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OCENA MORFOLOGII BLIZNY MACICY PO CIĘCIU CESARSKIM PRZY ZASTOSOWANIU ULTRASONOGRAFII DWUWYMIAROWEJ I TRÓJWYMIAROWEJ

ROZPRAWA DOKTORSKA

lek. Joanna Budny-Wińska

Promotor: dr hab.n.med. Michał Pomorski

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Składam najserdeczniejsze podziękowania Promotorowi mojej pracy,
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za nieocenioną pomoc, wsparcie, życzliwość i motywację do działania
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za wsparcie przy tworzeniu niniejszej rozprawy.

Z dedykacją dla Męża…

SPIS TREŚCI

1. WYKAZ PUBLIKACJI STANOWIĄCYCH ROZPRAWĘ DOKTORSKĄ

I. “Two- and three-dimensional transvaginal ultrasound in assessment of the impact of selected obstetric risk factors on cesarean scar niche formation: the case-controlled study”

Joanna Budny-Wińska, Aleksandra Zimmer-Stelmach, Michał Pomorski

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III. “UTERINE NICHE AFTER CESAREAN SECTION: a review of diagnostic methods”

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2. STRESZCZENIE

WSTĘP

Następstwem każdego cięcia cesarskiego jest wytworzenie się blizny w mięśniu macicy. W przypadku jej nieprawidłowego bądź niecałkowitego wygojenia się, może dojść do powstania tzw. niszy macicy po cięciu cesarskim. Większość małych ubytków blizny macicy po cięciu cesarskim jest bezobjawowa. Do objawów klinicznych związanych z obecnością niszy macicy po cieciu cesarskim - tzw. cesarean scar syndrome, zalicza się nieprawidłowe krwawienie maciczne, dyspareunię, zespół bólowy miednicy mniejszej i niepłodność wtórną. W przypadku kobiet ciężarnych następstwa wynikające z obecności niszy po cięciu cesarskim stanowią bezpośrednie zagrożenie zdrowia i życia. Związane są one z dehiscencją blizny macicy i jej pęknięciem, zaburzeniem placentacji, prowadzącym do powstania łożyska przodującego, wrastającego lub przerastającego mięsień macicy, czy z ciążą zlokalizowaną w bliźnie macicy. Powyższe następstwa stanowią, dlaczego tak ważne jest prawidłowe zdiagnozowanie niszy po cięciu cesarskim, wyodrębnienie czynników ryzyka prowadzących do jej powstania i ustalenie dalszego postępowania w przypadkach wymagających leczenia.

CELE

Przedmiotem niniejszej pracy jest ocena morfologii blizny macicy po cięciu cesarskim przy zastosowaniu ultrasonografii dwuwymiarowej i trójwymiarowej, jak również ocena zależności pomiędzy wystąpieniem położniczych i ogólnoustrojowych czynników ryzyka a powstaniem niszy macicy i jej morfologią. Celem niniejszego opracowania jest również przegląd i analiza metod diagnostycznych, mających zastosowanie w rozpoznaniu niszy macicy po cięciu cesarskim.

MATERIAŁ I METODY

Grupę badaną stanowiło 204 pacjentek, które przebyły cięcie cesarskie w II Klinice i Katedrze Ginekologii i Położnictwa we Wrocławiu w latach 2017-2019. Wszystkie kobiety przebyły cięcie cesarskie z zaopatrzeniem nacięcia macicy szwem jednowarstwowym ciągłym obejmującym całą grubość myometrium z wyłączeniem doczesnej. Uczestniczki badania zostały zaproszone do ultrasonograficznej oceny blizny macicy po cięciu cesarskim po 6-8 tygodniach od zabiegu. Diagnostykę obrazową wykonano przy zastosowaniu przezpochwowej ultrasonografii dwuwymiarowej oraz trójwymiarowej, używając aparatu

Voluson V8 Expert (General Electric Medical Systems) z sondą przezpochwową 3D 4–9 MHz i programu VOCAL. Oceniono następujące parametry niszy macicy: wysokość, szerokość, grubość części zrośniętej myometrium (ang. residual myometrial thickness, RMT), grubość myometrium przylegającego do niszy (ang. adjacent myometrial thickness, AMT), objętość niszy macicy, jak również współczynnik RMT/AMT, jak i stosunek grubości części zrośniętej myometrium wobec szerokości i wysokości niszy macicy.
W publikacji „Two- and three-dimensional transvaginal ultrasound in assessment of the impact of selected obstetric risk factors on cesarean scar niche formation: the case-controlled study" oceniono wpływ wystąpienia czynników położniczych takich jak: tryb przeprowadzenia cięcia cesarskiego (pilne vs elektywne), rozwarcie szyjki macicy (brak rozwarcia vs rozwarcie <10 cm), przeprowadzenia cięcia cesarskiego w II okresie porodu, sposobu otwarcia macicy (na ostro vs na tępo), przebytych cięć cesarskich w historii (przebycie co najmniej jednego cięcia cesarskiego w przeszłości vs pierwsze cięcie cesarskie), typ zgięcia macicy (przodozgięcie vs tyłozgięcie macicy), doświadczenie operatora (specjalista vs rezydent), na powstanie niszy macicy i jej morfologię.
W pracy pod tytułem „The impact of selected risk factors on uterine healing after cesarean section in women with single layer uterine closure: a prospective study using two- and three-dimensional transvaginal ultrasonography" oceniono wpływ czynników ryzyka takich jak: wiek ciążowy w momencie rozwiązania (poród przedwczesny vs rozwiązanie w ciąży donoszonej), wiek matki w momencie cięcia cesarskiego, historia dotycząca przebytych poronień, kolonizacja szyjki macicy przez drobnoustroje czy wystąpienie chorób wikłających ciążę takich jak: cukrzyca ciążowa, nadciśnienie tętnicze wywołane ciążą, niedoczynność tarczycy. Uzyskane wyniki zostały poddane analizie statystycznej.

W publikacji „UTERINE NICHE AFTER CESAREAN SECTION: a review of diagnostic methods" dokonano przeglądu dostępnej literatury dotyczącej metod diagnostycznych niszy macicy, przeszukując bazy danych Pubmed, Scopus i Google Scholar oraz podjęto próbę usystematyzowania wiedzy i wytycznych dotyczących procesu diagnostycznego blizny i niszy macicy po cięciu cesarskim.

WYNIKI

Średni wiek pacjentek wynosił 32,25 lat (SD 4,156). Wiek ciążowy w momencie rozwiązania wynosił średnio 37,863 t.c. (SD 2,43). 56 kobiet przebyło co najmniej jedno cięcie cesarskie w przeszłości. Spośród wszystkich badanych, u 153 stwierdzono obecność niszy po cięciu cesarskim. Jedynie u 5 pacjentek stwierdzono grubość zrośniętego odcinka

(RMT) <2.2mm, a u 35 stwierdzono stosunek RMT/AMT równy bądź mniejszy niż 0.5, co jest uznane za czynnik ryzyka ciężkich powikłań związanych z blizną macicy w kolejnych ciążach.

W pracy „Two- and three-dimensional transvaginal ultrasound in assessment of the impact of selected obstetric risk factors on cesarean scar niche formation: the case-controlled study" nie wykazano wpływu rozwarcia szyjki macicy, wystąpienia czynności skurczowej podczas cięcia cesarskiego, przeprowadzenia cięcia cesarskiego w II okresie porodu, sposobu otwarcia macicy, doświadczenia operatora czy uwarunkowań anatomicznych macicy (typu zgięcia macicy) na występowanie i morfologię niszy macicy po cięciu cesarskim. Stwierdzono, iż grubość zrośniętego odcinka myometrium (RMT), jak i stosunek RMT/AMT u kobiet, które w przeszłości przebyły co najmniej jedno cięcie cesarskie są mniejsze niż u kobiet, u których przeprowadzono cięcie cesarskie po raz pierwszy.

W publikacji „The impact of selected risk factors on uterine healing after cesarean section in women with single layer uterine closure: a prospective study using two- and three-dimensional transvaginal ultrasonography" nie stwierdzono wpływu obciążenia chorobami układowymi takimi jak cukrzyca ciążowa, nadciśnienie tętnicze wywołane ciążą, niedoczynność tarczycy, czy wiekiem matki i wiekiem ciążowym w momencie rozwiązania, przebyciem w przeszłości poronienia czy kolonizacją kanału szyjki macicy drobnoustrojami a częstością występowania niszy macicy, jak i jej morfologią.

Ponadto, wykonując kompleksowy przegląd literatury dotyczącej diagnostyki blizny i niszy macicy, dokonano posumowania obecnego stanu wiedzy na ten temat. Z uwagi na niejednoznaczne doniesienia naukowe dotyczące m.in. braku jednolitej definicji i sposobu klasyfikacji niszy macicy czy określenia optymalnego czasu po cięciu cesarskim do oceny blizny macicy, zwrócono uwagę na konieczność przeprowadzenia dalszych badań dotyczących tej tematyki i stworzenia jednolitych definicji i algorytmów diagnostyczno-terapeutycznych niszy macicy.

WNIOSKI

Wyniki zawarte w publikacji "Two- and three-dimensional transvaginal ultrasound in assessment of the impact of selected obstetric risk factors on cesarean scar niche formation: the case-controlled study" oraz "The impact of selected risk factors on uterine healing after cesarean section in women with single layer uterine closure: a prospective study using two- and three-dimensional transvaginal ultrasonography" oraz niejednoznaczne doniesienia wpływu ocenionych zmiennych w literaturze światowej na morfologię blizny macicy po

cięciu i występowanie niszy macicy, zwracają uwagę na to, że problem nieprawidłowego procesu gojenia się macicy po cięciu cesarskim jest problemem wieloczynnikowym.

Dla praktyki klinicznej ważnym jest, że zastosowanie zaopatrzenia nacięcia macicy szwem jednowarstwowym ciągłym obejmującym całą grubość myometrium z wyłączeniem doczesnej pozwala na uzyskanie prawidłowego zrostu mięśnia macicy po cięciu cesarskim, niezależnie od: trybu przeprowadzenia cięcia cesarskiego, doświadczenia operatora, uwarunkowań anatomicznych macicy, wystąpienia czynności skurczowej, postępu porodu w momencie cięcia cesarskiego, jak i obciążenia chorobami układowymi w ciąży, historii przebytych poronień czy wieku matki i ciążowego w momencie cięcia cesarskiego lub kolonizacji kanału szyjki macicy drobnoustrojami.

W związku z rosnącą liczbą cięć cesarskich i tym samym narastającym problemem coraz większej liczby dużych nisz macicy, które niosą ze sobą ryzyko poważnych konsekwencji zdrowotnych oraz z uwagi na brak jednoznacznych standardów diagnostycznych i klasyfikacyjnych nisz macicy po cięciu cesarskim, jak również sprzeczne doniesienia co do wpływu poszczególnych czynników na proces gojenia się blizny macicy po cięciu cesarskim, konieczne jest przeprowadzenie dużych badań prospektywnych na homogennych grupach pacjentek.

3. ABSTRACT

INTRODUCTION

Scar formation in the uterine muscle is the consequence of each cesarean section. When the healing process of uterine muscle is abnormal or incomplete, the cesarean scar niche is formatted. Most of the small uterine scar defects are asymptomatic. The clinical symptoms related to the presence of the cesarean scar niche - the so-called cesarean scar syndrome, include abnormal uterine bleeding, dysmenorrhea, and secondary infertility. Among pregnant women, the consequences of the presence of a niche after cesarean section pose a direct threat to health and life, as they are related to uterine scar dehiscence and uterine rupture, improper placentation process, leading to the formation of the placenta previa and placenta accreta spectrum disorders, or cesarean scar pregnancy. That is why it is so important to correctly diagnose the niche after cesarean section, as well as to identify risk factors leading to its formation, and to determine further treatment in cases requiring treatment.

AIM OF THE STUDY

The subject of this study is to assess the uterine scar morphology after cesarean section using two-dimensional and three-dimensional ultrasound, as well as to assess the relationship between the occurrence of obstetric and systemic risk factors and the prevalence of cesarean scar niche and its morphology. The aim of this study is also to review and analyze the diagnostic methods used in the detection of the uterine niche after cesarean section.

MATERIAL AND METHODS

The study group consisted of 204 patients who underwent cesarean section at the 2nd Clinic and Department of Gynecology and Obstetrics in Wrocław in years 2017-2019. All women underwent cesarean section with low transverse uterine incision with single-layer continuous suture covering the entire thickness of the myometrium, excluding the decidua. Participants of the study were invited to undergo ultrasonographic assessment of the cesarean section scar 6-8 weeks after the procedure. Ultrasound diagnosis of the uterine cesarean scar was performed using two-dimensional and three-dimensional transvaginal ultrasound, using the Voluson V8 Expert (General Electric Medical Systems) ultrasound machine with a 4–9 MHz transvaginal 3D probe and the VOCAL program. The following parameters of the

uterine niche were assessed: height, width, residual myometrial thickness (RMT), adjacent myometrial thickness (AMT), volume of the uterine niche, as well as the RMT / AMT ratio, the RMT/W ratio and RMT/D ratio.

In the publication "Two- and three-dimensional transvaginal ultrasound in assessment of the impact of selected obstetric risk factors on cesarean scar niche formation: the case-controlled study" the impact of obstetric factors such as: mode of cesarean section (emergency vs elective), cervical dilation (no dilation vs dilation <10 cm), cesarean section performed in the second stage of labor, uterine incision expansion (sharp vs blunt), number of previous cesarean sections (at least one previous cesarean section vs no previous cesarean sections), type of uterine flexion (anteflexion vs retroflexion), operator's experience (specialist vs resident); for cesarean scar uterine niche incidence and its morphology was assessed.

In the work entitled "The impact of selected risk factors on uterine healing after cesarean section in women with single layer uterine closure: a prospective study using two- and three-dimensional transvaginal ultrasonography", the impact of risk factors such as: pregnancy complicated by diseases such as gestational diabetes, gestational hypertension, hypothyroidism during pregnancy, gestational age at delivery (preterm delivery vs term delivery), maternal age at the time of cesarean section, miscarriage history, cervical colonization by pathogens; for cesarean scar niche prevalence and its morphology was assessed.

In the publication "UTERINE NICHE AFTER CESAREAN SECTION: a review of diagnostic methods", the available literature concerning the diagnostic methods of the uterine niche was reviewed by searching the Pubmed, Scopus and Google Scholar databases to systematize the knowledge and guidelines for the diagnostic process of the uterine scar and niche after cesarean section.

RESULTS

The mean age was 32.25 years (SD 4.156) and gestational age was 37.863 weeks (SD 2.43). In all, 56 (27%) participants had at least one cesarean section in the past, while 32 (16%) had at least 1 previous vaginal delivery. Out of all examined women, 153 had a niche after cesarean section (75%), but only five patients had a residual myometrium thickness

(RMT) <2.2 mm, and 35 had an RMT / AMT ratio of 0.5 or less, which is considered a risk factor for severe uterine scar complications in subsequent pregnancies.

In the publication "Two- and three-dimensional transvaginal ultrasound in assessment of the impact of selected obstetric risk factors on cesarean scar niche formation: the case-controlled study", no impact of: cervical dilation, performing cesarean section during second stage of labor, uterine incision expansion, the operator's experience, or the type of uterine flexion on the occurrence and morphology of the uterine niche after cesarean section was found. Based on the analysis, it was found that the residual myometrial thickness and RMT/AMT ratio among women who had previously undergone at least one cesarean section was lower than among women who underwent the cesarean section for the first time.

In the publication "The impact of selected risk factors on uterine healing after cesarean section in women with single layer uterine closure: a prospective study using two- and three-dimensional transvaginal ultrasonography", no impact of the presence of systemic diseases such as gestational diabetes, gestational hypertension, hypothyroidism during pregnancy, the mother's and gestational age at the time of delivery, history of miscarriage or colonization of the cervical canal by pathogens and the prevalence of the uterine niche after cesarean section and its morphology was found.

Moreover, by performing a review of the literature concerning the diagnosis of uterine scar and niche, the current state of knowledge on this subject was summarized. Due to the ambiguous reports concerning the diagnosis of cesarean scar niche, the further researches on the subject of uterine scar after cesarean section are needed to create uniform definitions, classifications, diagnostic and therapeutic algorithms.

CONCLUSIONS

The results included in the publication “Two- and three-dimensional transvaginal ultrasound in assessment of the impact of selected obstetric risk factors on cesarean scar niche formation: the case-controlled study” and “The impact of selected risk factors on uterine healing after cesarean section in women with single layer uterine closure: a prospective study using two- and three-dimensional transvaginal ultrasonography "and the ambiguous reports of the influence of the assessed risk factors in the literature concerning the morphology and occurrence of the uterine niche, prove that the improper uterine healing process after cesarean section is a multifactorial problem.

For clinical practice, it is important that the use of single-layer continuous suture covering the entire thickness of the myometrium, excluding the decidua, provide the proper uterine healing after cesarean section, regardless of the mode of cesarean section, the operator's experience, the type of uterine flexion, the progress of labor at the time of cesarean section, as well as the presence of systemic diseases in pregnancy, the history of miscarriages, the mother's and gestational age at the time of cesarean section, or colonization of the cervical canal by pathogens.

Due to the growing number of cesarean sections and thus the growing problem of the increasing number of large niches, and the lack of unambiguous diagnostic and classification standards for them, as well as conflicting reports of the impact of factors affecting the healing process of the uterine scar after cesarean section, it is necessary to conduct large prospective studies on homogeneous groups of patients.

4. WSTĘP

Zabieg cięcia cesarskiego jest najczęściej wykonywaną procedurą położniczą, której poddają się rocznie miliony kobiet na całym świecie. To operacja często ratująca zdrowie i życie matki i narodzonego dziecka. W ostatnich dekadach na całym świecie obserwuje się wzrost odsetka przeprowadzanych cięć cesarskich. W Polsce ten odsetek jest jednym z najwyższych w Europie i według raportu Głównego Urzędu Statystycznego z roku 2019 wynosi on 44.8%. Główne położnicze wskazania do cięcia cesarskiego stanowią zatrzymanie postępu porodu i zagrażająca śródporodowa wewnątrzmaciczna zamartwica płodu, jednak obserwuje się wzrastającą ilość elektywnych cięć cesarskich przeprowadzonych z uwagi na obecność blizny po cięciu cesarskim czy z uwagi na położenie miednicowe płodu.[1] W ostatnich latach wzrósł także odsetek cięć cesarskich z przyczyn pozapołożniczych, które coraz częściej są wykonywane z uwagi na tokofobię.[2]

Jak każda inwazyjna procedura, cięcie cesarskie niesie ze sobą możliwość wystąpienia niepożądanych następstw. Konsekwencją każdego cięcia cesarskiego jest utworzenie się blizny macicy w miejscu jej nacięcia. W przypadku nieprawidłowego lub niecałkowitego jej wygojenia dochodzi do powstania tzw. niszy macicy i możliwości wystąpienia związanych z nią objawów/następstw.

4.1. DEFINICJA I KLASYFIKACJA NISZY MACICY PO CIĘCIU CESARKIM

W dostępnej literaturze nie ma jednoznacznej definicji niszy macicy po cięciu cesarskim. Większość autorów określa niszę macicy jako brak ciągłości myometrium w miejscu histerotomii lub jako stwierdzony w przezpochwowym badaniu ultrasonograficznym hipoechogenny trójkąt, mający łączność z jamą macicy.[3-5] W opublikowanej w 2018r pracy pod tytułem „Sonographic examination of uterine niche in non-pregnant women: a modified Delphi procedure” zostały zawarte zasady oceny ultrasonograficznej niszy macicy po cięciu cesarskim, jak również przyjęto definicję niszy macicy jako wpuklenie w miejscu blizny po cięciu cesarskim o głębokości co najmniej 2 mm.[6]

Podobnie jak z definicją niszy macicy, w dostępnej literaturze brakuje jednorodnej klasyfikacji niszy macicy. Pierwszą próbę podziału nisz macicy podjęto w 2011r w pracy „Surgical hysteroscopic treatment of cesarean-induced isthmocele in restoring fertility: prospective study”, gdzie pogrupowano je z uwagi na pole powierzchni hipoechogennego

trójkąta w ultrasonograficznym badaniu przezpochwowym.[7] Kolejne klasyfikacje niszy macicy opierały się na grubości części zrośniętej myometrium (RMT) bądź na stopniu penetracji niszy macicy wobec przedniej ściany myometrium[3]. Według powyższych klasyfikacji duża nisza, to taka, w której grubość części zrośniętej myometrium (RMT) jest mniejsza bądź równa 2.2 mm w ultrasonograficznym badaniu przezpochwowym lub mniejsza bądź równa 2.5 mm w sonohisterografii lub gdy nisza stanowi powyżej 50% bądź 80% grubości myometrium. W klasyfikacji VTS zaproponowanej przez A. Ludwin et al. podzielono nisze macicy na klinicznie istotne i nieistotne na podstawie ich objętości, grubości części zrośniętej (RMT) czy obecności czynników dodatkowych (obecności odgałęzień niszy, pęcherza moczowego niepokrywającego niszy i podejrzenia głęboko naciekającej endometriozy w niszy po cięciu cesarskim).[8] Nisze macicy można również podzielić na dające objawy kliniczne lub asymptomatyczne.

4.2. EPIDEMIOLOGIA

Nie ma jednoznacznych danych dotyczących częstości występowania niszy macicy. Rozpowszechnienie jej po cięciu cesarskim różni się w badaniach w zależności od definicji, według której stwierdzano niszę macicy, użytej metody diagnostycznej czy grupy badanej (tylko objawowe pacjentki czy część populacji) itd. W dostępnej literaturze częstość występowania niszy macicy po cięciu cesarskim waha się pomiędzy 24-84%.[3 9-11]

4.3. NASTĘPSTWA GINEKOLOGICZNE WYNIKAJĄCE Z OBECNOŚCI NISZY MACICY PO CIĘCIU CESARKIM

Konsekwencją obecności objawowej niszy macicy jest wystąpienie tzw. cesarean scar syndrome, dla którego charakterystyczne są takie objawy jak: nieprawidłowe krwawienia maciczne, które stanowią przedłużające się i bolesne miesiączki, zespół bólowy miednicy mniejszej i niepłodność wtórna. [7 12-14]

Częstość występowania nieprawidłowych krwawień macicznych w grupie kobiet z niszą macicy wynosi 29%.[9] Wykazano korelację pomiędzy wielkością niszy macicy, a częstością występowania nieprawidłowych plamień.[15]

W pracy pod tytułem „Post-Caesarean section niche-related impaired fertility: hypothetical mechanisms" przedstawiono możliwe przyczyny niepłodności wtórnej związanej z obecnością niszy macicy.[16] Związane są one z m.in. wystąpieniem czynników upośledzających zagnieżdżenie zarodka takich jak: obecność płynu w jamie macicy, nasilenie miejscowego stanu zapalnego związanego z obecnością niszy czy wystąpienie

nieskoordynowanych skurczów macicy. Mogą być związane również z zaburzeniem ruchu plemników, który jest utrudniony przez nagromadzony w niszy macicy śluz i zalegającą w niej krew miesiączkową czy utrudnieniem transferu zarodka w przypadku silnie tyłozgiętej macicy i wystąpienia dużej niszy macicy. Mogą także wynikać z ograniczenia możliwości współżycia seksualnego w przypadku nasilenia objawów ginekologicznych wynikających z obecności niszy macicy, takich jak: plamienia, ból miednicy mniejszej czy dyspareunia lub wiążącego się z okresem rekonwalescencji po przebyciu operacji naprawczych niszy macicy.

4.4. NASTĘPSTWA POŁOŻNICZE WYNIKAJĄCE Z OBECNOŚCI NISZY MACICY PO CIĘCIU CESARSKIM

Do następstw położniczych niszy blizny macicy po cieciu cesarskim w kolejnej ciąży należą: dehiscencja blizny macicy po cięciu cesarskim i jej pęknięcie, zaburzenia związane z nieprawidłową placentacją (łożysko przyrośnięte, wrastające i przerastające) oraz ciąża zlokalizowana w niszy macicy po cięciu cesarskim. [17-19]

Śródporodowe pęknięcie macicy zdarza się rzadko. Najczęstszą przyczyną pęknięcia macicy jest jej pęknięcie w miejscu blizny macicy po poprzednim cięciu cesarskim.[20] W publikacji M. Fogelberg et al., w której przeanalizowano dokumentację medyczną dotyczącą cięć cesarskich, które odbyły się w latach 2005-2009 w Malmo, odsetek pęknięć macicy w miejscu blizny po uprzednim cięciu cesarskim wikłał 2.8% ciąż, natomiast dehiscencja blizny macicy po poprzednim cięciu cesarskim została stwierdzona w 10.1% przypadków. [21] W pracy „Prediction of uterine dehiscence using ultrasonographic parameters of cesarean section scar in the nonpregnant uterus: a prospective observational study” wykazano, iż stosunek wysokości niszy macicy wobec części zrośniętej myometrium (RMT) jest pomocny w przewidywaniu dehiscencji blizny macicy po cięciu cesarskim w kolejnej ciąży. [18]

Ciąża w bliźnie macicy to ciąża ektopowa, która zagnieździła się w obrębie/sąsiedztwie niszy macicy. Częstość występowania ciąży w bliźnie po cięciu cesarskim wynosi 1:1800-1:2216, ale wraz ze wzrostem odsetka cięć cesarskich, obserwuje się wzrost częstości jej występowania.[22] Z uwagi na duże ryzyko krwotoku z dróg rodnych i pęknięcia macicy stanowi ona bezpośrednie zagrożenie życia ciężarnej.[23] Uznaje się, że ciąża w bliźnie macicy stanowi wczesne stadium zaburzeń placentacji, prowadzących do rozwoju łożyska zarówno przodującego, jak i wrastającego czy przerastającego mięsień macicy. [24]

4.5. METODY DIAGNOSTYCZNE NISZY MACICY PO CIĘCIU CESARSKIM

Do metod diagnostycznych blizny po cięciu cesarskim zalicza się ultrasonografię przezpochwową i sonohisterografię, zarówno 2D i 3D/4D [8 18], histerosalpingografię, histeroskopię lub rezonans magnetyczny. [25]

W praktyce klinicznej badaniem pierwszego wyboru w ocenie mięśnia macicy po cięciu cesarskim jest przezpochwowe badanie ultrasonograficzne, które jest badaniem najbardziej dostępnym, najmniej inwazyjnym, najtańszym, ale ma też swoje ograniczenia - małe nisze po cięciu cesarskim mogą być nieuwidocznione lub ich parametry mogą być niedoszacowane. [26-28] Sonohisterografia jest badaniem czulszym w diagnostyce i potwierdzeniu obecności niszy macicy w porównaniu do ultrasonograficznego badania przezpochwowego bez użycia środka kontrastowego, dodatkowo pozwala ona na dynamiczną ocenę ubytku mięśniówki macicy po cięciu cesarskim. [4 9 29 30] Trójwymiarowe badanie ultrasonograficzne pozwala na dokładną ocenę parametrów niszy macicy, jak i na pomiar jej objętości, która m.in. stanowi jedno z kryteriów używanych w klasyfikacji VTS nisz istotnych i nieistotnych klinicznie.[8] Histeroskopia umożliwia bezpośrednie uwidocznienie i potwierdzenie obecności niszy macicy po cięciu cesarskim [31] oraz małoinwazyjną korektę ubytku mięśniówki macicy w miejscu jej blizny, co redukuje objawy ginekologiczne niszy pod postacią nieprawidłowych krwawień macicznych.[32] Podczas badania histeroskopowego nie jest możliwy pomiar grubości zrośniętej myometrium (RMT), co stanowi ograniczenie tej metody diagnostycznej.

Szczegółowy opis metod diagnostycznych blizny macicy po cięciu cesarskim znajduję się w ostatniej publikacji stanowiącej cykl prac - “UTERINE NICHE AFTER CESAREAN SECTION: a review of diagnostic methods” (patrz str. 35).

4.6. ULTRASONOGRAFICZNA OCENA BLIZNY MACICY PO CIĘCIU CESARSKIM

Blizna macicy po cięciu cesarskim znajduje się na przedniej ścianie macicy. Niszę macicy może stanowić hipoechogenny trójkąt bądź wielokształtna struktura, w której można wyodrębnić co najmniej jedno odgałęzienie. W 2018r opublikowano zasady ultrasonograficznej diagnostyki blizny macicy po cięciu cesarskim według zmodyfikowanego protokołu Delphi[6], co do których zastosowano się w badaniach stanowiących ten cykl prac. Według powyższej publikacji ocenę ultrasonograficzną powinno się rozpocząć od płaszczyzny strzałkowej. W tej płaszczyźnie, w przypadku obecności niszy macicy, ocenia się następujące parametry: długość, głębokość niszy macicy oraz grubość mięśniówki macicy przylegającej do niszy w miejscu, w którym są największe oraz grubość części zrośniętej

myometrium, w jej najmniejszym wymiarze. W przypadku braku obecności niszy jedynym pomiarem blizny, który można ocenić jest grubość części zrośniętej myometrium. Następnie w przekroju poprzecznym ocenia się szerokość niszy macicy oraz dokumentuje się występujące jej odgałęzienia. Rozszerzona ocena niszy macicy, która jest pomocna w planowaniu postępowania terapeutycznego, obejmuje pomiar odległości pomiędzy szczytem niszy a fałdem pęcherzowo-pochwowym oraz odległości między niszą a ujściem zewnętrznym szyjki macicy.

5. CELE PRACY

Przedmiotem niniejszej pracy jest:

a. ultrasonograficzna ocena blizny macicy po cięciu cesarskim przy pomocy ultrasonografii dwuwymiarowej i trójwymiarowej oraz stworzenie modeli nisz macicy w programie VOLCAL, jak również ultrasonograficzna ocena zależności pomiędzy morfologią blizny w mięśniu macicy po cięciu cesarskim w grupie pacjentek, u których nacięcie macicy zostało zaopatrzone szwem jednowarstwowym ciągłym a wybranymi czynnikami ryzyka - publikacja „Two- and three-dimensional transvaginal ultrasound in assessment of the impact of selected obstetric risk factors on cesarean scar niche formation: the case-controlled study" oraz „The impact of selected risk factors on uterine healing after cesarean section in women with single layer uterine closure: a prospective study using two- and three-dimensional transvaginal ultrasonography".
b. podsumowanie aktualnego stanu wiedzy dotyczącego metod diagnostycznych blizny macicy po cięciu cesarskim na podstawie przeglądu literatury - publikacja „UTERINE NICHE AFTER CESAREAN SECTION: a review of diagnostic methods".

6. PUBLIKACJE

6.1. “Two- and three-dimensional transvaginal ultrasound in assessment of the impact of selected obstetric risk factors on cesarean scar niche formation: the case-controlled study.”

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Two- and three-dimensional transvaginal ultrasound in assessment of the impact of selected obstetric risk factors on cesarean scar niche formation: the case-controlled study

Joanna Budny-Winska, Aleksandra Zimmer-Stelmach, Michal Pomorski

2nd Department and Clinic of Gynaecology, Obstetrics and Neonatology, Wroclaw Medical University, Wroclaw, Poland

ABSTRACT

Objectives: Incomplete healing of the uterine scar after cesarean section may result in formation of a niche. The aim of this study is to identify the potential risk factors for the improper uterine healing after cesarean section in women with single layer, full thickness uterine closure with the use of two- and three-dimensional transvaginal ultrasonography.

Material and methods: 204 women with a history of at least one low transverse cesarean section (CS) with a single layer uterine closure participated in the study. Residual myometrial thickness (RMT), adjacent myometrial thickness (AMT), width (W), depth (D) and volume of the niche, RMT/AMT, RMT/D, RMT/W ratio and clinical characteristics were analyzed.

Results: A niche after cesarean section was found in 153 cases. However only five patients had a RMT < 2.2 mm, and 35 had an RMT/AMT ratio ≤ 0.5. The RMT and RMT/AMT ratio among women who had undergone more than one cesarean section was lower than among women who underwent the first cesarean section. No statistically significant relationship was found between the incidence of niche, its parameters and cervical dilation, uterine contractions, cesarean section in the second stage of labor, type of uterus incision expansion and flexion, operator's experience.

Conclusion: Healing of the uterine cesarean section scar in women with single-layer continuous suture covering the entire thickness of the myometrium, excluding the decidua is not affected by the mode of caesarean section, type of uterine incision expansion and flexion, operator's experience, stage of labor at the time of caesarean section.

Key words: cesarean section; scar niche; single layer suture; 3D ultrasonography; VOCAL; risk factors

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INTRODUCTION

The consequence of each caesarean section is scar formation in the uterine muscle. In the case of incomplete healing, a niche is present within the scar. Symptoms related to the presence of uterine niches in non-pregnant women may include abnormal uterine bleeding, dysmenorrhea, chronic pelvic pain, infertility and dyspareunia [1]. According to some studies, large uterine niches eligible for surgery correction were the cause of prolonged postmenstrual spotting in 85% of patients, secondary infertility in 28% of patients and chronic pelvic pain in 14% of patients [2].

Moreover, the presence of a uterine scar niche can lead to uterine scar dehiscence/rupture in the subsequent pregnancy, as well as to caesarean scar pregnancy and to placenta accreta spectrum disorders [3, 4].

However, it needs to be stated that most small uterine niches are asymptomatic.

The aim of this study is to identify the potential risk factors for incomplete uterine healing after caesarean section in women with single layer, full thickness uterine closure with the use of two- and three-dimensional ultrasonography.

MATERIAL AND METHODS

In this case-controlled study, women who delivered by caesarean section (CS) at our institution from 2017 to 2019 were invited to undergo ultrasonographic assessment of the caesarean section scar 6–9 weeks after the caesarean section. The study protocol was accepted by the ethics committee and all participants signed the informed consent form before entering the study.

Corresponding author:
Joanna Budny-Winska
2nd Department and Clinic of Gynaecology, Obstetrics and Neonatology, Wroclaw Medical University, Poland
e-mail: Joanna.budny91@gmail.com

The examinations were conducted using a Voluson V8 Expert ultrasound machine (General Electric Medical Systems) with a 4–9 MHz transvaginal 3D probe.

According to the international definition, a niche was defined as indentation of the myometrium of at least 2 mm [5].

The measurements were obtained in the sagittal transection of the uterus. The following parameters of niche were assessed according to the modified Delphi protocol [5] (Fig. 1):

— width of the anechoic triangle — W (mm)
— height of the anechoic triangle — D (mm)
— residual myometrial thickness — RMT (mm),
— adjacent myometrial thickness — AMT (mm),
— the volume of the anechoic triangle.

Additionally, the following parameters were assessed:

— the ratio of the residual myometrial thickness to adjacent myometrial thickness — RMT/AMT ratio
— the ratio of the residual myometrial thickness to the width of the anechoic triangle — the RMT/W ratio,
— the ratio of the residual myometrial thickness to the height of the anechoic triangle — RMT/D ratio.

In completely healed CS scars, when the niche was not present, only the RMT value was measured.

To create a 3D models and calculate the volume of the niche after section we used the VOCAL program (Fig. 2). The following settings were used: manual trace and rotation angle 15°. The boundaries of the anechoic niche were manually outlined on the touch screen of the Voluson V8 Expert ultrasound machine.

The ultrasound examinations were performed by a single operator experienced in caesarean scar assessment.

Clinical information regarding maternal medical history, pregnancy and caesarean section course were collected from medical records and analyzed after ultrasonographic assessment of the CS scar.

The inclusion criteria were as follows: low transverse uterine incision, single layer continuous full thickness uterine closure and uneventful postoperative course. There were the following exclusion criteria: vertical or inverted "T" uterine incision, double-layer uterine closure, congenital uterine malformations.

The obtained data was collected and systematized using the Excel spreadsheet tools. The statistical examination was performed using the Statistica 13.3 PL package. For quantitative variables, basic descriptive statistics were calculated (for all patients and taking into account the assumed division into groups), while for qualitative variables the frequency of occurrence of their individual variants were calculated (also taking into account the assumed division). The non-parametric test was used in the analysis (Mann-Whitney U test, post and hoc comparisons for the Kruskal-Wallis ANOVA test and the non-parametric Spearman rank correlation). We used the test Chi ^ 2 of Pearson, Chi ^ Yates or Chi ^ 2 NW (depending on the group size) to search the differences in the distributions of qualitative variables. The criteria for statistical significance were set at $p < 0.05$.

RESULTS

A total of 204 patients participated in this study. The study group included women with mean age of 32.25 (SD 4.156) years and gestational age 37.863 (SD 2.43) weeks. Fifty-six patients had at least one cesarean section in the past. Out of all participants, in 153 (%) of them, a uterine niche after caesarean section was detected. The presence of the uterine niche was found in 72% of women after one caesarean section, 87% of women after two and 100% of women after three cesarean sections. Detailed characteristics of the study group are presented in Table 1.

Only five patients had a residual myometrial thickness (RMT) < 2.2 mm, and 35 had an RMT / AMT ratio of 0.5 or

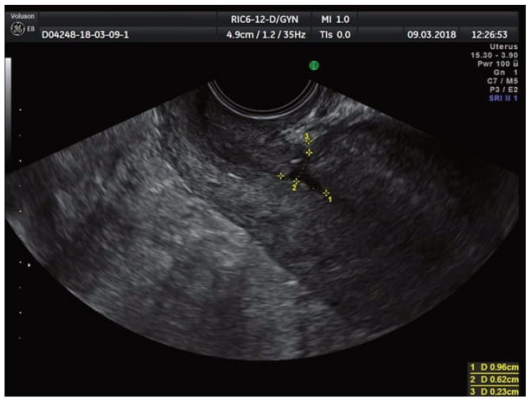

Figure 1. Measurement of the standardized cesarean section scar parameters

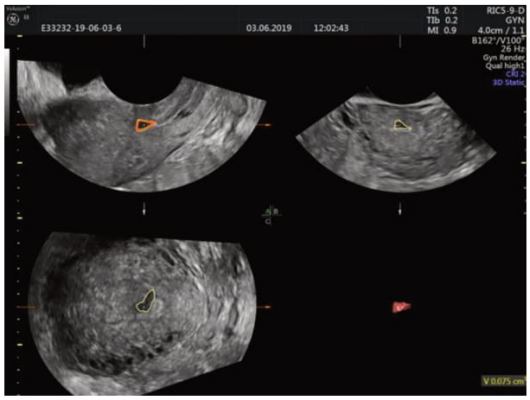

Figure 2. 3D model of cesarean scar niche

Table 1. Characteristics of the study group

Variable		Total	With niche	Without niche
Maternal age [mean (SD)]		32.25 (4,16)	32.21 (4,13)	32.27 (4,17)
Gestational age [mean (SD)]		37.83 (2,44)	37.86 (2,44)	37.87 (2,45)
Type of CS	Emergency [n (%)]	82 (40%)	63 (31%)	19 (9%)
	Planned [n (%)]	122 (60%)	92 (45%)	30 (15%)
Cervix dilatation	No [n (%)]	163 (80%)	123 (60%)	39 (11%)
	< 10 cm [n (%)]	41 (20%)	32 (16%)	9 (4%)
CS during II stage of labour	No [n (%)]	194 (95%)	147 (72%)	47 (23%)
	Yes [n (%)]	10 (5%)	8 (4%)	2 (1%)
Uterus incision expansion	Blunt [n (%)]	35 (17%)	27 (13%)	8 (4%)
	Sharp [n (%)]	169 (83%)	128 (63%)	41 (20%)
Number of previous CS	No previous CS [n (%)]	148 (73%)	106 (52%)	42 (21%)
	> 1 CS [n (%)]	56 (27%)	49 (24%)	7 (3%)
Flexion of uterus	Anteflexion [n (%)]	169 (83%)	128 (63%)	41 (20%)
	Retroflexion [n (%)]	35 (17%)	27 (13%)	8 (4%)
Operator's experience	Resident [n (%)]	101 (49%)	76 (37%)	25 (12%)
	Specialist [n (%)]	103 (51%)	79 (39%)	25 (12%)

SD — standard deviation; CS — caesarean section

less. Both parameters are considered risk factors for severe scar complications in subsequent pregnancies [6, 7].

The study did not reveal any statistically significant relationships between the parameters of the uterine caesarean scar (niche height, niche width, niche volume, residual myometrial thickness, the RMT/AMT ratio, RMT/W ratio, RMT/D ratio) and: cervical dilation, uterine contractions prior to cesarean section, caesarean section in the second stage of labor, type of uterine incision expansion (sharp vs blunt), operator's experience (resident vs specialist) or type of uterine flexion. Moreover, no statistically significant correlation was found between the occurrence of the uterine scar niche and the above-mentioned variables.

Based on the analysis, it was found that the residual myometrial thickness among women who had previously undergone at least one caesarean section was lower than among women who underwent the caesarean section for the first time [RMT = 0.69482 cm (SD = 0.37705) vs RMT = 0.88088 cm (SD = 0.30718); p = 0.000068]. Similar relationship was demonstrated for the RMT/AMT ratio. The individual results are presented in Tables 2, 3.

DISCUSSION

Due to the increasing number of caesarean sections and, consequently, the increasing number of side effects related to incomplete healing process of the uterine scar, there are worldwide efforts trying to define factors that affect uterine healing.

In this study, the evaluation of the uterine scar niche was performed using 2D and 3D unenhanced transvaginal ultrasound 6–9 weeks after caesarean section. Calculation of the niche volume and preparation of the 3D model of the niche, enabled precise evaluation of the niche. In most of previous studies the caesarean section scar was assessed only with the use of two dimensional ultrasonography [1–4, 7–12].

The aim of our study was to assess the dependence of niche parameters after caesarean section in relation to individual variables, to determine which factors can lead to the niche formation. Thus, each diagnosed niche was included in the statistical analysis, and not only those niches which can be classified as large [5] ^{v} or those which cause clinical symptoms [4].

In our study, as in other studies, the relationship between the number of previous caesarean sections and the risk of uterine niche formation was confirmed [1, 8–10]. The study found no correlation between the incidence of uterine scar niches and the mode of caesarean section (emergency/elective), which is supported by other studies [10, 13]. However, our study revealed that RMT, RMT/AMT ratio and RMT/W ratio are lower in women who underwent elective caesarean section versus those who underwent emergency caesarean section. Such relationship can be explained by the disproportion in size and heterogeneity of both groups.

In the search for potential factors that may affect the healing of the uterine scar after caesarean section, the influence of uterine contractions prior to caesarean section, dilation of the cervix, and thus the progress of labor, cannot

Table 2. Correlations between analyzed niche variables

Variable		Width (W) [cm]	Height (H) [cm]	RMT [cm]	AMT [cm]	RMT/AMT	RMT/W	RMT/H	Volume [cm^3]
Type of CS	Emergency	0.77	0.48	**0.89**	1.3	**0.62**	1.24	**2.08**	0.14
	Planned	0.85	0.51	**0.79**	1.26	**0.58**	1.08	**1.75**	0.16
Cervix dilatation	No	0.88	0.54	0.84	1.27	0.6	1.01	1.69	0.16
	< 10 cm	0.8	0.49	0.83	1.28	0.58	1.18	1.93	0.15
CS during II stage of labour	No	0.82	0.5	0.83	1.28	0.6	1.14	1.89	0.15
	Yes	0.73	0.44	0.83	1.19	0.62	1.17	1.74	0.09
Uterus incision expansion	Blunt	0.83	0.5	0.84	1.29	0.6	1.13	1.94	0.15
	Sharp	0.77	0.52	0.79	1.22	0.56	1.2	1.62	0.14
Number of previous CS	No previous CS	0.81	0.49	**0.88**	**1.32**	**0.62**	**1.2**	**2.01**	0.13
	> 1 CS	0.84	0.51	**0.69**	**1.17**	**0.55**	**1.02**	**1.61**	0.19
Flexion of uterus	Anteflexion	0.81	0.49	0.84	1.27	0.6	1.14	1.92	0.15
	Retroflexion	0.84	0.55	0.8	1.29	0.58	1.17	1.71	0.15
Operator's experience	Resident	0.82	0.51	0.85	1.29	0.59	1.14	1.88	0.13
	Specialist	0.82	0.49	0.81	1.26	0.6	1.15	1.88	0.16

Significant correlations at level of $p < 0.05$ are marked in bold; RMT — residual myometrial thickness; AMT — adjacent myometrial thickness; CS — cesarean section

Table 3. Correlations between incidence of uterine niche and analyzed variables

Variable	Type of CS		Contractions prior to CS		Uterus incision expansion		Operator's experience		Flexion of uterus	
	Emergency [n (%)]	Planned [n (%)]	Yes [n (%)]	No [n (%)]	Blunt [n (%)]	Sharp [n (%)]	Resident [n (%)]	Specialist [n (%)]	Anteflexion [n (%)]	Retroflexion [n (%)]
Niche	62 (40.52%)	91 (59.48%)	9 (17.65%)	121 (79.08%)	27 (17.65%)	126 (82.35%)	76 (49.67%)	77 (50.33%)	125 (82.24%)	27 (17.65%)
Non-NICHE	20 (39.22%)	31 (60.78%)	32 (20.92%)	42 (82.35%)	8 (15.69%)	43 (84.31%)	25 (49.02%)	26 (50.98%)	43 (84.31%)	8 (15.69%)
p value	p = 0.86903		p = 0.76218		p = 0.91461		p = 0.93556		p = 0.90008	

CS — cesarean section

be ignored. There are conflicting conclusions in the literature regarding the impact of these variables on the healing process of the uterus. In the study of Yazicioglu et. al. [11], it has been shown that smaller cervical dilatation at the time of caesarean section is a risk factor for incomplete uterine healing [xi]. However other studies have shown lower RMT values in women who underwent caesarean section in the second stage of labor [12]. In our study, no correlation was found between the incidence of niches after caesarean section and dilatation of cervix, contractions prior to caesarean section, performance of caesarean section during the second stage of labor. Also, no influence of the above-mentioned factors on niche parameters was found.

To the best of our knowledge this is the first study that assessed the type of uterine incision expansion (sharp vs blunt) and surgeons experience (specialist vs resident) on the healing of the caesarean section scar. In the previous studies, only the parameters related to the postoperative course were assessed. Thus, in the meta-analysis by Saad et al. [13] it was found that blunt opening of the uterus was associated with a lower decrease in hematocrit and postoperative hemoglobin level, a lower percentage of unintended openings and a shorter operation time. The analysis carried out in our study did not show a statistically significant difference between the frequency of the niche occurrence and the parameters of the niche depending on the type of uterine incision expansion and surgeons experience. This can be explained by the use of unified uterine closure technique — single layer, continuous full thickness suture, excluding the decidua.

Another issue assessed in the study was the type of flexion of the uterus. Our study found no correlation between the uterine retroflexion and the presence of the uterine scar niche, and no negative correlation between retroflexion and

residual myometrial thickness (RMT), despite the fact that such an association is reported in the literature [3, 7, 14]. Most likely, it is associated with a small group of women with uterine retroflexion in our study.

CONCLUSIONS

Healing of the uterine caesarean section scar assessed with the use of 2D/3D ultrasonography in women with single-layer continuous suture covering the entire thickness of the myometrium, excluding the decidua is not affected by the mode of caesarean section, type of uterine incision expansion, operator's experience, uterine flexion and stage of labor at the time of caesarean section.

Conflict of interest

None declared.

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6.2. “The impact of selected risk factors on uterine healing after cesarean section in women with single layer uterine closure: a prospective study using two- and three-dimensional transvaginal ultrasonography.”

AHEAD OF PRINT

Impact of selected risk factors on uterine healing after cesarean section in women with single-layer uterine closure: A prospective study using two- and three-dimensional transvaginal ultrasonography

Joanna Budny-Wińska[A–D], Aleksandra Zimmer-Stelmach[B,C], Michał Pomorski[D–F]

2nd Department of Gynecology and Obstetrics, Wroclaw Medical University, Poland

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;
D – writing the article; E – critical revision of the article; F – final approval of the article

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Address for correspondence
Joanna Budny-Wińska
E-mail: joanna.budny-winska@umed.wroc.pl

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Abstract

Background. Modern obstetrics must meet many challenges, including long-term complications resulting from the presence of a uterine niche after cesarean section.

Objectives. To assess the impact of selected risk factors on the uterine healing process after cesarean section. The uterus was closed with a single-layer continuous suture covering the entire thickness of the myometrium, excluding the decidua.

Materials and methods. A prospective, case-controlled study was carried out at 2nd Department of Gynecology and Obstetrics, Wroclaw Medical University, Poland. Women who delivered by cesarean section at our Department were invited to undergo an ultrasonographic assessment of the cesarean section scar from 6 to 9 weeks after the procedure. In all cases, the uterus was closed with a single-layer continuous suture. The ultrasound examination of the niche was performed according to the modified Delphi protocol. The volume of the niche was calculated and a 3D model was created. The obtained data were analyzed with clinical information from the maternal medical history and the course of the pregnancy.

Results. A total of 204 patients participated in the study. Five patients had a residual myometrial thickness (RMT) <2.2 mm and 35 had a residual myometrial thickness to adjacent myometrial thickness ratio (RMT/AMT) ≤0.5. In 45% of women, pregnancy course was complicated by gestational diabetes mellitus (GDM), gestational hypertension and hypothyroidism. The cervical canal was colonized with pathogenic flora in 22% of women. No correlation between maternal and gestational age at delivery, presence of medical complications during pregnancy, colonization of the cervical canal, and presence of niche and its parameters were found.

Conclusions. Our study revealed that the selected risk factors, such as systemic diseases during pregnancy and in the maternal medical history, as well as the colonization of the cervical canal, have no impact on uterine scar healing in women undergoing single-layer uterine closure spanning the entire thickness of the myometrium, excluding the decidua.

Key words: 3D ultrasonography, cesarean scar niche, risk factors of cesarean scar niche, systemic diseases during pregnancy, single-layer suture

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Background

Modern obstetrics must meet many challenges, including the increased frequency of cesarean sections and long-term complications resulting from the presence of a uterine niche after cesarean section. Additionally, worldwide, there has been an increased incidence and prevalence of systemic diseases appearing in pregnancy, such as gestational hypertension and gestational diabetes mellitus (GDM).[1,2] The another challenge for obstetricians is the increased rate of pregnancy among older women[3,4] due to the sociocultural changes in family planning that leads to the postponement of maternal plans, as well as the improved availability and effectiveness of assisted reproductive methods.

The consequence of cesarean section is a scar formation within the uterine muscle. In recent years, the rate of deliveries by cesarean section has increased all over the world. In Poland, the rate of cesarean section is 44.8% (data from Statistics Poland for 2019). The World Health Organization (WHO) recommends an ideal cesarean section rate of 10–15% of all births. This percentage is associated with a decrease in maternal and neonatal mortality. Above this level, the increased incidence of cesarean delivery is no longer associated with reduced mortality.[5]

With rising cesarean rates, the incidence of cesarean-related iatrogenic complications is also on the rise. In cases of incomplete healing, a niche can develop within the scar.

Various imaging methods including two- and three-dimensional ultrasonography, sonohysterography, hysterography, hysteroscopy, and magnetic resonance imaging (MRI) can be used to assess the anterior uterine wall and to diagnose a cesarean scar niche.[6–8] Despite the availability of various diagnostic methods, there are no clear diagnostic criteria for uterine niches after cesarean section. In 2019, the European Niche Taskforce defined a uterine niche as an indentation of at least 2 mm in the uterine myometrium at the site of the cesarean scar, assessed using transvaginal ultrasound.[9] The incidence of uterine niches varies widely in the literature, ranging from 24% to 84%.[10–13]

Differences in the frequency of uterine niches result from the use of different diagnostic criteria, the time elapsed after the cesarean procedure and the diagnostic method used. The incidence is often underestimated because many women are asymptomatic and clinicians may not consider a niche as a cause of a patient's symptoms, due to lack of awareness.[8]

Most of the small uterine niches after cesarean section are asymptomatic and do not pose a threat to the health or life of the patient. However, the consequences of the presence of the large and symptomatic cesarean scar niche include uterine bleeding, chronic pelvic pain, reduced fertility, complications in subsequent pregnancies (morbidly adherent placenta, placenta previa), as well as directly life-threatening conditions (uterine rupture, cesarean scar pregnancy).[6,14–17] Additionally, cesarean scar niches may increase the risk of complications in gynecological procedures such as embryo transfer and intrauterine device placement and removal.[18,19]

Due to the potentially dangerous consequences resulting from the presence of a uterine niche after cesarean section, it is necessary to develop preventive strategies aimed at reducing the risk of isthmocele formation, and thus preventing adverse outcomes. To achieve this, it is essential to identify related risk factors for the formation of a uterine niche after cesarean section, and to develop appropriate diagnostic and therapeutic protocols. Therefore, in the past several years, numerous studies have been published concerning the uterine scar niche, but most of them have been performed using selected populations of symptomatic women.

Objectives

This study aimed to assess the impact of the most common risk factors in obstetrics on the uterine healing process after cesarean section, using a prospectively collected and unselected population, in which the uterus was closed with a single-layer continuous suture covering the entire thickness of the myometrium, excluding the decidua.

Materials and methods

Study design

This prospective descriptive study was designed to assess the prevalence and risk factors for improper uterine healing after cesarean delivery and niche formation. This study is a continuation of our previous research, in which we assessed the impact of mode and number of previous cesarean sections, type of uterine incision expansion, operator's experience, uterine flexion, and stage of labor at the time of cesarean section on uterine healing.[20]

Setting and participants

The study was carried out at 2nd Department of Gynecology and Obstetrics, Wroclaw Medical University, Poland. The study protocol was accepted by the ethics committee (approval No. KB 221/2016 and No. KB 153/2020) and all participants signed an informed consent form before participating in the study. The study was conducted in accordance with the 1964 Declaration of Helsinki and its later amendments.

Women who delivered by cesarean section at our Department from 2017 to 2019 were invited to undergo an ultrasonographic assessment of the cesarean section

scar. They were recruited either before the cesarean delivery (elective surgery) or within 2 days after the operation (emergency cesarean delivery). Patients who agreed to participate in the study were scheduled for the ultrasound examination from 6 to 9 weeks after the cesarean section.

Surgical technique

The cesarean section procedures were performed by various obstetricians working in our Department using a standardized manner, i.e., low transverse uterine incision with a single-layer continuous suture covering the entire thickness of the myometrium, excluding the decidua. All physicians used the same suture material (Surgicryl® 910 polyglactine-braided synthetic absorbable suture; SMI AG, St. Vith, Belgium).

Ultrasound examination

The examinations were conducted using a Voluson V8 Expert ultrasound machine (General Electric Medical Systems, Chicago, USA) with a 4–9 MHz transvaginal 3D probe. All transvaginal ultrasound examinations were performed by the first author, who was blinded to clinical information. During the examination, the parameters of the niche were assessed and a 3D model was created. All data were saved on the internal hard drive of the ultrasound machine. According to the international definition, a niche was defined as an indentation in the myometrium of at least 2 mm.[9] All measurements were obtained on a sagittal view of the uterus. To standardize the ultrasound evaluation, all examinations were performed using the modified Delphi protocol, and the exams performed prior to the publication of the modified Delphi protocol were reloaded and recalculated in accordance with the guidelines.[9]

The following niche parameters were assessed according to the modified Delphi protocol: width (W [mm]), height (D [mm]), volume of the anechoic triangle, residual myometrial thickness (RMT [mm]), and adjacent myometrial thickness (AMT [mm]). Additionally, the following parameters were calculated: the RMT/AMT ratio, the RMT/W ratio and the RMT/D ratio.

The VOCAL program was used to create 3D models and calculate the volume of the niche. The following settings were used: manual trace and rotation angle of 15°. The boundaries of the anechoic niche were manually outlined on the touch screen of the Voluson V8 Expert ultrasound machine.

Clinical data analysis

Clinical information, such as laboratory results, maternal medical history pregnancy, and cesarean section course, was collected from the medical record and analyzed after ultrasonographic assessment of the cesarean section scar.

Inclusion and exclusion criteria

The inclusion criteria were low transverse uterine incision, single-layer continuous full thickness uterine closure, uneventful postoperative course and singleton pregnancy. The exclusion criteria included a vertical or inverted "T" uterine incision, congenital uterine malformations and the use of more than 3 additional hemostatic uterine sutures.

Statistical analyses

Data were collected and recorded using an Excel spreadsheet. Statistical analyses were performed using the STATISTICA v. 13.3 PL package (StatSoft Inc., Tulsa, USA). For quantitative variables, basic descriptive statistics were calculated (for all patients and taking into account the assumed division into groups), while the frequency of occurrence of their individual variants was calculated for qualitative variables (also taking into account the assumed division). The Mann–Whitney U test, post hoc comparisons for the Kruskal–Wallis analysis of variance (ANOVA) test and non-parametric Spearman's rank correlation test were used in the analysis of non-parametric data. The Pearson's χ^2 test and Fisher's exact test were used to evaluate the differences in the distributions of qualitative variables. The criterion for statistical significance was set at a p-value <0.05.

Results

A total of 204 patients participated in the study. The mean age was 32.25 years (standard deviation (SD) ±4.156) and the mean gestational age was 37.863 weeks (SD ±2.43). A total of 117 (57%) participants had no previous deliveries. Of the 204 patients, 56 (27%) had at least 1 cesarean section in the past, while 32 (16%) had at least 1 previous vaginal delivery. Eighty-two (40%) patients underwent emergency cesarean delivery and 122 (60%) underwent elective cesarean delivery. The most common reasons for elective cesarean delivery were previous cesarean delivery (40%) and breech presentation (9%). The most common reasons for emergency cesarean delivery were impending fetal asphyxia (40%) and prolonged labor (17%).

Out of all examined women, 153 were diagnosed with a niche after cesarean section (75%). Five of those patients had a RMT < 2.2 mm and 35 patients had an RMT/AMT ratio of 0.5 or less. The mean RMT value in the study group was 8.3 mm (SD ±3.37).

The course of pregnancy was uncomplicated by pregnancy-related systemic diseases in 55% (n = 112) of women. In this group, uterine scar niches were diagnosed after cesarean section in 71% (n = 79) of patients. In contrast, in 21 patients (10%) with GDM, a uterine niche was diagnosed after cesarean section in 91% of these women. In 11% of respondents, their pregnancy was complicated

8.

Table 1. Comparison of the analyzed variables and the occurrence of uterine niche after the cesarean section

Variable	Chronic diseases in pregnancy		Gestational diabetes		Gestational hypertension		Culture of cervical canal	
	yes	no	yes	no	yes	no	negative	positive
Niche, n (%)	75 (49)	78 (51)	18 (12)	135 (88)	14 (9)	139 (91)	92 (79)	24 (21)
Non-niche, n (%)	17 (33)	34 (67)	3 (6)	48 (94)	9 (18)	42 (82)	32 (76)	10 (24)
p-value*	0.0536		0.2949		0.1236		0.6665	

*Fisher's exact test.

Table 2. Characteristics of the parameters of the cesarean scar niche depending on the occurrence of systemic diseases during pregnancy and cervical colonization (Mann–Whitney U test)

Variable	Chronic diseases in pregnancy		Gestational diabetes		Gestational hypertension		Hypothyroidism in pregnancy		Culture of cervical canal	
	yes	no	yes	no	yes	no	yes	no	positive	negative
Height [cm]										
Mean (SD)	0.50 (0.24)	0.49 (0.20)	0.54 (0.24)	0.49 (0.22)	0.51 (0.33)	0.49 (0.21)	0.49 (0.21)	0.51 (0.23)	0.49 (0.18)	0.52 (0.23)
p-value	0.7150		0.5091		0.5491		0.7047		0.5346	
Width [cm]										
Mean (SD)	0.80 (0.36)	0.83 (0.37)	0.80 (0.33)	0.82 (0.37)	0.79 (0.43)	0.82 (0.35)	0.80 (0.34)	0.83 (0.37)	0.76 (0.24)	0.84 (0.40)
p-value	0.4332		0.9848		0.4332		0.6807		0.5435	
Residual myometrial thickness [cm]										
Mean (SD)	0.84 (0.35)	0.82 (0.33)	0.84 (0.30)	0.83 (0.34)	0.87 (0.32)	0.82 (0.34)	0.82 (0.35)	0.83 (0.33)	0.81 (0.29)	0.82 (0.35)
p-value	0.3905		0.9487		0.3905		0.8058		0.8590	
Adjacent myometrial thickness [cm]										
Mean (SD)	1.25 (0.38)	1.17 (0.38)	1.32 (0.41)	1.19 (0.38)	1.21 (0.32)	1.21 (0.39)	1.23 (0.38)	1.20 (0.39)	1.16 (0.28)	1.22 (0.41)
p-value	0.6636		0.4952		0.9373		0.6962		0.7239	
Residual myometrial thickness/adjacent myometrial thickness										
Mean (SD)	0.67 (0.21)	0.71 (0.22)	0.64 (0.16)	0.70 (0.22)	0.74 (0.24)	0.69 (0.21)	0.66 (0.21)	0.71 (0.22)	0.71 (0.22)	0.68 (0.23)
p-value	0.7392		0.9782		0.5172		0.8663		0.5840	
Residual myometrial thickness/width										
Mean (SD)	1.24 (0.88)	1.05 (0.57)	1.18 (0.62)	1.14 (0.76)	1.24 (0.73)	1.14 (0.74)	1.18 (0.76)	1.13 (0.73)	1.04 (0.49)	1.16 (0.81)
p-value	0.4332		0.6176		0.4332		0.9496		0.7950	
Residual myometrial thickness/height										
Mean (SD)	1.96 (1.40)	1.81 (1.19)	1.76 (0.90)	1.89 (1.34)	1.98 (1.15)	1.87 (1.31)	1.94 (1.49)	1.86 (1.20)	1.65 (0.74)	1.82 (1.30)
p-value	0.5153		0.9782		0.5153		0.8663		0.8740	
Niche volume [cm^3]										
Mean (SD)	0.15 (0.20)	0.15 (0.25)	0.12 (0.10)	0.15 (0.24)	0.18 (0.28)	0.14 (0.22)	0.14 (0.20)	0.15 (0.24)	0.09 (0.14)	0.17 (0.27)
p-value	0.9850		0.7231		0.9850		0.8728		0.0362	

SD – standard deviation.

by gestational hypertension (n = 28), and among them, 65% were diagnosed with a niche of the uterus after cesarean section. Out of the 59 (29%) patients who developed hypothyroidism during their pregnancy, 85% were diagnosed with a uterine niche after cesarean section. There was no statistical correlation between the prevalence or parameters of a uterine niche after cesarean section and the abovementioned medical complications of pregnancy.

In our study, there were no cases of postoperative, symptomatic infections. However, the influence of cervical canal colonization by microbes on the healing of uterine scars was evaluated. Swabs from the cervical canal were taken from 158 pregnant women on admission to the hospital. In 78% (n = 124) of pregnant women, a negative culture was reported. In 22% (n = 34) of women, the culture was positive for pathogenic flora such as *Staphylococcus agalactiae* spp (n = 8, 24%), Candida (including *C. albicans* spp, *C. glabrata* spp; n = 10.29%), Enterococcus (including *E. faecalis* spp; n = 4.12%), *Escherichia coli* spp (n = 6.18%), *Klebsiella pneumoniae* spp (n = 4.12%), and *Pseudomonas putida* spp (n = 1.3%). The percentage of identified niches in women with negative culture was 74% (n = 92). The same percentage of niches was found in the group of women with positive cultures from the cervical canal

Table 3. Comparison of the maternal age and the occurrence of uterine niche after cesarean section

Variable	≤25 years	25–30 years	31–35 years	36–40 years	>40 years
Niche, n (%)	8 (5)	45 (29)	73 (48)	21 (14)	6 (4)
Non-niche, n (%)	4 (8)	13 (25)	23 (45)	10 (20)	1 (2)
p-value	0.7346*				

*Pearson's χ^2 test, degrees of freedom (df) = 4.

Table 4. Comparison of the parameters of the cesarean scar niche depending on maternal age

Variable	≤25 years	25–30 years	31–35 years	36–40 years	>40 years	p-value*
H [cm], mean (SD)	0.49 (0.29)	0.47 (0.19)	0.50 (0.22)	0.52 (0.27)	0.47 (0.23)	0.8210
W [cm], mean (SD)	0.84 (0.21)	0.83 (0.42)	0.83 (0.37)	0.73 (0.24)	0.84 (0.22)	0.6992
RMT [cm], mean (SD)	0.9 (0.33)	0.87 (0.35)	0.81 (0.34)	0.80 (0.33)	0.80 (0.31)	0.6749
AMT [cm], mean (SD)	1.30 (0.40)	1.24 (0.39)	1.20 (0.38)	1.15 (0.41)	1.21 (0.45)	0.8959
RMT/AMT	0.72 (0.25)	0.70 (0.21)	0.68 (0.22)	0.71 (0.23)	0.68 (0.17)	0.8408
RMT/W	0.92 (0.40)	1.21 (0.69)	1.13 (0.80)	1.17 (0.79)	1.02 (0.57)	0.7671
RMT/H	1.61 (0.86)	2.06 (1.31)	1.83 (1.31)	1.81 (1.47)	1.90 (1.00)	0.5102
Niche volume [cm^3], mean (SD)	0.20 (0.21)	0.16 (0.30)	0.14 (0.20)	0.12 (0.11)	0.16 (0.25)	0.8994

H – height; W – width; RMT – residual myometrial thickness; AMT – adjacent myometrial thickness; SD – standard deviation; *Kruskal–Wallis analysis of variance (ANOVA) test.

Table 5. Comparison of the occurrence of uterine scar niche by gestational age and history of miscarriages

Variable	Preterm delivery		Miscarriage in the past	
	yes	no	yes	no
Niche, n (%)	11 (22)	40 (78)	10 (20)	41 (80)
Non-niche, n (%)	22 (14)	131 (86)	33 (22)	120 (78)
p-value*	0.2720		0.8448	

*Fisher's exact test.

(n = 25, 74%). In this study, no statistically significant correlation was found between the prevalence and parameters of the uterine scar niche and the colonization of the cervix by pathogens. Table 1 and Table 2 present the comparison data between the incidence and parameters of cesarean scar niche and systemic diseases appearing in pregnancy, and the colonization of the cervix by pathogenic bacteria.

The study group was divided into subgroups by age. Table 3 presents the detailed characteristics of each subgroup.

Also, the impact of gestational age at the time of cesarean section was assessed. In 16% of patients (n = 33), cesarean section was performed on a preterm pregnancy in which 67% (n = 22) of these resulted in a uterine niche. In women undergoing cesarean section at term (n = 171, 84% of patients), the percentage of uterine scar niches after cesarean section was 77% (n = 132). For women with a history of miscarriages (n = 43, 21% of patients), a niche was diagnosed in 33 (77%) of these patients. There was no statistical correlation between the prevalence or parameters of the niche after cesarean section and maternal age during cesarean section, preterm delivery and history of miscarriages (Table 4,5,6).

Discussion

Currently, there are no guidelines concerning the optimal timing for cesarean section scar assessment.

Most of the research concerning uterine niches after cesarean section have focused on examining women with symptoms related to its presence. The interval between cesarean section and evaluation of the cesarean scar varied in different publications. Most publications assessed the uterine scar from 6 to 8 weeks, 6 months,[21] 1 year,[22] or more than 5 years[23,24] after performing the cesarean section. This study aimed to evaluate the influence of individual factors and systemic diseases appearing during pregnancy on the process of uterine healing after cesarean section. In this study, every woman who had cesarean section with a single-layer, full thickness uterine closure excluding the decidua, was invited for a uterine scar examination. The examination was performed from 6 to 9 weeks after the operation, during which the uterine scar was still healing and no clinical symptoms are present. Van der Voet et al. found that the prevalence of niches did not change with time (niches found during an examination at 6–12 weeks after the cesarean section were also

Table 6. Comparison of analyzed parameters of cesarean scar niche depending on the history of miscarriages and gestational age

Variable	History of miscarriages			Gestational age		
	no	yes	p-value*	preterm delivery	term delivery	p-value*
H [cm], mean (SD)	0.50 (0.23)	0.50 (0.18)	0.4301	0.48 (0.24)	0.52 (0.22)	0.3757
W [cm], mean (SD)	0.80 (0.32)	0.90 (0.48)	0.3868	0.81(0.48)	0.82 (0.34)	0.3081
RMT [cm], mean (SD)	0.84 (0.34)	0.79 (0.34)	0.2912	0.89 (0.36)	0.82 (0.33)	0.2423
AMT [cm], mean (SD)	1.22 (0.39)	1.17 (0.35)	0.5697	1.23 (0.41)	1.21 (0.38)	0.8455
RMT/AMT	0.70 (0.21)	0.67 (0.87)	0.3472	0.73 (0.22)	0.69 (0.21)	0.3672
RMT/W	1.15 (0.65)	1.12 (1.01)	0.2202	1.16 (0.61)	1.14 (0.76)	0.5342
RMT/H	1.91 (1.27)	1.77 (1.40)	0.1832	2.03 (1.41)	1.86 (1.28)	0.7800
Niche volume [cm^3], mean (SD)	0.13 (0.17)	0.20 (0.37)	0.9947	0.23 (0.43)	0.13 (0.17)	0.9588

H – height; W – width; RMT – residual myometrial thickness; AMT – adjacent myometrial thickness; SD – standard deviation; *Mann–Whitney U test.

present on an examination performed 1 year after cesarean section).[25]

Transvaginal ultrasound examination at 6–9 weeks after cesarean section allows for the identification of patients with a potential risk of abnormal uterine healing after cesarean section, due to a large niche that may threaten the next pregnancy or be the cause of cesarean scar syndrome. Patients with a large niche and low RMT, as well as physicians treating them need to be aware of the risk of possible complications as soon as possible. Currently, in our clinical practice, we found many women with abnormal uterine bleeding related to the niche, who are unnecessarily treated by other doctors with oral contraceptives or invasive procedures such as dilatation and curettage. Moreover, women with extremely low RMT face life-threatening complications in subsequent pregnancies due to the risk of scar rupture at 21 weeks of gestation.[26] Taking into consideration the above problems and the limited knowledge gynecologists have of niche-related complications, we suggest cesarean section scar assessment be routinely performed in all women who have undergone cesarean section at the end of puerperium.

In this study, all niches, whether classified as small or large, were assessed using two and three-dimensional ultrasound.[7] Even though 2 meta-analyses have concluded single-layer closure to be associated with decreased RMT in comparison to double-layer sutures, in our study group, only 2.4% of women had a RMT < 2.2 mm. An RMT < 2.2 mm is considered a risk factor for severe scar complications in subsequent pregnancies.[9] Both of these meta-analyses have shown no differences in the risk of maternal morbidity or long-term outcomes between single- compared to double-layer uterine closure.[27,28]

This study is a continuation of our previous research in which we proved there was no correlation between an operator's experience and the prevalence and parameters of uterine niches after cesarean section.[20] The lack of a relationship between the operator's experience and the formation of a uterine niche after cesarean section is supported in the literature.[11] It should be emphasized that all cesarean sections were performed in a standardized manner, i.e., low transverse uterine incision with single-layer full thickness uterine closure using the same suture material.

There was also no correlation between the parameters of the niche, incidence of niches and a woman's age at the time of cesarean section, which is in line with other studies.[29] In the study by Pomorski et al., a positive correlation was found between the height of the niche and the mother's age.[30] In another publication, the presence of a niche was significantly associated with younger maternal age at the time of cesarean section. In this study, younger patients had cesarean section performed during the active phase of labor.[31] According to some studies, performing cesarean section during the active phase of labor or phase II of labor increases the risk of a large niche formation.[11,33] In our study, only 6 patients were in the active phase of labor (dilation >4 cm to full dilation of cervix) and 10 patients were in phase II of labor at the time of cesarean section. Therefore, due to the low numbers, we did not use these variables in the statistical analysis of the subgroups of maternal age.

There are conflicting reports in the literature regarding the impact of gestational age on niche formation. In our study, no relationship was found between gestational age at the time of delivery and the prevalence and parameters of the niche. This finding is supported by other studies.[29,30,32] On the other hand, Vikhareva and Valentin found that delivery before 37 weeks gestation was a predictor of large niches.[33] The study by Hayakawa et al. demonstrated a positive link between the gestational age of 37–41 weeks at delivery and the presence of wedge niches.[34]

The influence of medical conditions associated with pregnancy on uterine niche development was analyzed. No correlation was found between GDM and the prevalence and parameters of niches. However, Antila-Långsjö et al. found GDM and higher body mass index (BMI) to be positively correlated with the incidence of uterine niche after cesarean section.[11] Interestingly, such a correlation has not been found for pregestational diabetes. In our study, the mean prepregnancy BMI in women diagnosed with cesarean scar niche was 27.1 (±6.1) kg/m^2 compared to 25.1 (±5.3) kg/m^2 in women without a niche. Consequently,

it means that most of the women in this study were overweight. In other studies, no correlation was found between BMI and the presence of a uterine niche.[33,34]

Our study also evaluated the influence of gestational hypertension on uterine healing. No statistically significant correlation was found between the frequency of occurrence or parameters of a niche and the presence of gestational hypertension. To our knowledge, only 1 other study evaluated the effect gestational hypertension has on the incidence of uterine scar defect – and failed to show any correlation.[35] Considering the influence of pregnancy-related systemic diseases, it is impossible to ignore the influence of hypothyroidism on tissue metabolism. The correlation between hypothyroidism and a higher risk of perioperative complications has been known for a long time.[36] To date, no other studies have been performed to assess the effect of hypothyroidism on uterine healing after cesarean section. In our study, no relationship was found between hypothyroidism and uterine scar niche parameters. When assessing the impact of individual diseases on uterus healing and comparing conflicting reports in the literature, it should be remembered that each population has its own individual characteristics and the incidences of GDM, gestational hypertension and hypothyroidism vary worldwide.

In our study, the effect cervical colonization by microorganisms has on the prevalence and parameters of a uterine niche was evaluated, because previous studies have correlated the bacterial load of the cervix with the bacterial load within the uterine cavity.[37,38] This suggests that cervical microbiota may be a source of microbes for colonization of the uterine cavity and may influence the healing process of the cesarean section scar. However, our study showed no correlation between the cervical colonization and the prevalence and parameters of uterine niches after cesarean section. This may be due to the use of perioperative antibiotics for surgical prophylaxis. Although, further research is needed to confirm this hypothesis.

In other studies, the influence of inflammatory processes such as postpartum fever,[33,35] the application of antibiotics during childbirth,[39] perinatal and puerperal infection in the form of chorioamnionitis, postoperative wound infection, urinary tract infection, and endometritis[34] were analyzed, but no correlation between the abovementioned variables and the prevalence of niches after cesarean section was found.

Limitations

The main limitation of our study is the lack of comparison between a single-layer continuous uterine suture and a double-layer uterine suture closure, due to the single-layer continuous uterine suture being the standard of care at our Department. The other limitation is that we were checking the colonization of the cervical canal without uterine cavity colonization.

The etiology of a uterine niche after cesarean section is multifactorial. In our study, we evaluated a few potential factors that could disturb the proper healing process of the uterus. The effect of other important individual risk factors such as BMI, corticosteroid use, previous myomectomy and smoking status on the prevalence and parameters of cesarean section niche was not investigated in our study, which is a limitation.

Conclusions

Two- and three-dimensional ultrasonographic cesarean scar assessment revealed that the selected risk factors concerning systemic diseases during pregnancy, maternal medical history and colonization of the cervical canal have no impact on uterine scar healing in women with single-layer uterine closure covering the entire thickness of the myometrium, excluding the decidua.

ORCID iDs

Joanna Budny-Wińska https://orcid.org/0000-0002-3094-2213
Aleksandra Zimmer-Stelmach https://orcid.org/0000-0003-1114-6980
Michał Pomorski https://orcid.org/0000-0002-4501-353X

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6.3. “UTERINE NICHE AFTER CESAREAN SECTION: a review of diagnostic methods.”

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Uterine niche after cesarean section: a review of diagnostic methods

Joanna Budny-Winska, Michal Pomorski

2nd Department of Gynaecology and Obstetrics, Wroclaw Medical University, Wroclaw, Poland

ABSTRACT

The consequence of each cesarean section is the uterine scar formation. In some patients, uterine scar after cesarean section heals incompletely and as a result, the uterine niche is formed. Most of the small niches are asymptomatic, but the large cesarean scar niches in nonpregnant women may cause a cesarean scar syndrome, which manifest itself as abnormal uterine bleeding, dysmenorrhea and secondary infertility. Among pregnant women, the presence of large niches may be associated with potentially life-threatening consequences, such as cesarean scar dehiscence and uterine rupture, placenta accreta spectrum disorders, placenta previa, cesarean scar pregnancy. Due to the possibility of dangerous consequences related to the occurrence of a uterine niche, in recent years many studies have focused on the term of cesarean scar niche, its risk factors, diagnostic methods and treatment options. Uterine niche can be examined using two- or three-dimensional transvaginal ultrasonography, as well as two- and three-dimensional sonohysterography, hysterosalpingography, hysteroscopy or magnetic resonance imaging. However, neither of the above diagnostic method is considered as the "gold standard". There are no unambiguous guidelines on some aspect concerning the diagnosis of cesarean scar niche.
The aim of this study is to analyze and describe the diagnostic methods of cesarean section niche.

Key words: uterine niche; cesarean section niche; diagnostic methods; ultrasonography; sonohysterography

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INTRODUCTION

In recent years, many studies have focused on the term of uterine niche after cesarean section. It is well known that the consequence of each cesarean section is the formation of uterine scar. In 50–70% of patients after cesarean section, a niche develops due to defective tissue healing [1, 2] It is defined as myometrial indentation at the site of the cesarean section scar with a depth of at least 2 mm [3].

Most of the small niches are asymptomatic. The clinical symptoms related to the presence of large uterine niche, and so-called cesarean scar syndrome includes abnormal uterine bleeding, dysmenorrhea and secondary infertility [4–6]. Obstetric complications of large cesarean scar niche in pregnancy may pose a risk of serious consequences because they are associated with scar dehiscence and uterine rupture, placenta accreta spectrum disorders, placenta previa, cesarean scar pregnancy [1, 7, 8]. Therefore, it is so important to early and correctly diagnose the uterine niche and implement an appropriate management, in cases requiring treatment.

Uterine niche can be examined using two- or three-dimensional transvaginal ultrasonography, as well as two- and three-dimensional sonohysterography [9], hysterosalpingography, hysteroscopy or magnetic resonance imaging [2]. However, neither of the above diagnostic method is considered as the "gold standard".

The aim of this study is to analyze and describe the diagnostic methods of cesarean section niche.

TRANSVAGINAL ULTRASOUND (TVUS)

Transvaginal ultrasonography is the initial and least invasive diagnostic method used to evaluate the integrity of the uterus wall. The cesarean section scar may take the form of an isolated niche, a niche with fibrosis, an isolated fibrosis [10]. In TVUS, small niches may not be visible, or their parameters may be underestimated [11, 12].

There were no uniform standards for the uterine niche's assessment.

In 2007, in the study entitled "Ultrasonographic analysis of cesarean scar features in nonpregnant uterus" for the

Corresponding author:
Joanna Budny-Winska
2nd Department of Gynaecology and Obstetrics, Wroclaw Medical University, 213 Borowska St, 50-556 Wroclaw, Poland
e-mail: joanna.budny91@gmail.com

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first-time standardized ultrasound evaluation of the uterine niche was presented [13]. In 2012, the same parameters were introduced for ultrasound examination of pregnant uterus by Naji et al. [14].

In 2013, Tower et al. proposed a uterine niche classification based on RMT and RMT/adjacent myometrial thickness (AMT) ratio as the only ultrasound niche features [15].

In 2019, the guidelines for sonographic examination of uterine niche in non-pregnant women according to a modified Delphi procedure were introduced [3]. According to these guidelines, basic niche evaluation includes the measurement of its length, depth, width, RMT, AMT, along with documentation and measurement of the present niche's branches (Fig. 1). RMT, length, depth of the niche should be measured in the sagittal plane, while the transverse plane is used to measure the width and identify its branches. The assessment of the distance between the niche and the vesicovaginal fold, and between the niche and the external os of the cervix provide an extended niche assessment, which is helpful in surgical strategy planning. The use of Doppler imaging is not obligatory but can be useful in differentiating uterine niches from hematomas, adenomyomas, and fibrotic tissue. This publication also introduces the classification of niches according to their shape, with a division into simple niche, simple niche with one branch, complex niche [3].

SONOHYSTEROGRAPHY (SHG)

Sonohysterography is a diagnostic method in which transvaginal ultrasonography of the uterus is enhanced by instillation of fluid into the uterine cavity to provide an anechoic contrast medium. It may be the sterile saline solution (SCSH) or gel (GIS).

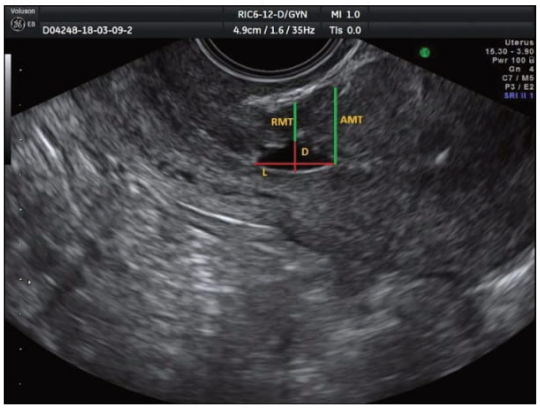

Figure 1. Basic evaluation of the simple niche according to the study of Jordans IPM, et al. "Sonographic examination of uterine niche in non-pregnant women: a modified Delphi procedure" [3]; L — length; D — depth; RMT — residual myometrial thickness; AMT — adjacent myometrial thickness

During sonohysterography the same parameters of the cesarean scar niche as with TVUS are measured, but it enables better visualization and demarcation of isthmocele. Additionally, it has increased sensitivity and specificity for the detection of uterine niches by enhancing the isthmocele and allowing its dynamic evaluation. Compared to transvaginal ultrasonography, it detects more niches [16, 17] and more of them are classified as large [18]. It is more invasive examination than TVUS and carries a low risk of complications (such as infections). During this examination, the cesarean scar niche may also be overestimated (about 1–2 mm) due to its overstretching by flushed into uterine cavity fluid [15]. The study by A. El-Mazny et al. showed that the detectability of the cesarean scar niche in SHG compared to hysteroscopy is 96%, while for intrauterine adhesions 91%, therefore SHG is a good alternative in the assessment of the uterine cavity [19].

THREE-DIMENSIONAL (3D) IMAGING

All niche parameters and its volume could be measured using 3D ultrasonography. The study by M. Alalfy showed that 3D sonohysterography is as accurate in assessing the uterine niche after cesarean section as 2D sonohysterography. However, the use of 3D sonography provide better characterization of the cesarean scar niche, because of superior evaluation of the RMT and niche width before the Intracytoplasmic Sperm Injection [20].

In the study by A. Ludwin et al. [21] to improve the reliability of volume estimation and morphological assessment of cesarean niche, as well as its classification (see below), the 3D-SCSH in conjunction with Sonography-based Automated Volume Count software (SonoHysteroAVC) or Virtual Organ Computer-aided AnaLysis (VOCAL) was used.9 Another study used 3D transvaginal ultrasonography to create a uterine niche's model and the VOCAL program to determine its volume (Fig. 2).

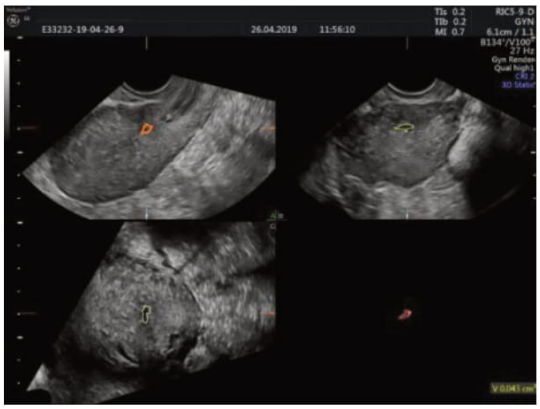

Figure 2. 3D model of cesarean scar niche

HISTEROSALPINGOGRAPHY (HSG)

Hysterosalpingography is a radiologic examination mainly used in the diagnosis of female factor infertility. It is done under fluoroscopy to visualize the uterine cavity and lumen of the fallopian tubes. This examination can identify the cesarean scar niches that can be the cause of secondary infertility after cesarean section. In the study by K. Suprapaneni and J. E Silberzweig, among 148 patients with history of cesarean section and technically adequate hysterosalpingograms, 60% of them had uterine cesarean scar niches [22].

Isthmocele in HSG is visualized as a leakage of contrast from the uterine cavity into a myometrial defect. HSG also allows classification of the uterine niches in terms of its shape and location [23].

The limitation of this diagnostic method is its inability to accurately measure RMT and other parameters of the niche. Moreover, if blood or mucus is accumulated in the isthmocele, HSG may not clearly identify the uterine niche [24].

MAGNETIC RESONANCE IMAGINING (MRI)

MRI relies upon the magnetic properties of living tissue. It detects the magnetic moment created by single protons in hydrogen atoms.

The use of MRI allows to determine all parameters of the niche, as well as niche and uterine cavity content on the sagittal T2-weighted views [2].

In study Marotta et al. [25] it has been shown that RMT measurements in MRI were related to those assess through TVUS.

MRI of the cesarean scar niche is not widely used due to its cost and availability. However, because it provides a comprehensive insight into the anatomy of the pelvis and its pathology, thanks to a higher tissue resolution and a wider field of view in comparison to TVUS, it is particularly useful in planning surgery, especially if there are other pathological conditions of the female's reproductive organs.

HYSTEROSCOPY

Diagnostic hysteroscopy is the "gold standard" in the diagnosis of uterine abnormalities. During this examination, the presence of the cesarean section scar niche can be directly visualized and confirmed [18, 26]. So far, the classification of the niches in hysteroscopic examination has not been described. The uterine niche in hysteroscopic examination is defined in various ways, e.g., a cavity with fibrotic ring, a pouch-like defect, a diverticulum with/without mucosa, a dome-shaped niche with nodules of endometrial hyperplasia/vascular hyperplasia [27]. There are no data in the literature on the relationship between the appearance of the uterine niche and the presence of clinical symptoms.

During hysteroscopy, which was performed in a group of women with abnormal uterine bleeding after cesarean section, the areas of profuse vascularization or polyps in niche were present [25, 28]. Hysteroscopy can also show the invagination of the myometrium with residual blood, which may correspond to the menstrual blood accumulating in the niche or related to endometriosis [28].

Histological analysis of samples taken after hysteroscopic treatment of uterine niches showed the presence of chronic inflammatory infiltration of the endocervix, fibrosis and necrosis, adenomyosis and polyps [6, 26, 29]

WHAT IS THE OPTIMAL TIMING FOR THE CESAREAN SECTION NICHE ASSESSMENT?

There are no unambiguous guidelines regarding the time after the cesarean section in which the uterine scar should be assessed.

In the study of L.F. van der Voet et al. [30] differences in cesarean scar niche's parameters dimensions were shown among patients, in whom the niche was the first time examined 6–12 weeks after the cesarean section, compared to the results of the examination performed one year after surgery. Contrary to changing uterine scar parameters, the incidence of uterine niche was unchanged. Other studies in which uterine niches were re-evaluated 6–24 months apart also showed a decrease in RMT over time after cesarean section [31].

The reduction in RMT or AMT /RMT ratio may be caused due to tissue reactions or a reduction in uterine muscle swelling during the healing process. Another theory involves the interaction of the uterus with adhesions between the uterus and the abdominal wall, resulting in an increase in niche depth and a decrease in RMT [32]. Moreover, uterine contractions can affect the RMT, and the accumulation of menstrual blood in the niche can increase the pressure on RMT, causing the change on its dimension [30].

IN WHICH PHASE OF MENSTRUAL CYCLE SHOULD WE ASSESS UTERINE NICHE?

There are no clear guidelines regarding the phase of the menstrual cycle in which a cesarean scar should be assessed [3]. According to some authors, the best time to perform an ultrasound examination is when the endometrial thickness is the smallest, it means immediately after the menstruation [33]. In another publication, the best time is during/after a few days after the menstruation [20]. According to the modified Delphi protocol, the ultrasound niche evaluation between 7.–14. cycle day may prevent the need for additional infusion fluid due to its natural intrauterine occurrence in the midfollicular phase [3].

A 3D-sonohisterography evaluation of the niche should be performed between the 17–25 day of the menstrual cycle because the cervical mucous during the preovulatory phase and blood deposits after menstruation may mix with the infused saline, which will deteriorate the quality of imaging [9].

HOW CAN WE CLASSIFY THE CESAREAN SECTION NICHES?

The literature lacks in uniform classification of cesarean scar niche. The first classification system of uterine niches was proposed by Gubbini in 2011 [6]. This classification was based on the measurement of the depth, base of the isthmocele and on calculation of its triangular area. This allowed to classify the uterine niches after cesarean section according to the size of its area.

In other studies, the large niche is when it penetrates to a depth of at least 50% or 80% of the uterine muscle or when RMT is ≤ 2.2 mm in transvaginal sonography and ≤ 2.5 mm in sonohysterography. In the situation, when there is no remaining defect over the isthmocele, it is a total defect of the uterine niche [34].

In the classification (VTS system) of cesarean section niches, which was proposed by A. Ludwin et al., the niche volume, RMT, presence supplementary features (niche's branches, urinary bladder not covering the niche and suspicion of deeply infiltrating endometriosis in the niche) were assessed [9]. Depending on the obtained total score, the niche is classified as probably clinically irrelevant or relevant.

CONCLUSIONS

There are still no unambiguous diagnostic and classification standards for uterine niches after cesarean section. Due to the growing number of cesarean sections and thus the growing problem of the increasing number of large uterine niches, which pose a risk of serious health consequences, it is necessary to create standardized diagnostic and therapeutic algorithms.

Conflict of interest

The authors state that there are no conflicts of interest to disclose.

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7. WNIOSKI

Na podstawie przeprowadzonych badań wyciągnięto następujące wnioski:

1. Nisza macicy po cięciu cesarskim została stwierdzona w badaniu ultrasonograficznym w odstępie czasowym 6-8 tygodni od zabiegu u 153 pacjentek (75%).
2. W badanej grupie, jedynie u 5 pacjentek (2.45%) stwierdzono grubość zrośniętego odcinka (RMT) <2.2 mm, a u 35 kobiet (17.15%) stwierdzono stosunek RMT /AMT ≤0.5, które według aktualnej wiedzy, stanowią czynnik ryzyka poważnych następstw w kolejnych ciążach.
3. Niszę macicy po cięciu cesarskim stwierdzono u 72% kobiet po przebytym wcześniej jednym cięciu cesarskim, u 87% pacjentek po przebytych wcześniej 2 cięciach cesarskich i u wszystkich pacjentek, które w historii przebyły 3 cięcia cesarskie.
4. W publikacji „Two- and three-dimensional transvaginal ultrasound in assessment of the impact of selected obstetric risk factors on cesarean scar niche formation: the case-controlled study" nie stwierdzono wpływu czynników ryzyka powstania niszy macicy takich jak: rozwarcie szyjki macicy podczas cięcia cesarskiego, wstąpienia czynności skurczowej przed cięciem cesarskim, przeprowadzenia cięcia cesarskiego w II okresie porodu, typu sposobu otwarcia macicy (na ostro vs na tępo), doświadczenia operatora (specjalista vs rezydent) czy typu zgięcia macicy (przodozgięcie vs tyłozgięcie) na parametry niszy macicy takie jak: wysokość szerokość i objętość niszy macicy, grubość zrośniętego odcinka, AMT, oraz współczynniki RMT/AMT, RMT/D, RMT/W, jak i na częstość występowania niszy macicy.
5. W publikacji „Two- and three-dimensional transvaginal ultrasound in assessment of the impact of selected obstetric risk factors on cesarean scar niche formation: the case-controlled study" stwierdzono, że grubość zrośniętego odcinka (RMT) u kobiet, które w przeszłości przebyły cięcie cesarskie jest mniejsza niż u kobiet, które przebyły cięcie cesarskie po raz pierwszy [RMT = 0.69482 cm (SD = 0.37705) vs RMT = 0.88088 cm (SD = 0.30718); p = 0.000068]. Podobna zależność została wykazana dla współczynnika RMT/AMT.

6. W publikacji „The impact of selected risk factors on uterine healing after cesarean section in women with single layer uterine closure: a prospective study using two- and three-dimensional transvaginal ultrasonography” wykazano brak wpływu czynników ryzyka powstania niszy macicy takich jak: występowanie chorób przewlekłych w ciąży, m.in. cukrzycy ciążowej, nadciśnienia tętniczego wywołanego ciążą, niedoczynności tarczycy czy kolonizacji drobnoustrojami szyjki macicy, wieku matki podczas cięcia cesarskiego, wieku ciążowego, historii przebytych poronień czy porodów przedwczesnych, na parametry niszy macicy takie jak: wysokość szerokość i objętość niszy macicy, grubość zrośniętego odcinka, AMT, oraz współczynniki RMT/AMT, RMT/D, RMT/W, jak i na częstość jej występowania.
7. W publikacji „UTERINE NICHE AFTER CESAREAN SECTION: a review of diagnostic methods” dokonano przeglądu literatury dotyczących metod diagnostycznych niszy macicy po cięciu cesarskim, wykazując w dostępnej literaturze brak jednoznacznych kryteriów diagnostycznych niszy macicy po cięciu cesarskim, brak jednoznacznego systemu klasyfikacji niszy macicy, brak wytycznych co do czasu po cięciu cesarskim, po którym nisza macicy powinna być oceniana, jak i brak jednoznacznych wytycznych co do fazy cyklu menstruacyjnego, w którym powinno się oceniać bliznę macicy po cięciu cesarskim.

8. PODSUMOWANIE

Na podstawie przeprowadzonych badań przy zastosowaniu przezpochwowej ultrasonografii dwuwymiarowej i trójwymiarowej nie stwierdzono wpływu czynników takich jak: rozwarcie szyjki macicy podczas cięcia cesarskiego, wstąpienia czynności skurczowej przed cięciem cesarskim, przeprowadzenia cięcia cesarskiego w II okresie porodu, typu sposobu otwarcia macicy (na ostro vs na tępo), doświadczenia operatora (specjalista vs rezydent), typu zgięcia macicy (przodozgięcie vs tyłozgięcie), jak i występowanie chorób przewlekłych w ciąży, m.in. cukrzycy ciążowej, nadciśnienia tętniczego wywołanego ciążą, niedoczynności tarczycy czy kolonizacji drobnoustrojami szyjki macicy, wieku matki podczas cięcia cesarskiego, wieku ciążowego, historii przebytych poronień czy porodów przedwczesnych na proces gojenia się macicy po cięciu cesarskim wśród pacjentek, u których nacięcie macicy zaopatrzono szwem jednowarstwowym ciągłym obejmującym całą grubość myometrium z wyłączeniem doczesnej.

W związku z rosnącą liczbą cięć cesarskich i tym samym narastającym problemem coraz większej liczby dużych nisz macicy, które niosą ze sobą ryzyko poważnych konsekwencji zdrowotnych oraz z uwagi na brak jednoznacznych standardów diagnostycznych i klasyfikacyjnych nisz macicy po cięciu cesarskim, jak również sprzeczne doniesienia co do wpływu poszczególnych czynników na proces gojenia się blizny macicy po cięciu cesarskim, konieczne jest przeprowadzenie dużych badań prospektywnych na homogennych grupach pacjentek. Dla praktyki klinicznej istotne jest również stworzenie odpowiednich algorytmów diagnostyczno-terapeutycznych, które pozwolą zmniejszyć ilość groźnych następstw związanych z obecnością niszy macicy po cięciu cesarskim.

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10. ZGODA KOMISJI BIOETYCZNEJ

KOMISJA BIOETYCZNA
przy
Uniwersytecie Medycznym
we Wrocławiu
ul. Pasteura 1; 50-367 WROCŁAW

OPINIA KOMISJI BIOETYCZNEJ Nr KB – 153/2020

Komisja Bioetyczna przy Uniwersytecie Medycznym we Wrocławiu, powołana zarządzeniem Rektora Uniwersytetu Medycznego we Wrocławiu nr 133/XV R/2017 z dnia 21 grudnia 2017 r. oraz działająca w trybie przewidzianym rozporządzeniem Ministra Zdrowia i Opieki Społecznej z dnia 11 maja 1999 r. (Dz.U. nr 47, poz. 480) na podstawie ustawy o zawodzie lekarza z dnia 5 grudnia 1996 r. (Dz.U. nr 28 z 1997 r. poz. 152 z późniejszymi zmianami) w składzie:

prof. dr hab. Jacek Daroszewski (choroby wewnętrzne, endokrynologia, diabetologia)
prof. dr hab. Krzysztof Grabowski (chirurgia)
dr Henryk Kaczkowski (chirurgia szczękowa, chirurgia stomatologiczna)
mgr Irena Knabel-Krzyszowska (farmacja)
prof. dr hab. Jerzy Liebhart (choroby wewnętrzne, alergologia)
ks. dr hab. Piotr Mrzygłód, prof. nadzw. (duchowny)
mgr Luiza Műller (prawo)
dr hab. Sławomir Sidorowicz (psychiatria)
prof. dr hab. Leszek Szenborn, (pediatria, choroby zakaźne)
Danuta Tarkowska (pielęgniarstwo)
prof. dr hab. Anna Wiela-Hojeńska (farmakologia kliniczna)
dr hab. Andrzej Wojnar, prof. nadzw. (histopatologia, dermatologia) przedstawiciel Dolnośląskiej Izby Lekarskiej)
dr hab. Jacek Zieliński (filozofia)

pod przewodnictwem
prof. dr hab. Jana Kornafela (ginekologia i położnictwo, onkologia)

Przestrzegając w działalności zasad Good Clinical Practice oraz zasad Deklaracji Helsińskiej, po zapoznaniu się z projektem badawczym pt.

„Ocena morfologii blizny po cięciu cesarskim macicy niecięŻarnej przy zastosowaniu USG 2D, 3D oraz programu VOCAL w zależności od wybranych parametrów"

zgłoszonym przez **lek. Joannę Budny-Wińską** zatrudnioną w II Klinice Ginekologii i Położnictwa Uniwersyteckiego Szpitala Klinicznego im. Jana Mikulicza-Radeckiego we Wrocławiu oraz złożonymi wraz z wnioskiem dokumentami, w tajnym głosowaniu postanowiła wyrazić zgodę na przeprowadzenie badania w II Klinice Ginekologii i Położnictwa Uniwersyteckiego Szpitala Klinicznego im. Jana Mikulicza-Radeckiego we Wrocławiu pod nadzorem dr. hab. Michała Pomorskiego **pod warunkiem zachowania anonimowości uzyskanych danych**.

Uwaga: Badanie to zostało objęte ubezpieczeniem odpowiedzialności cywilnej Uniwersytetu Medycznego we Wrocławiu z tytułu prowadzonej działalności:

Pouczenie: W ciągu 14 dni od otrzymania decyzji wnioskodawcy przysługuje prawo odwołania do Komisji Odwoławczej za pośrednictwem Komisji Bioetycznej UM we Wrocławiu

Opinia powyższa dotyczy: projektu badawczego będącego podstawą rozprawy doktorskiej

Wrocław, dnia 30 marca 2020 r.

BW

Uniwersytet Medyczny we Wrocławiu
KOMISJA BIOETYCZNA
przewodniczący
prof. dr hab. Jan Kornafel

11. OŚWIADCZENIA WSPÓŁAUTORÓW

Dr hab. n. med. Michał Pomorski
II Klinika i Katedra Ginekologii i Położnictwa
Uniwersytet Medyczny we Wrocławiu

Wrocław, 5.11.2021

OŚWIADCZENIE

Oświadczam, że w pracy:

1. "Two- and three-dimensional transvaginal ultrasound in assessment of the impact of selected obstetric risk factors on cesarean scar niche formation: the case-controlled study";
   Joanna Budny-Wińska, Aleksandra Zimmer-Stelmach, **Michał Pomorski**;
   Ginekologia Polska.2021;92(5): 378-382.doi:10.5603/GP.a2021.0024

   mój udział polegał na: pomocy w zaprojektowaniu badania, wsparciu merytorycznym w analizie i interpretacji wyników, pomocy przy pisaniu i korekcie manuskryptu.

2. "The impact of selected risk factors on uterine healing after cesarean section in women with single layer uterine closure: a prospective study using two- and three-dimensional transvaginal ultrasonography";
   Joanna Budny-Wińska, Aleksandra Zimmer-Stelmach, **Michał Pomorski**;
   Advances in Clinical and Experimental Medicine, 2021. doi: 10.17219/acem/142519

   mój udział polegał na: pomocy w zaprojektowaniu badania, wsparciu merytorycznym w analizie i interpretacji wyników, pomocy przy pisaniu i korekcie manuskryptu.

3. "UTERINE NICHE AFTER CESAREAN SECTION: a review of diagnostic methods";
   Joanna Budny-Wińska, **Michał Pomorski**;
   Ginekologia Polska.2021; 92(10): 726–730.doi: 10.5603/GP.a2021.0195

   mój udział polegał na: pomocy przy pisaniu i korekcie manuskryptu

(podpis)

lek. Aleksandra Zimmer-Stelmach
II Klinika i Katedra Ginekologii i Położnictwa
Uniwersytet Medyczny we Wrocławiu

Wrocław, 5.11.2021

OŚWIADCZENIE

Oświadczam, że w pracy:

"Two- and three-dimensional transvaginal ultrasound in assessment of the impact of selected obstetric risk factors on cesarean scar niche formation: the case-controlled study";
Joanna Budny-Wińska, **Aleksandra Zimmer-Stelmach**, Michał Pomorski;
Ginekologia Polska.2021;92(5): 378-382.doi:10.5603/GP.a2021.0024
mój udział polegał na: pomocy w rekrutacji pacjentek i pomocy w tworzeniu bazy danych

a w pracy:

"The impact of selected risk factors on uterine healing after cesarean section in women with single layer uterine closure: a prospective study using two- and three-dimensional transvaginal ultrasonography.";
Joanna Budny-Wińska, **Aleksandra Zimmer-Stelmach**, Michał Pomorski; Advances in Clinical and Experimental Medicine, 2021. doi: 10.17219/acem/142519
mój udział polegał na: pomocy w rekrutacji pacjentek i pomocy w tworzeniu bazy danych.

Aleksandra Zimmer-Stelmach
(podpis)