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Evaluation of Cesarean section scar using saline contrast sonohysterography in women with previous Cesarean scar pregnancy

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KEYWORDS: Cesarean scar pregnancy; saline contrast sonohysterography; ultrasound; uterine niche; uterine scar

CONTRIBUTION

What are the novel findings of this work?
Women with prior Cesarean scar pregnancy (CSP) who had a gestational sac protruding beyond the serosal line had a significantly greater uterine niche length and depth and lower residual myometrial thickness on saline contrast sonohysterography.

What are the clinical implications of this work?
These findings may guide individualized counseling as to the likelihood of development of a Cesarean scar defect, risk of recurrence of the CSP and indication for scar repair, and improve dialogue between physicians, who can use the same nomenclature.

ABSTRACT

Objective *To evaluate Cesarean scar defects using saline contrast sonohysterography (SCSH) in women with a history of Cesarean scar pregnancy (CSP).*

Methods *A cohort of 38 non-pregnant women with a history of CSP treated with combined local and systemic methotrexate was investigated prospectively by SCSH. For the purpose of analysis, they were classified, according to the modified Delphi consensus criteria for CSP in early gestation, into three subgroups based on the depth of the gestational sac herniation in the midsagittal plane. Subgroup A included eight (21.1%) cases, in which the largest part of the gestational sac protruded towards the uterine cavity; Subgroup B included 20 (52.6%) cases, in which the largest part of the gestational sac was embedded in the myometrium; and Subgroup C included 10 (26.3%) cases, in which the gestational sac was located partially outside the outer contour of the cervix or uterus.*

Results *SCSH revealed that all women in Subgroup C had a uterine niche. The median niche length (*$P = 0.006$*) and depth (*$P = 0.015$*) were significantly greater in Subgroup C than in Subgroups A or B. The median residual myometrial thickness (RMT) was significantly lower in Subgroup C than in Subgroups A or B (*$P = 0.006$*).*

Conclusions *Women with prior CSP who had a gestational sac protruding beyond the serosal line had a significantly greater niche length and depth, and lower RMT. This knowledge may guide individualized risk counseling.* © *2023 International Society of Ultrasound in Obstetrics and Gynecology.*

INTRODUCTION

A Cesarean scar pregnancy (CSP) is defined as blastocyst implantation within the uterine incision area of a previous Cesarean delivery (CD) and is considered to be a life-threatening condition. If left intact, some CSPs can result in massive hemorrhage, leading to hysterectomy, uterine rupture and placenta accreta spectrum[1].

To date, there are no available data on the rate of CSP. Reports tend to cite rough estimates ranging from 1/1800 to 1/2500 of all CDs[1]. Incidence has risen considerably because of the mounting rate of CD over the last 20 years[2], and due to growing awareness and more accurate diagnosis.

Although studies have grappled with the underlying pathological mechanisms and occurrence, CSP pathogenesis remains unclear. The lower uterine segment contains fewer muscle fibers than the upper segment and their numbers decrease toward the cervix[3–5]. Thus, the anatomical impact of a surgical procedure is more prominent in the lower segment, and the formation of

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what is known as the Cesarean scar defect or niche, which can be identified during a transvaginal ultrasound, is now well described[6–8]. Large niches are often characterized by a lack of re-epithelialization with a myometrial thickness that is frequently below 2 mm[6–8], implying permanent loss of almost all the myometrial thickness. Previous studies have pointed towards potential risks linked to Cesarean scar tissue in terms of endometrial biology, as well as uterine vascular changes[9,10]. This may explain the formation of a uterine niche and the possibility of greater iatrogenic obstetric complications in future pregnancies, including CSP[11] and placenta accreta spectrum[12,13].

Figures for the rate of uterine niche after CD differ considerably and range from roughly one-quarter to three-quarters of all subsequent pregnancies[8,14–16]. In an attempt to standardize niche assessments, the recent niche taskforce agreed on a list of ultrasound signs[17]. Most experts agreed that niche evaluation with saline contrast sonohysterography (SCSH) is of additional value compared with using standard two-dimensional sonography[17].

The aim of this study was to evaluate prospectively post-CD uterine wall integrity using SCSH in non-pregnant women with a history of CSP.

METHODS

This prospective cohort study was conducted at the Department of Obstetrics and Gynecology, The Yitzhak Shamir Medical Center, Zerifin, Israel, between December 2022 and April 2023. The sample was composed of non-pregnant women with a history of CSP treated with combined local and systemic methotrexate (MTX) and was investigated prospectively by SCSH. The study was approved by the institutional ethics committee (#0298-22), registered as a clinical trial (registration number: NCT05672563 (ClinicalTrials.gov)) and written informed consent was obtained from all participants.

Study population

We conducted a computerized database search for CSP cases diagnosed in our department between January 2008 and December 2022. Our department has extensive (> 25 years) experience managing patients with CSP[18–22]. All patients fulfilled the sonographic criteria for CSP[18] and were treated with combined administration of local MTX (injected directly into the ectopic sac under sonographic guidance) and systemic MTX, according to our department protocol[18–22]. The inclusion criteria for administration of MTX were: pregnancy with detectable heartbeat, up to 10 weeks of gestation, with increasing β-human chorionic gonadotropin (β-hCG) levels. The ultrasound scan determined the gestational age based on the last menstrual period and the correlation with crown–rump length when an embryonic pole is visible. All patients were asymptomatic, hemodynamically stable and desired to preserve fertility. They all agreed to undergo medical treatment with the required follow-up and had no contraindications for MTX treatment. In some cases, pregnancy tissue embedded in the scar (following undetectable levels of β-hCG level) was extracted via surgical intervention[18–22].

The medical records of all identified cases were reviewed retrospectively, and information on demographics, obstetric and gynecological history was collected. All CDs were performed with a low-transverse uterine incision and the uterus was closed in two unlocked layers.

Saline contrast sonohysterography

All SCSH procedures were performed by a single experienced sonographer (Y.M.). All women were scheduled for SCSH before the 14th day of their ovulatory cycle and after the cessation of menstrual bleeding from their previous period. Exclusion criteria were: declined to participate; surgical repair of Cesarean section scar; unprotected intercourse; intrauterine device *in situ*; profuse vaginal bleeding; or inflammation or infection of the genital tract (e.g. pelvic inflammatory disease or suspected sexually transmitted diseases (purulent vaginal discharge upon speculum insertion), salpingitis or tubo-ovarian abscess). A flowchart summarizing inclusion of women in the study is shown in Figure 1. After signing the written informed consent, an initial transvaginal scan to detect pelvic pathologies was conducted.

Once the woman was in the supine position, a vaginal speculum was introduced to visualize the cervix. After the cervix and vagina were flushed with iodine solution, a balloonless catheter with a soft tapered tip was inserted into the endocervical canal. There was no use of a tenaculum or a cervical dilatator. A transvaginal ultrasound probe was introduced after removing the speculum to avoid moving the catheter. A basic pelvic scan was performed (Figure 2a) and then normal saline was introduced slowly into the uterine cavity via the catheter until satisfactory distension and visualization of the uterine cavity was achieved (Figure 2b).

All examinations were conducted on a Voluson E8 or an E10 ultrasound system equipped with a V5–9-MHz endovaginal probe (GE Healthcare, Zipf, Austria). The

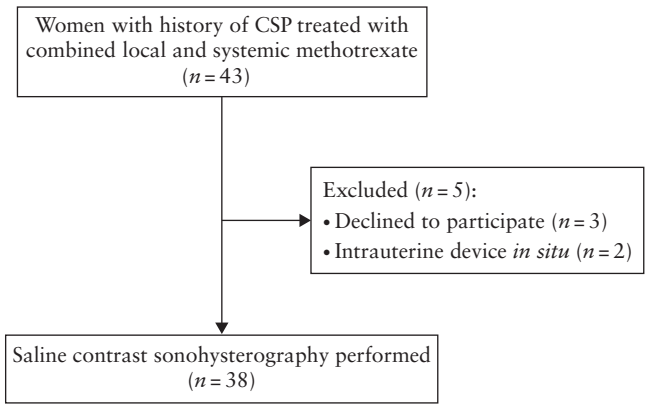

Figure 1 Flowchart summarizing inclusion of non-pregnant women with history of Cesarean scar pregnancy (CSP) in study population.

diagnosis of a niche was defined, according to the recent Delphi consensus, as an indentation at the site of the Cesarean scar with a depth of at least 2 mm[17]. Basic ultrasound measurements of the niche included length, depth and residual myometrial thickness (RMT) in the midsagittal plane.

For the purpose of analysis, women were classified, according to the modified Delphi consensus criteria for CSP in early gestation, into three subgroups based on the depth of the gestational sac herniation in the midsagittal plane[23]. Videoclips of CSPs were reviewed independently by two experienced sonographers (Y.M. and M.P.-Z.). After reviewing the videoclips, the CSPs were classified into the three subgroups[23]. Subgroup A included cases in which the largest part of the gestational sac protruded towards the uterine cavity, Subgroup B included cases in which the largest part of the gestational sac was embedded in the myometrium and Subgroup C included cases in which the gestational sac was located partially outside the outer contour of the cervix or uterus (Figure 3). There was 100% agreement between the two sonographers.

Statistical analysis

The SPSS version 25 (IBM Corp., Armonk, NY, USA) data package was used to analyze the data. The descriptive parameters are expressed as median (interquartile range) or as *n* (%). Mann–Whitney *U*-test with Bonferroni correction and Fisher–Freeman–Halton exact test were used for statistical comparisons as appropriate. A *P*-value < 0.05 was considered statistically significant.

RESULTS

During the study period, a total of 38 women who had been diagnosed with CSP and treated with combined local and systemic MTX underwent SCSH. Subgroup A included eight (21.1%) cases, Subgroup B included 20 (52.6%) cases and Subgroup C included 10 (26.3%).

The characteristics of the three groups are summarized in Table 1. The median gestational age at diagnosis of CSP was similar in all subgroups (6.1 (interquartile range (IQR), 6.1–6.4), 6.3 (IQR, 6.0–6.6), 6.3 (IQR, 6.0–6.6) weeks for Subgroup A, B and C, respectively; $P = 0.777$). There were no differences in maternal age, body mass index, gravidity, parity or previous CD across subgroups. The length of time from the previous CD to diagnosis of CSP was similar in all subgroups.

Comparison of ultrasound findings during SCSH is presented in Table 2. The median length of time from CSP to SCSH examination was similar in all subgroups (6.1 (IQR, 5.3–6.9), 6.0 (IQR, 5.1–6.7), 6.0 (IQR, 4.7–6.2) years for Subgroup A, B and C, respectively; $P = 0.799$).

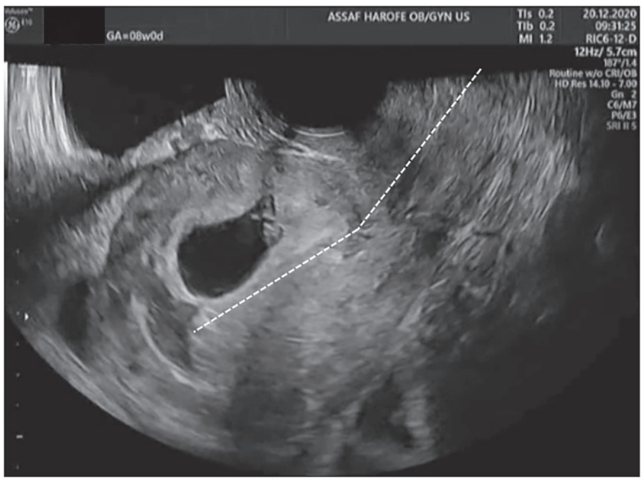

Figure 3 Grayscale transvaginal ultrasound image in midsagittal view showing Subgroup-C Cesarean scar pregnancy classified according to modified Delphi criteria[23], in which gestational sac protrudes over serosal line of uterus. ---, marking line through cervical canal and endometrial cavity.

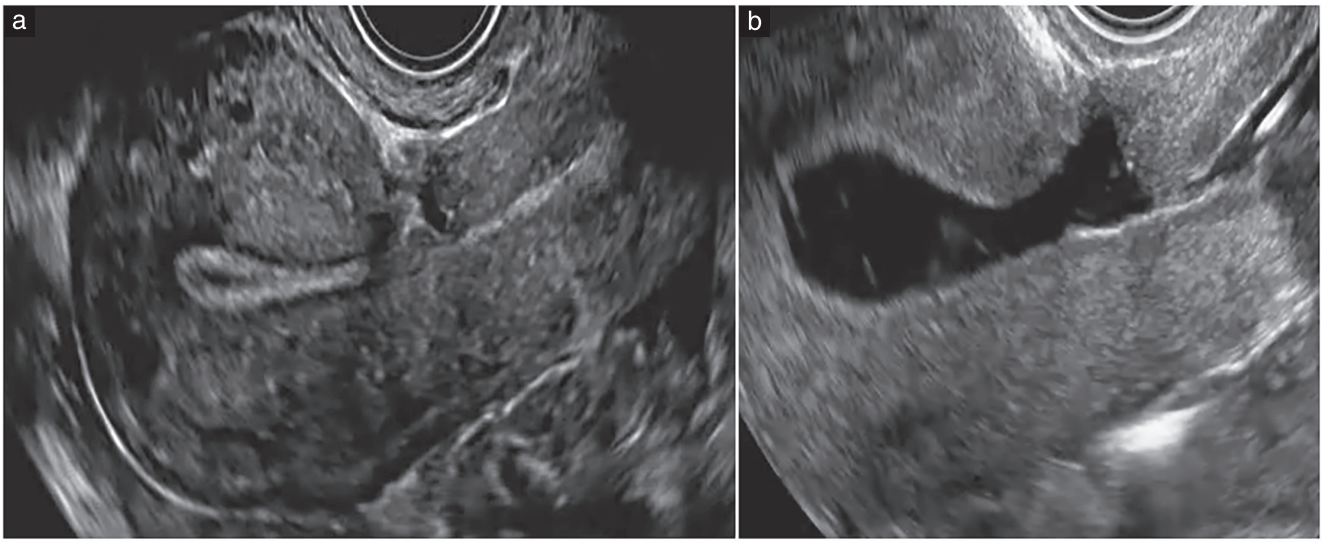

Figure 2 Grayscale transvaginal ultrasound images in midsagittal view showing: (a) uterus before saline contrast sonohysterography (SCSH) and (b) uterine niche on SCSH.

Table 1 Characteristics of 38 patients diagnosed with Cesarean scar pregnancy (CSP) treated with combined local and systemic methotrexate, according to classification by modified Delphi consensus criteria for CSP in early gestation[23]

Characteristic	*Subgroup A (n = 8)*	*Subgroup B (n = 20)*	*Subgroup C (n = 10)*	P*
Maternal age (years)	34.0 (32.0–37.5)	35.5 (33.0–39.0)	39.5 (39.0–42.2)	0.945
Body mass index (kg/m^2)	28.7 (25.0–30.0)	26.9 (25.1–33.0)	27.5 (25.4–30.0)	0.945
Gravidity	4 (3–5)	4 (3–5)	5 (4–6)	0.682
Parity	2 (2–3)	2 (2–3)	3 (2–4)	0.852
Number of CD	2 (2–3)	2 (2–3)	2 (2–3)	0.228
Interval from previous CD to CSP diagnosis (months)	33.5 (18.5–47.5)	26.0 (12.7–38.0)	25.0 (25.0–30.0)	0.237
GA at CSP diagnosis (weeks)	6.1 (6.1–6.4)	6.3 (6.0–6.6)	6.3 (6.0–6.6)	0.777

Data are given as median (interquartile range). *Mann–Whitney *U*-test with Bonferroni correction. CD, Cesarean delivery; GA, gestational age; Subgroup A, largest part of gestational sac protruded towards uterine cavity; Subgroup B, largest part of gestational sac embedded in myometrium; Subgroup C, gestational sac located partially outside outer contour of cervix or uterus.

Table 2 Ultrasound findings during saline contrast sonohysterography (SCSH) to evaluate Cesarean scar or niche in 38 patients, according to classification by modified Delphi consensus criteria for Cesarean scar pregnancy (CSP) in early gestation[23]

Parameter	*Subgroup A (n = 8)*	*Subgroup B (n = 20)*	*Subgroup C (n = 10)*	P
Interval from CSP to SCSH (years)	6.1 (5.3–6.9)	6.0 (5.1–6.7)	6.0 (4.7–6.2)	0.799*
Anteflexed uterine position	6 (75)	16 (80)	5 (50)	0.226†
Niche	2 (25)	12 (60)	10 (100)	0.002†
Niche length (mm)	5.2 (4.2–6.7)	9.6 (7.0–13.7)	14.5 (12.2–16.5)	0.006*
Niche depth (mm)	4.1 (3.2–4.3)	5.0 (4.0–6.2)	9.1 (8.3–10.3)	0.015*
Mean RMT of scar or niche (mm)	5.5 (3.6–6.3)	2.8 (2.0–3.9)	1.9 (1.4–2.1)	0.006*

Data are given as median (interquartile range) or *n* (%). *Mann–Whitney *U*-test with Bonferroni correction. †Fisher–Freeman–Halton exact test. RMT, residual myometrial thickness; Subgroup A, largest part of gestational sac protruded towards uterine cavity; Subgroup B, largest part of gestational sac embedded in myometrium; Subgroup C, gestational sac located partially outside outer contour of cervix or uterus.

All Subgroup-C women were found to have a uterine niche during SCSH examination (Figure 3). The median niche length ($P = 0.006$) and depth ($P = 0.015$) were significantly greater in Subgroup C than in Subgroups A or B. The median RMT was significantly lower in Subgroup C than in Subgroups A or B ($P = 0.006$).

DISCUSSION

Using the classification proposed by the CSP taskforce[23], we found that all women with a history of CSP in which the gestational sac protruded over the serosal line in the midsagittal plane presented with a uterine niche on SCSH and were more likely to have greater niche length and depth, and smaller RMT than those who had the largest part of the gestational sac protruding towards the uterine cavity or embedded in the myometrium.

Overall recurrence rate in women with previous CSP can vary across studies (9–25%)[24–27]. Timor-Tritsch *et al.*[28] found a higher rate of 34.3% and Ben Nagi *et al.*[29] argued that a very large niche could be the cause of CSP after CD. They noted, however, that a recurrence is 'more likely to be a chance event rather than being caused by a particular affinity of the pregnancy to implant into the deficient scar'. To diminish the risk of repeated CSP, Hasegawa *et al.*[30] suggested repairing uterine scars to reduce the dangers of recurrent CSP. By contrast, Ben Nagi *et al.*[29] argued that surgical correction of a CD niche involved its own numerous complications and could be more detrimental than beneficial to women hoping to preserve their fertility. Qian *et al.*[31] concurred and suggested that only large uterine defects should be repaired in recurrent instances or as a step to preserve fertility.

Several other factors are also suspected of having a direct impact on niche development. These include a retroverted uterus, multiple CDs and the split-thickness suturing technique (which excludes the endometrial layer)[6,32,33]. Other possible factors that could play a role in niche development include a very low incision through cervical tissue, inadequate suturing technique during closure of the uterine scar, surgical interventions that increase adhesion formation, or patient-related factors that impair wound healing or increase inflammation or adhesion formation[34].

In a previous study[18], we applied the CSP taskforce standardized sonographic evaluation criteria[23] and found that women who had a CSP in which the gestational sac protruded over the serosal line in the midsagittal plane tended to exhibit higher β-hCG levels at admission, required higher rates of repeated doses of MTX and surgical intervention, and longer hospital stays. These findings make it clear that applying the Delphi consensus criteria in cases of CSP in early gestation is valuable in clinical practice by guiding the determination of risk of adverse outcome. However, the findings of the current study showed that patient characteristics, which include patient age, body mass index, gravidity, parity or previous CD, were not different across subgroups and less likely to contribute to risk stratification for CSP implantation. The use of Delphi criteria may actually help providers stratify patients in terms of their risk of severe maternal morbidity and identify potential candidates for expectant management

vs immediate treatment. This may guide individualized risk counseling as to the likelihood of the development of a Cesarean scar defect, risk of recurrence of the CSP and indication for scar repair, and improve dialogue between physicians, who can use the same nomenclature.

This study has a number of strengths. The first is its prospective design and that the authors were blind to the identificatory data when applying the consensus criteria of the CSP taskforce[23]. The use of the taskforce criteria served to avoid the problem of differences in the definitions of what constitutes a CSP and its outcome, which could lead to selection bias. The small sample size is the major limitation of this study, since there were relatively small numbers of women in each arm, which limits the generalizability of the findings. It is also of note that the follow-up SCSH scans were conducted at different times after CD. This precluded us from generating longitudinal data on the possible evolution of the Cesarean scars and uterine niches over time after hysterotomy.

In conclusion, we have found that the subgroup of CSPs that protrude beyond the serosal line (Subgroup C) had a significantly larger and deeper niche, and presented with a lower median RMT compared with those CSPs embedded in the myometrium or protruding towards the uterine cavity, which may guide individualized risk counseling. Further studies are needed to confirm our findings.

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