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Morphological estimation of incomplete uterine scar rupture (dehiscence) in post-cesarean deliveries. Immunohistochemical studies

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ABSTRACT

Objectives: No studies were found that analysed the properties of the caesarean scar, therefore the new study analysed the myometrial immunohistochemical expression of elastin, collagen type VI, alpha smooth muscle actin, smooth muscle myosin heavy chain, and endothelial cell marker CD31.
The aim of the study was to determine the risk of uterine rupture in future pregnancies.

Material and methods: A total of 89 women of Caucasian ethnicity were eligible: 20 healthy pregnant women, who underwent repeat caesarean section complicated by incomplete uterine scar rupture before labour, and 69 healthy pregnant women, who underwent repeat caesarean section without subsequent uterine scar rupture as the control group. In all cases, uterine tissue sample from the scarred region was collected during the caesarean section operation.

Results: The lack of observed significant changes of elastin, collagen type VI, alpha smooth muscle actin, smooth muscle myosin heavy chain and endothelial cell marker CD31 concentrations in ruptured and unruptured uteri indicates that these components cannot be found to be a marker of risk of uterine rupture in future pregnancies.

Conclusions: It could be suggested that the examined components do not contribute to the mechanism of maintaining integrity and are not responsible for the biomechanical properties of the uterine scar.

Key words: uterine scar; elastin; collagen; actin; myosin; endothelial cell marker CD3

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INTRODUCTION

The latest data show an increased global trend in caesarean section (CS) rates, consistently increasing over the past five years [1]. The uterine scar seriously affects the integrity of the uterus [2, 3], and recently, many more cesarean scar defects have been found to lead to unexpected complications, such as: abnormal uterine bleeding, painful menstruation, pelvic pain, dyspareunia and infertility in non-pregnant women [4]. Additionally, primary CS delivery carries potential risks in subsequent pregnancies: cesarean scar pregnancy, placenta previa, accreta, increta or percreta, scar dehiscence or rupture of the uterus in pregnant women [3–5].

Uterine ruptures are usually divided into complete and incomplete (dehiscence) ruptures. Incomplete uterine rupture defines a process of gradual or full myometrial rupture where the serosa and amniotic sac are intact, and the patient is virtually always asymptomatic. Complete uterine rupture is used to refer to a situation in which a patient has a uterine rupture coexisting with strong clinical manifestations (intraabdominal haemorrhage, tachycardia, rebound abdominal tenderness) [6]. Compared to complete uterine rupture, uterine dehiscence relates to much lower maternal and neonatal mortality and morbidity. There is a little known about complex process of the uterine wound repair and healing after cesarean delivery [7]. Improper healing may lead to thinning of the anterior uterine wall. In most of investigations, anatomical defects resulting from previous cesarean sections, have been reported to be associated with a higher probability of complete uterine rupture during labor [5, 6]. The uterine closure technique during CS may influence on further biomechanical uterine wound proprieties during subsequent pregnancies and thereby determine the perioperative or long-term maternal outcomes. Based on a meta-analysis including twenty studies (15,053 women),

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it has been shown that double-layer unlocked sutures are more effective than single-layer locked sutures. In terms of wound healing and residual myometrium thickness has been found to be decreased by 1.26mm after single-layer closure when compared to double-layer closure technique [8]. Dysmenorrhea symptoms have been observed more often in the single-layer group, whereas incidence of uterine rupture was similar in both groups: with single- and double-layer sutures. [8].

In turn, in the CORONIS trial conducted in 13,153 women during the 3.8 years period, there was no evidence of any difference in the incidence of pelvic pain symptoms, dyspareunia and subsequent pregnancy outcomes, depending on single- or double-layer closure of the uterus [9]. Finally, it is suggested that double-layer uterine closure with unlocked first-layer suture during caesarean delivery appears to be the most accurate method in terms of postpartum uterine scar thickness [10, 11]. There is also evidence suggesting that locking a single-layer suture in primary CS may increase the risk of uterine rupture at a subsequent delivery. Regardless of whether the uterine incision is closed using one or two layers, thickness of uterine myometrium in the site of previous incision is reduced by about 50%. [12]. The current randomized controlled trial (2Close Study) results publication will surely help to choose the preferable technique of uterus closing during CS in relation to postmenstrual bleeding, fertility and the development of a niche, measured by ultrasound [13]. Though sonographic lower uterine segment (LUS) thickness seems to be a strong predictor for uterine scar defect and full LUS thickness of less than 2.3 mm is associated with severe complications during labor (uterine dehiscence, rupture, hemorrhage), no ideal diagnostic method can yet be recommended [14, 15]. The possible pitfalls in ultrasound diagnostics may lead to LUS diagnosis difficulties, as well as incorrect finding of valuable reference values for LUS thickness [16]. In cases of altered anatomy and impaired ultrasound conditions, the use of 3T magnetic resonance imaging (MRI) as an additional LUS diagnostic tool may be useful [16]. In studies focused on suturing operative techniques, it is suggested that full thickness uterine suturing technique plays a role by lowering the incidence of incomplete healing of the uterine incision after CS [17, 18]. Labour before previous CS and the use of synthetic sutures for the uterine closure may be associated with a thicker myometrial LUS [14]. It has been also proposed that prostaglandins used for uterine contractions induction may act locally by leading to biochemical modifications that weaken the scar and subsequently predisposed to rupture [19]. It is possible that an increased risk of incomplete healing after the uterine incision is related with cesarean operation in advanced labor (second stage of labor) [20, 21]. The occurrence of post caesarean scar defect may be also influenced by risk factors such as age > 30years, BMI > 27.3, premature rupture of membranes, elective caesarean section, postoperative anaemia and retroposition of the uterus [2]. Delivery may alter the viscoelastic proprieties of myometrium and the pattern of collagen organization. The regenerative ability of a uterus can be result of histological, mitotic and functional differences in biomechanical proprieties of the scarred myometrium after cesarean section. Tensile properties of the LUS can be also connected with its biochemical structure and sulfated glycosaminoglycans, hydroxyproline, pyridinoline — deoxypyridinoline concentrations [17, 22, 23]. Extracellular matrix (ECM) remodeling during healing process lead to new ECM forms creation that never achieve biomechanical proprieties (flexibility and strength) of the original unscarred tissue [24]. The tissue scarring process is proceeding in various ways, leading in some cases to abnormal ECM reconstruction with excessive scars formation (keloid or hypertrophic scar) [24]. The uterine scar alpha smooth muscle actin concentrations differences detected with use of IHC assay may facilitate understanding their role in the pathogenesis of reparative process [25], due to regenerative endothelial cells activity that is enhanced by smooth muscle cells [26]. In the ischemic organs the reparation process proceeds with new blood vessels formation, where the vascular network creation is stimulated by endothelial cells and smooth muscle cells [26].

Essential for wound repair, angiogenesis is regulating by signals coming from serum and ECM, providing scaffold support with non-collagenous laminins 8 and 10. This dynamic healing process is moderating with cooperative angiogenic cytokines regulation. Vascular endothelial growth factor, angiopoietin, fibroblast growth factor, transforming growth factor beta are the most important and well recognized angiogenic cytokines. Uterine wound healing process involves many other cells, such as connective tissue growth factor, basic fibroblast growth factor, platelet-derived growth factor, tumor necrosis factor alpha expression of some of these factors in the myometrial smooth muscle is suspected to be altered in cases of uterine dehiscence [7]. Therefore, the investigation of uterine scar proprieties with determination of elastin, collagen type VI, alpha smooth muscle actin, smooth muscle myosin heavy chain, endothelial cell marker CD31 concentrations may be helpful to recognize possible determinants of uterine rupture in scared uteri.

Collagens and elastic fibres are *ECM fibrous proteins* constituting networks, present in myometrium tissue. Type VI collagens have many functions, including clinical evidence of involvement of connective tissue [27–29]. Its deficiency is associated with morphological abnormalities of the tendons and large spectrum of collagen VI-related myopathies. It also acts throughout interaction with collagen IV of basement membrane. Elastin is a connective tissue polymeric protein,

Table 1. Characteristics of analyzed groups of patients

	Unruptured uterus	Ruptured uterus	p
The average age of women [years]	33.36 ± 4.6	32.95 ± 5.3	NS*
Mean gestational age [weeks]	39.22 ± 1.5	37.60 ± 1.2	NS*
Number of cesarean sections (n)	2.42 ± 0.8	3.10 ± 0.9	0.005
Period after previous cc [months] cesarean section [months]	70.40	59.2	NS*
Pregnancy complications	None	None	
Previous uterine incision closure technique	single-layer closure	single-layer closure	
Newborns' birthweight [grams]	3445.94	3045.50	0.002

NS — not significant

synthesized as a single chain protein, which undergoes organization into an elastic fiber in the extracellular space. It is likely elastin tissue distribution may help to explain the normal contractile function of myometrium during labor. We speculate that there is a correlation between the occurrence of uterine dehiscence or rupture incidence in term pregnant scarred uteri and biochemical changes in LUS structure, ascertained by myometrial immunohistochemical expression of elastin, collagen type VI, alpha smooth muscle actin, smooth muscle myosin heavy chain, endothelial cell marker CD31 (Platelet endothelial cell adhesion molecule - PECAM-1). Differences may occur in incompletely ruptured, fully ruptured or unruptured scarred uteri in term pregnancies.

MATERIAL AND METHODS

Test group

The study was conducted in Department of Perinatology, Obstetrics and Gynecology, Pomeranian Medical University in Szczecin, Poland in years 2016–2018. Institutional ethics approval from Pomeranian Medical University in Szczecin was received for all experiments and patients gave written consent for the investigation. During the three year prospective observation, total number of deliveries in our department was 4668 and the cesarean sections were performed in 2395 (51.3%) cases. From a total of 2395 cesarean sections, 20 (0.83%) were complicated by incomplete uterine scarred rupture. In all cases, the rupture of previously scarred uteri has occurred occasionally in the antepartum period. All analysed pregnant women were at term, without previous signs and symptoms of labor or regular uterine contractions. No pro-contractile agents have been administrated. All women who previously had one or more cesarean sections and did not accept vaginal route delivery after previous cesarean section, were qualified for elective cesarean section. Eighty-nine Caucasian ethnicity women took part in the study: 20 healthy pregnant women, who underwent repeat cesarean section complicated by incomplete uterine scar rupture before onset of labour and 69 healthy pregnant patients, who underwent repeat cesarean section without uterine scar rupture were analysed. The mean *age of* pregnant women in our total sample was 33.30 (SD ± 5.34) years with a range of 18 to 39 years. In all analysed women, a pre-pregnancy body mass index (BMI) had been calculated by dividing weight (kg) by height (m) squared. The BMI ranged between 19.8–29.0. Seventy-nine percent of the sample was classified as normal weight. There were no significant differences among analysed groups of patients in terms of age, gestational age and period after previous cesarean section. The time that had elapsed since the last caesarean section was generally longer than six years (Mean 6.1 SD ± 1.87) and did not statistically differ between either group. The mean number of cesarean sections in the group of women with unruptured and ruptured uterus was statistically significantly different, 2.42 (SD ± 0.61) and 3.10 (SD ± 0.72) respectively (Tab. 1).

Surgical procedures

All patients were operated under epidural anesthesia. Cesarean section was performed in sterile conditions. A transverse skin incision was made and carried through to the underlying layer of fascia. The fascia was incised in the midline and extended laterally. Once the abdomen was opened, the lower uterine segment in place of previous cesarean section was incised in transverse fashion. The infant was delivered atraumatically. After fetus removal, a uterine scar had been identified and a 2 × 2 cm sample of uterine lower segment was cut out. In all cases of incomplete uterine ruptures or unruptured uteri, an analogical procedure for collecting samples was performed. The uterine incision was closed by using one-layer closure technique with continuous lock stitches. No hysterectomy was required and there were neither maternal nor neonatal deaths.

Morphological study

Obtained tissues were fixed in 4% buffered paraformaldehyde and subsequently embedded in paraffin. The ovaries

were sectioned into slices of thickness of 3–5 µm with a Microtome HM 325. These sections were then mounted onto *poly-l-lysine coated slides*. The slides were stained with H-E (hematoxylin and eosin) for morphological study, and immunohistochemistry (IHC) was used to detect the presence of specific protein markers in uterine scars: CD31 (PECAM-1) endothelial cell marker; a-actin and myosin heavy chain — elements of myofilaments in smooth muscle cells; elastin and collagen type VI — elements of extracellular matrix. To visualize the proteins in myometrium scar, following mouse anti-human antibodies (Novocastra distributed by Leica Biosystems, Zalesie Gorne, Poland) were used: anti-CD31 (clone 1A10; optimally diluted); anti-smooth muscle actin, alpha (clone ASM-1; optimally diluted); anti-myosin heavy chain (smooth muscle) (clone S131; optimally diluted); anti-elastin (clone BA-4; diluted 1:100); anti-collagen type VI (clone 64C11; diluted 1:500). The deparaffinized sections were microwaved in citrate buffer (pH 6.0) for heat-induced epitope retrieval. After slow cooling to room temperature, the slides were washed in PBS twice for five minutes and then incubated for 60 minutes with primary antibodies. Next, the slides were incubated with Invitrogen Alexa Fluor Plus 488 goat anti-mouse IgG secondary antibody (Product # A32723) at a dilution of 1:1000 for 1 hr at room temperature (Invitrogen Thermo Fisher Scientific, USA).

The samples were viewed by fluorescent microscopy Olympus BX 46 and Olympus DP 25 camera. Additionally, samples were analyzed by high content screening for rapid quantitation and comparison of data from multiple samples. A digital computer-assisted analysis technique was based on the use of an image processing program (cell Sense Dimension 1.5), where three parameters were obtained: percentage of labeled cells, digital immunostaining intensity, and digital expression index. Sample images of staining analysed all the components shown in the picture below (Fig. 1 A–E).

Statistical analysis

To choose the right statistical analysis, we checked if the dependent variables were normally distributed using Shapiro-Wilk normality test. Because of non-normal data distribution, a nonparametric Mann-Whitney U test was used for determination of differences between analyzed groups. We compared mean, median scores of samples and performed one-way analysis of variance with the aid of Statistica10 statistical software (Oklahoma, Tulsa, USA). A $p \leq 0.05$ was considered to indicate statistical significance.

RESULTS

In our study, the majority of ruptures occurred in para 3–4, before trial of labour and uterine rupture was significantly more frequent, when the number of previous cesarean sections exceeded three. In turn, the period that had passed since the previous cesarean section and uterine incision closure technique previously used did not play a significant role. *Significant differences* were found between the birth *weight* of *newborns. In the group of unruptured uteri, the newborns* where significantly heavier when compared to those coming from the *ruptured uteri group* (Tab. 1).

Our study has demonstrated that collagen type VI, elastin, alpha smooth muscle actin, smooth muscle myosin heavy chain, endothelial cell marker CD31 are active and regular constituents of uterine scarred myometrium, which surround and associate smooth muscle cells (Tab. 2). Their concentrations, however, did not differ in the scarred unruptured and ruptured uterine tissue. The analysis of significance of the sample's correlation coefficient in two groups did show significant negative correlation between alpha smooth muscle actin and smooth muscle myosin heavy chain concentrations and elastin and CD31 concentrations in the unruptured uteri group as well (Tab. 3). Analysis of products of IHC reaction of tested components in myometrial scar did not show any significant differences in both groups of women delivered by cesarean section.

DISCUSSION

Cesarean section is the most frequent obstetrical procedure which the rate has dramatically risen in few last years. The presence of cesarean scar defect (CSD) in the lower uterine segment became a life-threatening problem mainly in cases when women wish to be pregnant more than once [18]. Previous caesarean section is known to be the main risk factor for incomplete and complete uterine rupture. Therefore, uterine scar rupture remains one of the most frightening late complications in obstetric care [5, 6]. Absence of peritoneal signs in incomplete uterine rupture in non-labouring women may delay its diagnosis, especially when connected with little or lack of bleeding into the abdominal cavity.

There is no consensus about the role of uterine closure technique for the risk of uterine rupture [8]. It is suggested that the risk of uterine rupture during labor after a single-layer closure is not significantly different from that after a double-layer closure [30]. In other studies, is postulated that a double-layer closure of the uterus during previous cesarean section is related to a thicker LUS, which may subsequently reduce the risk of LUS thickness lowering for less than 2mm and uterine dehiscence in the next pregnancies [11]. Contrarily, the type of used thread for uterine closure does not significantly influence on LUS thickness in next pregnancies [11]. There are also other factors that may have an impact on LUS integrity, such as: inter-cesarean interval longer than 54 months, maternal age beyond 35 years, cesarean section performed in labor, baby weighting more than 3000g, period longer

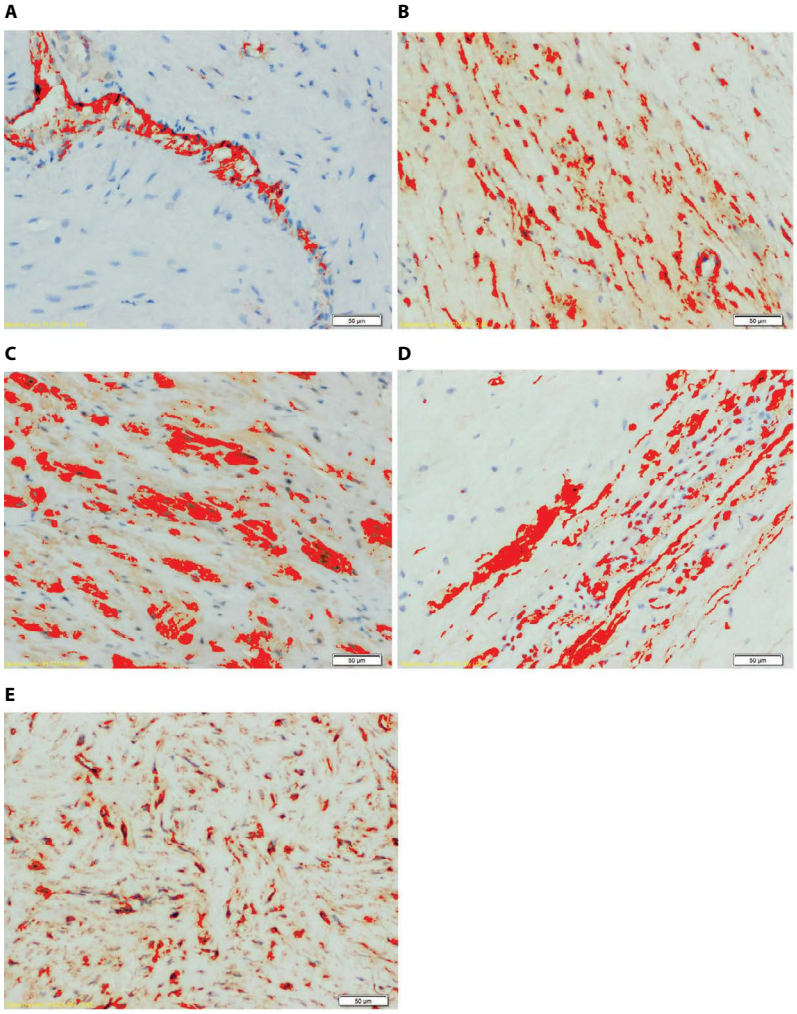

Figure 1. Representative IHC staining of **A.** CD31 (PECAM-1); **B.** Alpha smooth muscle actin; **C.** Smooth muscle myosin heavy chain; **D.** Elastin; **E.** Collagen type VI in ruptured uteri. Images were obtained under an ×20 magnification. Scale bar, 50 µm

Table 2. Relationship between immunohistochemical morphological parameters of unruptured and ruptured uterine cesarean scar

	alpha smooth muscle actin						smooth muscle myosin heavy chain					
	area [%]	**z**	**p**	**area fraction [µm²]**	**z**	**p**	**area [%]**	**z**	**p**	**area fraction [µm²]**	**z**	**p**
Unruptured uterus (n = 69)	23.14	–0.29	NS*	40755.87	–0.49	NS*	2.99	1.16	NS*	4 235.89	0.60	NS*
Ruptured uterus (n = 20)	29.86			46194.99			2.08			2 948.88		
	elastin						collagen type VI					
	area [%]	z	p	area fraction [µm²]	z	p	area [%]	z	p	area fraction [µm²]	z	p
Unruptured uterus (n = 69)	2.54	1.28	NS*	3 496.22	0.89	NS*	11.72	–0.47	NS*	4 235.89	–0.24	NS*
Ruptured uterus (n = 20)	2.06			2 936.05			12.15			2 948.88		
	CD31											
	area [%]	z	p	area fraction [µm²]	z	p						
Unruptured uterus (n = 69)	1.16	–1.05	NS*	1 857.15	–0.82	NS*						
Ruptured uterus (n = 20)	1.37			2 088.51								

NS — not significant

Table 3. Significance of the samples correlation coefficient in analyzed groups

Variables		Unruptured uterus n = 69 p	Ruptured uterus n = 20 p
Actin	Myosin	0.025	NS*
Actin	Elastin	NS*	NS*
Actin	Collagen	NS*	NS*
Actin	CD31	NS*	NS*
Myosin	Elastin	NS*	NS*
Myosin	Collagen	NS*	NS*
Myosin	CD31	NS*	NS*
Elastin	Collagen	NS*	NS*
Elastin	CD31	0.028	NS*
Collagen	CD31	NS*	NS*

NS — not significant

than 18 hours after rupture of membranes [21]. Myometrial discontinuity at the site of a previous cesarean section in nonpregnant women may be responsible for postmenstrual spotting, dysmenorrhea, dyspareunia and chronic pelvic pain. Moreover, patients after multiple cesarean sections have larger CSD followed by more severe clinical symptoms. It is reported that the CSD rate varies widely in range 0.3–19.4%, probably due to asymptomatic group of patients with CSD, who are not under control or at analysis [5, 19, 20].

Uterine wound repair has been analysed in just a few studies [17, 22]. It is likely that individual biochemical and biomechanical tissues' proprieties play a certain role in myometrium healing process [3].

Many investigations were focused on risk factors for uterine rupture and its prediction by LUS sonographic evaluation [2, 8, 15]. Until now, there is no evidence which factors have most significant and important impact on uterine healing process. There are a few data for the field of morphological and histological uterine wall repair process and there is little known about human uterine scar protein contents as well [17, 22]. The wound healing as a biological response for tissue injury can proceed as a repair and regeneration [23]. The wound repairing usually undergoes by patching, rather by restoring to its original structure. In normal conditions, wound repairing is processing through three phases: inflammation (onset of injury to days 4–6), tissue formation (days 4–14), tissue maturation and remodeling (week 1–year 1). A fibro-proliferative response involves mediators, blood cells and ECM parenchymal cells. The human myometrium is mainly composed of smooth muscle cells that have the ability to undergo hyperplasia and hypertrophy during pregnancy and can also regenerate as a repair response of injured tissue. The cells are interspersed with elements of ECM, a reservoir for matricellular proteins, growth factors, and cytokines [29]. Parallel to presence of smooth muscle cells, interstitial collagen fibrils are also detected. Collagens and elastic fibres are *ECM fibrous proteins* constituting networks, present in myometrium tissue. Type I, type III and type V are the predominant in human myometrium, additionally to type IV (basement membrane) and type VI that are present. The collagen VI plays a structural role as well as influences the migration of cells probably through fibronectin-dependent agents. [31]. Type VI collagens have many functions, including clinical evidence of involvement of connective tissue [27–29]. Its deficiency is associated with morphological abnormalities of the tendons and large spectrum of collagen VI-related myopathies. It acts also throughout interaction with collagen IV of basement membrane. The collagen VI homeostasis is regulating by capillary morphogenesis gene 2, also known as anthrax toxin receptor 2 (CMG2/ANTXR2). In cases of loss of CMG2 function, an accumulation of collagen VI lead to nodule formation in patients suffering from hyaline fibromatosis syndrome. In animal studies, a massive mice uterine collagen type VI accumulation induces progressive fibrosis and sterility. It is proposed, that CMG2 may mediate collagen VI intracellular degradation and plays a role of signalling receptor [32]. We suggest that over-accumulation of collagen VI may affect the uterine integrity by abnormal healing process, leading to changing the biomechanical wound proprieties. Another collagen VI function is an interaction with basement membrane collagen IV [28, 29]. In human wound collagen type VI is reported to be present after a post injury period of at least three days in a network connected with fibroblasts in the wound area. It can be also found in scar tissues and may play a role in modulation of haemostatic response to vascular injuries. Though the uterine scar collagen deposition after cesarean section is not the primary healing mechanism, collagen seems to be the most critical element, responsible for maintenance of tissue structural integrity. Pollio et al. demonstrated a higher collagen content in scarred lower uterine segment in cases of uterine dehiscence [17]. Our histological analysis of the uterine scar did not show any difference in scar integration and collagen type VI remodeling at the site of myometrial injury between ruptured and nonruptured uteri.

Elastin is a connective tissue polymeric protein, synthesized as a single chain protein, which undergoes organization into an elastic fiber in the extracellular space. The elastin is a stable element of ECM, and its myometrial tissue concentration remains unchanged even at pregnancy. In our investigation the myometrial elastin concentrations did not vary in groups of patients with ruptured and unruptured uterine scars. Our study provides tendency that there is a gradient of elastin uterine scar distribution and the scar seems to be more elastic in pregnancies uncomplicated by uterine rupture when compared to pregnancies complicated by uterine rupture.

It has been proven, that eNDOTHELIAL CELLS have many functions and play a role in the control of coagulation, thrombolysis, vascular tone, permeability, inflammation, tissue repair and angiogenesis [33]. The expression of anti-platelet-endothelial cell adhesion molecule-1 (endothelial cell marker CD31, 130-kDa transmembrane glycoprotein) has been recently demonstrated on surface of platelets, monocytes, macrophages [34]. Neoangiogenesis understood as a formation of new blood vessels, seems to be an essential process during wound healing. In our study we demonstrated the presence of endothelial cell marker CD31 in human uterine scar of ruptured and unruptured uteri as well. The CD31 expression and angiogenesis in the uterine scar may be associated with the inflammation phase of wound repairing after cesarean section, oxygen deliverance, nutrients, and inflammatory cells as well. Its angiogenic and facilitating leukocyte migration role, may be important in myometrial continuity repair process. We did not identify any significant differences in CD31 expression in scarred ruptured and non-ruptured uteri. In animal model studies, the formation of capillaries, reflected by expression of CD31 haven't been increased in uterine wound tissue [23]. The scarred and unscarred tissues are composed of the same molecules of extracellular matrix, but the ratios in scarred tissue are different when compared to normal tissue [24, 35], which was also partially confirmed in our studies in the analysis of actin and myosin in the unruptured uteri group (Tab. 3). The contractile smooth muscle activity is based on cytoplasmic structural proteins' microfilament system, where actin and myosin play a basic role and constitute about 55% of all the proteins of the smooth muscle cells. Immunoexpression of alpha smooth muscle actin (SMA) is found in vascular walls and muscularis mucosae of many organs, including uterus, therefore is reported to be useful in the identification of leiomyomas and leiomyosacomas pleomorphic adenomas. In our investigation we identified presence of SMA in scarred uteri and its concentration did not differ in ruptured and non-ruptured uteri. The smooth muscle myosin heavy chain (SM-MHC) that is major component of the contractile system also did not vary in analysed groups of patients. Our study can suggest indirectly that in unruptured scarred uteri the contractile uterus activity is less expressed than in ruptured uteri. Myometrial contraction is mediated *via* interaction of actin and myosin and regulated by enzymatic phosphorylation.

CONCLUSIONS

Our study demonstrated that collagen type VI, elastin, endothelial cell marker CD31, alpha smooth muscle actin, and smooth muscle myosin heavy chain, are active and regular constituents of ruptured and unruptured uterine scarred myometrium.

The obtained results indicated correlated distribution of actin and myosin as well as elastin and CD31 in unruptured uteri while this fact hasn't been observed in ruptured uteri.

There is no statistically significant difference between myometrial immunoexpression of studied fibrous proteins of extracellular matrix, endothelial cell marker and markers of smooth muscle cells in ruptured and unruptured scarred uteri. It suggests that myometrial wound healing is related to multicomplex cell interactions, where the direct mechanism of abnormal uterine healing and myometrial rupture remains unclear.

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Conflict of interest

The authors have not reported any conflict of interest.

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