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Clinical outcomes after resectoscopic treatment of cesarean-induced isthmocele: a prospective case-control study

L. MUZII, L. DOMENICI, F. LECCE, M. DI FELICIANTONIO, R. FRANTELLIZZI, C. MARCHETTI, M. MONTI, P. BENEDETTI PANICI

Department of Obstetrics, Gynecology and Urologic Sciences, "Sapienza" University, Rome, Italy

Abstract. – OBJECTIVE: Isthmocele represents a reservoir on the anterior wall of the uterine isthmus or of the cervical canal at the site of a previous cesarean delivery scar. Recently, it has been clarified that it might be the cause of several gynecologic symptoms, as most common abnormal uterine bleeding. Hysteroscopy and trans-vaginal ultrasound are considered the gold standard for the diagnosis of this defect. Resectoscopic treatment can be considered effective in small size defects, but no randomized clinical trials are available. This is a prospective controlled study to assess feasibility and efficacy of surgical hysteroscopic treatment of cesarean-induced isthmocele on symptom relief.

PATIENTS AND METHODS: Diagnostic hysteroscopy was performed as an office procedure in all 47 patients included in the study to confirm and identify the size of the defect. Surgical hysteroscopic treatment was performed in a selected group of patients (n = 23) having no more desire to conceive. Outcomes were measured three months later and compared in the operative hysteroscopy versus diagnostic hysteroscopy group.

RESULTS: The duration of periods shortened significantly ($p = 0.0003$) compared with the duration of menses before operative hysteroscopy in the treated group. Moreover, symptom relief was significantly better in treated patients compared with controls ($p < 0.0001$).

CONCLUSIONS: Resectoscopic treatment of isthmocele offers the possibility of an effective, safe and well-tolerated resolution of associated bleeding symptoms, having an excellent impact on the length of menses. To our knowledge, this is the first prospective controlled trial demonstrating better outcomes of resectoscopic treatment of isthmocele in solving symptoms compared with expectant management.

Key Words:

Isthmocele, Cesarean-induced defect, Resectoscopic treatment, Operative hysteroscopy, Abnormal uterine bleeding.

Introduction

Isthmocele is a reservoir-like pouch located on the anterior wall of the uterine isthmus at the site of a previous cesarean delivery scar[1].

This defect is mainly reported as a sonographic finding, and it has been described as a niche or as a triangular anechoic area at the supposed site of incision[2].

The prevalence of such anatomic defect is still debated. Using transvaginal ultrasonography (TVU), the stated prevalence of a niche varied between 24% and 70% in four studies in women with a history of one or multiple cesarean sections[3-6], whereas it ranged from 56 to 84% when assessed by sonohysterography[4,6-7].

Isthmocele is often diagnosed incidentally in patients presenting with symptoms such as spotting, postmenstrual abnormal uterine bleeding (PAUB), chronic pelvic pain or infertility. Secondary infertility may be associated with isthmocele, as the persistence of the menstrual blood in the cervix may negatively impact on the mucus quality, obstruct sperm transport through the cervical canal, or eventually interfere with embryo implantation leading to secondary infertility. Different imaging modalities, from hysterosalpingography to ultrasonographic evaluation, have been used to diagnose the defect of the anterior uterine wall. Nowadays, the diagnosis of isthmocele is feasible, but few literature data about the surgical treatment of this defect are currently available.

Various surgical techniques have been proposed to correct defects at the level of the cesarean section scar: hysteroscopic resection of fibrotic tissue[1,8-11], laparoscopic removal of the fibrotic tissue from the edges of the cesarean scar to access healthy myometrium and subsequent reconstruction[12] or robotic-assisted laparoscopic

Corresponding Author: Ludovico Muzii, Ph.D; e-mail: ludovico.muzii@uniroma1.it

repair of scar defect[13]. None of the above studies are either randomized or controlled, except for a single retrospective research comparing surgery versus cyclic oral contraceptives in PAUB associated with isthmocele[9].

The present work is a prospective case-control study, in which we compared the efficacy of the resectoscopic correction of the isthmocele (isthmoplasty) versus no treatment in the management of PAUB.

Patients and Methods

This prospective case-control study was performed from January 2012 through September 2014 at the Department of Gynecological, Obstetrical and Urologic Sciences of "Sapienza" University of Rome, in 47 consecutive patients (23 cases and 24 controls) with isthmocele, documented with TVU and diagnostic hysteroscopy, with associated postmenstrual abnormal uterine bleeding (PAUB).

Inclusion criteria were the presence of a sonographically documented isthmocele, and prolonged menstrual bleeding (more than 9 days), following at least one cesarean delivery in patients whose menses ranged from 2 to 7 days prior to delivery.

The exclusion criteria were the presence of an intrauterine device, coagulopathy, exogenous hormone treatments, desire of pregnancy and other gynecological conditions that could cause prolonged bleeding (polyps, adenomyosis, myomas, endometrial hyperplasia, malignancy).

The study was approved by the Institutional Review Board (IRB), and written informed consent was obtained from all patients.

Due to the lack of literature data on the impact of the resectoscopic correction of isthmocele on subsequent pregnancy and labour, patients were asked about their desire of pregnancy and then divided in two groups.

The first group consisted of patients who did not plan further pregnancies (Group A), to which the isthmoplasty procedure was proposed, and the second (Group B) consisted of patients desiring further pregnancies, to which expectant management was suggested. All patients agreed on the management proposed in both groups. Group A included 23 patients subjected to diagnostic hysteroscopy and resectoscopic isthmoplasty, whereas Group B included 24 women undergoing diagnostic hysteroscopy only (control group).

A complete medical history was collected, with particular attention to the number of previous pregnancies. All patients were asked to assess the length of menses and the impact on the symptoms (PAUB) on two menstrual cycles before the procedure.

The diagnosis of isthmocele was initially made at the transvaginal ultrasound (4-9 MHz endocavitary transducer, Voluson 730 Pro ultrasound machine; GE Healthcare, Milan, Italy) 3 to 7 days after last menstruation, as previously described[1,2]. The following measurements were taken: length, height of the defect and the thickness of the myometrium over the scar. Defect location was recorded dividing ideally the cervix in upper, middle and lower third.

Diagnostic Hysteroscopy

Diagnostic hysteroscopy was performed as an office procedure, without anaesthesia or cervical dilation, using the vaginoscopic approach and a 2.9 mm telescope (Hopkins II, 30 Forward-Oblique Telescope; Karl Storz GmbH & Co., Tuttlingen, Germany) and continuous flow sheath with saline solution as the distending medium.

Resectoscopic Treatment

Operative hysteroscopy was performed only in Group A patients, under general anaesthesia, using a 10-mm resectoscope (Karl Storz GmbH & Co.) and sorbitol-mannitol as a distending medium.

After positioning the bladder catheter, cervical dilation using Hegar dilators up to size 10 was performed. All operations were carried out under visual examination. After determining the site of the isthmocele, a cutting loop was used to remove the flap of fibrotic tissue that appeared underneath the pouch-like defect, from the limit of the defect to the endocervix, modulating the technique on the ground of the defect site until the myometrial tissue below was evident. The residual of the pouch was cauterized with a 3 mm roller-ball if needed.

Follow-up

Outcomes were measured three months after operative hysteroscopy in group A, and three months after diagnostic hysteroscopy in group B. Patients were evaluated by TVU and were asked about the resolution and/or improvement of menstrual disorders (in particular AUB and the length of menses reported in a pictorial chart).

The total duration of the menstruations was recorded, which included also the number of

days with PAUB and possible episodes of intermenstrual bleeding. Values are expressed as the mean duration of the menstrual cycle in two consecutive cycles before the surgical procedures and two consecutive cycles after the procedure excluding the first menstrual cycle after the procedure (operative hysteroscopy in Group A and diagnostic hysteroscopy in Group B). The first post-operative cycle was not considered for the evaluation of post-operative AUB, in order to exclude possible interference in bleeding in early post-operative period due to the healing process after operative hysteroscopy. Patients were requested to express their degree of satisfaction with the treatment on a five-grade scale (very satisfied, satisfied, uncertain, dissatisfied, very dissatisfied). We considered as positive treatment outcome only the definition of very satisfied-satisfied. TVU measurements were collected after three months since surgical procedure and compared in the two groups.

Statistical Analysis

Data are reported as mean (SD) or number (%) of cases, with 95% confidence intervals (CIs), when appropriate. Comparison of quantitative variables between the study groups was made using the two-sample *t*-test, and categorical variables were compared with Fisher's exact test. All tests used were two-tailed. A p value of < 0.05 was considered statistically significant.

Results

Mean patient age was 39.7 years (SD 4.0; 95% CI: 37.9-41.9) years in the treated group and 39.4 (SD 5.1; 95% CI: 37.3-41.6) in the control group. There was no evidence of endocrine disorders of the pituitary and ovary in any subject, nor any evidence of premature ovarian failure or premature menopause.

The operative hysteroscopy group included 23 women (Group A), and the diagnostic hysteroscopy only group included 24 women (Group B).

The two groups were similar for the following baseline features: age, parity, length of preoperative menses, preoperative symptoms, isthmocele size and defect location (Table I).

In Group A, resectoscopic correction of isthmocele was successfully achieved in all cases evaluated. No complications occurred during or after resectoscopic surgery.

Duration of menses in patients receiving resectoscopic therapy is shown in Table II. Three months after therapy, the duration of menses (7.8 days ± 3.4 SD; 95% CI: 6.3-9.3) shortened significantly ($p = 0.0003$) compared with the duration of menses before therapy (12.0 days ± 3.1 SD; 95% CI: 10.7-13.3).

Group B (control group of untreated patients) had no significant ($p = 0.534$) difference in post-procedure menses duration (12.3 days ± 4.0 SD; 95% CI: 10.6-14) compared with the length of menses before office hysteroscopy (11.7 days ± 3.9 SD; 95% CI: 10.1-13.3).

Furthermore, when compared to findings recorded at follow-up, Group A patients had significant lower numbers of days of menstrual bleeding ($p = 0.0009$) and were very satisfied related to Group B patients. Complete resolution of PAUB in 87% (n=20) treated *versus* 12.5% (n = 3) untreated patients was achieved ($p < 0.0001$).

Discussion

Isthmocele is defined as a defect in the anterior wall of the uterine cervical canal at the site of a

Table I. Clinical details of study population.

Variables	Group A (n = 23)	Group B (n = 24)	*p*-value
Age (mean ± SD)	39.7 ± 4.0 (95% CI: 37.9-41.9)	39.4 ± 5.1 (95% CI: 37.3-41.6)	0.824 (NS)
No. of previous cesarean section			
1	8	10	–
2	11	11	–
≥ 3	4	3	–
Symptoms before treatment (PAUB)	100%	100%	–
Localization of isthmocele			
Superior third (no., %)	10 (43.5%)	12 (50%)	
Mild third (no., %)	6 (26%)	4 (16.7%)	
Inferior third (no., %)	7 (30.5%)	8 (33.3%)	

Table II. Presurgical, postoperative and follow up outcomes.

Variables	Group A (n = 23)	Group B (n = 24)	*p*-value
Menstrual period length (mean ± SD)			
Pre-operative	12.0 ± 3.1 (95% CI: 10.7-13.3)	12.3 ± 4.0 (95% CI: 10.6-14)	0.775
Post-operative	7.8 ± 3.4 (95% CI: 6.3-9.3)	11.7 ± 3.9 (95% CI: 10.1-13.3)	0.0009
Improvement of symptoms after 3 mo. (no., %)	20 (87%)	3 (12.5%)	< 0.00001
Duration of menses after 3 mo. (mean ± SD)	6.9 ± 4.2 (95% CI: 5.1-8.7)	11.2 ± 3.7 (95% CI: 9.6-12.8)	0.0005

significant; no., number; SD, standard deviation; max, maximum.

previous cesarean section scar, causing PAUB, low pelvic pain, and secondary infertility[1-3].

Stewart reported the first publication on caesarean section scar defect in relation to bleeding symptoms in 1975[14].

In 1995, Morris[15] described for the first time the presence of anatomic and histologic distortions as well as scar tissue in the anterior isthmus at the place of the previous cesarean section. Samples were obtained after hysterectomy in women with abnormal uterine bleeding.

Isthmocele may result in the collection of menstrual blood within the niche that, in combination with a reduction of uterus contractility as a result of the development of fibrosis in the niche, alters the direct outflow of menstrual blood. This defect causes PAUB, pelvic pain, and secondary infertility. PAUB represents the most common symptom associated with the presence of the defect[1,8,15].

An in-depth analysis concerning the etiology and the prevention of the defective healing of the caesarean section scar is not available, although caesarean in advanced labour has been identified as a risk factor for the development of a scar defect[6,16].

The presence of these surgical sequelae should be suspected in women whit previous delivery by cesarean section, mainly in uteri in retroflexion[17]. In a random population of women with a history of cesarean section, the prevalence of a niche ranged from 56% to 84% when assessed by sonohysterography[18]. A Cochrane review showed fewer scar defects with single closure group in comparison with two layers suturing for closing the uterine incision[19]. As a consequence of the dramatic increase in the rate of cesarean section in recent decades, a similar increase has been observed in the use of surgical treatment of symptomatic isthmocele, even in the absence of clear scientific evidence to support surgical management.

Fabres et al[20] was the first author to suggest the removal of fibrotic tissue to facilitate blood drainage and resolve isthmocele-related symptoms.

Since then, several scholars have adopted different surgical modalities to treat the defect. Some literature data have suggested that the resectoscopic correction allowed the best results, despite the lack of literature evidences as yet.

In a prospective study on 26 women, Gubbini et al[8] reported the success of resectoscopic treatment in correcting the anatomic defect and in the reconstructing the cervical canal in the interested tract[1]. The same authors published the results of a prospective study on the efficacy of the operative hysteroscopy to solve symptoms and to restore fertility in women with cesarean-induced isthmocele and secondary infertility. In all cases, there was a complete resolution of symptoms and all 41 treated patients became spontaneously pregnant between 12 and 24 months after surgery[8].

Van der Voet et al[21] have recently underlined that evidences on the best treatment strategy of cesarean-induced isthmocele are still modest[21]. Randomized controlled trials or meta-analysis on the management of isthmocele are still lacking.

Florio et al[9] reported the only controlled study available in the literature so far. In a retrospective study conducted on 46 women symptomatic for isthmocele, they demonstrated that the resectoscopic correction was more effective than hormonal treatment in reducing pelvic pain and PAUB.

In our prospective, controlled study we obtained a complete control of isthmocele-related symptoms and a high degree of satisfaction in patients subjected to resectoscopic treatment (Group A). Hysteroscopic correction of the defect was able to reduce the duration of cycles significantly.

Patients were asked about their desire for pregnancy before resectoscopic correction because only seven studies[15,18,21-26] were reported on fertility and pregnancy outcomes after surgical treatment. A total of 78 women were reported to have fertility problems, of which 67 later conceived after hysteroscopic resection of isthmocele[21].

Notwithstanding limitations due to a limited number of patients and study design, we report that resectoscopic correction of isthmocele shortened menstrual period and led to complete resolution of symptoms in 87% of cases securely, with a significant difference compared to untreated patients. This study is to our knowledge the only controlled study comparing resectoscopic surgery to no treatment in patients with PAUB related to the presence of isthmocele.

Conclusions

Surgical intervention seems to be a valid means to treat patients who have symptoms of prolonged postmenstrual uterine bleeding caused by isthmocele. Data from this paper support that resectoscopy may be the first choice in the management of PAUB associated with TVU-documented isthmocele. In fact, this minimally invasive technique is able to yield excellent therapeutic results.

Nevertheless, to confirm these findings, randomized controlled investigations with large sample size are needed.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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