Changes in the uterine scar during the first year after a caesarean section; a prospective longitudinal study

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Submitted
Abstract

Aim
To study changes in a Cesarean Section (CS) scar during the first year after a CS using gel installation sonography (GIS).

Methods
Proof of concept study, prospective cohort study. 20 women who delivered by their first CS were evaluated by both transvaginal sonography and GIS 2 months and 1 year after CS. A niche was defined as an anechogenic space at the uterine caesarean scar with a depth > 2 mm. Primary outcome was any change in the thickness of the residual myometrium (RMT) as evaluated by GIS.

Results
Mean RMT changed in time from 11.9 mm at 2 months to 6.5 mm at 12 months after the CS (p<0.001). Niche prevalence did not change. The AM reduced from 15 mm to 12.4 mm (p=0.04) The ratio between RMT and AM with GIS decreased from 0.80 at 2 months to 0.54 at 12 months (p=0.002).

Conclusion
Residual myometrium thickness, the adjacent myometrium and the ratio between the RMT and AM reduces from 2 to 12 months after a CS. The prevalence did not change. This needs to be taken into account in timing of niche measurement and the interpretation of the RMT.
Introduction

Nowadays one third of women deliver their child by caesarean section (CS) worldwide. As a result there is a growing number of women experiencing complications of the caesarean section. These include caesarean scar pregnancies, uterine rupture, malplacentation and gynaecological symptoms such as post menstrual spotting and dysmenorrhea. The uterine caesarean scar is most frequently evaluated by transvaginal sonography (TVS) and saline infusion sonography (SIS) or Gel installation sonography (GIS). Often one can see contrast entering into the myometrium at the site of the scar forming a triangular echolucent space in a longitudinal view of the lower uterine segment that is colloquially known as a ‘niche’. Different nomenclature is used to describe this feature; a scar defect, niche, isthmocele, pouch or diverticula. The prevalence of a niche, using sonohysterography varies between 56% and 84% in random populations. GIS or SIS are more sensitive than TVS in detecting niches. And sonohysterography give the best inter and intraobserver agreement. Despite an increasing number of prospective cohort studies reporting on the prevalence and appearances of the uterine caesarean scar, a clear uniformly used definition is still lacking. In addition it is unclear what the best moment is to measure a niche after a CS, since it is unclear if a niche changes over time after a CS.

All prospective studies performed in a more or less random population are based on a single measurement of the scar with TVS or SIS or GIS. Longitudinal studies with a long term follow up of the caesarean scars among non-pregnant women are lacking. The aim of this study is to evaluate changes in the residual myometrial thickness, niche prevalence and size over time during a follow-up period of one year using both TVS and GIS in non-pregnant women after their first CS.

Methods

This study is a proof of concept study performed as a a prospective cohort study. The study was executed in a teaching hospital, Sint Antonius Hospital Nieuwegein, the Netherlands between November 2007 and September 2011. The trial was registered in the Nederlands trial register (www.trialregister.nl, trial number NTR-2887) The protocol was approved by the local medical ethics committee (VCMO NL18722.100.07 R-07.14A/SCAR). All women signed informed consent. Women included in this study are a subgroup of a larger prospective cohort study that aimed to evaluate the prevalence of a niche and its relation with bleeding disorders after a CS. Women were asked to participate during their stay in the ward immediately after CS. Women were asked to undergo a TVS and GIS 6-12 weeks after the CS and to complete a questionnaire at 6 weeks, 6 and 12 months after their CS. A subgroup was asked to participate additionally in the current ultrasound follow-up study. Eligible women for this ultrasound follow up study were women who had the CS performed
in their first pregnancy and without any previous uterine surgery and were willing to undergo a second GIS. They were asked after their first ultrasound 6-12 weeks after CS to undergo a second TVS and GIS 9-12 months after the CS. Women who gave their informed consent were contacted by telephone 9-12 months after CS and scheduled for a TVS and GIS at the outpatient clinic. Ultrasound was performed in a standard way, as previously described and briefly outlined below.8

The uterus was scanned in both transversal and sagittal plane and if a niche was present the sagittal plane with the largest depth was searched and niche characteristics were measured and registered in a CRF; presence of a niche (defined as an anechoic space at the presumed site of the caesarean scar with a depth equal or more than 2 mm), depth of the niche, thickness of the residual myometrium at the site of the uterine scar, the thickness of the adjacent myometrium (see Figure 1), the length and width of the uterus and the double endometrial thickness.

Immediately after the TVS a GIS was performed and the same measurements were taken. All ultrasound were performed using a 7.5–MHz transducer (Philips Sonicare HD 11.XE, Philips Medical Systems, Eindhoven, the Netherlands) by 2 experienced gynaecologist (LV and SV).

Indication and characteristics of the CS were recorded from the medical chart. A questionnaire was used to obtain details about contraceptive use, breastfeeding and bleeding pattern. All data were recorded in a CRF and a web based database by two research nurses. The results of the ultrasound scans were not recorded in the case notes, and women and their doctors were not informed on the ultrasound findings. Reporting was performed according to the guideline for reporting a prospective study (STROBE).12

![Figure 1 Measurement of the niche](https://example.com/figure1.png)

Figure 1 Measurement of the niche

1 = depth, 2 = residual myometrium, 3 = adjacent myometrium
Statistical Analysis
The primary outcome was the change in the thickness of the residual myometrium (RMT) from 2 to 12 months after the CS evaluated by GIS. Secondary outcomes are the prevalence of a niche using TVS and GIS, depth of the niche, the thickness of adjacent myometrium (AM), ratio RMT/AM, length and width of the uterus. IBM SPSS statistics version 22 (SPSS Inc., Chicago IL USA) was used for the statistical analyses. To compare the thickness of RMT, the depth of the niche, width and length of the uterus, thickness of adherent myometrium and the ratio RMT/AM Wilcoxon signed Rank test was performed because of non-normal distribution. McNemar test was used to compare the prevalence of a niche. To compare baseline characteristics chi-square and students t-test were performed. All test were performed two-sided, a two-tailed p value of <0.05 was considered statistically significant.

Sample size calculation
At the time of the study design we did not have any relevant data of comparable studies to base our sample size. Our study should be considered as a proof of concept study, we aimed to include 20 patients.

Results
Of the 115 women who had the CS performed in their first pregnancy during the first study 46 gave informed consent immediately after their first GIS to participate additionally in the ultrasound follow up study. Fourteen women withdrew at 9 to 12 months after CS and 12 women could not be reached 9 months after their first ultrasound. Finally 20 women showed-up for their second ultrasound. (see Figure 2)
Mean period between the CS and the first ultrasound was 7.3 weeks (SD1.1 range 6-10) and between the CS and the second visit was 48.9 weeks (SD13.1 range 24-68). Baseline characteristics of the women are shown in Table 1.
On the included women there were more planned CSs and gestational age was shorter compared to women who did not participate. All CSs were performed with a transversal incision in the low uterine segment. In all but one patients the uterus had been closed in one layer. Two CSs had been complicated by more than 1000 cc blood loss and one patient had had an eclamptic seizure during the CS. One women developed fever after CS, none of the women received antibiotics for more than 24 hours. Contraceptive use at the time of visit 1 and 2 are shown in Table 1.
Results of both TVS and GIS are shown in Table 2. All women underwent a TVS at the second visit and 15 women received a GIS. Of the five women without a GIS, two women were pregnant, two women were in the luteal phase of their cycle without use of contraceptives and one woman refused to undergo an additional GIS. There was a reduction in the mean RMT in time with both GIS and TVS, it reduced from 11.9 mm at 2 months to 6.5 mm at 12 months (p<0.001) using GIS, with a mean difference of 5.4 mm (95%CI 3.6-7.3) (Table 2, Figure 3,4a,4b). Reduction with TVS was from 10.1 mm at 2 to 7.0 mm at 12 months (p=.008), mean difference 2.82 mm (95% CI 0.61-5.02) (Table 2, Figure 4a,4b). A non-significant increase in niche depth was observed using GIS from 3.8 mm at 2 months to 5.3 mm at 12 months (p=0.46), while the mean niche depth remained 5.3 mm using TVS (Table 2). The adjacent myometrium reduced from 15 mm to 12.4 mm (p=0.048), mean differences 2.6 mm (95% CI 0.13-5.0) using GIS. Similar results were found using TVS. The ratio between RMT and AM decreased from 0.8 at 2 months to 0.54 at 12 months with GIS (p=0.008), mean differences 0.26 (95% CI 0.11-0.42). TVS results showed a non-significant decrease in the ratio RMT/AM (Table 2, Figure 4a,4b). The prevalence of a niche
did not change. In five women there was a change in the position of the uterus between 2 and 12 months. Four women had a uterus in retroversion position at six weeks and an anteversion position at 12 months. One woman had a uterus in straight position which was turned to retroversion position at twelve months. Four of these five women had a niche.

Table 1 Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>N=20 included</th>
<th>N=26 Not participated</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td>Age years mean (sd)</td>
<td>31 (2.8)</td>
<td>32 (3.4)</td>
<td>.352</td>
</tr>
<tr>
<td>Gestational age days (sd)</td>
<td>274 (8.7)</td>
<td>279</td>
<td>.046</td>
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<tr>
<td>Labour n(%)</td>
<td>9 (45)</td>
<td>22 (85)</td>
<td>.004</td>
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<tr>
<td>Cervical dilatation mean cm (sd)</td>
<td>4.1 (4.4)</td>
<td>5.8 (3.7)</td>
<td>.171</td>
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<tr>
<td>Augmentation oxytocine n(%)</td>
<td>7 (35)</td>
<td>13 (50)</td>
<td>.351</td>
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<tr>
<td>Induction of labour n(%)</td>
<td>21 (10)</td>
<td>6 (23)</td>
<td>.246</td>
</tr>
<tr>
<td>PIH/PE n (%)</td>
<td>4 (20)</td>
<td>7 (27)</td>
<td>.732</td>
</tr>
<tr>
<td>Blood loss&gt;1000 cc n (%)</td>
<td>2 (10)</td>
<td>3 (12)</td>
<td>.868</td>
</tr>
<tr>
<td>Niche *</td>
<td>11 (55)</td>
<td>14 (54)</td>
<td>.997</td>
</tr>
</tbody>
</table>

Visit 1 Visit 2

<table>
<thead>
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<th></th>
<th>Visit 1</th>
<th>Visit 2</th>
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</tr>
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<tbody>
<tr>
<td>Weeks after CS mean (sd)</td>
<td>7.3 (1.1)</td>
<td>48.9 (13.2)</td>
<td></td>
</tr>
<tr>
<td>Regular cycle n(%)</td>
<td>none</td>
<td>13 (65)</td>
<td></td>
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<tr>
<td>Breastfeeding n (%)</td>
<td>15 (75)</td>
<td>3 (15)</td>
<td></td>
</tr>
<tr>
<td>Oral contraceptive n (%)</td>
<td>5 (25)</td>
<td>10 (50)</td>
<td></td>
</tr>
<tr>
<td>Pregnancy n (%)</td>
<td>2 (10)</td>
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sd= standard deviation, n= number, PIH/PE= pregnancy induced hypertension/Pre-eclampsia. CS = caesarean section * niche measured with Gel Installation Sonohysterography

Table 2 Ultrasound characteristics

<table>
<thead>
<tr>
<th></th>
<th>TVS Visit 1 N=20</th>
<th>TVS Visit 2 N=20</th>
<th>P value</th>
<th>GIS Visit 1 N=20</th>
<th>GIS Visit 2 N=15</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length uterus (cm)*</td>
<td>7.1 (0.92)</td>
<td>6.8 (0.83)</td>
<td>0.38</td>
<td></td>
<td></td>
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<tr>
<td>Width uterus (cm)*</td>
<td>3.9 (0.65)</td>
<td>3.7 (0.52)</td>
<td>0.13</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Endometrial thickness (mm)*</td>
<td>3.4 (1.2)</td>
<td>5.0 (3.5)</td>
<td>0.16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Niche ≥ 2mm n(%)</td>
<td>12 (60)</td>
<td>10 (50)</td>
<td>0.69</td>
<td>11 (55)</td>
<td>9 (60)</td>
<td>0.69</td>
</tr>
<tr>
<td>Niche depth</td>
<td>5.3 (4.6)</td>
<td>5.3 (3.8)</td>
<td>0.92</td>
<td>3.8 (2.8)</td>
<td>5.3 (3.8)</td>
<td>0.67</td>
</tr>
<tr>
<td>Residual myometrium (mm)</td>
<td>10.1 (3.8)</td>
<td>7.0 (3.1)</td>
<td>0.008</td>
<td>11.9 (3.3)</td>
<td>6.5 (3.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Adjacent myometrium (mm)</td>
<td>14.5 (3.5)</td>
<td>10.8 (2.6)</td>
<td>0.001</td>
<td>15 (2.9)</td>
<td>12.4 (3.4)</td>
<td>0.048</td>
</tr>
<tr>
<td>RM/AM ratio</td>
<td>0.72 (0.22)</td>
<td>0.65 (0.23)</td>
<td>0.11</td>
<td>0.8 (0.20)</td>
<td>0.54 (0.26)</td>
<td>0.008</td>
</tr>
</tbody>
</table>

Given as mean (SD) unless stated different. VS = trans vaginal sonography. GIS= gel installation sonohystergraphy, RM/AM ratio= residual myometrium/adjacent myometrial ratio SD= standard deviation. * Excluding pregnant women at visit 2 did not change significantly the outcome of these measurements.
Chapter 4

Figure 3  Changes in thickness of residual myometrium in women evaluated with Gel installation Sonohysterography (GIS) n=15

Visit 1 = 2 months after caesarean section
Visit 2 = 12 months after caesarean section

Figure 4a  Residual myometrium

Figure 4b  Ratio residual myometrium/adjacent myometrium

TVS= trans vaginal sonography, GIS=gel installation sonohysterography
Discussion

Between 2 and 12 months after CS the residual myometrium, the adjacent myometrium at the site of the caesarean scar and the ratio RMT/AM decreased significantly using both GIS and TVS. However niche depth, prevalence of a niche, uterine length and width did not change in time. Our findings implicate that the myometrium at the site of the caesarean scar is not a static feature and changes over time.

A strength of our study is that we included patients immediately after their first CS, reducing the risk on bias to participate. Another strength is that we used both TVS and GIS at 2 and 12 months after CS. Sonohysterography increases the delineation of the niche and myometrium. A recent study shows the best inter- and intraobserver agreement of RMT measurements with contrast sonohysterography compared to other niche characteristics.6 Also in a 3D study the RMT has shown to have a good inter-observer agreement.13 In addition we used a standardized method for niche evaluation using predefined criteria.8

A limitation of this study is the small sample size due to the relatively high number of patients that did not want to undergo a second GIS after their first one due to its discomfort. There were no differences between the women who participated and women who did not participated in ultrasound findings at 12 weeks or gynaecological symptoms at 12 months after the CS. Women who participated in the current study had more often a planned caesarean section than the women who did not participate. However, given the fact that participating women were their own controls eventual selection bias would not have affected the outcomes but it may have consequences for the extrapolation of the result to other populations. Since the majority of the included women had a uterus closed in one layer, these results can not be extrapolated to women who received double layer closure of their uterus.

So far only two peer reviewed studies and four abstracts are published on longitudinal follow up within patients with niches by 2D or 3D ultrasound.14-19 They all evaluated niches with a follow up between 6 weeks and 24 months. Three of these studies also found a reduction of the RMT in time.14-16 A reduction in the RMT and the AM/RM ratio over time could be induced by the continuing tissue reaction or reduction of oedema during the healing process. Another theory includes retraction of adhesions between the uterus and the abdominal wall inducing an increase in niche depth and reduction of RMT.20 Also peristaltic contractions of the uterus could influence the traction on the residual myometrium and blood accumulation in the niche may induce a continuous pressure on the residual myometrium.

In women with symptomatic niches the RMT is one of the key parameters for the selection of different surgical approaches, hysteroscopic resection should in general only be considered in case of a RMT of at least 2.5-3mm to prevent bladder injury.21 The results of our study show that the RMT is a dynamic feature that changes during the first year after CS. Therefore measurement of the RMT after a CS should be timed carefully before considering surgical interventions. Also for research purposes it is relevant to realize that timing of measurement of the niche may affect the thickness of the RMT. Our results also
indicate that TVS may be a good alternative to assess changes of the niche over time in the same patient. However for the determination of treatment possibilities or in the assessment of possible risks for future pregnancies it remains important to perform GIS or SIS. Larger studies and longer follow-up are needed to know whether the changing of the scar continues after one year follow-up and to gain more insight in factors that affect wound healing of the uterine scar and niche development in order to develop preventive strategies.

Conclusion

The uterine scar after a CS is not a static feature and changes over time. The residual myometrium thickness between the niche and the bladder at the site of the CS scar measured with sonohysterography decreases significantly over time between 2 and 12 months after a CS.

Acknowledgments

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Disclosure of interests

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References


