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Prediction of scar integrity and vaginal birth after caesarean delivery (VBAC)

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Abstract

A statistically significant association with uterine rupture during a trial of labour after caesarean delivery was found in at least two studies for the following variables: interdelivery interval (higher risk with short interval), birthweight (higher risk if ≥ 4000g), induction of labour (higher risk), oxytocin dose (higher risk with higher doses), and previous vaginal delivery (lower risk). However, no clinically useful risk estimation model including clinical variables has been published. A thin lower uterine segment at 35-40 weeks as measured by ultrasound in women with a caesarean hysterotomy scar increases the risk of uterine rupture or dehiscence. However, no cutoff for lower uterine segment thickness can be suggested because of study heterogeneity, and because prospective validation is lacking. Large caesarean hysterotomy scar defects in non-pregnant women seen at ultrasound examination increase the risk of uterine rupture or dehiscence in subsequent pregnancy but the strength of the association is unknown. To sum up, we currently lack a method that can provide a reliable estimate of the risk of uterine rupture or dehiscence during a trial of labour in women with caesarean hysterotomy scar(s).

Key words: vaginal birth after caesarean; caesarean section; uterine rupture; ultrasonography
A INTRODUCTION/BACKGROUND

Uterine rupture is a rare but serious complication of a trial of vaginal birth after caesarean delivery (VBAC) [1-3]. Therefore, VBAC should be proposed only to women who are likely to have a low risk of uterine rupture. Is it possible to identify these women? A number of clinical factors might be important as well as the integrity of the hysterotomy scar and the thickness of the lower uterine segment assessed by imaging techniques. A simple and easily available imaging technique to use for this purpose is ultrasound. Possibly, ultrasound assessment of the hysterotomy scar or of the whole lower uterine segment could be used alone or in combination with clinical factors to estimate the likelihood of uterine rupture or dehiscence occurring spontaneously or during a trial of labour. Current evidence on our ability to predict uterine rupture or dehiscence using ultrasound or clinical variables is very limited. It is summarized below.

B How common is uterine rupture after caesarean delivery?

The answer is that we do not know for sure. In retrospective studies, the rate of uterine rupture during a trial of labour after caesarean delivery is around 1% [3-10]. These studies seem to have included only symptomatic uterine rupture. In prospective studies in which women, who had the thickness of their lower uterine segment measured with ultrasound, were followed up with regard to pregnancy outcome, the rate of uterine rupture or dehiscence is on average 6.6% (range 1% to 46%) [11]. The prospective studies include not only complete uterine rupture but also uterine dehiscence, and they also include diagnoses made at elective caesarean, not only rupture occurring during a trial of labour. In an ordinary clinical setting it is unlikely that all these cases would have been assigned an International Classification of Diseases (ICD) code indicating uterine dehiscence or
rupture. In a prospective observational study by Rozenberg et al [12], where uterine rupture and uterine dehiscence were diagnosed either at caesarean section or by uterine exploration after vaginal delivery, the latter being performed in all women who gave birth vaginally, the frequency of uterine rupture after caesarean delivery was 2.3% and that of uterine dehiscence 1.6%, for a total frequency of “uterine defect” of 3.9%.

Some might want to argue, that only symptomatic uterine rupture (in all likelihood resulting in an ICD code in the patient’s record) is clinically important, while asymptomatic uterine rupture and uterine dehiscence, irrespective of whether the latter is symptomatic or asymptomatic, are clinically unimportant. I disagree. Whether a uterus with a dehisced caesarean hysterotomy scar (or with an extremely thin myometrium in the scar area) will proceed to rupture is likely to depend on the management of labour and on the timing of caesarean delivery.

Uterine rupture before start of labour is extremely rare [13]. Vaknin et al [13] reported uterine rupture to occur before start of labour in seven of 120636 (i.e. in one in 17234) pregnancies ≥22 gestational weeks. In five of the seven cases the woman had a caesarean hysterotomy scar. Rupture of an unscarred uterus is also very rare [14]. Miller et al [14] reported rupture of an unscarred uterus during labour in ten of 168491 (i.e. in one of 16849) deliveries.

**B Which clinical factors are associated with uterine rupture after caesarean delivery?**
Researchers have tried to answer this question in retrospective cohort studies [4-8, 10, 15-24] or case control studies [3, 25-30] including women who underwent a trial of labour after caesarean delivery. These studies seem to have included only symptomatic uterine rupture. The following factors have been examined with regard to their ability to predict uterine rupture during a trial of labour after caesarean delivery: gestational age [4, 19], maternal age [15], interdelivery interval [5, 16], interpregnancy interval [7], suture technique for closing the hysterotomy [31], birth weight [18, 24], previous vaginal delivery [3, 6, 21], induction of labour [10, 28], ethnicity [22], pre-eclampsia or gestational hypertension [20], twin pregnancy [23], labour progress [27], and number of epidural doses [29]. A statistically significant association with uterine rupture was found in more than one study for the following variables: interdelivery or interpregnancy interval (higher risk with short interval, short interdelivery interval being defined as ≤ 24 months [16] or ≤ 18 months [5], and short interpregnancy interval as ≤ 6 months [7]), birthweight (higher risk if ≥ 4000g) [18, 24], induction of labour (higher risk) [10, 32], oxytocin dose (higher risk with higher doses) [8, 30], and previous vaginal delivery (lower risk of rupture if the woman ever delivered vaginally) [3, 6]. In addition, a systematic review including 12 studies, showed that locked single layer closure of the caesarean hysterorotomy increased the risk of uterine rupture compared with double layer closure [31].

Two research teams tried to create multivariate logistic regression models including clinical data to estimate the individual risk of uterine rupture (dehiscence not included) during a trial of labour after caesarean delivery [9, 32]. Both studies were retrospective. In a case-control study, Macones et al [32] created one model including four variables
(maternal age, gestational age, ethnicity, prior vaginal delivery) and another including six variables (maternal age, gestational age, ethnicity, prior vaginal delivery, cervical dilatation at admission, and labour induction). The variable “two or more previous caesarean deliveries” did not enter any model. No model performed well enough to be useful in clinical practice (area under the receiver operating characteristic curve 0.68 and 0.70, respectively). In a retrospective study including only women with a singleton term pregnancy after one pervious caesarean delivery, Grobman et al [9] constructed a logistic regression model including two variables, i.e. previous vaginal delivery (lower risk of rupture) and induction of labour (higher risk of rupture). However, the model had poor diagnostic performance (area under the receiver operating characteristic curve 0.63 and 0.60 on the training and test sets, respectively). Moreover, the predicted rupture risk did not agree well with the observed rate of rupture. Therefore, this model could also not be recommended for clinical use. To sum up current evidence, it seems not to be possible to provide a reliable estimate of the risk of uterine rupture during a trial of labour after caesarean delivery using only clinical information.

**B Can the thickness of the lower uterine segment as measured by ultrasound at 35 - 40 gestational weeks predict uterine rupture or dehiscence?**

Jastrow et al tried to answer this question in a systematic review published in 2010 [11]. The aim was to estimate the strength of the association between sonographic thickness of the lower uterine segment in women who had undergone caesarean delivery and uterine scar dehiscence or rupture, and to find the best cutoff value for the thickness of the lower uterine segment with regard to predicting uterine dehiscence or rupture.
The review comprises 12 studies published between 1988 and 2009 [12, 33-43] including together 1834 women with a previous low transverse caesarean hysterotomy who underwent ultrasound measurement of the thickness of the lower uterine segment at 35-40 gestational weeks. In seven of the 12 studies the full lower uterine segment thickness was measured [12, 33, 36, 38-40, 42], in four studies the myometrial thickness was measured [34, 35, 37, 43], and in one study both measurements were taken [41]. Because only three of the 12 studies reported the frequency of uterine rupture separately, the outcome measure was “uterine rupture or uterine dehiscence”, i.e. ”uterine scar defect”. It is uncertain if the definition of uterine rupture and uterine dehiscence was the same in all 12 studies. A common definition of uterine dehiscence is “subperitoneal separation of the uterine scar in the lower uterine segment with the chorionamniotic membrane visible through the peritoneum”. Uterine rupture is usually defined as a complete separation of the uterine scar with communication between the uterine and abdominal cavities. The rate of uterine scar defect was 6.6% (121/1834), the rate ranging from 1% to 46% in the different studies. Both the full lower uterine segment thickness and the myometrial thickness were associated with uterine scar defect: the area under the summary receiver operating characteristic curve for the full lower uterine segment thickness was 0.83 (SE 0.03) and that of myometrial thickness 0.75 (SE 0.05). However, because the 12 studies were very heterogenous, it was impossible to suggest an optimal thickness cutoff for predicting uterine defect. The cutoffs suggested for the full lower uterine segment thickness in the different studies varied between 2.0 mm and 3.5 mm and those for the myometrial thickness between 1.4 mm and 2.0 mm. It is of note that in nine of the 12 studies included in the review the ultrasound results were available to the staff managing the pregnancies and deliveries [33-35, 38-43]. This is inappropriate when estimating
sensitivity and specificity of a diagnostic test. Therefore, the results of these nine studies are likely to be biased. The study most likely to have yielded reliable results is the one by Rozenberg et al [12]. Another study of particular interest is the one by Bujold et al [41]. Both these studies are briefly outlined below.

C The prospective observational study by Rozenberg et al [12]

The aim of the study by Rozenberg et al [12] was to estimate the sensitivity and specificity of the full lower uterine segment thickness as measured by transabdominal ultrasound with regard to uterine rupture or dehiscence. It includes 642 women with a caesarean hysterotomy scar who had their full lower uterine segment thickness measured with transabdominal ultrasound at 36-38 gestational weeks by one single ultrasound examiner. The medical staff was blinded to the ultrasound results. Uterine rupture and uterine dehiscence were diagnosed either at caesarean section or by uterine exploration after vaginal delivery, the latter being performed in all women who gave birth vaginally.

The full lower uterine segment thickness varied between 1.6 and 12.3 mm. Uterine rupture was diagnosed in 15 (2.3%) women and uterine dehiscence in ten (1.6%) women, i.e. the rate of uterine defect was 3.9%. The thinner the full lower uterine segment the higher the risk of uterine rupture or dehiscence. In groups of women with full lower uterine segment thickness of 1.6 -2.5mm, 2.6 - 3.5mm, 3.6 - 4.5mm, and > 4.5mm the frequency of any uterine defect (either dehiscence or rupture) was 16%, 10%, 2% and 0, the frequency of uterine rupture was 10%, 7%, 0.6% and 0, and that of uterine dehiscence was 6%, 4%, 1% and 0. The authors themselves suggested a cutoff of 3.5mm to be optimal and suitable for clinical use, values for full lower uterine segment thickness
≤ 3.5 mm being taken to indicate a high risk of uterine rupture. In their study population, this cutoff had a sensitivity of 88% and a specificity of 73%. This corresponds to a positive likelihood ratio of 3.3 and a negative likelihood ratio of 0.16, which means that this test had poor – or at most moderate [44] – ability to predict uterine dehiscence or rupture.

C The prospective observational study by Bujold et al [41]

The study by Bujold et al [41] is the second largest study in the systematic review by Jastrow et al [11]. It includes 236 women who had the full lower uterine segment thickness and the myometrial thickness measured using both transabdominal and transvaginal ultrasound at 35-38 weeks of gestation. The measurement technique was described in detail (Figure 1). The frequency of uterine rupture was 1.3% (3/236) and that of dehiscence 2.5% (6/236). Using multivariate logistic regression the authors found that a thin lower uterine segment (full thickness < 2.3mm), single layer closure of the hysterotomy and short inter-delivery interval (< 18months) significantly and independently predicted uterine rupture or dehiscence. Unfortunately, the staff was not blinded to the ultrasound results, and so these results are likely to be biased. Moreover, the study was not large enough to allow assessment of interaction between variables, and with only nine cases of uterine defect the result of the multivariate analysis are unreliable because of the risk of overfitting. However, multivariate analysis including both clinical and ultrasound variables could be the way forward and should be used in future much larger studies.
B Have any of the cutoffs for lower uterine segment thickness been prospectively validated?

I know of no study that has prospectively validated any of the lower uterine segment thickness cutoffs suggested, i.e., it is not known how well they would perform in other populations than those where they were suggested, or in the hands of new examiners.

Rozenberg et al [42] introduced measurement of the lower uterine segment with the 3.5 mm cutoff into clinical practice after their observational study [12] had been closed. They compared the results for 1995 -1996 after the method had been implemented clinically with those in their observational study (1989-1994) with regard to the frequency of uterine dehiscence or rupture, the frequency of planned and emergency caesarean delivery, and the use of oxytocin in women with previous caesarean delivery. After measurement of the lower uterine segment had been introduced clinically, the frequency of uterine defect was lower (0.8% versus 3.9%), and the use of oxytocin was twice as common in women with previous caesarean delivery. Moreover, in women who had undergone only one previous caesarean delivery the frequency of elective caesarean delivery was higher (12% versus 6%) while that of emergency caesarean delivery was lower (20% versus 24%), and in women with two previous caesarean deliveries the rate of vaginal delivery was higher. Even though these results suggest that ultrasound measurement of the lower uterine thickness might improve the management of delivery in women with previous caesarean, they must be interpreted with caution, because the study uses historical controls. It is not a randomized controlled trial.
B How should the thickness of the lower uterine segment during pregnancy be measured by ultrasound?

Two ultrasound measurements have been reported to reflect the thickness of the lower uterine segment in the end of pregnancy and to possibly be predictive of uterine rupture or dehiscence: the “full lower uterine segment thickness” and the “thickness of the myometrial layer”. These measurements can be taken either transabdominally or transvaginally. There is no consensus on which measurement technique to use either for transabdominal or transvaginal ultrasound.

In studies reporting on measurements of the thickness of the lower uterine segment the measurement technique was described with varying detail [12, 33-43]. Therefore, it is unlikely that exactly the same transabdominal measurement technique or exactly the same transvaginal measurement technique was used in all studies: there may be differences between the degree of bladder filling, the site of measurement, the placement of the callipers, the number of measurements taken and in the measurement selected to be representative if more than one was taken. This means that the measurement results in different studies may not be directly comparable. Clearly, if to use a cutoff for the sonographic thickness of the lower uterine segment recommended by a certain research group, exactly the same measurement technique must be used as in the study where that particular cutoff was recommended.

The most detailed description of how the measurements of the lower uterine segment were taken is found in a paper by Bujold et al [41]. Their measurement technique (the same for transabdominal and transvaginal measurements) is described in Figure 1.

Figure 1 to be inserted here.
B. How thick is a “normal” lower uterine segment as measured by ultrasound at 35-40 gestational weeks?

To the best of my knowledge, no study reported on the sonographic thickness of the full lower uterine segment at 35-40 gestational weeks in women with an unscarred uterus. However, one study reported on the thickness of the myometrium at 36-38 gestational weeks in nulliparous women and in parous women who had only delivered vaginally [35]. The mean ± SD (range) myometrial thickness was 2.3 mm ± 1.1 (1.1–5.5) in nulliparous women and 3.4 mm ± 2.2 (1.0–10.3) in parous women. The corresponding thickness for women with caesarean hysterotomy scar(s) was 1.9 mm ± 1.4 (0–9.0).

A summary of published ultrasound measurements of the lower uterine segment thickness at 35-40 weeks in women delivered by caesarean is presented in Table 1 [12, 35, 41, 45-48] [34, 49]. It seems that the sonographic full thickness of the lower uterine segment at 35-40 weeks in women delivered by caesarean is on average 3–4 mm with a range from 2 to 19 mm, and that sonographic myometrial thickness ranges from 0 to 10 mm.

Insert Table 1 here

B Are ultrasound measurements of the thickness of the lower uterine segment reproducible?

The reproducibility of ultrasound measurements of the thickness of the lower uterine segment using different examination techniques has been examined in five studies [41] [45, 46, 48, 49]. To sum up, most intra- and inter-observer differences were ≤1 mm [46, 49], but the limits of agreement (the limits within which 95% of future measurements are
expected to fall) were wide, i.e., up to 4 mm for full lower uterine thickness and up to 1.5 mm for myometrial thickness [48]. Despite the imprecision in the measurements, the intra- and inter-observer agreement with regard to classifying the lower uterine segment as being thicker or thinner than a certain cutoff level was at least moderate in most studies, reported Kappa values ranging from 0.34 - 1.0. Clearly, if to use measurements of the thickness of the lower uterine segment clinically, ultrasound examiners would need to be properly trained and adopt a meticulous measurement technique.

B Which factors affect the thickness of the lower uterine segment as measured by ultrasound in the end of pregnancy?

To the best of my knowledge, there is only one study that has tried to answer this question [47]. That study includes 235 women with one previous caesarean delivery who had their lower uterine segment measured with ultrasound at 35 to 38 gestational weeks. A number of factors were evaluated with regard to their ability to predict the thickness of the lower uterine segment but only one, i.e., the stage of labour at caesarean, was found to be associated with the thickness of the lower uterine segment. The lower uterine segment was thinnest in women who were not in labour when caesarean was performed and thickest in women with cervical dilatation $\geq$ 4 cm when caesarean was carried out. These results are in agreement with those of one study but at variance with those of two studies evaluating the integrity of the hysterotomy scar with ultrasound in non-pregnant women [50] [51, 52], see below.

B Can the ultrasound appearance of the caesarean hysterotomy scar in the non-pregnant uterus predict uterine rupture or dehiscence in a subsequent pregnancy?
To the best of my knowledge, only one study has tried to answer this question [53]. In that study the definition of large scar defect at ultrasound examination was “thickness of the remaining myometrium over the defect < 2.5 mm in women who had undergone one caesarean and < 2.3 mm in women who had undergone two or more caesareans when saline contrast sonohysterography was performed [54], or “thickness of the remaining myometrium over the defect <2.2 mm in women who had undergone one caesarean and < 1.9 mm in women who had undergone two or more caesareans when unenhanced transvaginal ultrasound examination was used” [55]. The study includes 162 women who had their hysterotomy scar examined with ultrasound 6-9 months after a caesarean delivery. The women were followed up for 3-4 years with regard to the outcome of their subsequent pregnancies and deliveries. Both the clinical staff and the women themselves were blinded to the ultrasound results, and so the ultrasound findings played no role in the management of subsequent pregnancies. Sixty-nine women became pregnant again and 59 gave birth. Only the first delivery after the ultrasound examination was included in the statistical analysis. Uterine dehiscence or uterine rupture (this diagnosis was made at elective or emergency repeat caesarean, manual exploration of the uterus after vaginal delivery was not routinely performed) was diagnosed in four of the 59 women, i.e. in 7%. Five percent (1 of 19) of the women with no scar defect or a small scar defect had uterine rupture or dehiscence at repeat caesarean versus 43% (3 of 7) of the women with large scar defects diagnosed with ultrasound (P = 0.047). This corresponds to an odds ratio of 11.8 (95% CI 0.7 to 746). These results suggest that there is likely to be an association between large scar defects detected at transvaginal ultrasound examination of non-pregnant women and uterine rupture or dehiscence in subsequent pregnancy. However, it is not possible estimate with any precision the strength of this association.
B What is the ultrasound definition of a caesarean hysterotomy scar defect in non-pregnant women and how should a caesarean hysterotomy scar defect be measured?

There is no generally accepted definition of what is a “scar defect”, a “large” scar defect or a “clinically relevant scar defect” (in terms of, for example, risk of uterine rupture or dehiscence in subsequent pregnancy, risk of caesarean scar pregnancy, or risk of placenta accreta or placenta praevia) in non-pregnant women. There is no consensus on how a uterine scar defect in a non-pregnant woman should be measured [56].

B Which factors predict the size of a defect in a caesarean hysterotomy scar as measured by ultrasound in non-pregnant women?

In a study from my own research team [53] including 108 women who had undergone only one caesarean delivery, we found – using multivariate logistic regression analysis – that only one variable could predict a large scar defect using the definition described above [54, 55]: the stage of labour at caesarean. The odds of a large scar defect was 26 (95% CI 4-162) times greater if caesarean had been carried out at 5 - 8 cm cervical dilatation and 32 (95% CI 6-171) times greater if caesarean section had been carried out at cervical dilatation 9 cm or more than if caesarean had been carried out when the cervix was closed. These results are in agreement with those of Armstrong et al [51], who found fluid filled defects in caesarean hysterotomy scars exclusively in women who were in labour at caesarean. However, they seem to be at variance with those of Yazicioglu et al [50], who reported the prevalence of wedge defects in the caesarean hysterotomy scar 6 weeks postpartum to decrease with cervical dilatation at caesarean, and with those of Jastrow et al [47] who found that the lower uterine segment as measured by ultrasound
was thinnest in women who were not in labour when caesarean was performed and thickest in women with cervical dilatation ≥4 cm when caesarean was carried out. On the other hand, in the study by Yazicioglu et al [50], any wedge defect, however small, was taken into account, and measurements of lower uterine segment thickness are not directly comparable with assessment of hysterotomy scars in non-pregnant women. To sum up, it is not clear which factors are related to the ultrasound appearance of the hysterotomy scar area after caesarean delivery.

A Summary

Whether a scarred uterus will rupture or not is determined by a number of factors, not only by the strength of the scar but also by the strain on the scar. Clinical variables alone do not seem to be able to provide a precise estimate of the risk of uterine rupture during a trial of labour after caesarean. However, the following factors do seem to increase the risk of rupture: short inter-pregnancy or interdelivery interval, large baby, induction of labour, high doses of oxytocin and locked single layer closure of the caesarean hysterorotomy. Previous vaginal delivery seems to decrease the risk. Using ultrasound the integrity of the caesarean hysterotomy scar in non-pregnant women can be assessed, and the thickness of the lower uterine segment in pregnant women can be measured. However, there is no unequivocal relationship between what we see and measure with ultrasound and the strength of the scar or of the lower uterine segment. Moreover, there is no agreed upon ultrasound examination technique or ultrasound measurement technique when assessing a caesarean hysterotomy scar in non-pregnant women or the lower uterine segment in pregnant women. No cutoff for any ultrasound measurement can be recommended for prediction of uterine rupture or dehiscence. Nonetheless, there does seem to be an
association between large scar defects in non-pregnant women and uterine rupture or
dehiscence, and between a thin lower uterine segment at 35-40 gestational weeks and
uterine rupture or dehiscence. There is a need for more studies (large and well designed)
before ultrasound assessment of the non-pregnant or pregnant uterus can be introduced
into clinical practice to help select women for a trial of labour after caesarean.

A Conflict of interest

The author has no conflict of interest

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<th>Myometrial thickness, mm</th>
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No info, no information; IQR, interquartile range
* measurement technique not specified for the range of values reported
† Three-dimensional ultrasound
‡ In 10.8% of the women, transvaginal measurements were also taken, the smallest measurement being used for analysis
Legend

Figure 1. Measurement of the lower uterine segment using the technique of Bujold et al [41]. The measurements should be taken when the woman feels bladder fullness. The thinnest zone of the lower uterine segment is identified and the image magnified so that each slight movement of the calipers produces only a 0.1mm change in the measurement. The calipers are placed so that the inner edge merges with the limit line of the thickness that is measured, and the line of measurement must be exactly perpendicular to the measured wall. Full lower uterine thickness is measured with one cursor at the interface between urine and the bladder wall and the other at the interface between the amniotic fluid (or fetal scalp) and the decidua (a). The myometrium (myometrial thickness) is measured with one cursor at the interface of the bladder wall and the myometrium so that it includes only the hypoechogenic myometrial layer (a, b). At least three measurements should be taken and the lowest one is taken to be representative. B, bladder; FH, fetal head; FT, full thickness of the lower uterine segment; MT, myometrial thickness.


This is an example of a measurement technique. There is no agreed upon standardized measurement technique of the thickness of the lower uterine segment.