverse incision. The rate of uterine rupture after Krönig hysterotomy has been reported to be 0.8-1.5% [Adair et al., 1996; Landon et al., 2008].

Classical hysterotomy

A vertical incision is made in the contractile portion of the uterus above the insertion of the round ligaments. Although available data are limited, the risk of uterine rupture in this group of patients is considered to be 4-10% [Landon et al., 2008].

Repair of the uterus

Single-layer and double-layer closure

Traditionally, uterine incisions have been closed in two layers. After several studies in the 1990s had shown shorter operative times, less need for haemostatic sutures and similar postoperative infection rate with single-layer closure, this technique gained wide clinical acceptance [Hauth et al., 1992; Jelsema et al., 1993; Malkamy et al., 1993; Ohel et al., 1996]. However, there has been insufficient analysis of the effect of this closure technique on the rate of uterine rupture in subsequent pregnancies.

In a large study population, Bujold and colleagues showed that single-layer closure of the hysterotomy after caesarean delivery was the most influential factor, and was associated with a four-fold increase in the risk of uterine rupture compared with double-layer closure [Bujold et al., 2002]. Prior single-layer closure has also been associated with increased uterine dehiscence (3.5% versus 0.7%; $p=0.046$) at subsequent caesarean deliveries [Durnwald et al., 2003]. According to Bujold et al. [2009] the combination of full lower uterine segment thickness < 2.3 mm, measured by ultrasound between 35 and 38 weeks, and single-layer closure was strongly associated with uterine rupture during a trial of labour.

Number of prior caesarean deliveries

Multiple caesarean deliveries are strongly associated with significant risk of surgical morbidity, including bladder or urethral injury, bowel injury, adhesions, operative technique difficulties requiring longer operative times, postoperative haemoglobin deficit, and the need for blood transfusion. Such serious complications increase progressively with increasing number of caesarean deliveries [Silver et al., 2006; Makoha et al., 2004].

The risk of uterine rupture also increases after multiple caesarean deliveries. In a retrospective cohort study the risk of uterine rupture in women with a history of two prior caesarean deliveries was estimated to be almost five times greater than in those with only one prior caesarean delivery: 3.7% versus 0.8% [Caughey et al., 1999]. It has been reported that even prelabour ruptures occur in women having undergone multiple caesarean deliveries [Al-Zirqi et al., 2010].

Stage of labour at caesarean

Performing a caesarean in the later stages of labour can be a risk factor for incomplete healing of the uterine incision. Increasing cervical dilation, in particular cervical dilation of 9-10 cm, is an independent risk factor for intraoperative complications such as tears in the uterus or cervix, complicating the operative technique and requiring additional suturing. The intraoperative complication rate in this group has been reported to be 19.1% (Häger et al., 2004). In women with such complications the uterine incisions and/or closure cannot be classified using the standard classifications, and have to be categorized as “non-typical”. To the best of my knowledge no

studies have been published reporting the rate of uterine rupture or dehiscence in this patient group. According to Al-Zirqi et al. [2010] uterine rupture or dehiscence occurred even before labour in women with “uncommon” uterine incisions.

Aims

The overall aim of the work described in this thesis was to determine whether the evaluation of hysterotomy scars in non-pregnant women after caesarean delivery by transvaginal ultrasound could be used to predict the risk of severe complications in subsequent pregnancies.

The specific aims were:

- to determine the ability of transvaginal ultrasound (with and without hydrosoneography) to correctly identify hysterotomy scars after caesarean delivery,
- to estimate the prevalence of defective hysterotomy scars,
- to determine the size and localization of hysterotomy scars using conventional transvaginal ultrasound,
- to examine the agreement between the findings of transvaginal ultrasound examinations, with and without hydrosoneography, with regard to number, size, location and shape of caesarean scar defects,
- to determine which factors increase the risk of large caesarean scar defects as assessed using transvaginal ultrasound, and
- to determine if large defects in the hysterotomy scar after caesarean delivery, assessed using transvaginal ultrasound, are associated with increased risk of uterine dehiscence or rupture in subsequent pregnancies.

Subjects

All women were examined between October 2005 and December 2006 at the ultrasound unit of the Department of Obstetrics and Gynaecology at Malmö University Hospital. The 162 women with who had previously undergone caesarean deliveries who participated in Study I were followed up until January 2010 with regard to the outcome of subsequent pregnancies by scrutiny of their medical records. Informed consent was obtained from all participants after the nature of the procedures had been fully explained.

The number of women included in each study and the selection of study groups are described in Figure 2.

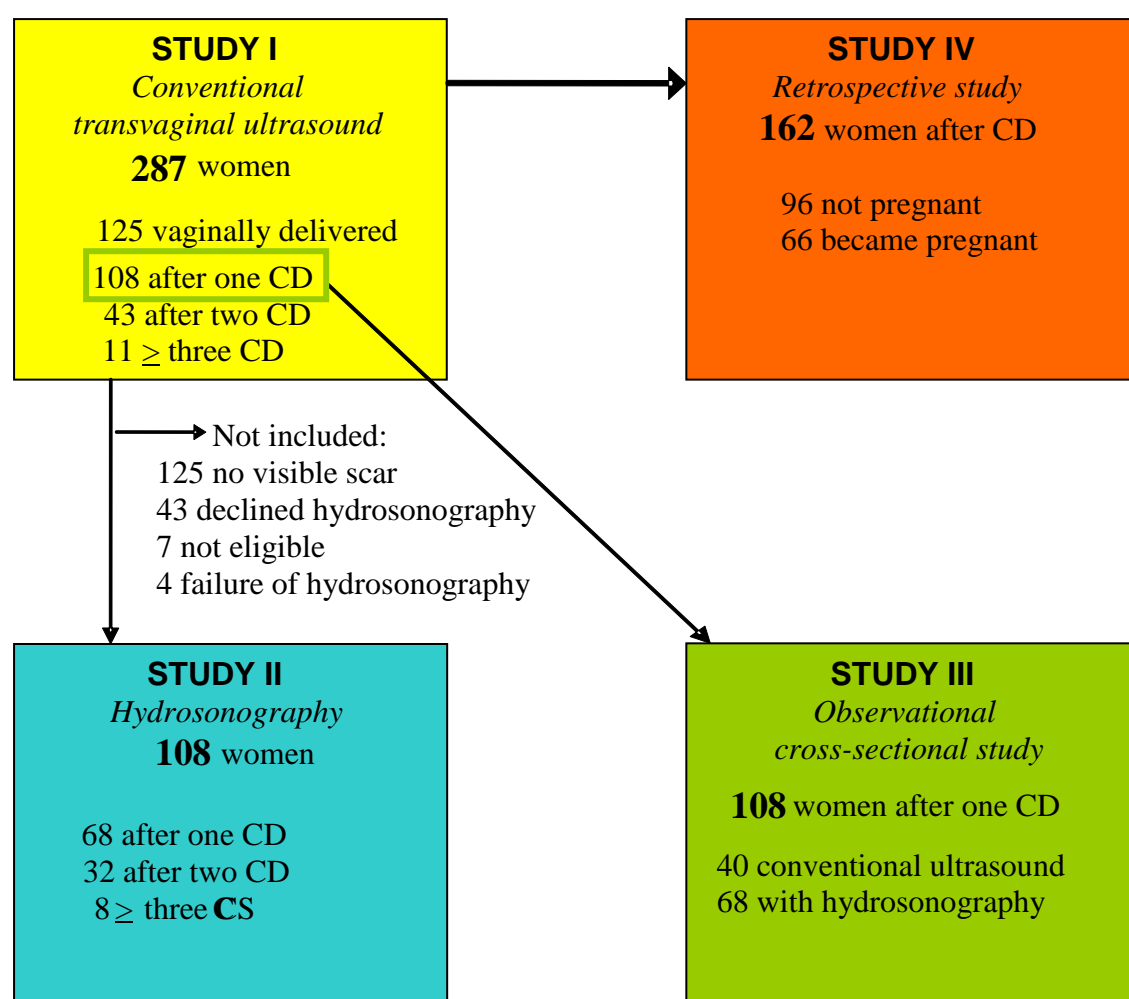


Figure 2. Flow chart describing the number of participants in each study, and the selection of the study groups. CD-caesarean delivery.

Methods

Ultrasound examinations

All ultrasound examinations were performed using a GE Voluson 730 Expert ultrasound system (General Electric, Zipf, Austria), and transvaginal scans were performed using a 5.0-7.0 MHz vaginal probe. The examinations were performed by the author. The abdomen of the woman to be examined was covered with a towel to hide any abdominal scar, and the women had been instructed not to reveal anything about their obstetric history to the ultrasound examiner. In this way, the ultrasound examiner was blinded to patient history.

Conventional ultrasound

The women were examined using conventional transvaginal ultrasound of the uterus 6 to 9 months after their latest delivery. A transvaginal ultrasound examination was carried out with the woman in the lithotomy position. The bladder was emptied before the examination. The uterus was scrutinized for the presence of caesarean hysterotomy scars and scar defects in both longitudinal and transverse sections through the uterus. The ultrasound images were evaluated during the ultrasound examination. All representative images were stored on a digital image storage system (Siemens Syngo Dynamics, version 5.0, Siemens Medical Solutions Health Services, USA, Inc.).

Ultrasound with hydrosonegography

Since it was discovered by chance that hydrosonegography facilitated the delineation of a caesarean hysterotomy scar defect, the conventional ultrasonography examination was supplemented with hydrosonegography. In 43% (46/108) of the women who participated in the second study, hydrosonegography was performed at the same visit, immediately after the conventional ultrasound examination. In the remaining women hydrosonegography was included at a second visit 10 weeks (median) after the conventional ultrasound examination. No premedication or prophylactic antibiotics were given before performing the procedure.

A polyethylene catheter (outer diameter 2.1 mm, inner diameter 1.7 mm) without an inflatable balloon (Prodimed, Neuilly-en-Thelle, France) was used to infuse about 20-30 ml of saline into the uterus, and the size of any caesarean scar defect was measured on a longitudinal scan through the uterus. Due to difficulties in delineating the defect on a transverse section of the uterus, the width of the defect could not be measured reliably when employing hydrosonegography.

Evaluation of ultrasound images and measurements

The ultrasound images were subjectively evaluated during the ultrasound examination. The following ultrasound features were noted: the uterine position (anteflexion or retroflexion), the presence of a scar, and a possible defect in the scar. If a defect was observed, the shape, size and location were noted.

A hypo- or hyperechoic line in the anterior wall of the uterus was defined as a hysterotomy scar resulting from caesarean delivery. Indentations in the scar were classified as scar defects. Caesarean hysterotomy scars were subjectively classified into three categories: intact scar, small defect and large defect (Figure 3A, B, and C).

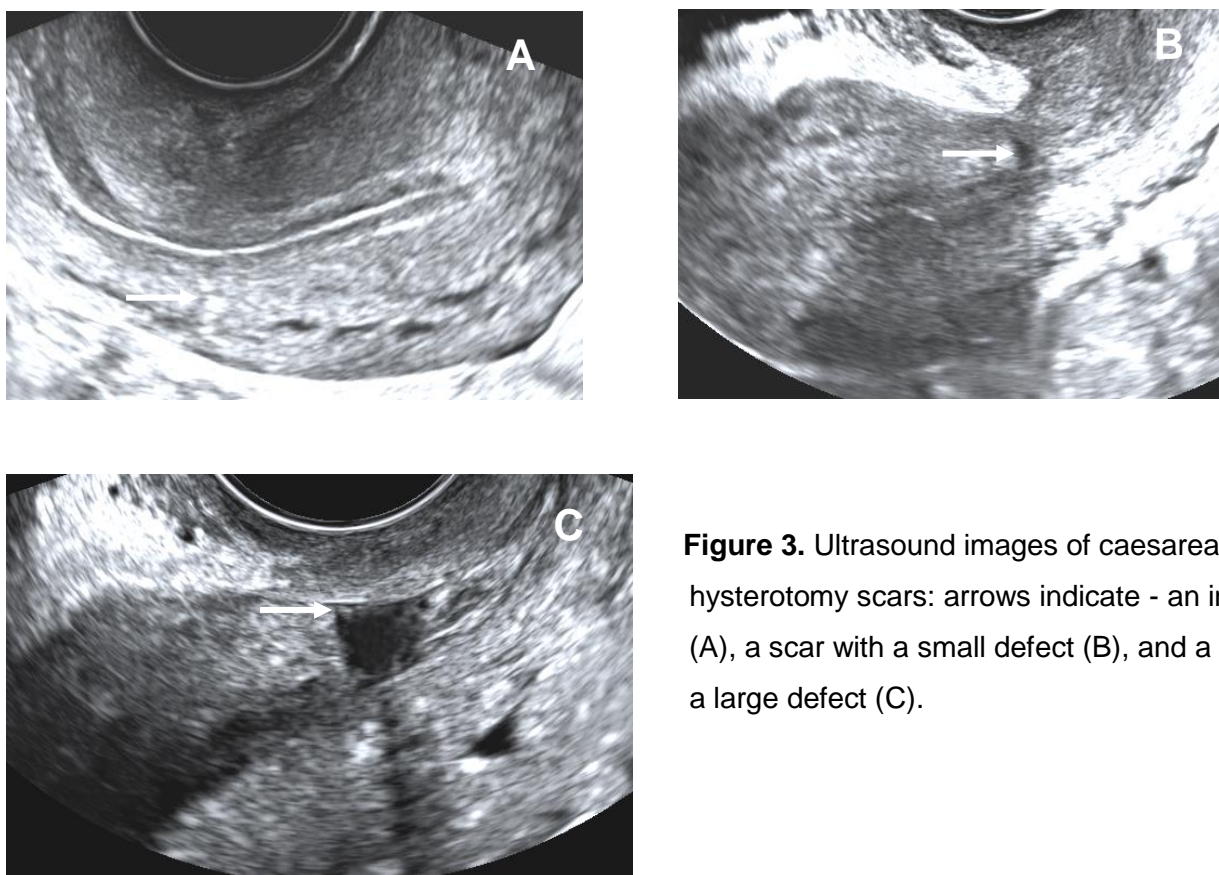


Figure 3. Ultrasound images of caesarean hysterotomy scars: arrows indicate - an intact scar (A), a scar with a small defect (B), and a scar with a large defect (C).

The level of the internal cervical os was defined as the position at which there is a slight narrowing of the uterus between the corpus and the cervix. This often corresponds to the lower boundary of the urinary bladder (Figure 4). The level of the internal cervical os is denoted “0 mm”. Measurements below the internal os are negative, measurements above are positive.

If more than one scar was seen, the scar located lowest in the uterus was denoted scar number one, and scars located closer to the fundus uteri were assigned the numbers two, three etc.

The size of the hysterotomy scar defects was also measured objectively. Measurements were made offline on a frozen ultrasound image immediately after the ultrasound examination, using callipers. The measurement technique is illustrated in Figure 5. The ratio between the thickness of the remaining myometrium covering the defect and the thickness of the myometrium adjacent to the defect was calculated (called the “ratio”).

All studies were approved by the Ethics Committee of the Medical Faculty of Lund University, Sweden.

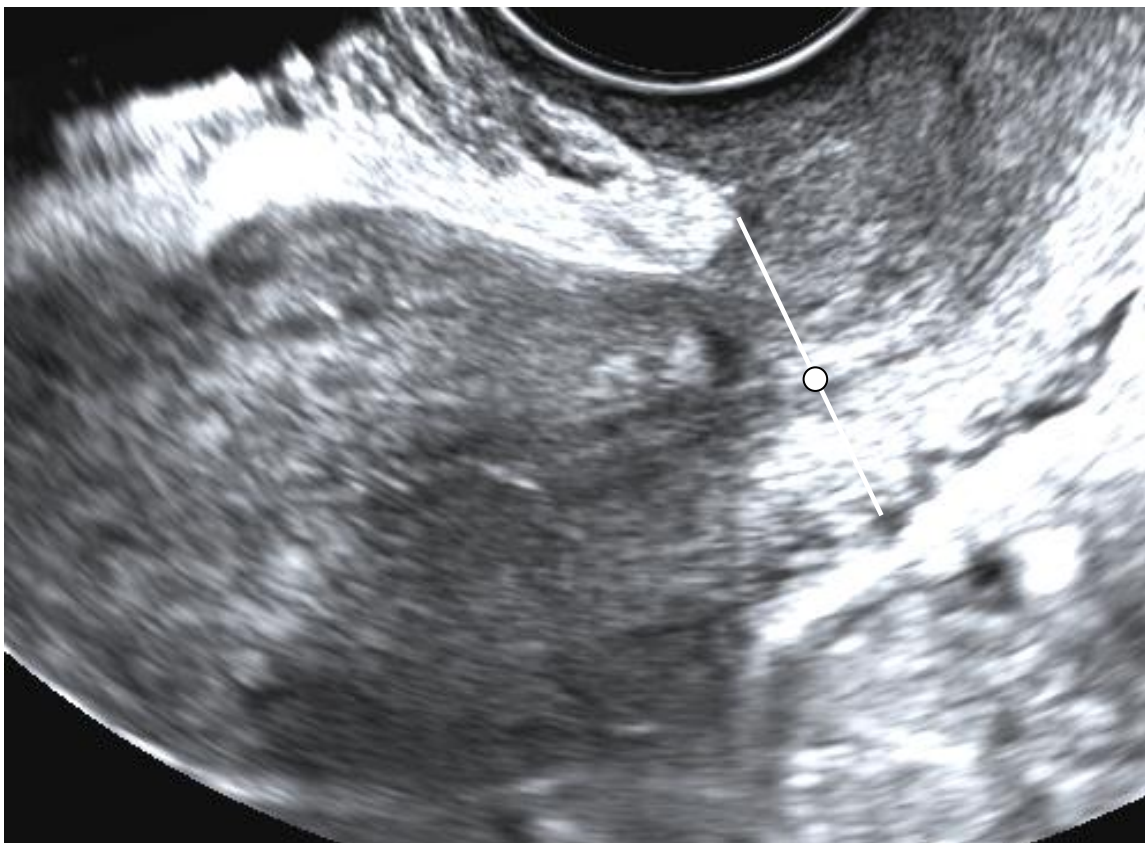


Figure 4. Ultrasound image illustrating the level of the internal cervical os (white spot).

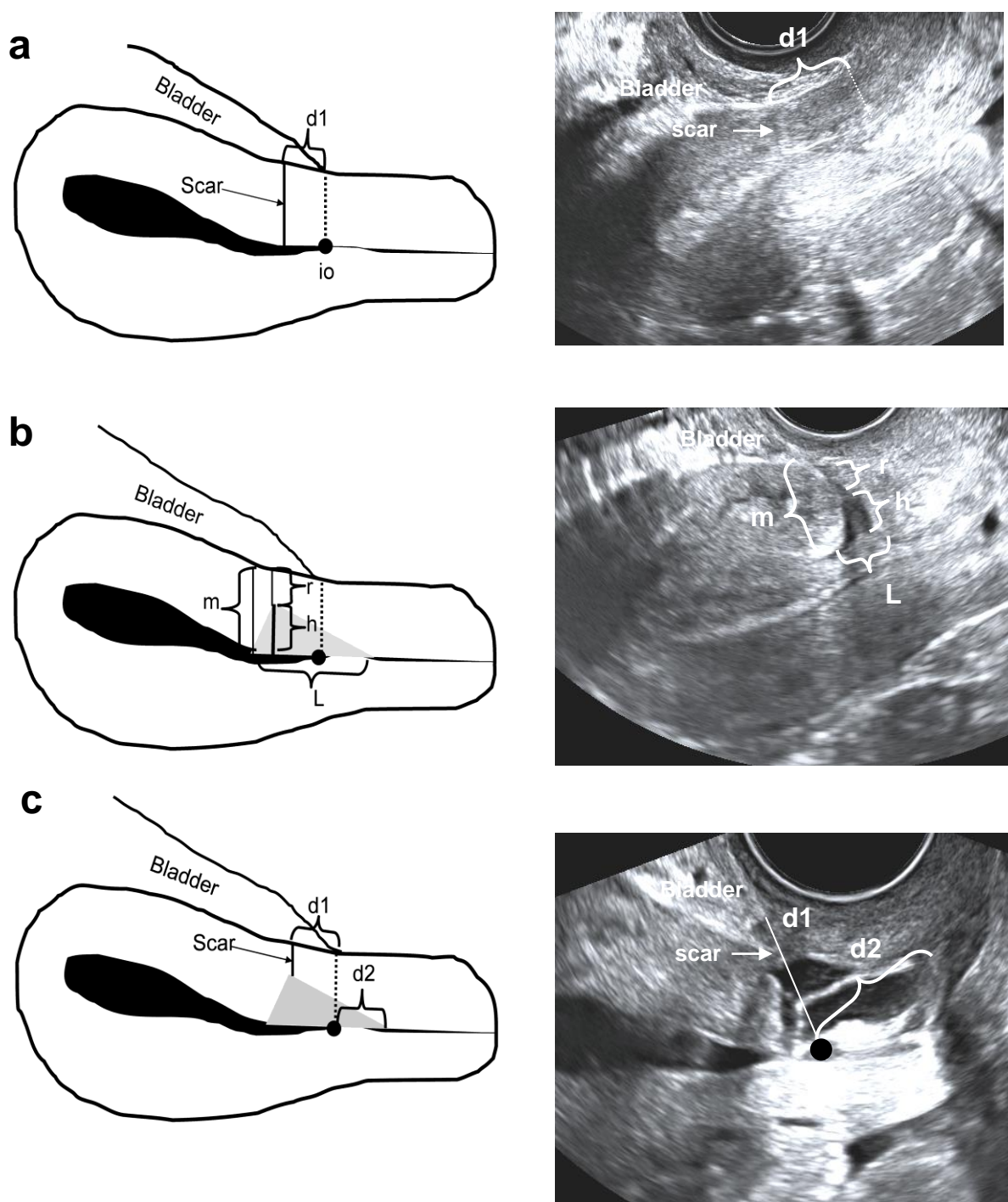


Figure 5. The distance between the inner cervical os and an intact scar ($d1$) was measured as shown in (a). The length (L) and height (h) of the defect, the thickness of the remaining myometrium over the defect (r) and the thickness of the myometrium close to and fundal to the defect (m) were measured as shown in (b). The distance between the inner cervical os (black spot) and a scar defect ($d1$) was measured as shown in (c). In the ultrasound image (c) distance ($d1$) is denoted “0 mm”. The distance between the inner cervical os and the lowest demarcation of the hysteroscopy scar defect ($d2$) was measured only in women

who were examined with hydrosonegography (c). The grey shaded triangular areas in (b) and (c) represent scar defects.

Data collection from medical records

Information on medical factors regarding the current pregnancy and delivery which could have affected the appearance of a hysterotomy scar after caesarean delivery at ultrasound examination was retrieved from our digitalized record system KIKA. This is a comprehensive information system developed at the Department of Obstetrics and Gynaecology in Malmö, serving as both a patient record-keeping system and a tool for quality control and other statistical purposes. Information on peri- and post-partum infection within six weeks was obtained from the electronic records system (Melior, the record system used at most Swedish hospitals).

The predictive capacity of the following continuous variables was tested:

- maternal age (years)
- maternal body mass index in the first trimester

and the following dichotomous and categorical variables:

- previous vaginal delivery
- diabetes mellitus (any type)
- chronic steroid treatment during pregnancy
- severe preeclampsia [Royal College of Obstetricians and Gynaecologists Guideline No.10 (A), March 2006]
- prolonged pregnancy (≥ 42 completed gestational weeks on the basis of foetometry at 15 – 20 gestational weeks [Persson and Weldner1986])
- duration of regular contractions before caesarean delivery, i.e. the duration of active labour (0 hours, 0.1 – 4 hours, 5 – 9 hours, 10 hours or more)
- cervical dilation immediately before caesarean delivery, as determined by the obstetrician in charge (0 cm, 1 – 4 cm, 5 – 7 cm, 8 cm or more)
- station of the presenting foetal part immediately before caesarean delivery, as determined by the obstetrician in charge (above or at the pelvic inlet versus below the pelvic inlet)
- oxytocin augmentation during labour
- immediate caesarean delivery (operation without delay, i.e. no bladder catheter, no scrubbing)
- suture technique (single-suture versus double-layer suture)

- intra-operative blood loss (< 1000 ml or \geq 1000 ml; blood loss was estimated by the surgeon immediately after the operation)
- intra-operative complications (e.g. tears in the uterus or cervix, urinary bladder lesions, other tissue damage that required extra suturing)
- infection peri- or post-partum within six weeks (chorioamnionitis, post-partum infection including wound infection, urinary tract infection, endometritis or infection of unknown origin)
- haemoglobin level at discharge from the hospital (99 g/l or less versus 100 g/l or more)
- uterine position at ultrasound examination (anteflexion or retroflexion)
- distance between the inner cervical os and the scar at ultrasound examination (0 mm versus > 0 mm; the level of the internal os is denoted 0 mm; the top of the caesarean delivery scar was never located below the internal cervical os).

Follow-up

All women who had undergone at least one previous caesarean delivery who participated in Studies I and II were followed up by scrutiny of their medical records with regard to the outcome of subsequent pregnancies concerning the rates of scar pregnancy, uterine rupture, dehiscence, extremely thin myometrium, placenta praevia and placenta accreta.

In the group of women with extremely thin myometrium at caesarean delivery, cases were included where the myometrium was described as “as thin as a leaf”, “membranous” or “transparent”. Uterine scar dehiscence was defined as subperitoneal separation of the uterine scar in the lower uterine segment with the chorion amniotic membrane being visible through the peritoneum. Uterine rupture was defined as complete separation of the uterine scar with communication between the uterine and abdominal cavities. These diagnoses were established at caesarean delivery in subsequent pregnancies. Women who gave birth vaginally were not routinely examined by exploration of the uterine cavity to detect uterine scar dehiscence or rupture.

In addition, information was collected on the rates of extremely thin myometrium, uterine rupture, uterine dehiscence, placenta praevia and placenta accreta by manual scrutiny of the patient records of all women with a caesarean scar delivered at Malmö University Hospital between 2005 and 2009. This information was collected in the same manner as for women who participated in Study IV. In cases where the operation report was unclear or difficult to interpret, the obstetrician who had performed the caesarean delivery was personally contacted and asked for details.

Statistics

Statistical calculations were performed using the Statistical Package for the Social Sciences, SPSS version 12.02 or 16.0 (SPSS Inc., Chicago, IL, USA).

The chi-squared test or Fisher's exact test was used to determine the statistical significance of differences in categorical data. P-values <0.05 were considered statistically significant.

The Mann-Whitney test, Kruskal-Wallis test or Wilcoxon's test was used to determine the statistical significance of differences in continuous data. P-values <0.05 were considered statistically significant.

A receiver operator characteristic (ROC) curve is a graphical plot of the sensitivity, or true positives, vs. (1-specificity), or false positives, for a binary classifier system as its discrimination threshold is varied. ROC curves were used to determine which measurements best predicted whether a scar defect in the lowest scar was subjectively perceived to be large by the ultrasound examiner. ROC curves were drawn separately for women who had undergone one or two caesarean deliveries. Since the defects had different appearances at conventional ultrasound examination and ultrasound with hydrosonegography, we chose different cut-off values to define a large defect using the two examination methods. The area under the ROC curve together with its 95% confidence interval (CI) was calculated. If the lower limit of the CI for the area under the ROC curve was > 0.5 , the measurement was considered to have discriminatory potential. The measurement with the largest area under the ROC curve was considered to be the best predictor of a defect being perceived to be large by the ultrasound examiner. The ROC curves were also used to determine the mathematically best cut-off value to predict whether a defect would be perceived as being large by the ultrasound examiner. The mathematically best cut-off value was defined as that corresponding to the point situated furthest away from the reference line.

Percentage agreement was used to determine the agreement between categorical data. The agreement between examinations performed with and without hydrosonegography with regard to subjective evaluation of the appearance of the scars (intact scar or scar with a defect) and the scar defects (shape, small or large defect, as perceived subjectively by the ultrasound examiner) was determined. The agreement between objective measurements of defect size was also determined.

Cohen's kappa [Cohen, 1960] was used to estimate the extent to which the percentage agreement exceeded that which would be expected by random chance alone [Kundel and Polansky 2003; Cicchetti and Feinstein 1990]. Kappa values of 0.81-1.0 indicate excellent agreement, 0.61- 0.80 good agreement and 0.41-0.60 moderate agreement [Brennan and Silman, 1992].

The mean difference, the 95% CI of the mean difference, and limits of agreement were used to determine the agreement between measurements made with conventional ultrasonography and those with

hydrosonography [Bland and Altman 1986]. If zero fell within the 95% CI of the mean difference no bias was assumed to exist between the measurements made with and without hydrosonography.

Univariate and multivariate logistic regression analysis was performed using the likelihood ratio test to determine which factors predicted large caesarean scar defects. A two-tailed p-value < 0.05 (likelihood ratio test) was considered statistically significant and was a pre-requisite for including a variable in a logistic regression model. To avoid overfitting, only two variables were used in each logistic regression model. ROC curves were drawn to evaluate the ability of single continuous ultrasound variables and of logistic regression models to predict large scar defects.

The odds ratio is a measure of the size of the effect, and describes the strength of association or non-independence between two binary data values. It is used as a descriptive statistic, and plays an important role in logistic regression.

Results and discussion

Evaluation of caesarean hysterotomy scars with ultrasonography and hydrososonography

None of the 125 women who had only given birth vaginally had a visible scar in their uterus, while all the women who had undergone caesarean delivery had at least one visible scar, observed upon conventional ultrasound examination (Paper I). This confirms that transvaginal ultrasound can accurately detect hysterotomy scars after caesarean delivery. Among the women who had undergone two caesarean deliveries two scars were seen in 37% (Figure 6).

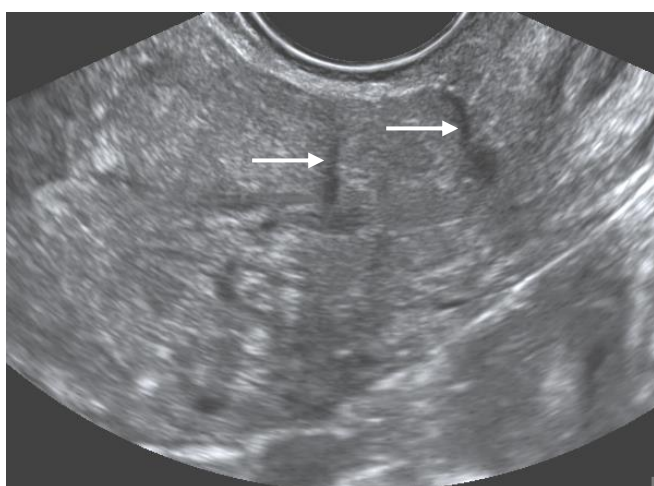


Figure 6. Ultrasound image illustrating two separate hysterotomy scars indicated by the arrows.

However, in 63% of the women who had undergone two caesarean deliveries, only one scar was seen, and in the eleven women who had undergone three or more caesarean deliveries no more than two scars could be seen (Paper I). The more caesarean deliveries, the more difficult it was to evaluate individual scars. This can probably be explained by the formation of fibrotic tissue formed during healing, disturbed anatomy and scar defects interfering with the ability to visualize each individual scar.

Any indentation in the hysterotomy scar was called a scar defect. A high prevalence of deficient scars was found (Table 1). It was higher than reported in other studies (19% [Ofili-Yebovi et al., 2008], 42% [Armstrong et al., 2003] and 43% [Menada Valenzano et al., 2006], respectively). This discrepancy is most likely to be explained by significant differences in study populations, i.e. differences in stage of labor at caesarean, indications for caesarean delivery, operative complications and by different definitions of hysterotomy scar defects.

The defect was classified as large by using the ultrasound examiner's subjective evaluation of the size of the defect. As seen in Table 1, the proportion of women with large scar defects as judged subjectively by the ultrasound examiner increased with the number of caesareans. Median myometrial thickness at the level of the isthmus decreased with increasing number of caesareans: the more caesareans the thinner the myometrium. This association seems natural because healing conditions are likely to be poorer in tissue where there is already a scar [Pollio et al., 2006; Wound healing chronic wounds. <http://www.emedicne.com/plastic/topic477.htm>, 2007; Alison, 1992; Whaley and Burt, 1992].

Table 1. Ultrasound characteristics of the uterine isthmus and caesarean hysterotomy scars in patients with a history of one, two or three or more caesareans by using the ultrasound examiner's subjective evaluation

Parameter	Vaginal	1CD	2CD	≥3CD	p-value
Scar defect, %	-	61	81	100	0.002
Large defect, %	-	14	23	46	0.029
Myometrium thickness, mm	11.6	8.3	6.7	4.7	0.000

CD: caesarean delivery

Subjectively, the margins of the defects were much more clearly demarcated at hydrosography than at unenhanced ultrasound examination. Ultrasound images illustrating the clearer demarcation of defects at hydrosography are shown in Figure 7.

Results of study II have shown that defects are more often detected in caesarean hysterotomy scars at hydrosography than at unenhanced ultrasound examination, and that most caesarean hysterotomy scar defects appear to be larger at hydrosography by subjective evaluation.

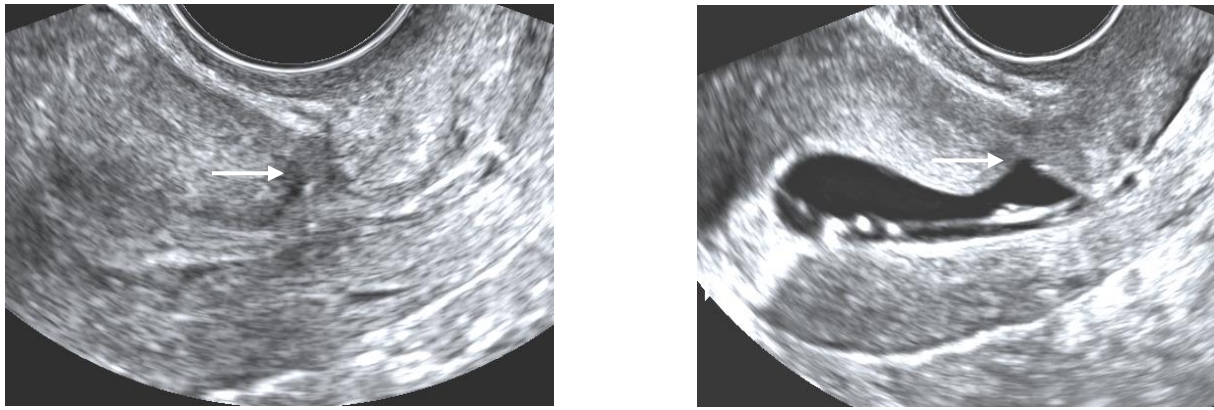


Figure 7. Ultrasound images a) before and b) at hydrosonography from the same woman. The arrow points to the defect. The images illustrate that the limits of scar defects were more clearly seen at hydrosonography than before.

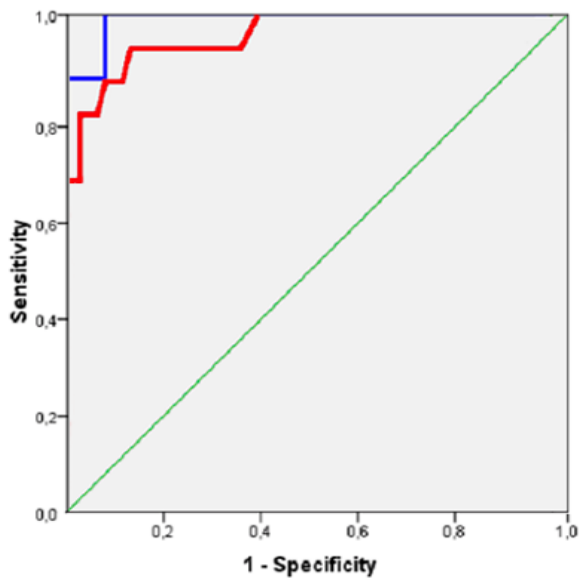
Table 2. Difference in subjective evaluation of cesarean scars before and at hydrosonography

Conventional ultrasound	Hydrosonography	Number of women
Intact	Defect	20
Not large	Large	15
Not total	Total	5
Defect	Intact	6
Large	Not large	0
Total	Not total	2

Table 2 shows that 40 out of 108 women had more advanced defects and 8 had less advanced defects at hydrosonography than at unenhanced ultrasound.

However, we realized that if in the future one would like to design studies to determine the clinical importance of caesarean hysterotomy scar appearance for complications in subsequent pregnancies or the effect of different surgical techniques on the prevalence of hysterotomy scar defects one would need an objective definition of ‘large defect’, and we have tried to provide such a definition. Using receiver operating characteristic curves we found that only the thickness of the remaining myometrium over the defect and the “ratio” predicted whether a defect would be perceived to be large or not by the ultrasound examiner using subjective evaluation and these two measures had virtually identical predictive performance. We decided to use the thickness of the remaining myometrium over the defect to define a large defect. We found it logical to believe that the thinner the myometrium the greater the risk of complications such as

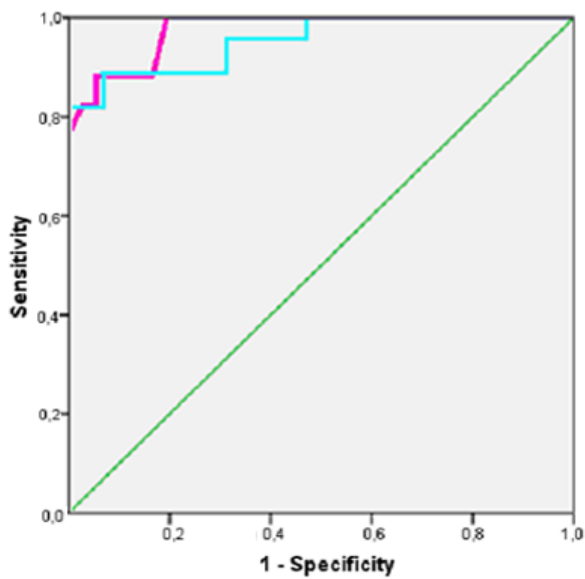
rupture and dehiscence. This is in agreement with the results of showing that a thin uterine wall in the isthmic part of the uterus in the third trimester in women who have undergone caesareans increases the risk of uterine rupture/dehiscence in the same pregnancy [Jastrow *et al.*, 2010]. Theoretically, the thickness of the endometrium (cycle day, contraceptive pills) could affect the appearance of a caesarean scar at ultrasound examination and thereby the classification of defects as small or large. However, the thickness of the remaining myometrium over the defect is unlikely to be affected by the thickness of the endometrium or by the intrauterine pressure changes during menstrual cycle [Ekström, 1991]. The ROC curves for remaining myometrium over the defect with regard to a defect being perceived to be large by the ultrasound examiner for women who had undergone one or two caesareans are shown in Figures 8. These ROC curves shown separately for unenhanced ultrasound and hydrosoundography. The defects were larger at hydrosoundography than before by objective evaluation: mean difference in base base2 mm and mean difference in height 1 mm in women who had undergone one caesarean. Mean difference in base was 4 mm and mean difference in height 2 mm in the lowest scar in women who had undergone 2 caesareans. The shape and localization of the scar defects did not change at hydrosoundography.



a) Unenhanced ultrasound.

■ For women after one CD (n=66). Area under the ROC curve, 0.96 (95% CI, 0.90–1.0). The best cut-off mathematically for the thickness of the remaining myometrium over the defect for predicting a large defect was 2.2 mm.

■ For women after two CD (n=35). Area under the ROC curve, 0.99 (95% CI, 0.97-1.0). The best cut-off mathematically for the thickness of the remaining myometrium over the defect for predicting a large defect was 1.9 mm.



b).Hydrosonography

■ For women after one CD (n=53). Area under the ROC curve, 0.98 (95% CI, 0.94–1.0). The best cut-off mathematically for the thickness of the remaining myometrium over the defect for predicting a large defect was 2.5 mm.

■ For women after two CD (n=31). Area under the ROC curve, 0.95 (95% CI, 0.89-1.0). The best cut-off mathematically for the thickness of the remaining myometrium over the defect for predicting a large defect was 2.25 mm.

Figure 8. Receiver–operating characteristics (ROC) curves for the thickness of the remaining myometrium over a caesarean scar defect with regard to a being perceived to be large by the ultrasound examiner. *CD-caesarean delivery*

Transvaginal ultrasound in non-pregnant women was found to be a useful tool in evaluating caesarean hysterotomy scars. It is very important to find an optimal internationally standardized measurement technique in order to develop a consensus for obstetric management of women with previous caesarean.

Factors affecting the risk of large defects

We found that scars with defects were located lower in the uterus than intact scars or small defects. In the women who had undergone one caesarean delivery, the median distance between an intact scar and the internal cervical os was 4.6 mm (range 0 – 19) and that between a deficient scar and the internal cervical os was 0 mm (range 0 – 26); $p=0.000$ at unenhanced ultrasound. The lowest demarcation of large scar defects was located lower in the uterus than the lowest demarcation of small scar defects (median distance -3.4 mm, range -9.3 to 8.6 for large defects versus 0 mm, range -6.8 to 16.1 for small defects; $P = 0.012$) at hydrosoneography. During labour, the cervix undergoes a process of dilatation and cervical tissues are drawn up into the lower uterine segment in the late stage of labour. Due to contractions the lower uterine segment becomes thinner and expands as it is pulled upward. It was observed by a few experienced obstetricians at the Department of Obstetric and Gynaecology in Malmö that sometimes hysterotomy at caesarean is performed with no attention to the changed anatomy of the lower uterine segment in the late stage of labour. It is likely that sometimes in such cases cervical tissue was incised and included in the suture (Figure 9). This might have a negative influence on the healing process.

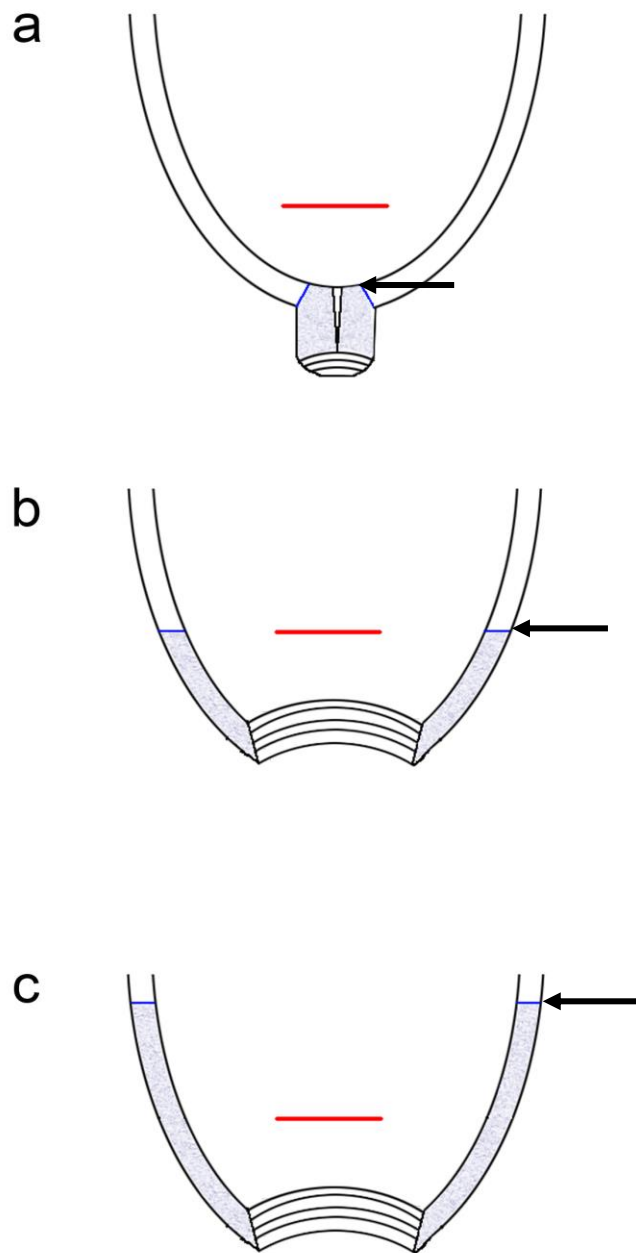


Figure 9. The level of hysterotomy at caesarean (indicated by the red line) likely to be performed in various stages of labour. **a)** elective caesarean without contractions **b)** caesarean at fully dilated cervix after normal progression of cervical dilatation **c)** caesarean at in case of dystocia.

Arrows indicate fibromuscular junction – the junction between the cervix uteri which is mainly fibrous and the corpus uteri which is mainly muscular. It is located near the lower end of the isthmus uteri [Danforth, 1947; Danforth, 1954]

Table 3. Association between cervical dilatation at caesarean and other variables

	Cervix dilated 0 - 4 cm	Cervix dilated ≥5cm	PP-value
Age, years; median (range)	33 (21-43)	29 (20-41)	0.001*
Ever delivered vaginally, % (n)	22.4 (17/76)	6.2 (2/32)	0.054†
Oxytocin augmentation during labour, % (n)	9.2 (7/76)	68.8 (22/32)	<0.001‡
Distance between the caesarean scar and the internal cervical os§, % (n)			<0.001†
= 0 mm	55.3 (42/76)	96.9 (31/32)	
> 0 mm	44.7 (34/76)	3.1 (1/32)	

* Mann-Whitney Test

† Fisher's Exact Test

‡ Pearson Chi-Square

§ The top of the caesarean scars was never located below the internal cervical os. The level of the internal os is denoted as 0 mm.

Low incisions are likely to be more common if caesarean is carried out in active labor than before start of labor, and this assumption is in accordance with our results (Table 3).

Zimmer et al. [2004] reported that caesarean hysterotomy scars were located lower in the uterus if the caesarean had been performed in active labour.

We found that women who underwent caesarean at cervical dilatation of 5 cm or more were younger than those who were delivered earlier in labour, and if the caesarean was carried out at cervical dilatation of 5 cm or more, the woman was less likely to have had a previous vaginal delivery, and more likely to have received oxytocin augmentation and have a scar located low in the uterus (Table 3). This suggests co-variation of maternal age, parity, oxytocin augmentation, and scar location with cervical dilatation at caesarean. The changes in odds when adding these factors to cervical dilatation at caesarean in multivariate logistic regression also support co-variation: substantial changes in odds ratios occurred when these variables were added to cervical dilatation at caesarean.

The risk of a large scar defect increased if the caesarean was carried out after 5 hours of active labour or at cervical dilatation of 5 cm or more. Multivariate logistic regression showed that no variable added information to cervical dilatation at caesarean or to the station of the presenting fetal part at caesarean. However, the station of the presenting fetal part and the position of the uterus at ultrasound examination added information to the duration of

active labour , with the risk of large defects increasing if the presenting part was below the pelvic inlet or if the uterus was in retroflexion at ultrasound examination (Table 4).

Table 4. Results of multivariate logistic regression and area under the receiver operating characteristic curve (AUC) of the logistic regression models

	Odds ratio		P-value	AUC (total model)	
	Point estimate	95% CI		Point estimate	95% CI
Duration of labour			0.006	0.857	0.764 to 0.950
0 hour, reference	1.0				
0.1-4 hours	1.459	0.115 to 18.497			
5-9 hours	18.607	1.346 to 55.017			
≥10 hours	14.795	2.419 to 90.463			
Station of presenting part	3.941	1.053 to 14.747	0.039		
Duration of labour			<0.001	0.869	0.788 to 0.951
0 hour, reference	1.0				
0.1-4 hours	2.312	0.186 to 28.803			
5-9 hours	15.258	2.404 to 96.836			
≥10 hours	39.688	7.225 to 218.008			
Uterine position	4.256	1.072 to 16.900	0.035		

The finding that duration of active labour and cervical dilatation at caesarean predicted a large scar defect is in accordance with the results by Armstrong et al. [2003] who reported that defect scars were seen only in women who were in labor at caesarean. This is perhaps not surprising since there is an association between the degree of cervical dilatation (in particular dilatation of 9 cm or more) at caesarean and uterine or utero-cervical lacerations and extensive blood loss causing surgical difficulties [Häger et al., 2004]. Such difficulties could theoretically affect the healing process. Another possibility is that changes in the myometrium induced by labour [Buhimschi et al., 2006] could affect healing negatively.

Large defects were seen more often in women with uterus in retroflexion compared to antelexion, 30% versus 16%. These findings are in agreement with results reported by Ofili-Yebovi et al. [2008]. They suggested that mechanical tension of the lower uterine segment in a retroflexed uterus might impair blood perfusion and oxygenation of the tissues under healing, and that this could affect wound healing negatively. Tissue oxygenation is an important factor for wound healing [Schugart et al., 2008].

We found that 16% (5/31) of the women with an intact scar had had their hysterotomy closed with two suture layers versus 18% (10/55) of those with a small defect and 9% (1/22) of those with a large defect. In our study, large scar defects were seen twice as often in women, who had undergone one-layer uterine closure as two-layer uterine closure, but the difference was not statistically significant, and the suture technique was not an independent predictor of large scar defects in multivariate analysis. It cannot be excluded that our inability to show an effect of uterine closure technique on the risk of large scar defects is explained by our study being under-powered for this specific purpose. For example, in multivariate analysis, uterine closure technique (one or two suture layers) added almost statistically significantly ($p=0.09$) to cervical dilatation at caesarean. A few publications have been examining the effect of suture techniques on the appearance of caesarean scars at ultrasound examination. Two studies that examined the importance of single layer versus double layer uterine closure presented conflicting results [Hamar et al., 2007; Hayakawa et al., 2006]. In a small randomised trial including 30 patients, it was shown that the uterine closure technique had no effect on the 'scar thickness' as measured by ultrasound 48h, 2 weeks and 6 weeks after the caesarean [Hamar et al., 2007]. In a non randomised study including 137 patients, double layer closure decreased the odds of finding a 'wedge defect' at least 5 mm in height in the scar at ultrasound examination 30-38 days after delivery [Hayakawa et al., 2006]. The third study, a randomised trial including 78 patients, showed that full thickness suturing technique decreased the rate of incomplete healing of the uterine incision as assessed by ultrasound 40-42 days after the caesarean [Yazicioglu et al., 2006]. Recently, in a prospective cohort study, it was demonstrated that women who previously had caesarean where the hysterotomy had been closed by single-layer suture and in the following pregnancy exhibited a thin lower uterine segment by sonography (<2.3 mm) at 35-38 weeks gestation had a higher risk of uterine rupture [Bujold et al., 2009]. According to Bujold et al. [2002] single-layer closure was associated with a 4-fold increased risk of uterine rupture compared with a double-layer closure.

The appearance of caesarean hysterotomy scars – clinical importance

Among the 69 women who became pregnant after the ultrasound examination there were 99 pregnancies and 65 deliveries: 53 women gave birth once and six women gave birth twice, while ten women experienced only miscarriage, termination of pregnancy, or ectopic pregnancy.

Early transvaginal ultrasound was carried out in 81% of the 99 pregnancies. No scar pregnancy was found. There were no placental complications (placenta previa, placenta accreta/increta/percreta).

The outcome of the first delivery after the ultrasound examination is shown separately for women with different types of hysterotomy scars (Table 5).

Table 5. Outcome of the first delivery after the ultrasound examination in relation to the ultrasound appearance of the caesarean hysterotomy scar

	Ultrasound appearance of the caesarean hysterotomy scar			Total n=59
	Intact scar n=12	Small defect n=34	Large defect n=13	
Current pregnancy and delivery				
Time between latest CD and the current delivery, years; median (range)	2.6 (1.1 – 4.1)	2.1 (1.0 – 4.8)	3.0 (1.1 – 4.1)	2.1 (1.0 – 4.8)
Gestational age at delivery, completed weeks †; mean ± SD	39.3 ± 1.2	39.1 ± 2.1	39.4 ± 0.9	39.2 ± 1.7
Uncomplicated vaginal delivery, n (%)	7 (58)	13 (38)	4 (31)	24 (41)
Instrumental vaginal delivery because of failure to progress, n (%)	1 (8)	3 (9)	1 (8)	5 (8)
because of fetal distress, n (%)	1 (8)	2 (6)	1 (8)	4 (7)
Triall of labour, n (%)	10 (83)	23 (68)	10 (77)	43 (72)
Extremely thin myometrium at CD, n (%)	0	0	0	0
Uterine dehiscence at CD, n (%)	0	0	2 (15)	2 (3.0)
Uterine rupture at CD, n (%)	0	1 (3)	1 (8)	2 (3.0)

CD: caesarean delivery

There were no clinical signs of uterine rupture in the women who gave birth vaginally. The 5-minute Apgar score was ≥ 7 in all newborns.

Uterine dehiscence and uterine rupture were diagnosed in 6.8% (4/59) of the women: in 2.2% (1/46) of the women with an intact scar or a small scar defect versus in 23.1% (3/13) of the women with a large scar defect (P=0.018). This corresponds to an odds ratio of 13.5, 95% CI 1.3 to 143.6, for uterine rupture or dehiscence in women with a large scar defect. Among the women delivered by caesarean, 5.3% (1/19) of those with an intact scar or a small scar defect were found to have uterine dehiscence or rupture at the caesarean versus 42.9% (3/7) of the women with a large defect (P=0.026). This corresponds to an odds ratio of 13.5, 95% CI 1.1 to 165.9, for uterine rupture or dehiscence in women with a large scar defect. These results confirm that large defects in the hysterotomy scar after a caesarean detected by transvaginal ultrasound in non-pregnant women increase the risk of uterine rupture or dehiscence in subsequent pregnancies. Even though our data point strongly towards an association between large caesarean scar defects detected at ultrasound examination of non-pregnant women and uterine dehiscence/rupture in a subsequent pregnancy, we cannot determine with any precision the strength of this association (see confidence intervals). Moreover, the study population is not large enough to explore interaction between variables, nor to determine if there are other factors than the ultrasound appearance of the uterine scar, for example the number of previous caesareans, complications in the current pregnancy or previous pregnancies, or maternal disease, that contribute to uterine rupture or dehiscence in women who have undergone caesarean delivery.

Between 2005 and 2009 there were 21420 deliveries at our institution, the rate of caesarean was 13.7% (2928/21420), the rate of repeat caesarean was 3.3% (709/21420). The number of repeat caesareans and findings at the caesarean operation is shown separately for women delivered during these years and in our study population (Table 6).

Table 6. Number of repeat caesareans and findings at the caesarean operation in our total population of women delivering in 2005 and 2009 and in our study population

Parameter	2005 n = 112	2006 n =152	2007 n = 123	2008 n =135	2009 n = 187	2005-2009 n = 709	Our study n = 26
Uterine rupture, n (%)	3 (2.7)	3 (2.0)	4 (3.2)	3 (2.2)	7 (3.7)	20 (2.8)	2 (7.7)
Dehiscence, n (%)	4 (3.6)	6 (3.9)	5 (4.1)	7 (5.2)	11 (5.9)	33 (4.6)	2 (7.7)
Extremely thin myometrium, n (%)	6 (5.4)	10 (6.6)	6 (4.9)	5 (3.7)	12 (6.4)	39 (5.5)	0
Uterine rupture, uterine dehiscence or extremely thin myometrium, n (%)	13 (11.6)	19 (12.5)	15 (12.2)	15 (11.1)	30 (16.0)	92 (13.0)	4 (15.4)
Placenta previa, n (%)	1 (0.9)	1 (0.7)	1(0.8)	3 (2.2)	3 (1.6)	9 (1.3)	0
Placenta accreta, n (%)	2 (1.8)	1 (0.7)	0	1 (0.7)	1 (0.5)	5 (0.7)	0
Postpartum hysterectomy, n%	2 (1.8)	3 (2.0)	0	1 (0.7)	1 (0.5)	7 (1.0)	0

The rate of uterine rupture was higher in our study group than in our total population of women undergoing repeat caesarean between 2005 and 2009 (7.7% vs. 2.8%), and the rate of uterine dehiscence was also higher (7.7% versus 4.7%). This raises the question whether our study population was in some way selected. The women in our study were volunteers who had been invited to undergo ultrasound examination to check the integrity of their hysterotomy scar after caesarean. It cannot be excluded, that women with previous complicated pregnancies and complicated caesarean deliveries were more eager to accept our invitation than women with uneventful pregnancies and less complicated deliveries, and that women who participated in our study were therefore at greater risk of uterine rupture and scar dehiscence than women declining our invitation. On the other hand, the combined rate of extremely thin myometrium, uterine dehiscence and uterine rupture was similar in our study group and in all women giving birth via repeat caesarean between 2005 and 2009 (15.4% vs. 13.0%). Research in this area is difficult because the International Classification of Diseases (ICD) does not have a code for incomplete uterine rupture

(dehiscence) or extremely thin myometrium. A study of coding practice of intrapartum ruptures showed that in all cases of dehiscence occurring during 2003 in Oslo University Hospital, an ICD code was used that could not identify the condition in the Medical Birth Registry of Norway [Al-Zirgi et al 2010]. We found that during the period from 2005 and 2009 in our hospital, too, none of women with dehiscence had an ICD code that made it possible to identify the condition in our electronic record system. Moreover a few patients where operative descriptions made the diagnosis (complete uterine rupture) clear missed the ICD coding. We found that the descriptions in the surgery reports of the condition of the uterine wall at caesarean sometimes were difficult to interpret. For example, it was not always clear whether there was an extremely thin myometrium or a true dehiscence. When confronted with the operation report the obstetrician who had performed the caesarean could sometimes not recall the details necessary for correct classification. We have been conservative in our classification and used the term dehiscence only when this diagnosis was unequivocal. Furthermore women who gave birth vaginally were not routinely examined with exploration of the uterine cavity to detect uterine scar dehiscence or rupture. Even though possible undiagnosed dehiscence or ruptures did not cause symptoms during the current delivery, they might complicate future pregnancies, and thereby be clinically relevant. However all three conditions represent a weakness of the myometrium and are likely to be a spectrum of the same condition. In a woman in labour, an extremely thin myometrium may rupture and develop into uterine dehiscence or complete rupture, and so the timing of the caesarean will determine which of the three diagnoses will apply. Three of the four women with uterine dehiscence or rupture had undergone only one previous caesarean, all three having a large scar defect, while one had undergone two previous caesareans and had a small scar defect. It is an interesting observation that the only woman with uterine rupture and a small scar defect had undergone two previous caesareans. Even though there may seem to be an intact scar or only a small defect in the hysterotomy scar at ultrasound examination, the tension capacity of the lower uterine segment in a woman who has undergone two or more caesareans may be reduced, and so her uterus may be prone to rupture even if the scar appears to be virtually intact. After all, ultrasound cannot tell us anything about the quality of the scar tissue or myometrium. It has been shown that the morphology of the tissue in a dehiscence area - and possibly its functional behavior - differs from that of normal myometrium in the isthmus [Wojdecki and Grynsztajn, 1970]. However, our current knowledge about myometrial repair and regeneration after caesarean is very limited. It is also an interesting observation in our study that intervention for failure to progress was highest in women with large scar defects. Possibly, the presence of a large scar defect counteracts coordinated labor.

On the basis of current knowledge, it is not possible to know whether a defect in a caesarean hysterotomy scar detected by ultrasound in a non-pregnant woman is more or less predictive of uterine rupture or dehiscence than the thickness of the myometrium in the uterine isthmus measured by ultrasound in late pregnancy. Rozenberg and colleagues found, that women with myometrial thickness in the lower uterine segment $>3.5\text{mm}$ at 36-38 weeks gestation (when the lower uterine segment is fully developed) as determined by transabdominal ultrasound had a

low risk of uterine rupture [Rozenberg et al., 1996]. We do not know how an intact scar or a scar with a small defect in a non-pregnant woman will develop during pregnancy. Even if the remaining myometrium over the defect is thick in the non-pregnant state, it may have reduced elasticity because of scarring and reduced ability to stretch when the fetus grows.

It is an interesting observation that between 2005 and 2009 among women with extremely thin myometrium verified at caesarean at our institution, 44% (17/39) attempted trial of labour before the caesarean versus 59% (19/33) of women with uterine dehiscence and 85% (17/20) of those with uterine rupture. In our study population 75% (3/4) of women with uterine defects (one of them with uterine rupture and two with dehiscence) were in active labor before the caesarean. This fact might indicate that trial of labor carries greater risk of uterine rupture. Al-Zirgi et al. [2010] reported the same findings and they considered that women with higher risk for failed attempt at vaginal birth after previous caesarean would not be recommended trial of labour in order to reduce the rate of uterine rupture. This indicates that it is of importance to recognize the subgroup of women with higher risk of uterine rupture or dehiscence in subsequent pregnancies in order for a correct management of labour. According to Grobman et al. [2008] and Macones et al. [2006] uterine rupture cannot be predicted only by analyzing clinical factors. A strong association has been found between the degree of lower uterine segment thinning measured near term and the risk of uterine rupture during labour [Rozenberg et al., 1996; Jastrow et al., 2010]. The obstetrician often gets the information about sonographic findings “too late” when the individual delivery plan already has been made independent of sonographic results. At that time it is difficult or almost impossible to change the planned management.

Possibly, an analysis of clinical factors combined with an ultrasound examination in the non-pregnant state could be used as an early obstetric scoring system to make it easier to correctly select women with previous caesareans contemplating trial of labour. It could also give support to obstetricians in decision making and planning the delivery. A correct delivery plan and careful intrapartum management could lead to increased successful vaginal deliveries with a very low rate of uterine rupture among women with scarred uterus.

Conclusions

The principal findings of the present thesis can be itemized as follows.

- Caesarean hysterotomy scars could be reliably detected by ultrasound
- Myometrial thickness at the level of the isthmus uteri decreased with the number of caesareans and the frequency of large defects increased
- Caesarean hysterotomy scars with defects were located lower in the uterus than intact scars.
- More women were found to have scar defects and large scar defects at hydrosography than at unenhanced ultrasound
- Hydrosonography was superior to unenhanced ultrasound for evaluation of caesarean hysterotomy scar defects
- Caesarean in advanced labour was associated with increased risk of large defect in the uterine incision as determined by transvaginal ultrasound
- Large defects in the hysterotomy scar after caesarean detected by transvaginal ultrasound in non-pregnant women increased the risk of dehiscence or uterine rupture in subsequent pregnancies

Populärvetenskaplig sammanfattning på svenska

Målsättning

Att ta reda på hur ultraljudsundersökning av livmoderärret hos icke gravida kvinnor med tidigare kejsarsnitt kan användas för att bedöma risken för att livmodern brister i kommande graviditet.

Bakgrund

Kejsarsnittsfrekvensen ökar världen över och därmed också den för mor och barn livshotande komplikationen livmoderbristning och inväxt av moderkakan i livmodermuskeln i efterföljande graviditet. Dessa komplikationer kan leda till livshotande blödningar hos modern och livshotande syrebrist hos barnet.

Det ökade bruket av ultraljud har medfört möjlighet till icke-invasiv identifiering av kejsarsnittsärar med eller utan defekt. Flera studier har visat att defekter i kejsarsnittsärar verifierade med ultraljud hos icke gravida kvinnor inte är ett ovanligt fynd. Det är emellertid ej känt om det finns samband mellan defekter i livmoderväggen efter kejsarsnitt fastställda med ultraljud hos icke-gravida kvinnor och komplikationer under följande graviditet och förlossning. Det är också okänt om stora defekter innebär större risk för komplikationer än intakta ärar eller ärar med små defekter men det är logiskt att förmoda att stora defekter i kejsarsnittsärar enligt ultraljud kan avspegla dålig läkning av livmoderväggen.

Syfte

- Att utvärdera möjligheten att identifiera ärar i livmoderväggen efter kejsarsnitt
- Att uppskatta förekomsten av defekta ärar
- Att uppskatta storleken och lokalisering av ärar med ultraljud
- Att beräkna överensstämmelsen mellan ultraljudsundersökning med och utan koktsaltinfusion (hydrosonografi) med hänsyn till antal, storlek, lokalisering och form av ärardefekter efter kejsarsnitt
- Att framställa vilka faktorer som ökar risken för uppkomst av stora defekter i kejsarsnittsärar som fastställts med ultraljud
- Att framställa om stor defekt i livmoderärar efter kejsarsnitt som fastställt med ultraljud är associerat med högre risk för glipa i livmoderväggen och brusten livmodern i efterföljande graviditet

Studiepopulation

Avhandlingen bygger på fyra studier omfattande 287 kvinnor som hade förlöst sex till nio månader innan studiestart på Kvinnokliniken vid Universitetssjukhuset MAS i Malmö.

Alla ultraljudsundersökningar utfördes på samma klinik av författaren under perioden 2005-2006.

I studien rörande möjligheter att identifiera och utvärdera livmoderärr efter kejsarsnitt undersöktes kvinnor efter naturlig förlossning och efter ett, två och tre eller fler kejsarsnitt.

Undersökaren var ovetande om patientens sjukhistoria. För jämförelse mellan transvaginal ultraljudsundersökning med och utan koktsaltinfusion (hydrosonografi) undersöktes kvinnor efter ett eller fler kejsarsnitt där undersökaren var ovetande om antal kejsarsnitt.

För undersökningen gällande vilka faktorer som ökar risken för uppkomst av stora defekter i livmoderärr användes gruppen med kvinnor som enbart genomgått ETT kejsarsnitt.

För studien om den kliniska betydelsen av ultraljudsutvärdering av livmoderärrs för komplikationer under följande graviditet och förlossning användes gruppen med kvinnor efter ett eller flera kejsarsnitt som hade deltagit i föregående studier och kunde följas upp efteråt.

Resultat

I de arbeten som ingår i avhandlingen har visats att kejsarsnittsärr kan tillförlitligt påvisas med ultraljud. Vidare har visats :

- Att ultraljud med koktsaltinfusion (hydrosonografi) är en bättre metod än konventionell ultraljudsundersökning för att värdera eventuella defekter i ärrret.
- Att 20 % av kvinnor som genomgått kejsarsnitt har stora defekter i livmoderärrret.
- Att stora defekter är vanligare hos kvinnor som genomgått fler än ett kejsarsnitt än hos dem som bara genomgått ett (14 % av kvinnor som genomgått ett kejsarsnitt har stora defekter, 23 % av dem som genomgått två kejsarsnitt och 46% av dem som genomgått tre eller fler kejsarsnitt; p-värde 0.029).
- Att stora defekter är vanligare hos kvinnor med bakåtriktad livmoder 30% respektive 15% .
- Att hos kvinnor som genomgår sitt första kejsarsnitt ökar risken för stor defekt om kejsarsnittet görs i långt framskridet värkarbete (ju senare desto högre risk), och att risken ökar drastiskt om snittet görs då livmoderhalsen är öppen 5 cm eller mer.
- Att ärr med stora defekter sitter längre ner i livmodern än ärr med små eller utan defekter.
- Att kvinnor som har stora defekter i sitt livmoderärr vid ultraljudsundersökning då de inte är gravida löper ökad risk att i en efterföljande graviditet drabbas av livmoderbristning eller glipande livmodervägg.

Den studie som visade samband mellan stor defekt och livmoderbristning i efterföljande graviditet var emellertid liten och styrkan av sambandet mellan stor defekt och ruptur kunde därför inte avgöras med precision (OR 13.3, 95% CI 1.269 to 143.641). Vidare var antalet kvinnor med livmoderbristning och glipande livmodervägg alldeles för

litet för att vi skulle kunna analysera om andra faktorer än ärrets utseende vid ultraljudsundersökningen hade betydelse för om livmodern skulle brista eller ej.

Slutsats

Det har visats ett samband mellan stora defekter i livmoderärret fastställda med ultraljud och livmoderbristning och glipande livmodervägg i efterföljande graviditet. Sambandets styrka och dess betydelse i förhållande till andra faktorer är dock oklart men kommer att fastställas i en större studie, som nu planeras. För att minska risken för livmoderbristning i efterföljande graviditet är det angeläget att minska antalet stora defekter i livmoderärret.

Vi fann nämligen att kejsarsnitt i långt framskridet förlossningsskede kraftigt ökar risken för stora defekter fastställda med ultraljud.

Vi fann också att defektläkta ärr var lokaliserade närmare inre modermunnen än intakta ärr. Detta kan bero på att livmodern vid kejsarsnittet öppnats nära inre modermunnen och detta kan ha påverkat läkningen av livmodern negativt.

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