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The incidence of isthmocele may be higher than reported

İsthmocele'in insidansı bildirilenden daha fazla olabilir

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Abstract

Aim: Isthmocele, a long-term complication of Cesarean section (CS) surgery, has drawn increasing worldwide interest. However, not all women with this Cesarean scar defect (CSD) present with clinical symptoms. We studied a group of non-pregnant women with a CS history to determine the prevalence of isthmocele, the potential risk factors for its development, and the most common clinical complaints.

Methods: This study included women who had a cesarean operation more than 6 months ago, who were not pregnant between January 2017 and April 2017 and applied to the gynecology clinic for any reason. The exclusion criteria were the patients in the menopause period. Data was collected on 115 participants, including age, body mass index, duration after CS, and the number of CS surgeries that had been performed. Standardized scar parameters (residual myometrial thickness (RMT) and the depth and width of the triangular hypoechoic niche) were measured using transvaginal-ultrasonography (TVS). Isthmocele symptoms were categorized as asymptomatic, postmenstrual spotting, menometrorrhagia, chronic pelvic pain, dysmenorrhea, and infertility. Associations between isthmocele and menstrual complications were investigated. The relationship between isthmocele development and the reasons for the CS surgery were evaluated.

Results: TVS examination diagnosed 17 women (14.78%) with isthmocele. Women who had undergone recurrent CS surgeries tended to have more visible isthmocele than those with a single CS surgery. The average isthmocele depth was 6.006 ± 0.7970 mm. Among the women with isthmoceles, elective CS surgery had been performed in six (35.3%), while 11 (64.7%) had the surgery at parturition. The presence of an isthmocele was frequently symptomatic, predominantly as postmenstrual spotting. Women with an isthmocele had significantly lower RMT values (5.57 ± 0.60 mm versus 8.78 ± 0.22 mm) than those without an isthmocele. There was no correlation between age, body mass index, and the presence of an isthmocele ($p > 0.05$).

Conclusions: The incidence and prevalence of CSD is greater than most gynecologists realize. Isthmoceles can develop after just one CS surgery, leading to long-term complications that morbidly effect women for the rest of their lives. A reduction in the number of CS surgeries is the most effective way to decrease the prevalence of isthmoceles.

Keywords: Isthmocele, Uterine niche, Postcoital bleeding, Pelvic pain

Öz

Amaç: İsthmosel, dünyada gittikçe yaygınlaşan sezaryen operasyonunun uzun dönem bir komplikasyonudur. Ancak sezaryen skar defektli kadınların (SSD=İsthmosel) tamamında semptom görülmez. Biz çalışmamızda isthmosel prevalansı, gelişimi için risk faktörleri ve en yaygın semptomlarını araştırmak istedik.

Yöntemler: Bu çalışmaya 6 aydan daha uzun bir süre önce sezaryen operasyonu olan, 2017 Ocak ve 2017 Nisan tarihleri arasında gebe olmayan, jinekoloji polikliniğine herhangi bir nedenle başvuran kadınlar dahil edildi. Menapoz döneminde ki hastalar çalışma dışı bırakılma kriteri olarak alındı. Sezaryen olan 115 kadının verileri yaşı, vücut kitle indexi, sezaryen sonrası geçen süre ve geçirilmiş sezaryen sayısını içerecek şekilde kayıt altına alındı. Standardize edilen skar parametreleri (residual myometrial kalınlık (RMK), triangular hipoekoik nishe'in genişlik ve derinliği ölçümü) transvajinal ultrasonografi (TVUSG) ile yapıldı. İsthmosel semptomları asemptomatik, postmenstrual spotting tarzı kanama, menoraji, kronik pelvik ağrı, dismenore ve infertilite olarak kategorize edildi. İsthmosel ve menstruel komplikasyonlar arasındaki ilişki araştırıldı. İsthmosel gelişimi ve sezaryen sebebleri arasındaki ilişkiler değerlendirildi.

Bulgular: Hastaların TVUSG ile değerlendirmesinde 17 tanesinde (%14,78) isthmosel tespit edildi. Birden fazla sezaryen olan hastalar tek sezaryen olan hastalara göre daha fazla isthmosel geliştirme eğilimindeydiler. Ortalama isthmosel çapı 6,006 ± 0,7970 mm'di. İsthmoselli kadınların 6 tanesi (%35,3) elektif alınan sezaryen vakalarında gelişmiş iken, 11 tanesi (%64,7) doğum eylemi başladıktan sonar yapılmıştı. İsthmosel olan hastaların çoğunluğu semptomatikti ve daha çok spotting tarzda kanama görülüyordu. İsthmosel görülen kadınların RMK değerleri isthmosel görülemyenlerden belirgin olarak düşüktü (5,57 ± 0,60 mm vs 8,78 ± 0,22 mm).

Sonuç: SSD prevalans ve insidansı kadın doğum hekimlerinin tahmin ettiğinden çok daha fazladır. İsthmosel bir sezaryen sonrası bile gelişebilir ve o kadınlarda uzun vadeli yaşamları boyunca morbidite sebebi olarak görülür. Sezaryen oranlarının azaltılması isthmosel prevalansını azaltmada çok etkili olacaktır.

Anahtar kelimeler: İsthmosel, Uterin niş, Postkoital kanama, Pelvik ağrı

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Introduction

Cesarean section (CS) surgery is often preferred by obstetricians to terminate high risk labor, and the number of recurrent CS surgeries is increasing in clinical practice around the world [1]. CS delivery provides a healthy birth for the baby. For the mother, however, this procedure can cause long-term complications related to defects in the surgical incision scar [2].

Cesarean scar defects (CSD) are clinically encountered as uteroperitoneal fistula, niche, or isthmocele and can be detected by ultrasonographic and hysterosonographic imaging as a hypoechoic area in the CS scar [3]. The term isthmocele was first described in 1995 by Dr. Hugh Morris [4]. This anatomic defect is a diverticulum that comprises a thin insufficient myometrium on the anterior wall of the uterine isthmus at the presumed incision site. In women who underwent emergency CS surgery, the defect can be located distally near the internal cervical os, while in women who had elective surgery, the defect is located proximally on the lower uterine segment. There is currently no standardization for isthmocele assessment [5]. Several factors may affect isthmocele development, including a retroflexed uterus. Smoking or uncontrolled diabetes may cause the wound to heal poorly. Surgical techniques such as low (cervical) hysterotomy, single or double layer closure, or the use of locking sutures as well as recurrent operations could contribute to defect formation [6].

Most isthmoceles are asymptomatic, and there is no consensus on the determining characteristics of size and location [7,8]. Isthmocele prevalence has been reported in a wide range (24–70%) when the condition is assessed by transvaginal-ultrasonography (TVS) [9]. The exact incidence is unknown, but it could be as high as 61% after a primary CS and 100% after three CS surgeries [10,11].

Isthmocele may cause dysmenorrhea, dyspareunia, menometrorrhagia, and secondary infertility as well as obstetrical complications, such as uterine rupture, Cesarean scar pregnancies, and abnormal placental implantation in future pregnancies [12,13]. The intensity of symptoms is directly related to the defect size. Small uterine scar defects can be asymptomatic, while the larger scar defects seen after multiple CS surgeries generally cause more symptoms [14].

This cross-sectional study sought to identify the prevalence of isthmocele in non-pregnant women with a history of CS surgery as well as the primary symptoms of the condition and the potential risk factors for its development.

Materials and methods

In this cross-sectional study, women who were in their reproductive period and who had delivered by CS at hospital from 2012 to 2017 were invited to undergo ultrasonographic evaluation of their CS scar at least six months after the operation. All the CS surgeries were performed using Kerr techniques for the uterine incision and a single layer continuous locking suture for closure. The study protocol was accepted by ethics committee on 17 October 2017 (approval no 2017-78), and all participants signed an informed consent form before they were included the study. The study was conducted in accordance with the 1964 Helsinki declaration and its later amendments.

The examinations were made by two gynecologists using a Mindray DP-5 (B&W Ultrasound System) ultrasound machine with a 6.5 MHz endocavity probe. All subjects were assessed three to six days after menstruation, when the endometrial stripe was thin. A standardized definition for imaging and measuring a CS scar with TVS was applied [15-17]. Isthmocele was diagnosed by the presence of a hypoechogenic zone under the myometrial layer of the lower uterine segment, at the site of the hysterotomy incision. The measurements were obtained in the sagittal plane of the uterus. The residual myometrial thickness (RMT) was defined as the distance between the apex of the hypoechoic triangle and the serosa at the site of the hysterotomy incision. The depth of the isthmocele was defined as the distance between the apex of the hypoechoic triangle and the posterior base of the endometrial cavity. The width of the isthmocele was defined as the distance from the widest point of this triangle to the surface of the endometrium in the posterior uterine wall (Figure 1).

The pregnancy and operation histories of the participants were reviewed, and the applicability of clinical symptoms such as postmenstrual spotting, dysmenorrhea, chronic pelvic pain, and dyspareunia was determined by a questionnaire after the women had been screened.

Women with a history of uterine surgery (other than low transverse incision) were excluded as well as those having other uterine pathologies (such as polyps, hyperplasia, myomas, malignancy, or congenital uterine malformations), chronic corticosteroid administration, or a recent pregnancy.

Statistical analysis

The statistical analysis was performed using the GraphPad Prism version 6.00 (GraphPad Software, La Jolla California USA). The data was expressed as a mean ± standard deviation (SD). One Way ANOVA was used for the descriptive statistics. To determine the statistical significance of the differences between the groups, the student t test was used for continuous variables, and the chi-squared test was used for categorical data. Results were evaluated within a 95% confidence interval, and the criteria for statistical significance were set at $p < 0.05$.

Results

The study included 115 non-pregnant women with a previous CS surgery. After the women were assessed by TVS, 17 (14.78%) were diagnosed as having an isthmocele. An intact CS scar without an isthmocele was detected in 98 women (85.22%). The average depth of the isthmoceles was 6.006 ± 0.7970 mm. Women with an isthmocele had significantly lower RMT values (5.57 ± 0.60 mm versus 8.78 ± 0.22 mm) than those without an isthmocele ($p < 0.05$). There was no statistically significant difference between the two groups in terms of age, height, weight, time to CS surgery, and the duration of the CS surgery (Table 1).

CS surgery had been performed electively in 91 women (79.1%), and in 24 women (20.9%) it was performed at parturition with cervical dilatation. Women who had undergone recurrent CS surgeries tended to have a more visible isthmocele than those who had undergone a single operation.

The relationship between complaints and the presence of an isthmocele is presented in Table 2. The presence of an isthmocele was frequently symptomatic. Postmenstrual spotting (35.3%) was the most common symptom, followed by menometrorrhagia (23.5%). Six women with an isthmocele were asymptomatic.

Study participants without an isthmocele had more regular menses than those with an isthmocele. This difference was statistically significant ($p < 0.05$). However, eleven of the women with an isthmocele had regular menstruations (64.7%) (Table 3). The development of an isthmocele was frequently seen in women who had had a CS surgery while in parturition (64%), but this statistical value did not reach significance (Table 4). There was no statistical significance between the group of women with an isthmocele and the group of women without an isthmocele with indications of a CS delivery ($p > 0.05$) (Table 5). There was no correlation between the size of the isthmocele and the magnitude of the symptoms (Table 6).

Table 1: Comparison of the groups with and without an isthmocele in terms of demographic and ultrasonographic parameters

	Isthmocele (+) (n = 17)	Isthmocele (-) (n = 98)	p
Age (years)	36.29 ± 1.2	36.79 ± 0.65	0.926
Height (cm)	158.2 ± 1.13	161.3 ± 0.61	0.063
Weight (kg)	69.94 ± 3.32	69.93 ± 1.86	0.822
The duration after CS (years)	6.94 ± 1.14	7.46 ± 0.52	0.855
RMT (mm)	5.57 ± 0.60	8.78 ± 0.22	< 0.001*
CS times	1.88 ± 0.20	1.68 ± 0.067	0.435

Values were given as mean ± standar deviation, CS: Cesarean section, RMT: Residual myometrial thickness, * There was statistical significance between the groups ($p < 0.05$)

Table 2: The ratio of complaints in the groups with and without an isthmocele

	Isthmocele (+) (n = 17)		Isthmocele (-) (n = 98)		χ^2	p
	n	%	n	%		
Asymptomatic	6	35.3	62	63.4		
Spotting	6	35.3	4	4		
Menometrorrhagia	4	23.5	17	17.4	17.77	0.001*
Pelvic pain	1	5.9	9	9.2		
Dysmenorrhea	-	-	2	2		
Infertility	-	-	4	4		

* There was statistical significance between the groups ($p < 0.05$)

Table 3: The relationship between the presence of an isthmocele and menstrual period complications

	Isthmocele (+) (n = 17)		Isthmocele (-) (n = 94)		χ^2	p
	n	%	n	%		
Regular menstruation	11	64.7	80	85.1	4.056	0.04*
Irregular menstruation	6	35.3	14	14.9		

* There was statistical significance between the groups ($p < 0.05$)

Table 4: The ratio of the timing of the CS operation in the groups with and without an isthmocele

	Isthmocele (+) (n = 17)		Isthmocele (-) (n = 98)		χ^2	p
	n	%	n	%		
CS in parturition	11	64.7	41	41.8	3.058	0.08*
Elective CS	6	35.3	57	58.2		

* There was no statistical significance between the groups ($p > 0.05$)

Table 5: The distribution of the indications of CS delivery in subjects with and without an isthmocele

	Isthmocele (+) (n = 17)		Isthmocele (-) (n = 98)		χ^2	p
	n	%	n	%		
Unprogressive labor	4	23.6	13	13.3		
Maternal option	4	23.6	40	40.8		
Breech presentation	2	11.7	17	17.4	4.973	0.290*
Fetal distress	5	29.4	13	13.3		
Dystocia	2	11.7	15	15.2		

* There was no statistical significance between the groups ($p > 0.05$)

Table 6: The relationship between the isthmocele size and the diversity of complaints

	Complaints				
	None (n=6)	Spotting (n=6)	Irregular menses (n=4)	Pelvic pain (n=1)	p
Isthmocele extension (mm)	5.2 ± 0.8	7.1 ± 2.0	5.5 ± 1.0	6.0 ± 0	0.50

* There was no statistical significance between the groups ($p > 0.05$)

Discussion

The clinical significance of a CSD is mostly benign; however, an isthmocele is typically identified in women who have undergone at least one previous CS surgery and who are presenting with complaints such as postmenstrual spotting, dysmenorrhea, dyspareunia, chronic pelvic pain, and infertility [11]. Isthmocele prevalence has been reported to be as high as 52% after one CS surgery [18]. The likelihood of development increases with recurrent CS surgeries [19], and these women often experience one or more symptoms [14]. In our study population, we detected an isthmocele prevalence of 14.78%, less than the rates reported in the literature. Our low rate may be because all the surgeons in our hospital used the Kerr incision, a unique surgical technique, for the uterine gash and a single layer continuous locking suture for closure.

TVS is an easily accessible, noninvasive, low-cost imaging method that should be considered the first step in screening for an isthmocele [20]. As shown by TVS, the isthmocele image is defined as an anechoic zone shaped like an isosceles triangle that exists between the uterus isthmus and the cervical canal. The best interval during a woman's cycle to display the isthmocele with TVS is a few days after menses. We examined all subjects three to six days after their menses by TVS with a high-resolution transducer. Residual myometrium on the isthmocele was characterized by erythro-ectasic vessels covered by a flabby mucosa. In the early proliferative phase, the cavity was filled with menstrual blood that could be presented by TVS examination [21]. In our study, TVS examination identified isthmoceles in 14.78% of the women, a prevalence that is lower than in some other reports [22]. Notably, we only used TVS to determine whether an isthmocele was present. If our study had also applied hysteroscopy and sonohysterography, the numbers of detected isthmoceles could have been much higher.

When patients who have had a CS surgery complain of postmenstrual bleeding or intermittent spotting, isthmocele should be considered as a potential cause. Non-coordinated muscle contractions can allow the menstrual blood to accumulate in the reservoir-like pouch [11]. Chronic inflammatory fibrin debris induces distortions and widens the lower uterine segment; endometrial congestion, lymphocytic infiltrations, and capillary dilatation with inflamed blood cells in the endometrial stroma have been found at the site of scar formation [23]. The isthmocele size (width and depth) expands, and the thickness of the myometrium (in one that is insufficiently contractible) decreases without discharging the redundant product [14]. Menstrual blood flows heavily through a cervical canal with an isthmocele, allowing the coagulant blood to accumulate in the pouch and depress the contractility of the uterine muscles around the defect [24]. Continuous incoming blood and densely viscous mucus production that are not fully drained can accumulate in the reservoir-like pouch [25].

The combination of persistent menstruation accumulation and blood with an increased local mucous secretion due to abundant vascularization may lead to postmenstrual abnormal uterine bleeding (PAUB) [13]. PAUB is a clinical symptom in which dark hematic spotting or discharge occurs days after menstruation. The presence of an isthmocele

has been implicated in underdiagnosed PAUB in non-pregnant women who have had a CS surgery. Increased CSD awareness may help physicians identify the cause of PAUB in more patients. In our study, the most common symptoms in women with isthmocele were postmenstrual spotting and irregular menstruation.

Secondary infertility is also common with isthmocele, likely due to the accumulated blood degrading the sperm and the cervical mucus quality obstructing sperm transportation through the cervical canal and the endometrial cavity, interfering with embryo implantation [26]. In addition, the presence of local inflamed fibrotic tissue in the isthmocele causes pelvic pain such as dysmenorrhea and dyspareunia [27].

A high prevalence of isthmocele in women whose CS surgery was performed intrapartum implies that the hysterotomy incision was made through effaced and dilatated cervical tissue, which is difficult to distinguish from the uterine wall during uterine contractions [28]. This could explain why there appears to be a greater risk of isthmocele development in women with cervical dilatation of more than 5 cm and duration of labor longer than five hours [29]. We detected fewer isthmocele in women who had elective CS surgery; however, that difference was not statistically significant. While data was collected on CS indications such as unprogressive labor, maternal option, breech presentation, fetal distress, and dystocia, the study did not include information about cervical dilatation and effacement at the time of the CS surgery. Surgical materials used in surgery can be effect on isthmocele development [30].

Our study was limited in that the women were only examined by TVS to identify the presence of an isthmocele. This practice may have underdiagnosed the number of women with isthmoceles in our study group. A unique feature of our study was that the same CS surgical technique (a Kerr incision and a single layer continuous locking suture closure) had been performed on all women during their previous CS surgeries. This made the standardization of variables easy to assess.

Conclusion

Not all women with a CS history develop a visible isthmocele, so it is important to define the risk factors that may lead to the principal symptoms. If the percentage of CS deliveries continues to increase, the long-term complications will be seen more and more in daily practice. If the use of CS can be minimized, potential clinical ailments such as isthmoceles will be reduced.

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