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The effect of suture materials with different absorption times on isthmocele: a retrospective study

Short title: Suture materials effect on isthmocele

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ABSTRACT

Objectives: With the increasing rate of cesarean operations, the formation of niches and related early and late complications have been observed more frequently. In this study, we examined the effects of using a suture material that can be absorbed faster than conventional sutures on the formation of niches.

Material and methods: This study was designed as a retrospective study and completed with a total of 101 patients. During the cesarean operation, the uterus was closed with Rapide Vicryl® in 49 patients and Vicryl® in 52 patients. The uterine niche was measured with a sonohysterogram 6 months after the operation. The primary outcome of the study was determined as uterine niche formation and the secondary outcome was the post-menstrual spotting (PMS) rate.

Results: Duration of surgery, intraoperative/postoperative blood loss, and hospitalization time were similar between the two groups. Niche formation was significantly lower in the Rapide

Vicryl group (22.4%) when compared to the Vicryl group (42.3%) (p = 0.046). Also, PMS was observed significantly lower in the Rapide Vicryl group (16.2% and 52.8% in Rapide Vicryl and Vicryl groups, respectively; p = 0.002).

Conclusions: The formation of niches and associated PMS rates were less with suture materials that were absorbed faster.

Key words: cesarean; Vicryl; Rapide Vicryl; isthmocele; niche; scar

INTRODUCTION

Cesarean operations are an increasing form of delivery in the world, and it is becoming more frequent in Türkiye [1]. This delivery leads to early complications such as infection and bleeding in the early stages, as well as ureter, bladder, and bowel injuries that may occur during surgical procedures. Consequently, these complications can lead to abnormal placentation secondary to the cesarean scar tissue and in this region, scar pregnancies, secondary infertility because of post-menstrual spotting (PMS), and intrauterine fluid accumulation [2].

The cesarean technique has been standardized. Upon healing of the incision after uterine suturing in the cesarean operation, the myometrial thickness decreases. This induced formation is called the isthmocele, uterine niche, or cesarean scar defect. There are many hypotheses that relate the duration of active labor, cervical dilatation, location of the hysterotomy, surgical uterine closure techniques, adhesion development, and predisposition to impaired wound healing. As the uterine cavity creates an indentation towards the myometrium, menstrual blood accumulates and causes PMS, endometritis, and infertility by disrupting the integrity of the endometrial cavity *via* accumulated blood that flows backward from the isthmocele space. In addition to studies to reduce the cesarean rate, many centers have been conducting studies to eliminate the niche left by surgical sequelae. The differences in healing between single or double-layer suturing, locked or non-locked continuous sutures during the closure of the uterus have been discussed; however, no significant differences were observed in suturing techniques [3, 4].

If possible, sutures should be removed within 1–2 weeks of their placement, depending on the anatomic location. Prompt removal reduces the formation of suture marks, and the risk of infection and tissue reaction also decrease [5]. Therefore, rapid absorption of suture materials may lead to a faster amelioration of the cesarean scar incision, and consequently, formation of a smaller isthmocele space in the myometrium. Nonetheless, there is few data in the literature regarding this issue.

Objectives

The aim of this study is to examine the effect of suture materials on the recovery of the uterine wall, and niche formation in the cesarean section incision site by comparing polyglactin multifilament suture (Rapide Vicryl®), which has a faster absoption time, with the conventionally used polyglactin multifilament suture (Vicryl®).

MATERIAL AND METHODS

This study was conducted at an obstetrics and gynecology clinic of a university hospital in between April 2020 and January 2021 with a total of 110 patients. This study was approved by Baskent University Institutional Review Board (Project no: KA22/59) and supported by Baskent University Research Fund.

The inclusion criteria were age range of 18–45 years, primipara with singleton pregnancy, no previous uterine surgery, and no previous cesarean section.

The exclusion criteria were pregnancy or uterine surgery in the time period from the cesarean section to ultrasonography and having a disease that affects wound healing (inflammatory bowel disease, systemic lupus erythematosus, rheumatoid arthritis, and insulin dependent diabetes mellitus).

Surgical procedure and post-operative evaluation

Seven surgeons working in the same clinic and using the same surgical technique participated in the study. A Pfannenstiel incision was applied to the abdominal wall and a lower segment transverse incision was applied to the uterine wall. During the closure step, two different suture materials were used: no. 1 Vicryl® (Ethicon, Raritan, NJ, USA), as control group; no. 1 Rapide Vicryl® (Ethicon) as study group. A single layer locked continuous suture was applied without passing a layer through the decidua. The location and number of the sutures were noted, in case of additional suture requirements. Next, the visceral peritoneum was left open, and the parietal peritoneum was closed. The time for uterine closure, duration of the operation, postpartum hemorrhage requiring transfusion, wound infection, endometritis, and hospitalization period were recorded.

Transvaginal sonohysterography was performed once by a single doctor experienced in sonohysterography and blinded to the closure suturing material. The sonohysterography was performed 5–6 months after the cesarean section with a GE Voluson S6 ultrasonography device. During sonohysterography, the presence of niche in the scar area, 3-dimensional niche

thickness (in x, y, z axes), and residual and total (adjusted) myometrial thickness (RMT and AMT) were evaluated (Fig. 1). This procedure was performed while the patient was on the gynecological table, after the cervix and vagina were cleaned with povidone iodine. Ultrasonography was performed by applying a sterile saline solution with an insemination cannula (Wallace® SureView, Trumbull, CT, USA). The presence of a hypoechogenic area (niche) in the cesarean scar area in the endometrial cavity was determined by measuring along three axes: the length, depth, and width. Furthermore, the patients were questioned in terms of inguinal pain, menstrual pain, and post-menstrual bleeding in the form of spotting and other abnormal bleeding patterns. Scar defects that were > 2 mm were considered positive for isthmocele. PMS was defined as brownish bleeding between menstrual cycles or exceeding the patient's normal menstrual period by more than two days.

The primary outcome of the study was formation of uterine niche, and the rate of post-menstrual spotting (PMS) was determined as the secondary outcome.

Statistical analysis

The sample size was calculated using a previous study [6]. The G-Power 3.1.9.7 program was used for the sample calculation of the "Residual myometrial thickness (mm)" outcome. With 95% GA and 90% power, a total of 102 patients were needed. However, considering the pandemic conditions and possible losses, 101 patients were included (Fig. 2).

IBM SPSS 25 was used for data analysis.

In the first stage of the study, descriptive statistics were specified with frequencies and mean-standard deviation. The normality assumptions of the variables were conducted according to the study by Tabachnick and Fidell [7]. According to this study, skewness and kurtosis values between −1.5 and 1.5 were accepted as normal distribution and necessary analyses were made. When the assumptions were validated in the analysis, differences between the groups were determined by the independent groups t-test. Yates and Fisher's exact test was used to determine the relationship between categorical variables. The statistical significance level was 0.05 in all tests.

RESULTS

No differences were identified between the demographic characteristics of the patients, as summarized in Table 1. No statistical differences in emergency cesarean and patients in labor and cervical dilatation rates, which may affect the formation of niches after cesarean section, were identified (Tab. 1).

Surgical procedures

While the proportion of patients who needed additional sutures during the operation was similar, the average number of additional sutures applied to each patient was statistically less in the Rapide Vicryl group ($p = 0.028$).

There was also no difference between uterine closure time and duration of operation. Blood loss was negligible in both groups and no blood transfusion was used for any patients. Wound infection and endometritis did not develop in any patient, and no difference was identified in the length of the hospitalization.

Ultrasonographic findings

Number of patients with a niche depth greater than 2 mm were significantly fewer in the Rapide Vicryl group when compared to the Vicryl group (22.4% and 42.3% in Rapide Vicryl and Vicryl groups, respectively; $p = 0.046$). When the niche depth was accepted as 1 mm, the scar defect rate was again significantly lower in the Rapide Vicryl group (73.4% and 92.3% in Rapide Vicryl and Vicryl groups, respectively; $p = 0.002$). The mean scar defect depth of 1.52 ± 0.88 mm in the Rapide Vicryl group was statistically less than in the Vicryl group (2.43 ± 1.35 mm) ($p = 0.001$). Among other ultrasonographic findings, the mean width of the scar defect was statistically less in the Rapide Vicryl group ($p = 0.008$); however, no significant difference was observed between the mean length of the scar defect, mean RMT, and AMT (Tab. 2).

The PMS rate of the Rapide Vicryl group was significantly less than the Vicryl group (Tab. 2) ($p = 0.002$).

The use of additional sutures was not significant in terms of scar defect formation > 2 mm in the Vicryl and Rapide Vicryl groups ($p = 0.2$, $p = 0.89$).

DISCUSSION

In this retrospective study, Rapide Vicryl suture, which is absorbed faster during the fusion of uterine incision edges, is demonstrated to cause a smaller niche formation when compared to the conventionally used Vicryl suture. Niche formation, which was considered as a space of 2 mm and greater in depth, was significantly lower at patients in the Rapid Vicryl group. As for the secondary outcome of the study, frequency of PMS was also significantly lower in the Rapide Vicryl group when compared to the Vicryl group.

The niche, isthmocele cesarean scar defect was accepted as at least 2 mm indentations of discontinuation of the myometrium in the lower uterine segment after cesarean section. The isthmocele incidence rate is up to 70% [8, 9].

Studies to prevent or reduce the formation of niches after cesarean operation have been conducted for many years. The systematic review and meta-analysis published by Roberge S. et al. examined 20 randomized controlled trials (RCTs) and there was no difference between single and double uterine closures in terms of niche formation [10]. Similar results were observed in the systematic review and meta-analysis published in 2017 by Di Spiezio Sardo A. et al. [11], where no difference was observed between closing the uterus in one layer or two layers. In our previous study [12], the effects of the conventionally used Vicryl sutures on the formation of niches were examined by closing the uterus in a single or double layer, and no difference was observed. Yasmin et al. [13] examined wound healing by closing the uterus using locked or unlocked suturing and showed a decreased myometrial thickness in the locked group. Ceci et al. [14] demonstrated that a continuous locked single-layer compared with an interrupted, unlocked, single-layer suture had a larger scar defect ($p = 0.001$) according to sonographic evaluation.

The effects of different types of suture materials on cesarean scar defects have been examined by Başbuğ A. et al. and Sevket O. et al. [6, 15]. In both studies, the difference between monofilament and conventionally used multifilament sutures was examined, and both groups observed that monofilament sutures formed less niche. They suggested that monofilament sutures produced less inflammation than multifilament sutures.

Acute wounds normally have orderly healing, with overlapping phases of inflammation, epithelialization, fibroplasia, and maturation. The fibroplasia phase starts at the acute wound site at 24 hours and reaches a maximum on the 10^{th} day [16]. However, there is no human study examining daily uterine wound healing. When the uterus from a patient who underwent a hysterectomy 18 days after cesarean was examined, granulation tissue progressing towards fibrosis was observed in the cesarean scar area [17].

Suture material, which is a foreign body implanted into human tissue, may trigger foreign-body tissue reaction. Utilization of a rapidly absorbed suture rather than conventional sutures may lessen tensile strength and decrease the tenting in the endometrium and myometrium, which may allow a proper fusion of the wound sides. Polyglactin sutures (Vicryl, Ethicon), which are conventionally used during uterine closure, lose 50% of their tensile strength at 21 days post-operation. The suture we used in our study (Rapide Vicryl, Ethicon), which has the same polyglactin structure, can dissolve in a shorter time and loses

50% of its strength on the 5th day [18]. By the using Rapide Vicryl, myometrial and endometrial tissues become anatomically mutual at an earlier stage and thus had a smaller space niche before the scar tissue was completed.

At a niche depth of 1 mm or 2 mm, the niche ratio was significantly lower in the Rapide Vicryl group. When the average scar depths were also examined without determining a cut-off ratio of the niche, mean scar defect depth was again significantly less in the Rapide Vicryl group. These data support better wound healing.

van der Voet et al. reported that PMS is a long-term side effect of niche formation and is more common in patients with niche formation [8]. In our study, among the patients who had menstrual cycles after cesarean section, PMS was demonstrated to be significantly lower in patients who were in the Rapide Vicryl group when compared to the patients in the Vicryl group. Thus, Rapide Vicryl can reduce niche formation, as well as related ultrasonography findings and clinical complications.

The major strength of our study is that there is a very rare study that examines the formation of a niche by closing the uterus with sutures that can dissolve faster than classical sutures. The homogeneity of the patients participating in the study, the formation of a niche, the cesarean section performed by surgeons with similar surgical techniques, and the 6-month follow-up period are additional strengths of the study. The fact that the patients were selected from those who previously had not had a cesarean section or other uterine surgery also enabled a more objective evaluation of wound healing.

One of the limitations of the study may be that the uteruses were single-layer locked and continuous or double-layer results were not studied. Moreover, the lack of an objective criterion to measure the PMS and instead evaluate according to the patients' statements may also be a factor that limits the strength of the study.

CONCLUSIONS

In this study, it is demonstrated that a more rapidly absorbed suture material can contribute to reduced formation of post-cesarean niche, and decrease the rate of related PMS. In future studies, different surgical techniques utilizing rapidly absorbed suture materials may be used in closure of the uterine incision in order to reach the least amount of niche formation. Prevention, rather than treatment, of this pathology should be focused on.

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Conflict of interest

All authors declare no conflict of interest.

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Table 1. Main patient characteristics and surgical properties

	Vicryl Rapide (n = 49)	**Vicryl (n = 52)**	**p**
Age, y	29.49 ± 4.02	29.54 ± 4.46	0.955
Body mass index, kg/m^2	30.09 ± 2.29	30.54 ± 2.42	0.885
Gestational age, week	38.56 ± 1.74	38.07 ± 1.95	0.19
Smoking, n (%)	1 (2%)	2 (3.8%)	1
Hypertension, n (%)	1 (2%)	4 (7.7%)	0.363
Diabetes mellitus, n (%)	5 (10.2%)	4 (7.7%)	0.736
Emergency cesarean, n (%)	6 (12.2%)	10 (19.2%)	0.491
Patients in labor, n (%)	8 (16.3%)	8 (15.4%)	1
Patient with cervical dilatation, n (%)	8 (16.3%)	8 (15.4%)	1
Needing additional suture, n (%)	26 (53.1%)	34 (65.4%)	0.29
Mean additional suture, n	0.96	1.5	0.028
Duration of uterine closure, min	4.47 ± 1.83	4.31 ± 1.61	0.63
Duration of operation, min	25.11 ± 5.16	25.86 ± 5.26	0.43

min — minute; n — number; y — year

Table 2. Study data

	Vicryl Rapide (n = 49)	**Vicryl (n = 52)**	**p**
> 2 mm scar depth, n	11 (22.44%)	22 (42.30%)	0.046
> 1 mm scar depth, n	36 (73.46%)	48 (92.30%)	0.002

Mean depth of scar defect, mm (range)	1.52 ± 0.88	2.43 ± 1.35	0.001
Mean length of scar defect, mm (range)	5.11 ± 1.49	5.97 ± 1.84	0.188
Mean width of scar defect, mm (range)	5.35 ± 2.25	8.29 ± 3.40	0.008
Mean RMT, mm (range)	7.47 ± 1.21	6.27 ± 2.68	0.169
Mean AMT, mm (range)	13.59 ± 1.63	12.46 ± 1.92	0.106
PMS	6/37 (16.2%)	19/36 (52.8%)	0.002

AMT — adjacent myometrial thickness; PMS — post-menstrual spotting; RMT — residual myometrial thickness

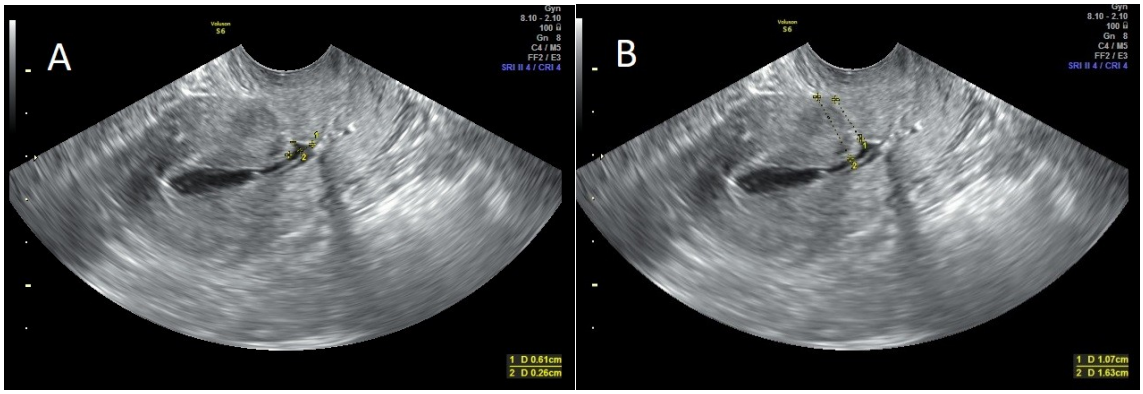

Figure 1. Transvaginal sonohysterography assessment. Sagittal transvaginal sonography views of a uterus presenting with an isthmocele. (A) The width (1) and depth (2) of the scar defect and (B) RMT (1) and AMT (2) measurements.

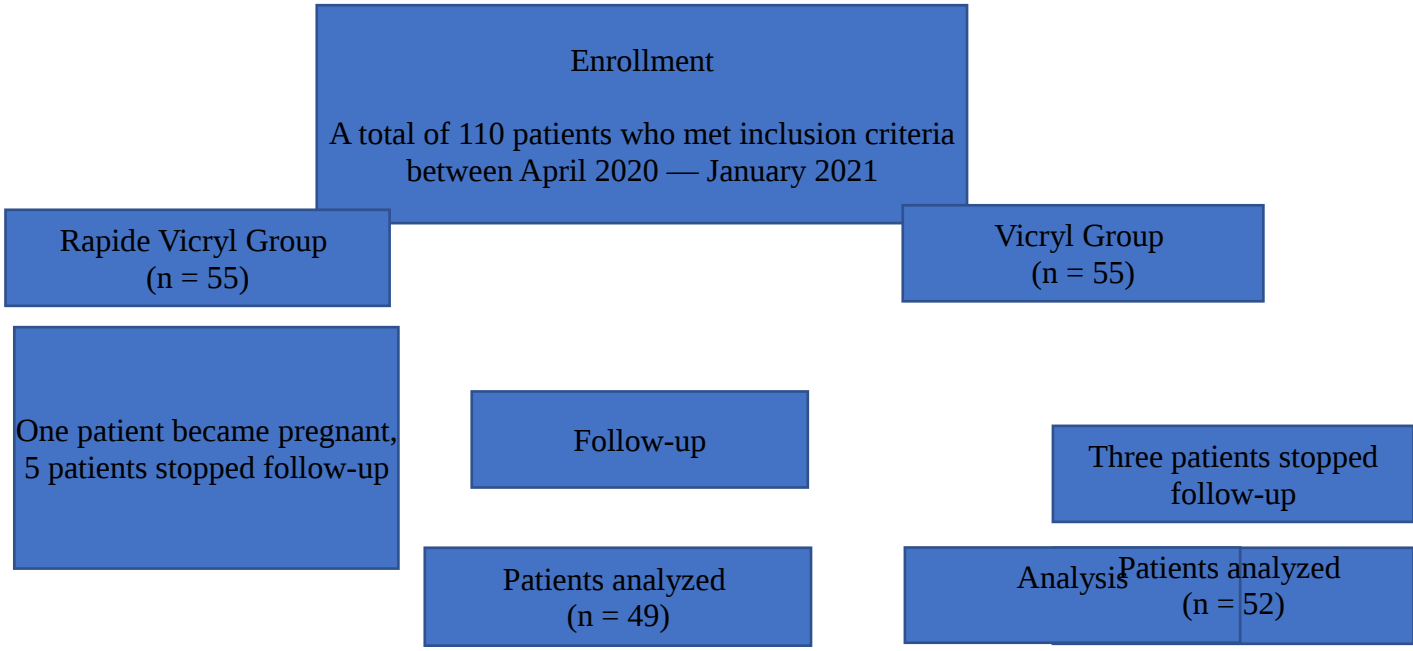

Figure 2. Patient selection flowchart