Niches after cesarean section in a population seeking hysteroscopic sterilization.

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Abstract

Objective
To study the prevalence of hysteroscopically evaluated disruptions of the integrity of the uterine wall (‘niches’) in women with and without a previous cesarean section.

Study Design
A prospective cohort study was performed in a teaching hospital in the Netherlands. Women seeking hysteroscopic sterilization were included. A hysteroscopic evaluation of the anterior wall of the uterus and cervix to identify the existence of disruptions (niches) was performed in a standard manner. Primary outcome was the presence of a uterine niche, defined as any visible defect, disruption, or concavity (gap) in the anterior wall. Secondary outcome was to develop a registration form of niche features for hysteroscopic evaluation.

Results
In total, 713 women were included, 603 without and 110 with a previous cesarean section. In women with a previous cesarean section 83 (75%) niches were observed using hysteroscopy. Anterior wall disruptions were not observed in women without a cesarean section. The following niche features were identified and incorporated in a registration form: polyps, cysts, myometrium defect, fibrotic tissue, (abnormal) vascular pattern, lateral branches, mucus production inside the defect, and bleeding.

Conclusion
In a prospective cohort study among women undergoing hysteroscopic sterilization, a uterine niche could be detected by hysteroscopy in 75% of women with a previous cesarean section.
Introduction

In the last decades there has been an increase in the rate of cesarean sections (CS) worldwide. In a non-pregnant uterus the cesarean scar can be visualized with transvaginal ultrasound, hysterosalpingography, sonohysterography or hysteroscopy. The scar can be visualized as an echogenic stripe, but it has also been reported as an anechoic triangle at the presumed site of the cesarean scar filled with fluid, called a niche. The prevalence of a niche in several cross-sectional cohort studies varies between 24%-70% using transvaginal ultrasound and between 56%-84% using sonohysterography. The prevalence of niches evaluated with hysteroscopy has only been evaluated in selected populations with gynaecological symptoms and varies between 31%-100%. Various symptoms have been reported in association with a niche, in particular post-menstrual spotting. Several surgical strategies to treat niche-related bleeding disorders have been proposed. According to recent publications treatment is also offered in asymptomatic women. A niche is a frequent feature after a CS and it does not always lead to symptoms. A limited number of papers report on the evaluation of cesarean scars and niches by hysteroscopy. However, these evaluations were only carried out in symptomatic women and in women with a previous CS. Characteristics of a niche during hysteroscopic evaluation were not described, a hysteroscopic classification is thus still lacking. The aim of our study is to determine the prevalence of a niche in a more or less asymptomatic population of women undergoing a hysteroscopy for a hysteroscopic sterilization, with and without a previous CS. The second goal is to identify different aspects and features of niches observed during hysteroscopy in order to develop a registration form for future classification of niches.

Material and methods

This study was performed in a teaching hospital with office-hysteroscopy facilities. From January 1st, 2006 to December 31st, 2010 all women with a request for hysteroscopic sterilization were asked consecutively to participate and, after written consent, were enrolled in this study. Women were excluded if the indication for hysteroscopy differ from sterilization. Consenting women were asked to complete a questionnaire about their obstetric history, previous (intrauterine) surgery, contraceptive use at the time of sterilization, and vaginal bleeding patterns (including length of menstrual cycle, days of bleeding, and intermenstrual blood loss). All included women underwent a hysteroscopy in an office setting without the use of a speculum, tenaculum, or local anesthetics (vaginoscopic approach), using a 5.5 mm continuous-flow hysteroscopic system (Olympus©) with 5-French working channel and 30-degree optics. Sterilization was performed by placement of Essure® devices in both fallopian tubes in the postmenstrual phase of the cycle. After placement of the Essure® devices, the anterior wall of the uterus and cervix were evaluated in a standard manner by withdrawing the hysteroscope from the fundus of the uterus to the external cervical os. At this stage the hysteroscope was turned towards the anterior wall and with the use of 30-degree optics the complete anterior wall was evaluated.
A niche or anterior-wall defect was defined as any defect, disruption, or concavity (gap) in the anterior wall at the level of the cervical isthmus. Besides the presence of a niche, a description of different features and aspects of the niche were recorded in a subgroup of women evaluated in 2010. Abnormalities, lining of the surface, shape of the niche, and presence of vessels or other substance in the niche were registered. Two gynaecologists, both with more than 10 years experience in hysteroscopy, performed all hysteroscopic procedures and examination of the anterior uterine wall. The Institutional Review Board approved this study (IZ16.056/W16.064).

**Statistics**

The primary outcome of our study was the prevalence of a niche in women seeking hysteroscopic sterilization with a previous cesarean section. There are no data on the prevalence of niches in a more or less asymptomatic population. We intended to include at least 100 women with a previous cesarean section for this purpose. To objectivate differences between baseline characteristics we used the independent student’s t-test for the comparison of continuous variables in case of normal distribution. Otherwise non-parametric tests were used. Chi-square or Fisher’s exact tests were used to compare proportions. Women whose hysteroscopic evaluation of the uterus failed were analyzed according to their obstetric history (previous or no previous cesarean section). These women could not be included in the analyses of niche-related factors. All tests were performed two-sided and \( p<.05 \) was considered statistically significant. IBM SPSS statistics version 22 (SPSS Inc., Chicago IL USA) was used for the statistical analyses. Reporting was performed according to the guideline for reporting a prospective study (STROBE).^{14}

**Results**

Between January 1st, 2006 and December 31st, 2010, 794 women underwent hysteroscopy for sterilization. 713 women were included in the study and completed the questionnaire about their obstetric history.(see Figure1) Assessment of the anterior wall failed in six women: due to collapse of the patient (3 women), due to cervical stenosis (1 woman), and in two cases the reason was not registered. Five of these women had no previous cesarean section. Of the 713 women, 55 were nulligravida, 80 were nullipara, 523 women had a history of at least one vaginal delivery without a CS, 73 women had a history of one CS, 33 women 2 CSs, and 4 women 3 CSs (Table 1). Mean age was 38.8 (SD 4.5). In this group 83 niches (75%) were observed using hysteroscopy. In all other women a normal appearance of the anterior wall was observed at the level of the cervical isthmus, without any signs of a gap or disruption of the integrity of the endometrium or myometrium. Anterior wall defects were not observed in women without a previous CS. Of those women investigated in 2010, the features of the observed niches were recorded. In women with anterior wall defects the following items could be identified in the niche or at the surface: polyp-like structures, cyst-like formations, visible serosa (a complete
defect of myometrium), fibrotic tissue, (abnormal) vascular pattern, lateral branches, mucus production inside the defect, and bleeding within the defect. On the basis of these features a registration form was developed (see Figure 2). Of the 713 participating women, 679 records (95%) were complete with respect to bleeding pattern or contraceptive use. Baseline characteristics were not significantly different between women with CS and with vaginal delivery apart from body mass index (BMI), as women with a previous CS had a higher BMI (see Table 1). In our population 46 women (6%) reported a menstrual bleeding disorder, 32 women (4%) reported intermenstrual bleeding (8 of them used levonorgestrel-intra uterine systems and 7 oral contraceptives), and 14 women (2%) reported regular heavy menstrual bleeding. There were no significant differences in bleeding disorders between women with or without a CS and no differences between women with or without a niche. There were no significant differences in baseline characteristics regarding BMI, age, parity, or contraceptive use between women with or without a niche (see Table 1).
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Discussion

In 75% of women with a previous CS undergoing a hysteroscopic sterilization, a uterine niche was observed. As expected disruptions of the uterine integrity of the anterior uterine wall were not observed in women without a previous CS confirming that even small indentations or disruptions are a result of the caesarean section and not of the pregnancy itself. Niche features during hysteroscopic evaluation are: polyp-like structures, cyst-like formations, complete defect of myometrium, fibrotic tissue, (abnormal) vascular pattern, lateral branches, mucus production inside the defect, and bleeding within the defect.

To our knowledge, this is the first study comparing uterine integrity in women with and without a previous CS using hysteroscopy. This study is also the first study that evaluated niches in women who are investigated by hysteroscopy with no gynaecologic complaints. Although the data are obtained between 2006 and 2010 and not reported earlier we still think it is relevant to report because there are no data on prevalence of a niche with hysteroscopy in asymptomatic women. Another advantage of our study is that all women

Table 1 Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total n</th>
<th>No CS</th>
<th>previous CS</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total n</td>
<td>713</td>
<td>603</td>
<td>110</td>
<td></td>
</tr>
<tr>
<td>Age mean (SD)</td>
<td>38.8 (4.5)</td>
<td>38.9(4.4)</td>
<td>38.6(4.6)</td>
<td>.52</td>
</tr>
<tr>
<td>BMI mean (SD)</td>
<td>24.7 (6.2)</td>
<td>24 (6.3)</td>
<td>26.1(5.3)</td>
<td>.02</td>
</tr>
<tr>
<td>Nulligravida n</td>
<td>55</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nullipara n</td>
<td>80</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Niche n (%)</td>
<td>83 (12%)</td>
<td>0</td>
<td>83 (75%)</td>
<td>.32</td>
</tr>
<tr>
<td>Oral contraceptive use n(%)</td>
<td>316 (44%)</td>
<td>262 (44%)</td>
<td>54 (49%)</td>
<td>.27</td>
</tr>
<tr>
<td>IMB n(%)</td>
<td>32(4%)</td>
<td>27(4%)</td>
<td>5 (5%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Menorrhagia n(%)</td>
<td>14 (2%)</td>
<td>14(2%)</td>
<td>0</td>
<td>.20</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Previous CS (n=110)</th>
<th>(1 missing)</th>
<th>Niche n=83</th>
<th>No niche n=26</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age mean (SD)</td>
<td>38.6(4.6)</td>
<td>38.4 (4.7)</td>
<td>39 (4.4)</td>
</tr>
<tr>
<td>BMI mean (SD)</td>
<td>26.1(5.3)</td>
<td>26.2 (5.0)</td>
<td>26.2(6.1)</td>
</tr>
<tr>
<td>Parity mean (SD)</td>
<td>2.1 (0.99)</td>
<td>2.1(1.1)</td>
<td>1.88(0.7)</td>
</tr>
<tr>
<td>CS mean(SD)</td>
<td>1.37(0.6)</td>
<td>1.4 (0.6)</td>
<td>1.3(0.5)</td>
</tr>
<tr>
<td>1 CS (1 missing)</td>
<td>73(66%)</td>
<td>53 (73%)</td>
<td>19(26%)</td>
</tr>
<tr>
<td>2 CsS</td>
<td>33(30%)</td>
<td>27(82%)</td>
<td>6(18%)</td>
</tr>
<tr>
<td>3 CsS</td>
<td>4 (4%)</td>
<td>3 (75%)</td>
<td>1(25%)</td>
</tr>
<tr>
<td>IMB (6 missing)</td>
<td>5 (5%)</td>
<td>5 (6%)</td>
<td>0</td>
</tr>
</tbody>
</table>

SD=standard deviation, BMI = body mass index, IMB = intra menstrual bleeding, CS= caesarean section
were evaluated in a standardized manner by hysteroscopy, enabling the development of a concept registration system for niches using hysteroscopy. A limitation of this study is the fact that the gynecologists performing the hysteroscopies were not blinded for the patient’s obstetric history. In addition, this study was not designed to study the relation between bleeding disorders and niches in a general population. Selection bias with respect to bleeding pattern was intentional because women with indications for hysteroscopy other than sterilization were excluded. Also evaluation of the uterine cavity regarding abnormalities as polyps and myoma were kept outside this study. Our results concerning bleeding symptoms and its relation to niches should therefore not be extrapolated to a general population. In addition, patients with previous bleeding disorders are more likely to be advised to continue their oral contraceptives or levenorgestrel intra uterine systems rather than opt for sterilization since these serve as contraceptives and may have a positive effect on the bleeding disorders.

Although we used standardized methods for evaluating the uterus the assessment of the signs of a disruption remains subjective. Niches have different presentations as illustrated by the different items the gynecologists have scored, such as presence of polyps, abnormal vascular pattern, cyst-like formations. There are no studies that report standard description and classification of niches. With the items found in this study we defined a concept registration system for hysteroscopic evaluation of niches (see Figure 2). This registration form is used in a randomised controlled trial. A hysteroscopic classification system has to be formed using these registrations and its correlation with clinical symptoms needs to be examined. Its clinical usefulness requires evaluation in other populations.

The presented prevalence of uterine niches is comparable to the reported prevalence of uterine niches using (sono)hysterography in random populations after CS. In four other studies performed in random populations in women with a previous CS the prevalence varied between 58% and 69%. These studies mostly used a cut-off level for niche depth of at least one or two millimetre. We were not able to correlate the hysteroscopy outcome with ultrasound or measure niche depth in our study. Any indentations were defined as a niche, possibly explaining the high prevalence, even in asymptomatic women. Previous reported prevalence during hysteroscopic evaluation ranged between 30 and 100%. All these studies included symptomatic women, and this wide range could be explained by the use of different definitions of a niche (from any abnormalities to complete defect) and the difference in population characteristics. (see Table 2)

We found a slightly lower BMI in women who had no CS compared to women with a previous CS. It is known that obesity is a risk factor for a CS. There was no relation between the presence of niches and BMI.
Table 2  Hysteroscopic studies on niche prevalence's

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of participants</th>
<th>Inclusion criteria</th>
<th>Hysteroscope</th>
<th>Definition niches</th>
<th>Prevalence niches</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borges 2010</td>
<td>43</td>
<td>post menstrual spotting and previous CS</td>
<td>Outpatient Vaginoscopic 2,9-4.0 mm 30 degree rigid scope, saline</td>
<td>Cavity at scar site, fibrotic ring</td>
<td>88%</td>
</tr>
<tr>
<td>El-mazny 2010</td>
<td>75</td>
<td>Infertility, menstrual disorders or recurrent pregnancy loss and previous CS</td>
<td>4 mm, 30 degree rigid scope, saline</td>
<td>Defect (or pouch) and unhealthy scar(fibrotic)</td>
<td>31% (defect) 45% (unhealthy scar)</td>
</tr>
<tr>
<td>Fabres 2002</td>
<td>32</td>
<td>Previous CS, abnormal bleeding</td>
<td>3mm hysteroscope, sorbitol</td>
<td>Cleft of the anterior wall</td>
<td>100%</td>
</tr>
</tbody>
</table>

CS= cesarean section

The relation between niches and bleeding disorders has been demonstrated in several studies. The large number of women with asymptomatic niches in our population underlines the fact that not all niches are symptomatic. The indication for surgery should be based on symptoms and other causes of bleeding disorders should be excluded first. Although some authors suggest that a wish to conceive is an indication for surgery there is no evidence to substain this conclusions. More well-designed trials are necessary to evaluate the relation between niches and both sub fertility and pregnancy outcomes. Also more well designed trials are mandatory to evaluate the pregnancy outcome after surgical therapy for niches. Although most studies report normal pregnancy outcomes, the amount of pregnancies evaluated is still small and a recent study by Tanimura showed 25-30 % premature delivery after a laparoscopic or vaginal niche repair. To allow the development of prognostic models for symptomatic niches, additional prospective studies in general populations are needed. Preferably, these studies should include the development of hysteroscopic and sonohysterographic classification of niches, which relate symptoms to the location, shape, size, and appearance of niches (such as presence of vessels, polyps, mucus production, and cyst formation).

Conclusion

We found a niche prevalence of 75% in women with a previous CS in a selected population without gynecological complaints seeking hysteroscopic sterilization. No disruptions of the anterior wall were seen in women without a previous CS. More research is needed to evaluate the association of niches with both sub fertility and pregnancy outcomes, and there is a need for a hysteroscopic classification system.
Hysteroscopic evaluation of niches

1. Concavity in Anterior Wall

2. Mucosa

3. Abnormal Vascular Pattern

4. Serosa visible / Defect Myometrium

5. Lateral Branches

6. Cystic Formations

7. Polyp like Structures

Figure 2. Registration form
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Disclosure of interests
JHU received two grants of ZonMw, a Dutch organization for Health Research and development for 1) To compare the effect of a hysteroscopic niche resection versus no treatment in women with postmenstrual spotting (Hysniche study, ZonMw project number 80-82305-97-12030) and 2) The (cost)effectiveness of double layer closure of the caesarean (uterine) scar in the prevention of gynaecological symptoms in relation to niche development (ZonMw project number 843002605) and received grants from Samsung Medison and Gedeon Richter outside the submitted work. HBR received grants from Olympus and Gynesonics and non-financial support from Samsung Medison, outside this study. SV is consultant for Bayer and Norvartis. He is member of the advisory board of Hologic and Johnson and Johnson. And SV is patentee for a new hysteroscopy.

Contribution to authorship
This study was conceived by LV, HB, SV and JH. SV performed the hysteroscopy and LV and TL collected the data. Analysis of the data was performed by LV and JH. The first draft was written by LV and JH, and TL, AT, HB, and SV supervised the article to the final draft.

Details of Ethics Approval
The study received ethics approval from the united committee on research involving human subjects (VCMO), Nieuwegein, the Netherlands (T23348/Z16.056/W16.064).

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No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.
Hysterocopic evaluation of niches

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