

Gynecological and obstetrical outcomes after laparoscopic repair of a cesarean scar defect in a series of 38 women

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Objective: To evaluate gynecological and obstetrical outcomes, as well as remaining myometrial thickness, after laparoscopic repair of a cesarean scar.

Design: Observational study and prospective evaluation of the remaining myometrium before and after repair.

Setting: Academic department in a university hospital.

Patient(s): A series of 38 symptomatic women with cesarean scar defects and remaining myometrial thickness of less than 3 mm, according to magnetic resonance imaging.

Intervention(s): Laparoscopic repair of the defect.

Main Outcomes Measure(s): Increase in myometrial thickness at the site of cesarean section, gynecological and obstetrical outcomes, and histological analysis of the defect after excision.

Result(s): The mean thickness of the myometrium increased significantly from 1.43 ± 0.7 mm before surgery to 9.62 ± 1.8 mm after surgery. All but three patients were free of symptoms. Among the 18 women with infertility, eight (44%) became pregnant and delivered healthy babies by cesarean section at 38–39 weeks of gestation. Histological analysis, performed in all 38 cases, revealed the presence of endometriosis in eight women (21.1%). Muscle fiber density was significantly lower compared with adjacent myometrium.

Conclusion(s): In symptomatic women with residual myometrial thickness of less than 3 mm who wish to conceive, laparoscopic repair could be considered an appropriate approach. (Fertil Steril® 2017;107:289–96. ©2016 by American Society for Reproductive Medicine.)

Key Words: Cesarean scar defect, niche, laparoscopic repair, hysteroscopy, myometrial thickness

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Over recent decades, the number of cesarean sections (CSs) has continued to rise worldwide.

In the United States, the proportion of CSs performed in 2007 was over 30%

(1–4), while rates in China climbed as high as 35%–58% in 2010 and up to 80% in the private sector in Brazil.

This growing CS rate has stimulated interest in a frequently encountered

morbidity described as a cesarean scar defect, also termed “niche” by some authors (5, 6).

Anomalies in a cesarean scar can be visualized by hysterosalpingography, transvaginal sonography (TVS), saline infusion sonohysterography (SIS), hysteroscopy, and magnetic resonance imaging (MRI) and are characterized by a defect within the myometrium, reflecting a breach at the site of a previous CS (7, 8) (Fig. 1).

CS scar defects are increasingly described, and the reported incidence is as high as 61% after one CS, reaching 100% in women undergoing at least three (9).

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O.D. has nothing to disclose. J.D. has been a member of the Scientific Advisory Board (SAB) of PregLem S.A. since 2007; held PregLem stocks related to SAB activities that were sold in October 2010 upon PregLem's full acquisition by the Gedeon Richter Group; there is no relationship between the stock payment value and future commercial performance of the studied drug. R.O. has nothing to disclose. M.-M.D. has nothing to disclose.

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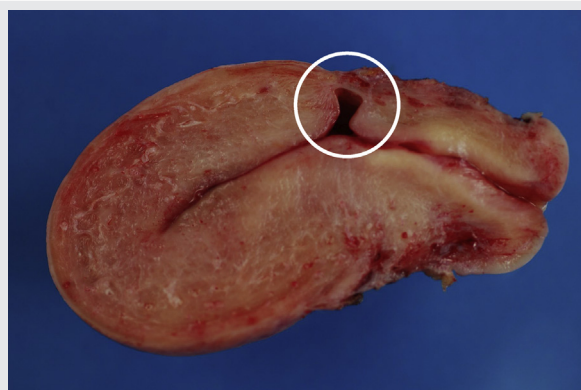
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FIGURE 1



Sagittal view of a frozen section from a hysterectomy specimen. A deep anterior defect covered with a thin layer of myometrium (white circle) can be observed at the level of the supposed site of CS.

Donnez. Laparoscopic repair of cesarean scar defects. *Fertil Steril* 2016.

The most useful discriminating measurement is the thickness of the remaining myometrium (9, 10). Although the risk of cesarean scar defects remains unclear, there is obviously an association between large defects detected in nonpregnant women and dehiscence or uterine rupture in subsequent pregnancy (odds ratio [OR], 11.8; 95% confidence interval [CI], 0.7–746) (10). The risk of uterine rupture or dehiscence was reported to be even higher in another study in women with large defects (OR, 26.05; 95% CI, 2.36–287.61) (11).

In a review, Bij de Vaate et al. (12) defined niches as large when the remaining myometrial thickness was 2.5 mm based on SIS evaluation, while Bujold et al. (13) determined a lower uterine segment median value of 2.8 mm as the cutoff for risk of uterine rupture. A cutoff value of 3 mm was chosen by Donnez et al. (7) and Marotta et al. (14) on the basis of MRI evaluation.

Intermenstrual spotting, dysmenorrhea, dyspareunia, and chronic pelvic pain are the most commonly observed symptoms. According to the literature (15–17), subsequent fertility may be impaired, with the risk of infertility estimated to be between 4% and 19%. Accumulation of mucus or blood in the defect, leading to the presence of intrauterine fluid, could prevent penetration of sperm cells or embryo implantation (12,15–18).

The first laparoscopic repair of a uteroperitoneal fistula caused by CS was performed by the group of Nezhat (19). Laparoscopic repair of large defects was subsequently described by Donnez et al. in 2008 (7), showing an increased risk of uterine rupture, and the first series of 13 patients was reported several years later (14).

In the present paper, we report the largest series ($n = 38$) of symptomatic women who have undergone laparoscopic repair of large cesarean scar defects with a remaining myometrium of less than 3 mm. This series incorporate patients from prior small series of the same group. All of them were evaluated both pre- and postoperatively by MRI. This is also the first study reporting histological data on cesarean scar defects.

MATERIALS AND METHODS

No Institutional Review Board approval was required for this study. The surgical technique was first described by the authors (7) in 2008 and later recognized as an appropriate approach for correction of the CS defects in symptomatic patients (14). The present study is a prospective evaluation of a larger series.

The characteristics of the 38 patients are summarized in Table 1 (this number includes the previously reported series of 13 women). Twenty-five of them had undergone one CS, 12 had undergone two CSs, and one had undergone three. Only one patient had experienced a vaginal delivery, followed by two CSs.

Patients were selected according to their symptoms (bleeding, pain, or infertility) and the presence of a remaining myometrium measuring less than 3 mm at MRI evaluation (Fig. 2A–2C). All the women underwent TVS and MRI to preoperatively evaluate the defect and thickness of the remaining myometrium (Table 1). Correction of the defect was proposed to patients who were fully informed about the procedure and possible surgical outcomes, as reported in our previous papers (7, 14). All patients consented to participate after receiving clear information on the advantages and disadvantages of both hysteroscopic and laparoscopic approaches. As stated by Nezhat et al. (20), standard practice would have involved performing hysteroscopic resection of the defect in patients who no longer wished to conceive (20, 21). However, in our series, hysteroscopic resection was not offered due to the risk of bladder injury and uterine perforation in patients with myometrial thickness of less than 3 mm. This was clearly stated in one of our previous papers (14).

Surgical Technique

All surgical procedures reported in this series were performed by two of the authors (J.D., $n = 4$; and O.D., $n = 34$). The complete surgical technique is described in detail in one of our previous publications (8), but the most important steps of the procedure are summarized below.

Using CO₂ laser (Lumenis-Sharpplan), we opened up the scar from one end to the other (Supplemental Fig. 1A). Fibrotic tissue was then excised from the edges of the defect (Supplemental Fig. 1B) to access healthy myometrium and facilitate further healing. Before closing the defect, a Hegar probe was inserted into the cervix to preserve the continuity of the cervical canal with the uterine cavity. For the first layer, three separate sutures were placed to close the scar using 2-0 Vicryl SH (Johnson & Johnson; Supplemental Fig. 1C). A second layer of separate stitches was applied to achieve double-layer closure. The peritoneum was then closed using Monocryl 0 MH+ (Johnson & Johnson) running suture (third layer; Supplemental Fig. 1D). Vervoort et al. (22) suggested that retroflexion of the uterus may impair wound healing after CS and encourage formation of cesarean scar defects. For this reason, the round ligaments were shortened bilaterally in case of a retroflexed uterus. At the end of surgery, hysteroscopy was performed to visualize the repair of the cervical

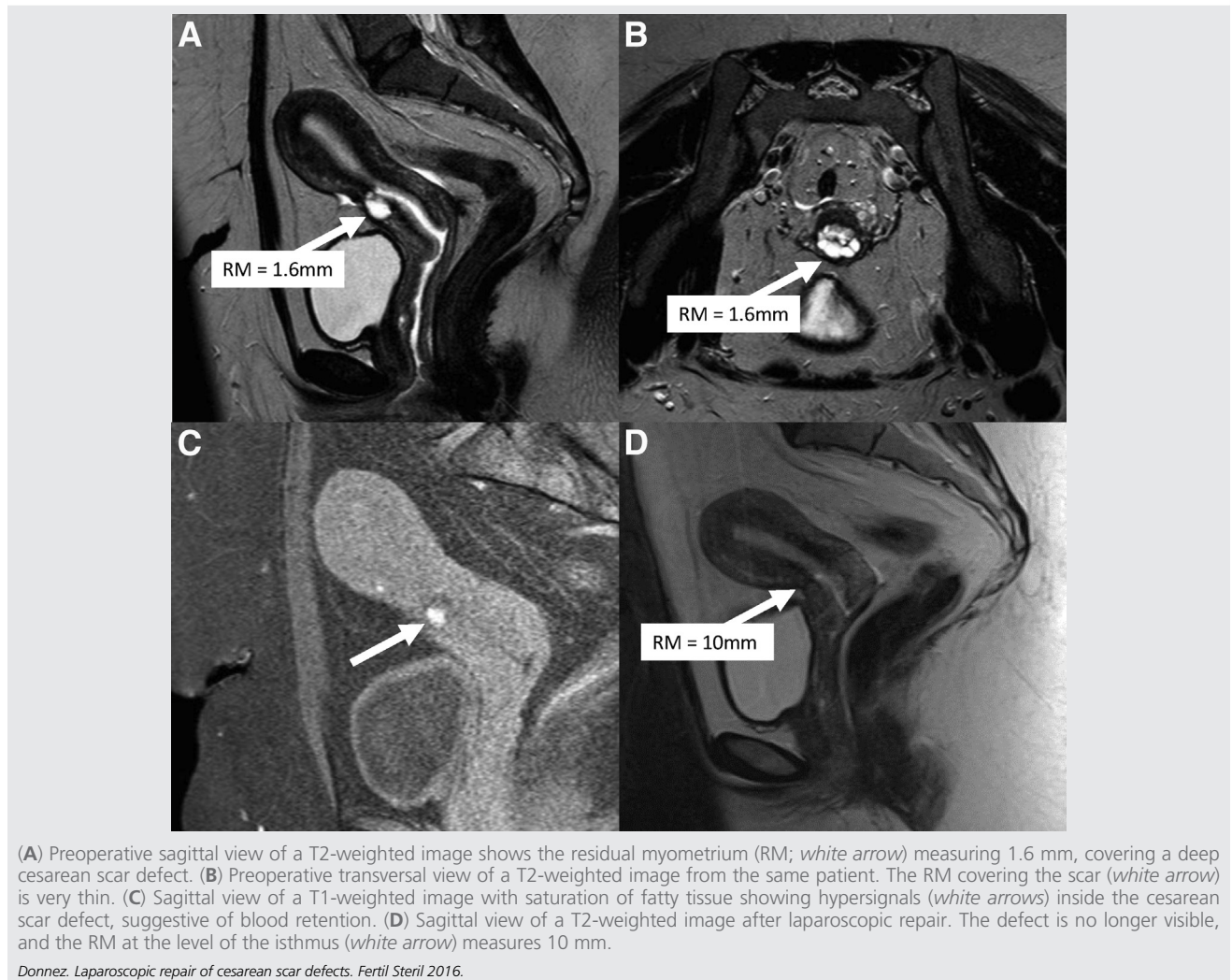
TABLE 1

Symptoms and preoperative and postoperative evaluation of the remaining myometrium by vaginal ultrasound and MRI, histological analysis.

Patient	Age (y)	Previous CS	Infertility	Symptom	Preoperative residual myometrium (mm)		Anatomopathology measure (mm)	Anatomopathology findings	Postoperative (mm) MRI	Pregnancy after laparoscopic repair
					Ultrasound	MRI				
1	32	1	+	IMB, infertility	0.8	1	NA	Fibrosis	11	CS 38w5
2	33	1	+	IMB, infertility	NA	2.2	2.27	Fibrosis	8.3	3 CS at 38w, 38.3w, and 38.4w
3	33	2	+	DIII, IMB, CPP, infertility	1.6	2.2	1.74	Endometriosis	8.9	CS 39w
4	35	2	+	Infertility	1.5	2.7	1.09	Fibrosis	11.2	CS 38.5
5	32	1	+	Infertility	0.0	0	0	Fibrosis	8.4	CS 38.3
6	37	1	+	DII, IMB, DDP, infertility	NA	0	0.2	Fibrosis	11.7	CS 38.2
7	29	1	+	CPP, infertility	1.0	0.9	1.1	Fibrosis	7.2	CS 38.5
8	42	1	+	IMB, infertility	1.3	1.3	1.24	Fibrosis	9.1	CS 34w3
9	32	1	+	IMB, infertility	NA	1.6	NA	Fibrosis	10.5	
10	31	2	+	Infertility	NA	0.7	0.81	Endometriosis	9.3	
11	35	1	+	IMB, infertility	0.0	0.7	0.5	Fibrosis	8.7	
12	28	2	+	DIII, IMB, CPP, infertility	NA	1.9	1.06	Endometriosis	10.9	
13	22	1	+	DDP, infertility	NA	1.6	1.53	Endometriosis	10	
14	33	1	+	Infertility	1.0	1.7	0.91	Endometriosis	10	
15	37	1	+	DI, Méno, IMB, CPP, infertility	3.0	1.7	1.5	Fibrosis	9.1	
16	42	2	+	Infertility	2.5	1.7	0.82	Fibrosis	11.3	
17	40	1	+	DIII, infertility	2.5	2.1	2	Fibrosis	11.6	
18	36	1	+	DII, Méno, IMB, infertility	2.5	2.3	2.69	Endometriosis	8.2	
19	39	1		CPP, DII, IMB,	1.9	2	2	Fibrosis	6.4	
20	33	1		DIII, IMB, CPP, DDP	NA	0.9	0.45	Fibrosis	11.4	
21	28	2		DIII, IMB, CPP	NA	2.3	2.59	Endometriosis	10.4	
22	31	3		DIII, IMB, CPP, DDP	1.6	1.8	1.7	Fibrosis	5	
23	33	1		DII, CPP	3.2	1.5	1	Fibrosis	9.8	
24	30	2		CPP	0.8	0.8	NA	Fibrosis	9.4	
25	36	2		CPP	2.1	2.1	NA	Fibrosis	10.1	
26	27	1		DIII, CPP, DDP	NA	0	1.52	Fibrosis	9.5	
27	21	2		DIII, DDP	0.0	1.1	1.21	Fibrosis	12.7	
28	44	1		Méno, IMB, DDP	1.3	2.4	0.66	Fibrosis	11.2	
29	31	1		DIII, CPP, IMB	3.2	2.6	2.5	Endometriosis	8.3	
30	40	1		DIII, IMB, CPP	1.2	1.1	1.4	Fibrosis	9	
31	32	2		DIII	2.2	2	2.27	Fibrosis	6.9	
32	31	2		CPP, IMB, DDP	1.8	0	1.77	Fibrosis	10.7	
33	33	1		CPP, IMB	2.4	1.8	2.64	Fibrosis	5.7	
34	18	1		DDP, DIII IMB	2.0	1.1	2	Fibrosis	10.1	
35	25	1		IMB, CPP	4.1	2	1.5	Fibrosis	11.2	
36	29	1		CPP	1.9	0.9	3	Fibrosis	11	
37	32	1		DIII, IMB, CPP	1.1	0.9	0.8	Fibrosis	10.5	
38	35	2		DIII, CPP, IMB	0.0	0.4	0.5	Fibrosis	12	
Mean	32.6				1.7	1.4210526	1.440294118		9.65	
SD	5.631				1.05293744	0.7644669	0.770641155		1.771966384	

Note: CPP = chronic pelvic pain; CS = cesarean section; DDP = deep dyspareunia; DI = grade I dysmenorrhea (tolerable pain, without pain killers); DII = grade II dysmenorrhea (moderate pain, justifying oral pain killers); Méno = menorrhagia; w = weeks of gestation; NA = not available.

Donnez. Laparoscopic repair of cesarean scar defects. *Fertil Steril* 2016.

FIGURE 2

canal, which showed complete correction of the defect and normal patency of the cervix. All the patients were discharged from hospital within 24 hours of surgery. After a period of 3 months and subsequent pelvic MRI, the women were told they could attempt pregnancy.

Histology

Histology was done in all patients, while immunohistochemical analyses were performed in the last 26 patients of the series (26/38) to evaluate the muscular density of the remaining myometrium and the presence of ectopic endometrial tissue. Two areas were evaluated: myometrium covering the scar and myometrium directly adjacent to the scar. A comparison was made with eight patients (control group) who had previously undergone CS without developing a cesarean scar defect and had been treated by laparoscopic hysterectomy for intramural fibroids located more than 3 cm from the scar. These patients were aware of the specific analysis carried out at the level of CS scar and consented. Even though the

number was low (which could constitute a limitation), this control group was homogeneous (women with intramural fibroids) with a history of CS without cervical or endometrial pathology. Moreover, the number of subjects allowed statistical analysis. Hematoxylin-eosin was used for histology, and specific actin antibody for immunohistochemistry (monoclonal mouse anti-human smooth muscle actin; Dako). All sections were scanned with the Leica SCN400 scanner (Leica Biosystems), and image acquisition was performed with the Tissue IA system (Leica Biosystems). Image J software was applied for immunohistochemical quantification and morphological analysis, using the color deconvolution plugin to isolate the DAB channel.

RESULTS

Symptoms

The main complaints were bleeding or spotting, chronic pelvic pain, dyspareunia, and dysmenorrhea. Indeed, an association of dysmenorrhea, chronic pelvic pain, and intermenstrual

bleeding (or spotting) is frequently encountered and was observed in 12 women in our series (31%) (Table 1). Fifteen women presented with an association of two of the symptoms, four complained of chronic pain, one had dysmenorrhea, and one experienced only intermenstrual bleeding. Five women showed no symptoms of pain or abnormal bleeding, but these five patients presented with secondary infertility (with no explanation other than the defect). According to our previously published criteria (14), they were considered to be suitable candidates for laparoscopic repair, as there were no other identifiable causes of infertility in these five couples.

Remaining Myometrial Thickness

Ultrasound (TVS) revealed a mean myometrial thickness of 1.7 ± 1 mm (median, 1.6 mm; range, 0–3.2 mm). All of the women also underwent preoperative MRI, yielding a mean thickness of 1.4 ± 0.7 mm (median, 1.5 mm; range, 0–2.7 mm; Fig. 2A–2C). Five patients had no visible myometrium (thickness evaluated at 0 mm).

MRI confirmed a normal pelvis in all cases. On T1-weighted images with saturation of fatty tissue, hypersignal spots (Fig. 2C) were detected in the niche due to the presence of residual menstrual blood in 34 patients (89%). In the other four cases, the signal was present, but less intense, revealing the presence of mucus.

All operated women underwent MRI 3 months after surgery. The mean thickness of the myometrium was 9.6 ± 1.8 mm (median, 9.5 mm; range, 5–11.6 mm; Fig. 2D). This thickness was significantly increased ($P < .001$) compared with values before surgery.

Follow-up from 1 Year to 6 Years

In this series, all but three patients, all of whom had experienced pain and/or bleeding before surgery, were free of symptoms. We thus observed a 91% rate of symptom relief among the 33 patients presenting with pain and/or bleeding. One of the limitations of this follow-up is that the symptomatology was not assessed by means of an anonymous questionnaire evaluating objective data. Nevertheless, the fact that only three patients required repeat surgery could be considered an objective criterion.

Two patients continued to experience pelvic pain despite laparoscopic repair, and MRI detected the presence of blood at the level of the CS scar, with the residual myometrium measuring 11.2 mm and 11.7 mm. Because the thickness remained significantly increased, hysteroscopic resection was performed, yielding symptom relief and resulting in conception in one of the patients within 4 months. The other woman had no desire for pregnancy.

One patient presented with aggravation of pain and dysmenorrhea after laparoscopic repair and underwent laparoscopic hysterectomy. MRI revealed residual myometrium measuring 5 mm, with the defect much larger than before surgery. As the patient had undergone three previous CSs and did not wish to conceive again, further correction was not proposed and laparoscopic hysterectomy was performed.

Among the 18 patients consulting for infertility alone ($n = 5$) or infertility associated with pain and/or bleeding ($n = 13$), eight (44.4%) became pregnant, and all of them delivered healthy babies by CS at 38–39 weeks of gestation. One of the women underwent three CSs after the repair.

Histology

Histological analysis was performed in all 38 cases, yielding similar results to MRI. Indeed, at histological analysis, the mean thickness of the myometrium covering the scar was 1.44 ± 0.77 mm, comparable to preoperative MRI measurements. In 30 cases (78.9%), pathological findings revealed the presence of fibrotic tissue. The remaining eight cases (21.1%) showed signs of endometriosis (Fig. 3C), defined as the presence of endometrial glands inside the scar unconnected to the endometrial surface on serial sections. Endometriosis was evidenced in 25% ($n = 6/24$) of patients presenting with pain and/or bleeding and 40% ($n = 2/5$) of patients presenting with infertility alone.

The muscular density of the residual myometrium covering the scar (Fig. 3A and 3B) was found to be significantly lower ($P < .001$) than that of healthy myometrium directly adjacent to the scar (Supplemental Fig. 2). In the control group, however, the two were not statistically different ($P = .2786$).

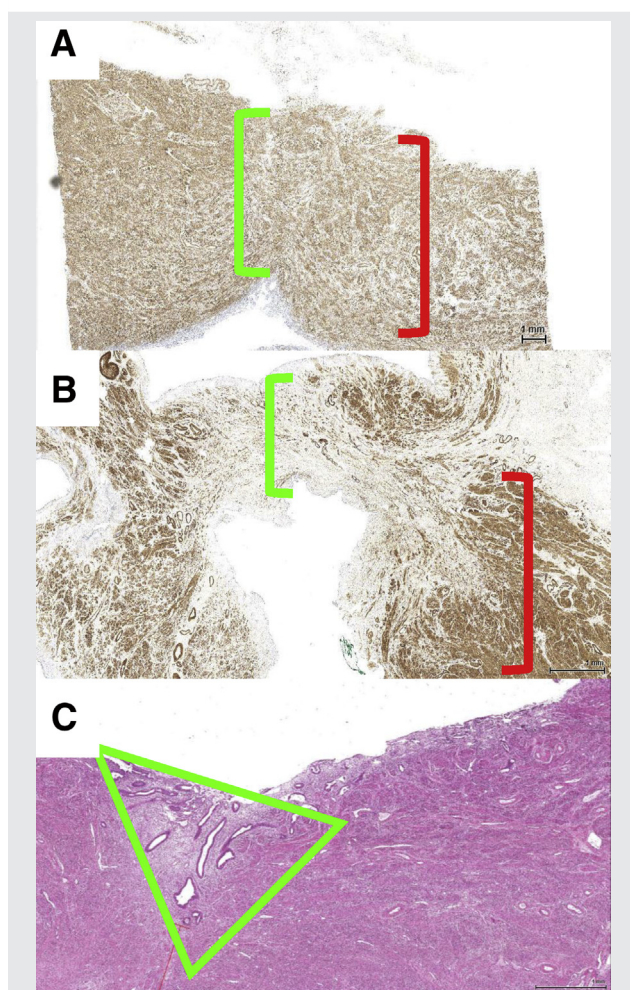
DISCUSSION

Worldwide, CS rates are on the rise, resulting in increasing obstetrical sequelae, such as placenta accreta, scar dehiscence, and ectopic scar pregnancy due to incomplete healing of the CS incision. Described for the first time as an “isthmocoele” by Morris in 1995 (23), a defect on the anterior wall of the uterine isthmus located at the site of previous CS is also known as a “cesarean scar defect” or “niche.” As reported by Vervoort et al. (22), a number of hypotheses may explain cesarean scar defect development: [1] a very low incision through the cervical tissue; [2] inadequate suturing or incomplete closure of the uterine wall due to a single-layer endometrial-saving closure technique or use of locking sutures; and [3] surgical interventions that encourage adhesion formation (namely, nonclosure of the peritoneum, inadequate hemostasis, visible sutures, etc.).

Gynecological sequelae, such as abdominal bleeding, chronic pelvic pain, dysmenorrhea, dyspareunia, and infertility, have also been increasingly reported in the last decade in case of cesarean scar defects. Collection of menstrual blood in the uterine defect, with intermittent passage through the cervix, may explain the occurrence of vaginal bleeding or spotting. Retention of blood inside the uterine scar defect can originate from endometriotic lesions but also from typical hypervascularization (14) or the inability of the myometrium covering the defect to exhibit sufficient contractility to expel blood from endometrial shedding during menstruation. This might be due to the significant decrease in muscular density we observed in the myometrium covering the defect compared with adjacent myometrium (present paper).

This is the first time that microscopic residual myometrium has been correlated to ultrasound and MRI

FIGURE 3



(A) Actin immunostaining in a hysterectomy specimen. The muscular density of the myometrium covering the cesarean scar (green bracket) is similar to adjacent healthy myometrium (red bracket). (B) Actin immunostaining in an excised cesarean scar defect. The muscular density of myometrium covering the cesarean scar (green bracket) is significantly decreased compared with adjacent healthy myometrium (red bracket). (C) Microscopic appearance of a cesarean scar defect (hematoxylin-eosin staining). Endometriotic glands (green triangle) can be seen in the myometrium covering the scar.

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measurements. MRI and ultrasound are thus appropriate tools to determine the thickness of residual myometrium. Moreover, we found 21.1% of endometriotic lesions inside resected tissue. These results confirm those of Tanimura et al. (24), who observed 27.2% of endometrial glands and stroma in the deepest part of the scar defect. These endometriotic lesions may well be responsible for pain and dysmenorrhea, but also for blood retention due to abnormal bleeding. However, 78.9% of resected specimens in our series revealed only fibrotic tissue, demonstrating that other mechanisms can influence pain and abnormal bleeding. The presence of hyper-vascularized areas and dendritic vessels with hemorrhage, observed by the same authors (14, 24) at hysteroscopy,

could suggest that the bleeding originates from the scarred area. The virtual absence of remaining myometrium as well as the very low muscular density encountered in the present study may explain the retention itself and why the accumulation remains permanent. Fertility might be impaired by the presence of fluid, blood, or mucus in the cervical canal or uterine cavity, interfering with penetration of sperm cells and blastocyst implantation (25, 26). This toxic environment could be responsible for the decrease in fertility, even though the association between a cesarean scar defect and infertility has never been proved owing to the absence of studies on this particular topic. Nevertheless, some mechanisms may be speculated to play a role. Bloody fluid or bleeding from the cesarean scar flows into the vagina and also the uterine cavity, which could result in infertility via a process similar to hydrosalpinx (27). The cytotoxicity of iron is well known, and an excess of iron after degradation of hemoglobin in the uterine cavity (28, 29) may be embryotoxic and/or impair embryo implantation via disturbed endometrial receptivity, as in case of endometriosis (26) or disrupted expression of the cytokine cascade (24).

A recent meta-analysis of 85,728 women who underwent CS (13) found the probability of future pregnancy to be reduced by 10% compared with vaginal delivery. In another retrospective analysis including 1,047,644 women, the same authors (14) evaluated the risk of subsequently decreased fertility according to the indication for and type of CS performed. This risk was evaluated to be 4% in case of CS for breech presentation, 19% for other indications, and 9% in case of emergency CS.

As stressed by Vervoort et al. (22), even if the true figure reflecting the decline in fertility is probably closer to 4% than 19%, it nevertheless has a considerable impact in view of the large numbers of CSs performed globally.

In the present series, only symptomatic women complaining of abnormal uterine bleeding and pain and/or infertility were included, as there is no consensus on the treatment of asymptomatic women (14, 20, 21). Moreover, the cutoff to decide the need for surgery was the thickness of the remaining myometrium covering the defect (7, 14). The main argument in favor of this cutoff threshold was the risk of uterine rupture or dehiscence in case of large defects when the residual myometrium measured ≤ 2.2 mm (10, 30). Sen et al. proposed a critical cutoff value of 2.5 mm to allow trials of labor after CS (31). In our study, all the women had a remaining myometrial thickness of ≤ 2.7 mm, with 36 of the 38 showing a figure of ≤ 2.5 mm. Of course, the majority of women exhibit myometrial thickness of more than 3 mm after several CSs, but our study was limited to women with a remaining thickness less than 3 mm to have a homogeneous group of symptomatic women. The mean value determined by MRI was 1.4 ± 0.77 mm (1.5 mm by ultrasound).

The advantages of MRI are reproducibility of measurements and a clearer view of the defect before surgery. However, its use may be disputed, as preoperative residual thickness values were found to be similar by both MRI and ultrasound. Further studies are needed to identify the most accurate

means of imaging, taking into account the cost-effectiveness of both methods.

Concerning the surgical approach, resection of the cesarean scar defect is the most commonly reported technique (18–21, 26, 32–35). Hysteroscopic and laparoscopic approaches were reviewed by Api et al. (21), who concluded that hysteroscopic treatment most likely corrects the scar defect but does not strengthen the uterine wall, while laparoscopic repair of the defect may potentially reinforce myometrial endurance.

In a review of the literature, Api et al. (21) reported that existing evidence on the management of cesarean scar defects is mostly based on case series. There is still no clear evidence to confirm whether laparoscopy is as effective as or superior to hysteroscopy.

In our series of 38 cases, all the women underwent pre- and postoperative MRI. Residual myometrial thickness increased from 1.4 ± 0.76 mm to 9.6 ± 1.8 mm, proving adequate reinforcement of the myometrium. We thus confirm that our surgical technique, described for the first time in 2008, is able to restore the thickness of the anterior uterine wall. In our series, we were able to achieve 9.65 ± 1.77 mm of residual myometrium covering the scar after correction. These results are comparable to those obtained by Tanimura et al. (24) but superior to those achieved by Chang et al. (34). However, despite residual myometrial thickness being considered the best discriminating factor (9, 10, 31), this important information was missing from the last series of Zhang et al. (36) and Li et al. (37). Our technique is also associated with high success rates in terms of symptoms, as 91% of our patients were asymptomatic after laparoscopic repair. Only two women underwent hysteroscopic resection to treat residual intermenstrual bleeding, despite a good anatomical result, and one of them was able to achieve pregnancy. It is important to note one serious failure occurring in a patient with three previous CSs. The myometrium was unable to heal correctly, which could have been due to excessive fibrotic tissue surrounding the scar or the inability of the surgeon to distinguish healthy tissue after three CSs.

Our personal series proved, on the basis of MRI evaluation in all cases, that the laparoscopic approach not only eliminates the cesarean scar defect but also strengthens the myometrial wall. In this series, eight women (44.4%) conceived and subsequently delivered by CS. As these women were followed in other institutions, no data are available on myometrial thickness during pregnancy, but none of them showed the presence of uterine dehiscence during pregnancy (ultrasound evaluation) and at surgery (repeated CS for all deliveries). We nevertheless acknowledge that the clinical benefits of increased myometrial thickness could not be evaluated during labor, as all of them underwent CS.

Most series on hysteroscopic management do not provide any information (18,19, 26, 32–35) on residual myometrial thickness before and after surgery, although myometrial thickness before and after hysteroscopy was reported to be similar in a series of 24 women treated by hysteroscopy (4.4 mm vs. 5.3 mm) (21).

Gubbini et al. (25, 26) published their prospective series of 37 patients who delivered by CS after hysteroscopic resection at the level of the cesarean scar defect. Unfortunately, as the

investigators failed to provide information on residual myometrial thickness before and after surgery, no conclusions could be drawn on the efficacy of the technique in terms of preventing uterine dehiscence or rupture. We do, however, agree with Tanimura et al. (24) and Nezhat et al. (20) that hysteroscopic resection should not be undertaken when residual myometrial thickness is less than 2.5–3 mm, as the risk of anterior wall perforation and subsequent bladder injury remains a real concern.

Conclusions

In symptomatic women with residual myometrial thickness of less than 3 mm who wish to conceive, laparoscopic repair should be proposed, as it was demonstrated that it significantly strengthens the myometrial wall. In case of symptoms like dysmenorrhea, bleeding, or pelvic pain, hysteroscopic resection may be carried out if the residual thickness is more than 3 mm.

Of course, in case of incidental diagnosis in asymptomatic women, surgery is not recommended. Nevertheless, as stated by Nezhat et al. (20), asymptomatic women who wish to conceive in the future may also require surgical repair owing to the high risk of uterine rupture, and the pros and cons should at least be discussed with the patient. More studies are clearly needed to shed further light on this specific issue.

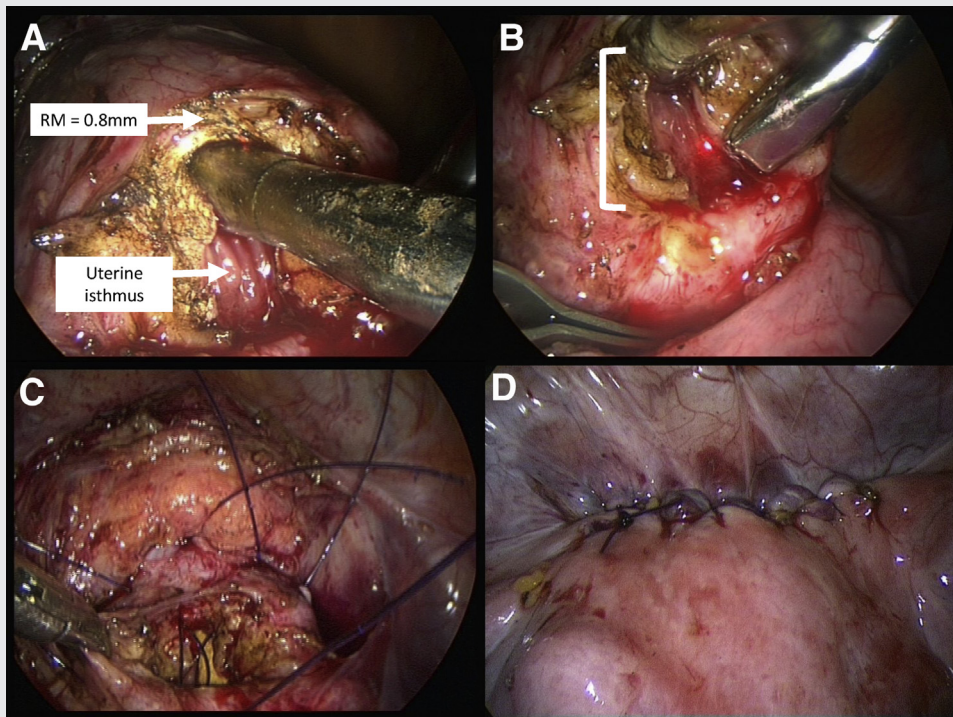
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REFERENCES

1. Souza JP, Gülmezoglu A, Lumbiganon P, Laopaiboon M, Carroli G, Fawole B, et al, the WHO Global Survey on Maternal and Perinatal Health Research Group. Cesarean section without medical indications is associated with an increased risk of adverse short-term maternal outcomes: the 2004–2008 WHO Global Survey on Maternal and Perinatal Health. *BMC Med* 2010;10:71.
2. Hamilton BE, Martin JA, Osterman MJ, Curtin SC, Matthews TJ. Births: final data for 2014. *Natl Vital Stat Rep* 2015;64:1–64.
3. Martin JA, Hamilton BE, Ventura SJ, et al. Births: final data for 2009. *Natl Vital Stat Rep* 2011;60:1–70.
4. Menacker F, Hamilton BE. Recent trends in cesarean delivery in the United States. *NCHS Data Brief* 2010;35:1–8.
5. Monteagudo A, Carreno C, Timor-Tritsch IE. Saline infusion sonohysterography in non-pregnant women with previous cesarean delivery: the “niche” in the scar. *J Ultrasound Med* 2001;20:1105–15.
6. Bij de Vaate AJ, Brölmann HA, van der Voet LF, van der Slikke JW, Veersema S, et al. Ultrasound evaluation of the cesarean scar: relation between a niche and postmenstrual spotting. *Ultrasound Obstet Gynecol* 2011;37:93–9.
7. Donnez O, Jadoul P, Squifflet J, Donnez J. Laparoscopic repair of wide and deep uterine scar dehiscence after cesarean section. *Fertil Steril* 2008;89:974–80.
8. Naji O, Daemen A, Smith A, Abdallah Y, Saso S, Stalder C, et al. Visibility and measurement of cesarean section scars in pregnancy: a reproducibility study. *Ultrasound Obstet Gynecol* 2012;40:549–56.
9. Osser OV, Jokubkiene L, Valentin L. High prevalence of defects in Cesarean section scars at transvaginal ultrasound examination. *Ultrasound Obstet Gynecol* 2009;34:90–7.

10. Vikhareva Osser O, Valentin L. Clinical importance of appearance of cesarean hysterotomy scar at transvaginal ultrasonography in nonpregnant women. *Obstet Gynecol* 2011;117:525–32.
11. Roberge S, Boutin A, Chaillet N, Moore L, Jastrow N, Demers S, et al. Systematic review of cesarean scar assessment in the nonpregnant state: imaging techniques and uterine scar defect. *Am J Perinatol* 2012;29:465–71.
12. Bij de Vaate AJ, van der Voet LF, Naji O, Witmer M, Veersema S, Brölmann HA, et al. Prevalence, potential risk factors for development and symptoms related to the presence of uterine niches following Cesarean section: systematic review. *Ultrasound Obstet Gynecol* 2014;43:372–82.
13. Bujold E, Jastrow N, Simoneau J, Brunet S, Gauthier RJ. Prediction of complete uterine rupture by sonographic evaluation of the lower uterine segment. *Am J Obstet Gynecol* 2009;201:320.
14. Marotta ML, Donnez J, Squifflet J, Jadoul P, Darii N, Donnez O. Laparoscopic repair of post cesarean section uterine scar defects diagnosed in non-pregnant women. *J Min Inv Gynecol* 2013;20:386–91.
15. Guro-Urganci I, Bou-Antoun S, Lim CP, Cromwell DA, Mahmood TA, Templeton A, et al. Impact of Caesarean section on subsequent fertility: a systematic review and meta-analysis. *Hum Reprod* 2013;28:1943–52.
16. Guro-Urganci I, Cromwell DA, Mahmood TA, van der Meulen JH, Templeton A. A population-based cohort study of the effect of Caesarean section on subsequent fertility. *Hum Reprod* 2014;29:1320–6.
17. CORONIS Collaborative Group, Abalos E, Addo V, Brocklehurst P, El Sheikh M, Farrell B, Gray S, et al. Caesarean section surgical techniques (CORONIS): a fractional, factorial, unmasked, randomised controlled trial. *Lancet* 2013;382:234–48.
18. Fabres C, Arriagada P, Fernández C, Mackenna A, Zegers F, Fernández E. Surgical treatment and follow-up of women with intermenstrual bleeding due to cesarean section scar defect. *J Minim Invasive Gynecol* 2005;12:25–8.
19. Jacobson MT, Osias J, Velasco A, Charles R, Nezhat C. Laparoscopic repair of uteroperitoneal fistula. *JSL* 2003;7:367–9.
20. Nezhat C, Grace L, Solimannjad R, Meshkat Razavi G, Nezhat A. Cesarean scar defect: What is it and how should it be treated? *OBG Manag* 2016;28(4). Available at: <http://www.mdedge.com/obgmanagement/article/107745/surgery/cesarean-scar-defect-what-it-and-how-should-it-be-treated/pdf>. Accessed October 25, 2016.
21. Grace L, Nezhat A. Should cesarean scar defect be treated laparoscopically? A case report and review of the literature. *J Minim Invasive Gynecol* 2016;23:843.
22. Vervoort AJ, Uittenbogaard LB, Hehenkamp WJ, Brölmann HA, Mol BW, Huirne JA. Why do niches develop in Caesarean uterine scars? Hypotheses on the aetiology of niche development. *Hum Reprod* 2015;30:2695–702.
23. Morris H. Surgical pathology of the lower uterine segment caesarean section scar: is the scar a source of clinical symptoms? *Int J Gynecol Pathol* 1995;14:16–20.
24. Tanimura S, Funamoto H, Hosono T, Shitano Y, Nakashima M, Ametani Y, et al. New diagnostic criteria and operative strategy for cesarean scar syndrome: endoscopic repair for secondary infertility caused by cesarean scar defect. *J Obstet Gynaecol Res* 2015;41:1363–9.
25. Gubbini G, Casadio P, Marra E. Resectoscopic correction of the “isthmocoele” in women with postmenstrual abnormal uterine bleeding and secondary infertility. *J Minim Invasive Gynecol* 2008;15:172–5.
26. Gubbini G, Centini G, nascetti D, Marra E, Moncini I, Bruni L, Petraglia F, Florio P. Surgical Hysteroscopic Treatment of Cesarean-Induced Isthmoele in restoring Fertility: Prospective Study. *JMIG* 2011;18:234–7.
27. Strandell A, Lindhard A. Why does hydrosalpinx reduce fertility? The importance of hydrosalpinx fluid. *Hum Reprod* 2002;17:1141–5.
28. Defrère S, Lousse JC, González-Ramos R, Colette S, Donnez J, Van Langendonck A. Potential involvement of iron in the pathogenesis of peritoneal endometriosis. *Mol Hum Reprod* 2008;14:377–85.
29. Van Langendonck A, Casanas-Roux F, Donnez J. Iron overload in the peritoneal cavity of women with pelvic endometriosis. *Fertil Steril* 2002;78:712–8.
30. Donnez J, Donnez O, Orellana R, Binda M, Dolmans MM. Endometriosis and infertility. *Minerva Med* 2016;58:143–50.
31. Sen S, Malik S, Salhan S. Ultrasonographic evaluation of lower uterine segment thickness in patients of previous cesarean section. *Int J Gyn Obstet* 2004;87:215–9.
32. Florio P, Filippeschi M, Moncini I, Marra E, Franchini M, Gubbini G. Hysteroscopic treatment of the cesarean-induced isthmocoele in restoring infertility. *Curr Opin Obstet Gynecol* 2012;24:180–6.
33. Feng YL, Li MX, Liang XQ, Li X. Hysteroscopic treatment of postcesarean scar defect. *J Minim Invasive Gynecol* 2012;19:498–502.
34. Chang Y, Tsai E, Long CY, Lee CL, Kay N. Resectoscopic treatment combined with sonohysterographic evaluation of women with postmenstrual bleeding as a result of previous cesarean delivery scar defects. *Am J Obstet Gynecol* 2009;200:370.e1–4.
35. Wang CJ, Huang HJ, Chao A, Lin YP, Pan YJ, Horng SG. Challenges in the transvaginal management of abnormal uterine bleeding secondary to cesarean section scar defect. *Eur J Obstet Gynecol Reprod Biol* 2011;154:218–22.
36. Zhang Y. A comparative study of transvaginal repair and laparoscopic repair in the management of patients with previous cesarean scar defect. *J Minim Invasive Gynecol* 2016;23:535–41.
37. Li C, Tang S, Gao X, Lin W, Han D, Zhai J, et al. Efficacy of combined laparoscopic and hysteroscopic repair of post-cesarean section uterine diverticulum: a retrospective analysis. *Biomed Res Int* 2016;2016:1765624.

SUPPLEMENTAL FIGURE 1



(A) Laparoscopic view of the cesarean scar defect with a probe inserted into the cervix. The residual myometrium (RM) covering the scar measures 0.8 mm. (B) Laparoscopic view of the anterior wall after resection of fibrotic tissue and the cesarean scar defect. (C) Laparoscopic view of the first layer of suture before the knots are tightened. (D) Final laparoscopic view after covering the double-layer suture with a bladder flap.

Donnez. Laparoscopic repair of cesarean scar defects. *Fertil Steril* 2016.

SUPPLEMENTAL FIGURE 2

