Influence of Cesarean Section Scar on the Mean Pulsatility Index of the Uterine Artery Doppler between 20 and 34 Weeks of Gestation

Auswirkung der Kaiserschnittnarbe auf den mittleren Doppler-Pulsatilitätsindex der Arteria uterina in der 20. bis 34. Schwangerschaftswoche

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Schlüsselwörter

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ABSTRACT

Objective

The aim of this study was to assess the influence of the cesarean section scars on the mean pulsatility index (PI) of the uterine artery Doppler between 20 and 34 weeks of gestation. A secondary objective was to assess the association between previous cesarean section and adverse maternal/perinatal outcomes.

Methods

A retrospective cohort study was conducted with pregnant women who had their deliveries between March 2014 and February 2023. PI of the uterine arteries Doppler was performed transvaginally between 20–24 weeks and transabdominally between 28–34 weeks. The following variables were considered adverse perinatal outcomes: birth weight < 10 th percentile for gestational age, preeclampsia, premature birth, placental abruption, perinatal death, postpartum hemorrhage, neonatal intensive care unit (NICU) admission.

Results

A total of 479 pregnant women were included in the final statistical analysis, being that 70.6 % (338/479) had no (Group I) and 29.4 % (141/479) had at least one previous cesarean section (Group II). Pregnant women with a previous cesarean had higher median of mean PI (1.06 vs. 0.97, p = 0.044) and median MoM of mean PI uterine arteries Doppler (1.06 vs. 0.98, p = 0.037) than pregnant women without previous cesarean section at ultrasound 20–24 weeks. Pregnant women with a previous cesarean section had higher median of mean PI (0.77 vs. 0.70, p < 0.001) and mean MoM PI uterine arteries Doppler (1.08 vs. 0.99, p < 0.001) than pregnant women without previous cesarean section at ultrasound 28–34 weeks. Pregnant women with ≥ 2 previous cesarean sections had a higher median of mean PI uterine arteries Doppler than those with no previous cesarean sections (1.19 vs. 0.97, p = 0.036). Group II had a lower risk of postpartum hemorrhage (aPR 0.31, 95% CI 0.13–0.75, p = 0.009) and composite neonatal outcome (aPR 0.66, 95% CI 0.49–0.88, p = 0.006). Group II had a higher risk of APGAR score at the 5 th minute < 7 (aPR 0.75, 95% CI 1.49–51.29, p = 0.016).

Conclusion

The number of previous cesarean sections had a significant influence on the mean PI uterine arteries Doppler between 20–24 and 28–34 weeks of gestation. Previous cesarean section was an independent predictor of postpartum hemorrhage and APGAR score at the 5 th minute < 7. Pregnancy-associated arterial hypertension and number of previous deliveries influenced the risk of composite neonatal outcome, but not the presence of previous cesarean section alone.

ZUSAMMENFASSUNG

Zielsetzung

Ziel dieser Studie war es, die Auswirkung von Kaiserschnittnarben auf den mittleren Doppler-Pulsatilitätsindex (PI) der A. uterina zwischen der 20. and 34. Schwangerschaftswoche zu beurteilen. Das sekundäre Ziel war, die Assoziation zwischen vorheriger Kaiserschnittentbindung und dem mütterlichen/perinatalen Outcome zu evaluieren.

Methoden

Es wurde eine retrospektive Kohortenstudie durchgeführt mit schwangeren Frauen, die zwischen März 2014 und Februar 2023 entbanden. Die Doppler-Sonografie zur Messung des PI der A. uterina wurde vaginal in den 20. –24. Schwangerschaftswochen und abdominal in den 28.–34. Wochen durchgeführt. Die folgenden Variablen wurden als ungünstiges perinatales Outcome bewertet: Geburtsgewicht < 10. Perzentile in Bezug auf das Gestationsalter, Präeklampsie, Frühgeburt, vorzeitige Plazentalösung, perinataler Tod, postpartale Blutungen, Verlegung auf eine neonatale Intensivstation (NICU).

Ergebnisse

Insgesamt wurden 479 schwangere Frauen in die letzte statistische Analyse eingeschlossen. Davon hatten 70,6% (338/479) keine (Gruppe I) und 29,4% (141/479) mindestens eine (Gruppe II) vorherige Kaiserschnittentbindung. Bei der Ultraschalluntersuchung in den 20.–24. Wochen hatten schwangere Frauen mit vorheriger Kaiserschnittentbindung einen höheren Median des durchschnittlichen PI (1,06 vs. 0,97; p = 0,044) und höheres medianes MoM des durchschnittlichen PI der A. uterina (1,06 vs. 0,98, p = 0,037) verglichen mit schwangeren Frauen ohne vorherige Kaiserschnittentbindung. Bei der Ultraschalluntersuchung in den 28.–34. Schwangerschaftswochen hatten schwangere Frauen mit vorheriger Kaiserschnittentbindung einen höheren Median des durchschnittlichen PI (0,77 vs. 0,70; p < 0,001) und ein höheres durchschnittliches MoM des PI der A. uterina (1,08 vs. 0,99; p < 0,001) verglichen mit schwangeren Frauen ohne vorherige Kaiserschnittentbindung. Schwangere Frauen mit ≥ 2 vorherigen Kaiserschnittentbindungen hatten einen höheren Median des durchschnittlichen PI der A. uterina verglichen mit Frauen ohne vorherige Kaiserschnittentbindung (1,19 vs. 0,97; p = 0,036). Gruppe II hat ein geringeres Risiko für eine postpartale Blutung (aPR 0,31; 95%-KI [0,13–0,75], p = 0,009) und für ein negatives neonatales Outcome (aPR 0,66; 95%-KI [0,49–0,88], p = 0,006). Gruppe II hatte ein höheres Risiko für einen APGAR-Score < 7 nach 5 Minuten (aPR 0,75; 95%-KI [1,49–51,29], p = 0,016).

Schlussfolgerung

Die Anzahl vorhergehender Kaiserschnittentbindungen hatte eine signifikante Auswirkung auf den mittleren Doppler-PI der A. uterina zwischen den 20.–24. und 28.–34. Schwangerschaftswochen. Eine vorherige Kaiserschnittentbindung war ein unabhängiger Prädiktor für eine postpartale Blutung und einen APGAR-Score < 7 nach 5 Minuten. Schwangerschaftsassoziierter Bluthochdruck und die Anzahl vorheriger Entbindungen haben Auswirkungen auf das Risiko eines negativen neonatalen Outcomes, nicht aber eine vorherige Kaiserschnittentbindung an sich.

Introduction

Globally, there has been a clear increase in the rate of cesarean sections, which has led to an increase in the number of previous cesarean sections [1]. Brazil has one of the highest cesarean section rates in the world, with an overall rate of 56% between 2014 and 2016 [2]. As a result of this increase in cesarean sections, there has also been an increase in scientific research on the topic. Evidence in the literature suggests that women who undergo cesarean sections in a subsequent pregnancy are more likely to experience adverse pregnancy/perinatal outcomes, such as preeclampsia, low birth weight, preterm birth, or stillbirth. However, the pathophysiological mechanisms associated with these outcomes remain to be elucidated [3, 4, 5].

Uterine artery Doppler ultrasound is one of the methods used to assess the progress of pregnancy to identify possible alterations in fetal development. It is a non-invasive method for detecting defects in uteroplacental circulation and placental implantation [6]. Using Doppler of the uterine arteries, it is possible to assess vascular resistance using pulsatility index (PI), resistance index (RI), and systolic/diastolic ratio (S/D). Of these, PI is the most commonly used index [7].

There seems to be some conflict regarding the Doppler of the uterine arteries in a new pregnancy in women who have previously undergone cesarean section. In the study by Santos-Filho et al. [8], the authors reported that there was no effect of the previous cesarean scar on the Doppler of the uterine arteries assessed between 26 and 32 weeks of gestation. However, in the study by Torabi et al. [9], cesarean section appeared to be associated with an increased risk of impaired placental function and adverse perinatal outcomes in subsequent pregnancies, particularly in women with a placenta located close to the previous uterine scar.

The aim of this study was to assess the influence of the cesarean section scars on the mean PI of the uterine artery Doppler between 20 and 34 weeks of gestation. A secondary objective was to assess the association between previous cesarean section and maternal/perinatal outcomes.

Methods

Study design

A retrospective cohort study, prospectively collected, was conducted at the Fetal Medicine Unit of the Gynecology and Obstetrics Sector of the University Hospital Mário Palmério, Uberaba-MG, Brazil and Sabin Diagnostic Medicine, Uberaba Unit, through an active search of the Astraia database (2000–2015 Astraia Software GmbH, Munich, Germany) and electronic medical records using the SOUL MV system (MV Informática Nordeste Ltda., Recife, Brazil) in pregnant women who had their deliveries between March 2014 and February 2023. The study was approved by the Ethics Committee of the University of Uberaba (CAAE: 69 833 723.4.0000.5145). Patients were grouped according to the presence of previous cesarean section: Group I – without previous cesarean section; Group II – at least one previous cesarean section.

Inclusion criteria were:

1. women less than 40 years of age with singleton pregnancies whose gestational age was confirmed by first trimester ultrasound and who had undergone ultrasound between 20 and 24 weeks and 28 and 34 weeks of gestation;
2. women not using heparin or aspirin;
3. women with no history of uterine surgery other than cesarean section;
4. absence of fetal malformations and/or chromosomal defects diagnosed during pregnancy or in the postpartum period.

Assessed variables

The following maternal/perinatal variables were assessed: ethnicity, mode of conception, parity, body mass index (BMI), smoking, alcohol consumption, maternal history of diabetes mellitus, pregnancy-associated arterial hypertension, systemic lupus erythematosus, antiphospholipid syndrome, placental location at the 20–24-week ultrasound scan, type of delivery, gestational age at delivery, birth weight, APGAR score at the 1 st minute, and APGAR score at 5 th minute. The following variables were evaluated to characterize the obstetric ultrasound examinations: gestational age at the time of the ultrasound examination, estimated fetal weight, mean PI of uterine artery Doppler, and mean multiples of median (MoM) PI of uterine artery Doppler.

The following were considered adverse perinatal outcomes: birth weight < 10 th percentile for gestational age [10], pre-eclampsia, premature birth, placental abruption, perinatal death, postpartum hemorrhage, neonatal intensive care unit (NICU) admission. The presence of at least one adverse perinatal outcome was considered a composite adverse perinatal outcome. Birth weight centile was calculated according to Nicolaides et al. [10].

Ultrasound examination

The ultrasound examinations were carried out by just two examiners with Fetal Medicine Foundation (FMF) accreditation and ten years' experience in obstetric ultrasound. All examinations were carried out transvaginally between 20–24 weeks and transabdominally between 28–34 weeks, using a Voluson E6 apparatus (General Electric, Healthcare, Zipf, Austria).

The PI of the uterine arteries Doppler was assessed transvaginally according to the following steps:

1. pregnant women were asked to void their bladder and placed in the classic dorsal lithotomy position, and
2. a sagittal view of the cervix was obtained.

The probe was swept laterally until the paracervical vessels were visualized. Color Doppler was activated to identify the uterine artery at the level of the internal cervical os. The uterine artery was evaluated at this point just before it bifurcates into the arcuate arteries. The uterine arteries Doppler have peak velocities above 50 cm/s, which can be used to differentiate this vessel from the arcuate arteries [11]. Routinely at our center, after correcting the insonation angle (< 30°), the spectral Doppler window was positioned over the entire width of the vessel to calculate the PI and peak systolic velocity of the uterine arteries. The PI of the right and left uterine arteries Doppler was calculated when at least three consecutive similar velocity waves were obtained [12, 13].

The PI of the uterine arteries Doppler was assessed abdominally according to the following steps:

1. the transabdominal probe was placed longitudinally in the lower lateral quadrant of the maternal abdomen, tilted medially in the parasagittal plane. Color Doppler flow mapping is useful to identify the uterine artery as it crosses the external iliac artery;
2. to obtain the best angle of insonation, the position of the probe was adjusted according to the orientation of the uterine artery;

3. the sample volume was placed 1.0 cm downstream of this crossing point. In a small proportion of cases, the uterine artery branches off before crossing the external iliac artery. In these cases, the sample volume should be placed in the uterine artery just prior to its bifurcation;
4. the same procedure was repeated for the contralateral uterine artery [14, 15].

The arithmetic means of the PI of the right and left uterine arteries Doppler was calculated when assessment was performed by the abdominal and transvaginal routes. Placental location as diagnosed by ultrasound was classified as lateral, fundic, anterior or posterior based on the area covered by more than 50 % of the placental mass. To calculate the MoM PI of the uterine arteries Doppler, the mean PI of the uterine arteries of pregnant women was divided by the median of the mean PI of the uterine arteries for gestational age, BMI, parity, diabetes mellitus during pregnancy, and pregnancy-associated arterial hypertension.

Sample size calculation

The GPower 3.1 program was used to calculate the sample size. Using an effect size of 0.25, a power of 80 % with 95 % confidence interval (CI), and a significance level of 0.05 (5 % probability of error), a sample size of at least 299 participants in the no prior cesarean section scar and 149 participants in the prior cesarean section scar group would be required to assess the effect of prior cesarean scar on the mean PI of the uterine arteries Doppler. Using an effect size of 0.25, a power of 80 % with 95 % CI, and a significance level of 0.05 (5 % probability of error), a total sample size of at least 180 participants in the none, one, two, and three or more previous cesarean section scar groups will be required to assess the effect of the number of previous cesarean section scars on the mean PI of uterine arteries Doppler. Using an effect size of 0.25, a power of 80 % with 95 % CI, and a significance level of 0.05 (5 % probability of error), a sample size of 95 participants would be required to evaluate the correlation between the number of cesarean scars and the mean PI uterine arteries Doppler. Using an effect size of 0.25, a power of 80 % with 95 % CI, and a significance level of 0.05 (5 % probability of error), a sample size of 206 participants would be required to evaluate the association between presence of cesarean scars and adverse perinatal outcomes. Using an odds ratio (OR) of 1.5, a power of 80 % with 95 % CI, and a significance level of 0.05 (5 % probability of error), a total sample size of at least 242 participants would be required to assess whether the presence of a previous cesarean section would be predictor of adverse perinatal outcomes. Using an OR of 1.5, a power of 80 % with 95 % CI, and a significance level of 0.05 (5 % probability of error), a total sample size of at least 146 participants would be required to calculate the prevalence ratio adjusted for confounding factors.

Statistical analysis

Data were collected in an Excel 2007 spreadsheet (Microsoft Corp., Redmond, WA, USA) and analyzed using SPSS version 20.0 (SPSS Inc., Chicago, IL, USA) and Prisma GraphPad version 7.0 (GraphPad Software; San Diego, CA, USA). The D'Agostino and Pearson normality tests were used to analyze whether the values were Gaussian distributed. Non-parametrically distributed variables were presented as medians and minimum and maximum values. The Mann-Whitney and Kruskal-Wallis tests were used to compare variables between groups. The Wilcoxon test was used to compare paired continuous variables. Categorical variables were described using absolute and percentage frequencies and presented in tables. The chi-squared test was used to assess the association between the presence of a previous cesarean section and the categorical variables. Spearman's correlation test was used to determine the association between the number of cesarean sections and the mean PI of the uterine arteries Doppler. To calculate the OR of adverse outcomes during pregnancy, binary logistic regression was used. The adverse maternal/perinatal outcomes of patients with history of previous cesarean section were compared with those without previous cesarean section. Effect estimates were reported as prevalence ratios (PR) with 95 % CI. When comparing the population with a history of prior cesarean section with those without previous cesarean section, we calculated adjusted prevalence ratios using modified Poisson regression models, adjusted for confounding factors (number of previous deliveries, BMI, pregnancy-associated arterial hypertension, diabetes mellitus during pregnancy, and type of delivery), with robust variance estimation to account for differences in baseline characteristics. The significance level for all tests was alpha < 0.05.

Results

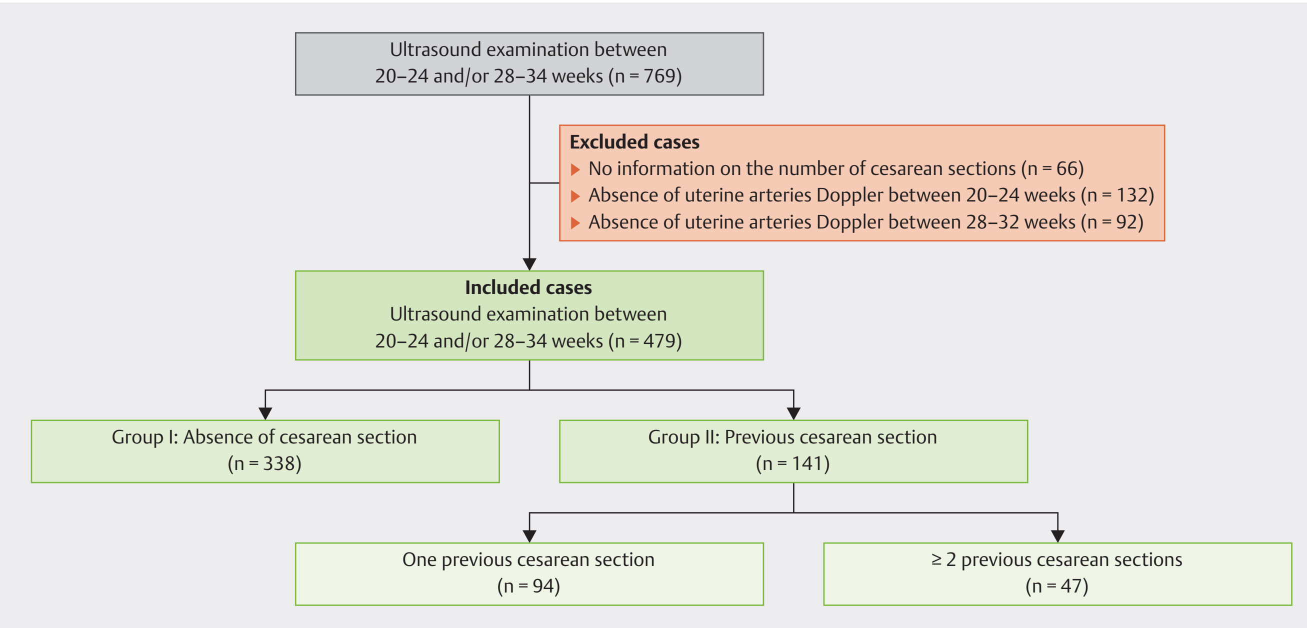
Maternal characteristics of the studied population

A total of 769 pregnant women who underwent an obstetric ultrasound examination between 20–24 weeks and/or 28–34 weeks were evaluated. Sixty-six cases were excluded due to lack of information on the number of cesarean sections in the medical records, 132 cases due to lack of uterine artery Doppler between 20–24 weeks, and 92 cases due to lack of uterine artery Doppler between 28–24 weeks. For the final statistical analysis, 479 pregnant women who underwent ultrasound between 20–24 weeks and 28–34 weeks of gestation were included. Of the pregnant women included, 70.6 % (338/479) had no previous cesarean section (Group I) and 29.4 % (141/479) had at least one previous cesarean section (Group II). Among pregnant women with previous cesarean sections, 66.6 % (94/141) had one previous and 33.4 % (47/141) had two or more previous cesarean sections (▶ **Fig. 1**).

Pregnant women with a previous cesarean section had a higher number of deliveries (1.0 vs 0.0 deliveries, p < 0.001), a higher BMI (29.7 vs 26.3 kg/m^2, p < 0.001), a higher alcohol consumption (6.5 % vs 1.5 %, p = 0.003), diabetes mellitus during pregnancy (14.9 % vs 6.8 %, p = 0.005), pregnancy-associated arterial hypertension (16.3 % vs 7.1 %, p = 0.002) and cesarean section in the current pregnancy (90.6 % vs 54.7 %, p < 0.001) (▶ **Table 1**).

Influence of the presence of a previous cesarean section on uterine arteries Doppler indices

When evaluating the influence of the presence of cesarean scar on ultrasound characteristics, pregnant women with a previous cesarean had higher median of mean PI (1.06 vs. 0.97, p = 0.044) and median MoM of mean PI uterine arteries Doppler (1.06 vs. 0.98,



▶ **Fig. 1** Flowchart of the cases included in the study.

p = 0.037) than pregnant women without a previous cesarean when the ultrasound examination was performed at 20–24 weeks' gestation. When the ultrasound examination was performed between 28–34 weeks of gestation, pregnant women with a previous cesarean section had higher median of mean PI (0.77 vs. 0.70, p < 0.001) and median MoM of mean PI uterine arteries Doppler (1.08 vs. 0.99, p < 0.001) than pregnant women without a previous cesarean section (▶ **Table 2**).

Influence of cesarean section scar and placental location on uterine arteries Doppler indices

When evaluating the influence of cesarean section scar and placental location on uterine arteries Doppler parameters, it was found that pregnant women with previous cesarean section and an anterior placenta, between 28–34 weeks of gestation, had a higher median MoM of mean PI uterine artery (1.10 vs 0.99, p = 0.049) compared to pregnant women without previous cesarean section. In addition, pregnant women with a previous cesar-

▶**Table 1** Maternal and perinatal characteristics of the studied population.

Variable	Group I (n = 338)	Group II (n = 141)	p
Maternal			
Ethnicity			**0.104**§
White	48.6 % (153/315)	51.5 % (69/134)	
Black	18.4 % (58/315)	17.9 % (24/134)	
Mixed	32.7 % (103/315)	29.1 % (39/134)	
Asiatic	0.3 % (1/315)	1.5 % (2/134)	
Mode of Conception			**0.431**§
Spontaneous	98.8 % (334/338)	100 % (141/141)	
Induction without IVF	0.9 % (3/338)	0.0 % (0/141)	
IVF	0.3 % (1/338)	0.0 % (0/141)	
Number of previous deliveries	0.0 (0–5)	1.0 (0–7)	< 0.001†
BMI (kg/m^2)	26.3 (16.2–55.7)	29.7 (16.8–57.5)	< 0.001†
Smoking	8.3 % (28/336)	12.2 % (17/139)	0.187§
Alcohol consumption	1.5 % (5/336)	6.5 % (9/139)	0.003§

▸**Table 1** continued

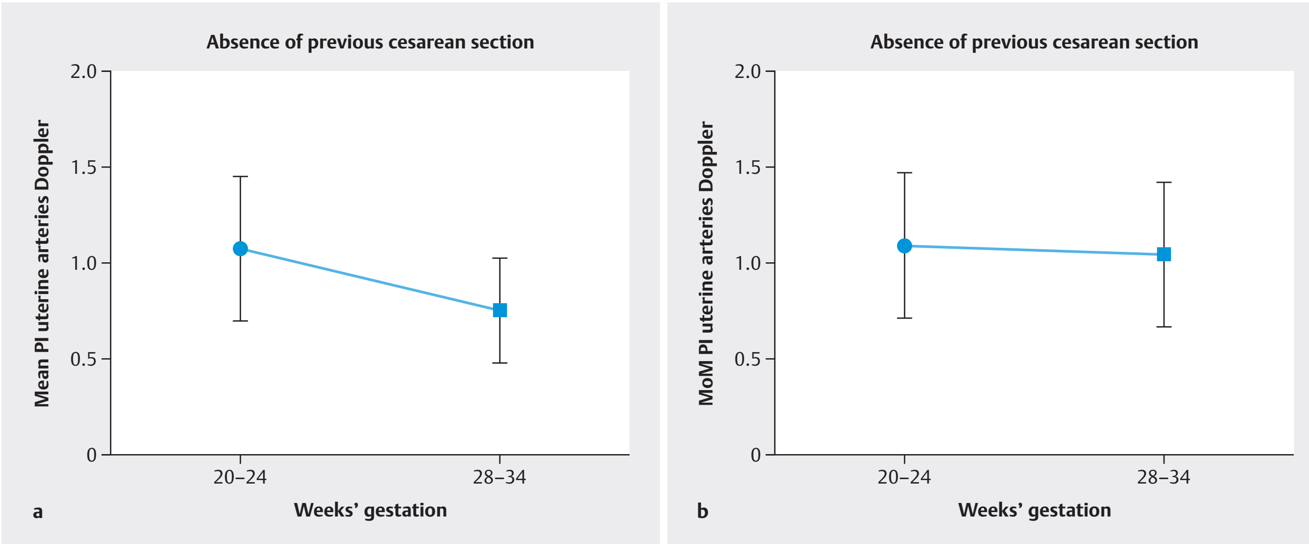
Variable	Group I (n = 338)	Group II (n = 141)	p
Diabetes mellitus during pregnancy	6.8 % (23/338)	14.9 % (21/141)	0.005§
Pregnancy-associated arterial hypertension	7.1 % (24/338)	16.3 % (23/141)	0.002§
Systemic lupus erythematosus	0.6 % (2/338)	0.0 % (0/141)	0.360§
Antiphospholipid syndrome	N/D	N/D	N/D
Placental location			**0.131§**
Anterior	48.5 % (164/338)	38.3 % (54/141)	
Fundic	1.8 % (6/338)	2.8 % (4/141)	
Lateral	3.0 % (10/338)	5.7 % (75/141)	
Posterior	46.7 % (158/338)	53.2 % (75/141)	
Perinatal			
Type of delivery			**< 0.001§**
Vaginal	44.4 % (146/329)	9.4 % (13/138)	
Cesarean section	54.7 % (180/329)	90.6 % (125/138)	
Forceps	0.9 % (3/329)	0.0 % (0/138)	
Gestational age at delivery (weeks)	39.0 (28.1–41.4)	39.0 (30.3–41.1)	0.800†
Birth weight (grams)	3140.0 (880–4300)	3205 (1070–4505)	0.408†
APGAR score at the 1 st minute	9.0 (1–10)	9.0 (2–10)	0.306†
APGAR score at the 5 th minute	9.0 (1–10)	9.0 (6–10)	0.835 †

BMI = body mass index; IVF = in vitro fertilization; N/D = no cases described.
Mann Whitney †: median (minimum-maximum); Chi-Squared §: percentage (n/N); * statistical test could not be used due to the absence of at least 3 cases in one of the groups. $p < 0.05$.

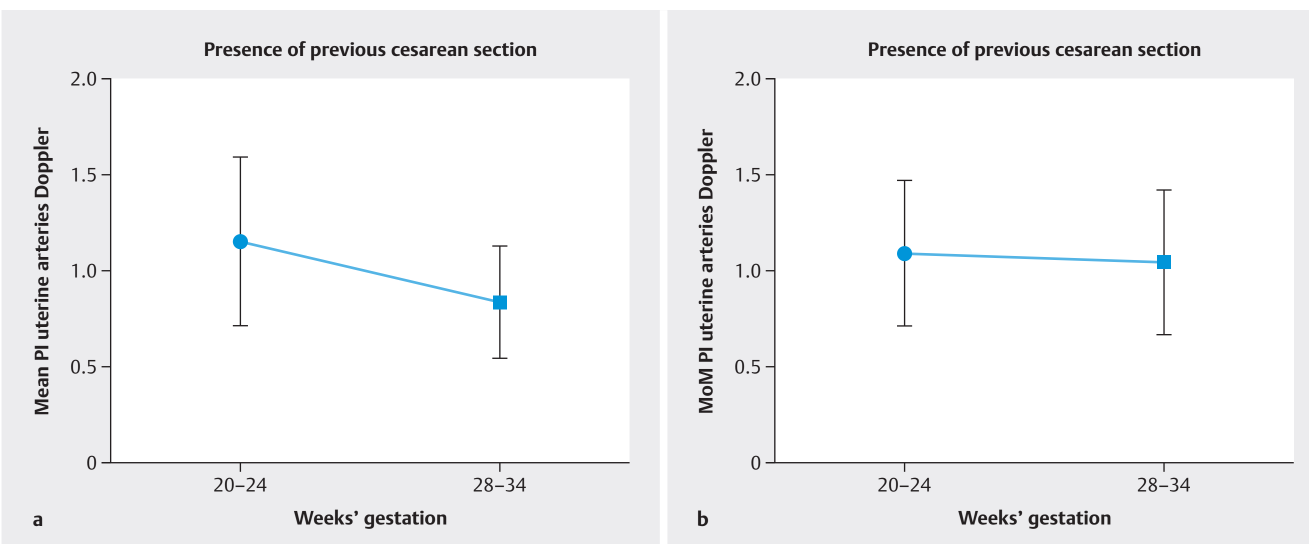
▸**Table 2** Influence of the presence of a previous cesarean section on the pulsatility index (PI) of the uterine arteries Doppler, gestational age at the time of ultrasound examination and estimated fetal weight.

Ultrasound examination	Group I (n = 338)	Group II (n = 141)	p
20–24 weeks' gestation			
Gestational age at US scan (weeks)	22.4 (20.0–24.7)	22.4 (20.0–24.9)	0.490†
Estimated fetal weight (grams)	493.0 (276.0–769.0)	483.0 (290.0–813.0)	0.814†
Median of mean PI uterine arteries Doppler	0.97 (0.50–2.96)	1.06 (0.58–3.44)	0.044†
Median MoM of mean PI uterine arteries Doppler	0.98 (0.49–2.85)	1.06 (0.59–3.21)	0.037†
Increased mean PI uterine arteries Doppler	14.8 % (50/338)	14.9 % (21/141)	0.977§
28–34 weeks' gestation			
Gestational age at US scan (weeks)	30.1 (28.0–34.9)	29.9 (28.0–34.9)	0.585†
Estimated fetal weight (grams)	1495.0 (853.0–2866.0)	1502.0 (881.0–2798.0)	0.939†
Median of mean PI uterine arteries Doppler	0.70 (0.35–2.77)	0.77 (0.36–2.41)	< 0.001†
Median MoM of mean PI uterine arteries Doppler	0.99 (0.52–4.26)	1.08 (0.49–3.26)	< 0.001†
Increased mean PI uterine arteries Doppler	7.1 % (24/338)	10.6 % (15/141)	0.197§

MoM = multiples of the median. Mann Whitney; US = ultrasound. †: median (minimum-maximum), Chi-squared §: percentage (n/N). $p < 0.05$.



▶ **Fig. 2** Influence of the time of ultrasound examination on the mean pulsatility index (PI) (**a**) and the multiples of the median (MoM) of mean PI of the uterine arteries Doppler (**b**) in pregnant women with no previous cesarean section (**b**). Wilcoxon test. p < 0.05.



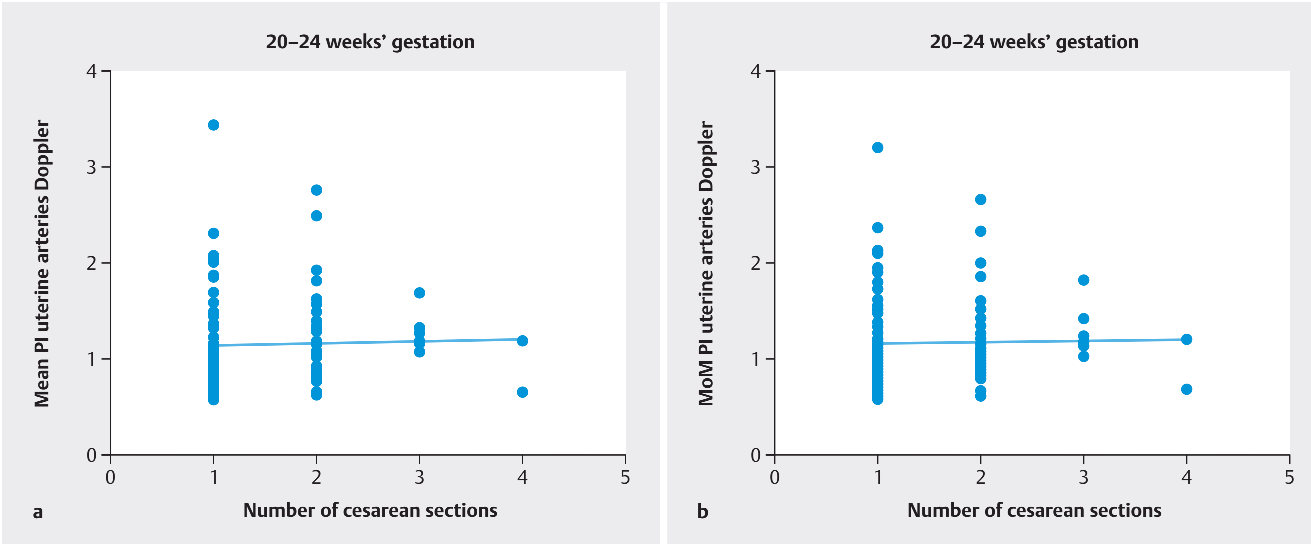
▶ **Fig. 3** Influence of the time of ultrasound examination on mean pulsatility index (PI) (**a**) and multiples of median (MoM) of mean PI uterine arteries Doppler (**b**) in pregnant women with previous cesarean section. Wilcoxon test. p < 0.05.

ean section and a posterior placenta, between 28–34 weeks of gestation, had a higher median of mean PI of uterine artery (0.68 vs 0.75, p = 0.025) and higher median MoM of mean PI uterine artery (0.94 vs 1.04, p = 0.005) than pregnant women without a previous cesarean section (**Table S1**, online).

Influence of previous cesarean section at 20–24 and 28–34 weeks of gestation on uterine arteries Doppler indices

In pregnant women without previous cesarean section, a significant reduction in mean PI and MoM of mean PI uterine arteries Doppler was observed between 20–24 weeks and 28–34 weeks of gestation. The median difference was − 0.28 (p < 0.0001) and − 0.03 (p = 0.0031) for mean PI and MoM of mean PI uterine arteries Doppler, respectively (▶ **Fig. 2**).

In pregnant women with previous cesarean section, there was a significant reduction in mean PI and MoM of mean PI uterine arteries Doppler between 20–24 and 28–34 weeks of gestation. The median difference was − 0.28 (p < 0.0001) and − 0.03 (p = 0.0031) for mean PI and MoM of mean PI uterine arteries Doppler, respectively (▶ **Fig. 3**).



▶ **Fig. 4** Correlation between the number of previous cesarean sections and the mean pulsatility index (PI) (**a**) and multiples of the median (MoM) of mean PI of the uterine arteries Doppler (**b**) performed between 20–24 weeks of gestation. Spearman's correlation test. $p < 0.05$.

▶**Table 3** Influence of the number of previous cesarean sections on the mean pulsatility index (PI) and multiples of median (MoM) of mean PI of the uterine arteries Doppler.

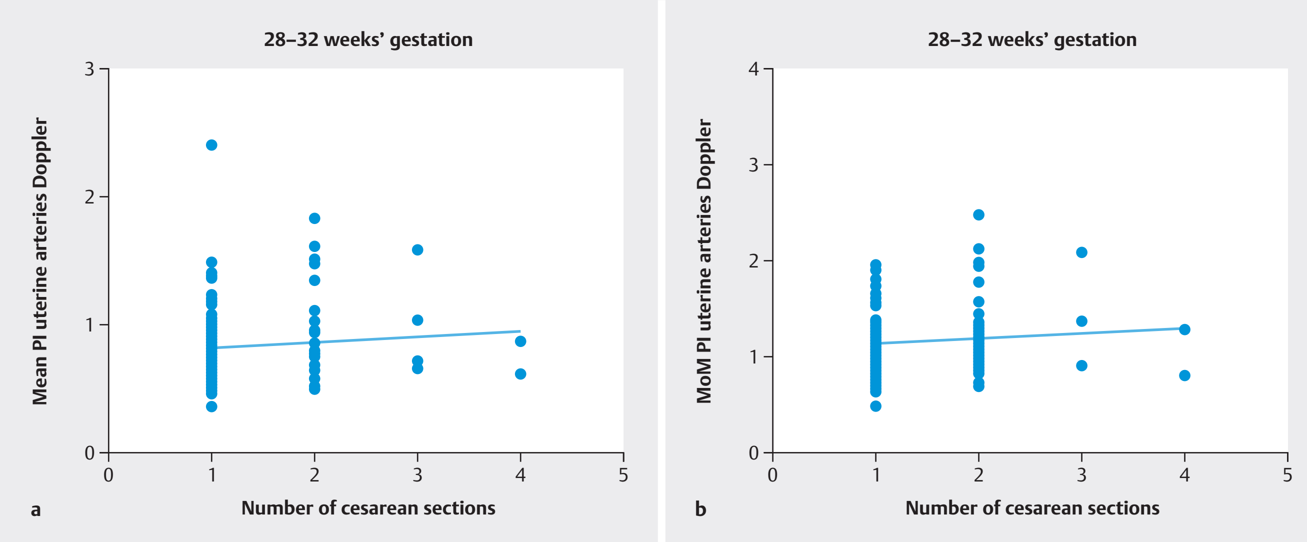
Variable	Absence of previous cesarean section (n = 338)	One previous cesarean section (n = 94)	≥ 2 previous cesarean sections (n = 47)	p§
20–24 weeks' gestation				
Mean PI uterine arteries Doppler	0.97 (0.50–2.96)[B]	1.04 (0.58–3.44)	1.10 (0.63–2.77)	0.047
MoM PI of mean uterine arteries Doppler	0.98 (0.49–2.85)	1.02 (0.59–3.21)	1.12 (0.62–2.66)	0.083
28–34 weeks' gestation				
Mean PI uterine arteries Doppler	0.70 (0.35–2.77)[A,B]	0.74 (0.36–2.41)	0.81 (0.50–1.83)	< 0.001
MoM of mean PI uterine arteries Doppler	0.99 (0.52–4.26)[A,B]	1.04 (0.49–3.26)	1.14 (0.71–2.48)	< 0.001

[A]: absence vs. one previous cesarean section; [B]: absence vs. ≥ 2 previous cesarean sections. Kruskal-Wallis §: median (minimum-maximum). $p < 0.05$.

Influence of number of previous cesarean sections on uterine arteries Doppler indices

There was a significant influence of the number of previous cesarean sections on the median of mean PI uterine arteries Doppler performed between 20 and 24 weeks of gestation ($p = 0.047$). Pregnant women with ≥ 2 previous cesarean sections had a higher median of mean PI uterine arteries Doppler than those with no previous cesarean sections (1.19 vs. 0.97, $p = 0.036$). There was no significant influence of the number of previous cesarean sections on median MoM of mean PI uterine arteries Doppler ($p = 0.083$) (▶ **Table 3**). Although there was a significant influence of number of previous cesarean sections on mean PI uterine arteries Doppler, there was no significant correlation between number of previous cesarean sections and mean PI ($r = 0.08$, $p = 0.333$) and MoM of mean PI uterine arteries Doppler ($r = 0.05$, $p = 0.507$) (▶ **Fig. 4**).

There was a significant influence of the number of previous cesarean sections on the median of mean PI ($p < 0.001$) and median MoM of mean PI uterine arteries Doppler ($p < 0.001$) performed between 28 and 34 weeks of gestation. Pregnant women with one previous cesarean section (0.74 vs. 0.70, $p = 0.009$) and ≥ 2 previous cesarean sections (0.81 vs. 0.70, $p < 0.001$) had higher median of mean PI uterine arteries Dopplers than pregnant women with no previous cesarean sections. Pregnant women with one previous cesarean section (1.04 vs. 0.99, $p = 0.013$) and those with ≥ 2 previous cesarean sections (1.14 vs. 0.99, $p < 0.001$) had higher median MoM of mean PI uterine arteries Doppler than those with no previous cesarean sections (▶ **Table 3**). Although there was a significant influence of the number of previous cesarean sections on mean PI and MoM of mean PI uterine arteries Doppler, there was no significant correlation between the number of previous cesarean sections and mean PI ($r = 0.11$, $p = 0.183$) and MoM of mean PI uterine arteries Doppler ($r = 0.11$, $p = 0.172$) (▶ **Fig. 5**).



▶ **Fig. 5** Correlation between the number of previous cesarean sections and the mean pulsatility index (PI) and multiples of median (MoM) of mean PI of the uterine arteries Doppler performed between 28–34 weeks of gestation. Spearman's correlation test. p < 0.05.

▶ **Table 4** Association between previous cesarean sections and adverse maternal/perinatal outcomes.

Variable	Group I (n = 338)	Group II (n = 141)	OR (95% CI)	aPR (95% CI)
Birth weight < 10 th percentile	21.6% (73/338)	15.6% (22/141)	0.67 (0.39–1.13), p = 0.134	0.72 (0.46–1.33), p = 0.160
Preeclampsia	2.7% (9/338)	6.4% (9/141)	2.49 (0.96–6.42), p = 0.051	1.17 (0.41–3.33), p = 0.767
Preterm birth	8.6% (29/338)	9.2% (13/141)	1.08 (0.54–2.15), p = 0.820	0.74 (0.39–1.39), P = 0.352
Placental abruption	0.0% (0/338)	0.0% (0/141)	*	*
Postpartum hemorrhage	9.5% (32/338)	4.3% (6/141)	0.42 (0.17–1.04), p = 0.054	0.31 (1.31–0.75), p = 0.009
NICU admission	4.4% (15/338)	7.8% (11/141)	1.82 (0.81–4.07), p = 0.139	1.42 (0.58–3.48), p = 0.442
APGAR score at the 1 st minute < 7	7.7% (26/338)	6.4% (9/141)	0.81 (0.37–1.79), p = 0.616	0.95 (0.44–2.02), p = 0.900
APGAR score at the 5 th minute < 7	1.5% (5/338)	2.1% (3/141)	1.45 (0.34–6.14), p = 0.614	8.75 (1.49–51.29), p = 0.016
Perinatal death	0.0% (0/338)	0.0% (0/141)	*	*
Composite adverse perinatal outcomes	40.5% (137/338)	32.6% (46/141)	0.71 (0.47–1.07), p = 0.104	0.66 (0.49–0.88), p = 0.006

aPR = adjusted prevalence ratio; CI = confidence interval; n = absolute number of patients; N = total number of patients; N/D = no cases described; NICU = neonatal intensive care unit; OR = odds ratio. Percentage (n/N). OR calculated by binary logistic regression. Adjusted PR with modified Poisson model after adjustment for confounding factors. p < 0.05.

Influence of previous cesarean section and adverse maternal/perinatal outcomes

▶ **Table 4** shows the rate of adverse maternal/perinatal outcomes in pregnant women who have previous cesarean section and those who did not have a previous cesarean section. A binary logistic regression was performed to identify if the previous cesarean section was a predictor of maternal/perinatal adverse outcomes.

After binary logistic regression, Poisson logistic regression with robust estimation was performed using previous cesarean section, pregnancy-associated arterial hypertension, diabetes mellitus during pregnancy as cofactors and number of previous deliveries, BMI as covariates to identify the best predictor of maternal/perinatal adverse outcomes (**Table S2**, online).

Previous cesarean section was an independent predictor of postpartum hemorrhage (aPR 0.31, 95% CI 0.31–0.75, p = 0.009), APGAR score at the 5 th minute < 7 (aPR 8.75, 95% CI 1.49–51.29, p = 0.016) (▶ **Table 4** and **Table S2**, online). The model including previous cesarean section (aPR 0.66, 95% CI 0.492–0.889, p = 0.006) (▶ **Table 4**), pregnancy-associated arterial hypertension (aPR 1.46, 95% CI 1.05–2.06, p = 0.026) and the number of previous deliveries (aPR 1.10, 95% CI 1.01–1.22, p = 0.049) (**Table S2**, online) was the best predictor of the composite neonatal outcome. Previous cesarean section was not predictive of birth weight

< 10 th percentile (aPR 0.72, 95% CI 0.46–1.33, p = 0.160), preeclampsia (aPR 1.17, 95% CI 0.41–3.33, p = 0.767), preterm birth (aPR 0.74, 95% CI 0.39–1.39, p = 0.352), NICU (aPR 1.42, 95% CI 0.58–3.42, p = 0.442), APGAR score at the 1 st minute < 7 (aPR 0.95, 95% CI 0.44–2.02, p = 0.900) (▶ **Table 4**).

The model with diabetes mellitus during pregnancy (aPR 0.25, 95% CI 0.06–0.96, p = 0.045) and pregnancy-associated arterial hypertension (aPR 1.95, 95% CI 1.18–3.23, p = 0.009), was the best model for predicting birth weight < 10 th percentile. Number of previous deliveries (aPR 1.14, 95% CI 0.97–1.33, p = 0.092) and BMI (aPR 0.97, 95% CI 0.95–1.00, p = 0.150) were not predictive of birth weight < 10 th centile. Number of previous deliveries (aPR 1.44, 95% CI 1.01–2.07, p = 0.044) was an independent predictor of preeclampsia. Diabetes mellitus during pregnancy (aPR 1.67, 95% CI 0.53–5.21, p = 0.374), pregnancy-associated arterial hypertension (aPR 2.30, 95% CI 0.60–8.85, p = 0.220), and BMI (aPR 1.03, 95% CI 0.97–1.09, p = 0.308) were not predictors of preeclampsia. Diabetes mellitus during pregnancy (aPR 2.32, 95% CI 1.18–4.53, p = 0.014) was an independent predictor of preterm birth. Pregnancy-associated arterial hypertension (aPR 2.22, 95% CI 0.99–4.97, p = 0.051), the number of previous deliveries (aPR 1.12, 95% CI 0.83–1.52, p = 0.433) and BMI (aPR 1.00, 95% CI 0.96–1.05, p = 0.827) were not predictors of preterm birth. Diabetes mellitus during pregnancy (aPR 1.59, 95% CI 0.63–4.03, p = 0.320), pregnancy-associated arterial hypertension (aPR 0.86, 95% CI 0.26–2.79, p = 0.803), the number of previous deliveries (aPR 1.04, 95% CI 0.79–1.52, p = 0.135) and BMI (aPR 1.04, 95% CI 0.99–1.09, p = 0.106) were not predictors of postpartum hemorrhage. Diabetes mellitus during pregnancy (aPR 3.25, 95% CI 1.34–7.89, p = 0.009) and pregnancy-associated arterial hypertension (aPR 3.11, 95% CI 1.08–8.97, p = 0.036) were predictors of NICU admission. Number of previous deliveries (aPR 0.97, 95% CI 0.64–1.48, p = 0.917) and BMI (aPR 0.97, 95% CI 0.92–1.03, p = 0.0.402) were not predictors of NICU admission. Diabetes mellitus during pregnancy (aPR 2.99, 95% CI 1.34–6.71, p = 0.008) was an independent predictor of APGAR score at the 1 st minute < 7. Pregnancy-associated arterial hypertension (aPR 1.32, 95% CI 0.49–3.59, p = 0.578), number of previous deliveries (aPR 0.66, 95% CI 0.41–1.09, p = 0.107) and BMI (aPR 1.01, 95% CI 0.95–1.07, p = 0.750) were not predictors of APGAR score at the 1 st minute < 7. Diabetes mellitus during pregnancy (aPR 4.94, 95% CI 0.95–25.47, p = 0.056), pregnancy-associated arterial hypertension (could not be calculated), number of previous deliveries (aPR 0.13, 95% CI 0.01–1.91, p = 0.139) and BMI (aPR 0.95, 95% CI 0.81–1.09, p = 0.473) were not predictors of APGAR score at the 5 th minute < 7. Diabetes mellitus during pregnancy (aPR 1.22, 95% CI 0.84–1.78, p = 0.282), and BMI (aPR 0.99, 95% CI 0.98–1.09, p = 0.904) were not predictors of composite neonatal outcome (**Table S2**, online).

There were no cases of placental abruption and perinatal death observed in the study (▶ **Table 4**).

Discussion

Cesarean section rates have increased dramatically worldwide in recent decades, particularly in middle- and high-income countries, despite a lack of evidence of substantial maternal and perinatal benefits. Between 1990 and 2014, Latin America and the Caribbean had the highest cesarean section rates (40.5%) [16]. Brazil, in particular, is a country with one of the highest cesarean section rates in the world. Data from the Brazilian Live Birth Information System between 2014 and 2017 showed that 11 774 665 deliveries occurred during this period, with cesarean section being the most common (55.8%) [17]. In a private health service in Southeast of Brazil, the cesarean section rate was high as 91.8% (536/584), being 8.5% for maternal cause indications, 30.41% for fetal causes, and 17.17% were elective [18]. The causes of this tremendous increase in cesarean section rates are several such as cesarean section on request, advanced maternal age at first pregnancy, decrease of vaginal delivery after one cesarean section, rare vaginal breech delivery, increased estimated fetal weight, maternal chronic diseases as arterial hypertension and diabetes mellitus [19]. In a systematic review including 1328 articles that assessed the risks of maternal complications associated with cesarean section without medical indication, the pregnant women had higher risks of maternal death and postpartum infections and lower risk of hemorrhage [20].

In addition, elective cesarean section is associated with adverse perinatal outcomes. Nakashima et al. [21] studied 684 neonates delivered by elective cesarean section at 37 weeks' gestation and observed a higher incidence of NICU admission, adverse respiratory complications, low birth weight, and hypoglycemia than those delivered at 38 weeks. The same matter, a Danish population-based cohort study including 145 821 low-risk primiparous women, 4039 were cesarean sections and 141 782 vaginal deliveries. Pregnant women with planned cesarean section had a slightly higher risk of wound infections than vaginal deliveries [22]. In our study, we observed an increased risk of APGAR score at the 5 th minute < 7 and a decreased risk of postpartum hemorrhage and composite adverse perinatal outcome in pregnant women with previous cesarean sections. We used an unselected population and the majority has only one previous cesarean section 66.6% (94/141). Kaboré et al. [23] compared the maternal/perinatal complications in pregnant women with trial of labor after a one previous cesarean section were and an elective repeated cesarean section. When only the low-risk population was analyzed, no difference was observed between the groups.

The uterine arteries are branches of the internal iliac artery and provide the main blood supply to the uterus. Coordinated remodeling of the segments of the uteroplacental vasculature occurs at different times during pregnancy. Such remodeling underlies the decrease in vascular resistance, facilitating an increase in uterine blood flow from approximately 45 ml/min in the nonpregnant state to 750 ml/min during pregnancy, in time to meet the increasing demands of the fetoplacental unit [24]. Clark et al. [25] have shown that incomplete spiral artery remodeling alone is unlikely to cause abnormal uterine arteries Doppler waveforms as increased resistance in these arteries can be "buffered" by upstream anastomoses. Increased uterine arteries Doppler indices are associated with maternal complications and adverse perinatal outcomes such as preeclampsia, fetal growth restriction, and stillbirth [26, 27, 28].

The indication as well as the surgical technique of cesarean section can cause devascularization of the uterine tissue and scarring, which may lead to impaired implantation and consequent complications such as placental accreta spectrum and fetal growth restriction. The same matter, the uterine blood vascularization can also be compromised [29]. Complete implantation of a gestational sac within the myometrial defect is a first trimester predictor of morbidly adherent placenta with consequent poor maternal/perinatal outcome [30]. According to our hospital protocol, the technique used to open the uterus consists of a transverse uterine incision. In selected cases, a vertical incision (low vertical or classic) was used by the surgeons. The hysterotomy began with a small incision made with a scalpel. After making an incision approximately 2 to 3 cm wide in most of the uterine wall, the surgeon used the index finger of the dominant hand to bluntly enter the uterine cavity in a blunt fashion. For uterine closure, the uterus was exteriorized or not according to the surgeon's preference, and a two-layer continuous full-thickness closure was performed with delayed absorbable synthetic suture. The first layer included the myometrium plus the decidual edge to achieve hemostasis, and the second imbricating layer covered the exposed myometrial edges. In addition to the blood supply provided by the uterine arteries, the ovarian arteries also play an important role in the perfusion of the uterus. There are at least 5 arterial anastomoses that contribute to the adequate perfusion of the female pelvis: tubal branch of the ovarian artery with the tubal branch of the uterine artery, pubic branch of the external iliac artery with the pubic branch of the obturator artery, internal pudendal artery with the obturator artery, superior rectal artery with the middle rectal artery, and superior rectal artery with the internal pudendal artery. Anastomoses also help meet the increased blood demand of the uterus during pregnancy, ensuring that the fetus has adequate oxygen and nutrients. They are also important for tissue healing and regeneration, reducing the risk of ischemia in the area of the anterior uterine scar. Thus, arterial anastomoses minimize the negative effects of previous uterine surgery [31]. Therefore, we believe that the absence of increased risk of birth weight < 10 th percentile, preeclampsia, preterm birth, placental abruption, NCIU admission, APGAR score at the 1 st minute < 7, and perinatal death in our study may be influenced by the function of the arterial anastomoses of the female pelvis in ensuring adequate blood supply and adequate healing of the uterine tissue.

In our study, pregnant women with previous cesarean section had higher PI of uterine artery Doppler between 20–24 and 28–32 weeks of gestation than pregnant women without previous cesarean section. Işıkalan et al. [32] evaluated uterine artery Doppler comparing 77 pregnant women without and 80 pregnant women with previous cesarean section between 18 and 24 weeks of gestation. They observed significantly higher MoM PI and increased PI in pregnant women with previous cesarean section. Torabi et al. [9] studied 400 pregnant women (200 without and 200 with previous cesarean section) between 18 and 22 weeks of gestation. They observed that pregnant women with previous cesarean section had higher uterine artery PI and persistent notch than pregnant women without cesarean section. These results are in agreement with ours, proving that previous cesarean section modifies local placentation. Different from these two cited studies [9, 32], we evaluated the uterine arteries Doppler during two different periods (20–24 and 28–34 weeks), showing that the local uterine modification persists in the third trimester of pregnancy.

Although the PIs vary significantly between groups, these values are quite close to each other, we believe that it may not have clinical significance. Indeed, there was no difference between the groups regarding some variables used in the population characterization, such as birth weight and APGAR score. However, after adjusting the regression model for confounders, we observed a higher risk of APGAR score at the 5 th minute < 7 and a lower risk of postpartum hemorrhage and composite neonatal outcome. So, the connection with increased risk of APGAR < 7 is not between cesarean section and uterine arteries Doppler, but rather with the pathologies used in the adjustment of the model. Our study was not designed to evaluate the association of increased uterine PIs with adverse maternal/perinatal outcomes. Therefore, the higher uterine PIs in pregnant women with prior cesarean section may not influence the increased risk of these adverse maternal/perinatal outcomes. Prospective randomized studies should be conducted in this field to better analyze the influence of cesarean section on the adverse maternal/perinatal outcomes.

We also observed that pregnant women with and without previous cesarean section showed a significant decrease in mean PI uterine arteries Doppler between 20–24 and 28–34 weeks of gestation. Yapan et al. [33] performed a prospective observational case-control study of singleton pregnancies in which ultrasound examinations with uterine artery Doppler were performed in four periods: 11–13 + 6, 19–24 + 6, 30–34 + 6, and 35–37 + 6 weeks. The pregnant women were divided into two groups: 267 (no cesarean section) and 261 (previous cesarean section). They observed in both groups that the mean MoM PI showed a significant biphasic pattern; an initial decrease between the first and second trimester of pregnancy, followed by a continuous increase from the second trimester, early and late third trimester of pregnancy. Flo et al. [29] performed a cross-sectional case-control study between 17 and 20 weeks of gestation, including 36 with previous and 32 without cesarean section. They did not observe significant differences between the groups. The reduction in mean uterine artery PI in late stages of pregnancy in previous publication was supported by data from preclinical studies of uterine arterial system remodeling from the paracrine effects of trophoblastic invasion, mostly conducted in primates [34].

There are conflicting results in the literature regarding the effect of parity on uterine artery Doppler indices. In a study by Goynumer et al. [35], the authors observed that parity did not affect mean uterine artery PI values in 19–24 weeks' gestation. In another study, the mean PI was significantly higher in nulliparous women than in multiparous women at 17–18 weeks' gestation [36]. Another study on 430 pregnant women suggested that there was a positive correlation between parity and uterine artery PI indices [37]. Işıkalan et al. [30], in a secondary analysis, showed a significant effect of the number of cesarean sections on the MoM of mean PI uterine artery Doppler. Consistent with the previous study [32], we showed that MoM of mean PI uterine artery Doppler were not significantly different between pregnant women with no previous and those with one or ≥ 2 previous cesarean sections at 20–24 weeks' gestation. On the other hand, the mean uterine artery PI Doppler was higher in pregnant women with ≥ 2 previous cesarean sections than in patients without previous cesarean section. To our knowledge, our study was the first to analyze the effect of the number of cesarean sections on uterine artery PI in the third trimester of pregnancy. We showed that also mean uterine artery PI as MoM of mean uterine artery PI was higher in pregnant women with ≥ 2 previous cesarean sections than in pregnant women without previous cesarean section. In the study by Yapan et al. [33], in the cesarean section group, 97 % had only one previous cesarean section and 3 % had ≥ 2 previous cesarean sections. In the study of Flo et al. [29], in the cesarean section group, 90.7 % had only one previous cesarean section and 9.3 % had ≥ 2 previous cesarean sections. In contrast, in our study, 66.6 % had only one previous cesarean section and 33.4 % had ≥ 2 previous cesarean sections. We believe that the greater the number of previous cesarean scars, the greater the uterine decidualization and the worse the local vascularization, contributing to a decrease in resistance in the uterine arteries.

As the placenta accreta spectrum (PAS) has a significant impact on the management of pregnancies after previous cesarean section, changes in uterine artery PI may indicate abnormal placentation. Cho et al. [38] performed an interesting retrospective analysis showing a reduction in mean PI measured by uterine artery Doppler in patients with placenta accreta compared to those without placenta accreta. The combination of uterine artery Doppler values and cesarean section history could potentially improve the diagnostic accuracy of placenta accreta. Although the study by Cho et al. [38] had a large sample size, prospective studies with higher levels of evidence may strengthen these findings. In our study, there were no cases of placenta accreta to analyze the effect of uterine artery PI on the diagnostic accuracy of PAS. However, pregnant women with previous cesarean section and a posterior placenta, between 28 and 34 weeks of gestation, had a higher median of mean uterine artery PI and a higher median MoM of mean uterine artery PI than pregnant women without previous cesarean section. At the same interval of gestational age, pregnant women with previous cesarean section and anterior placenta had a higher median MoM of mean PI uterine artery than pregnant women without previous cesarean section. Osmanağaoğlu et al. [39] described a case of placenta percreta with bladder invasion. Cesarean section with supracervical hysterectomy, partial excision of the bladder and bilateral hypogastric artery ligation was carried out in the 36 th week of pregnancy. A part of the placenta was excised manually and the remaining placenta was left in situ.

The strengths of this study include the large sample size and the analyses of uterine artery PI and MoM of mean uterine artery PI in the second and third trimesters of pregnancy. The main limitation of this study is the fact that we performed a retrospective analysis and did not measure uterine artery volume blood flow or maternal cardiac output; these measures could have helped to improve our understanding of the pathophysiology and our interpretation of the results.

The uterine arteries Doppler has not been shown to be a marker of adverse maternal/perinatal outcomes in pregnant women with previous cesarean scars. We believe that uterine artery Doppler should not be routinely performed during pregnancy as a predictor of adverse perinatal outcomes in women with previous cesarean scars. However, future prospective studies with larger case numbers are needed to prove our findings.

Conclusion

In summary, pregnant women with previous cesarean section had higher uterine artery resistance and the number of previous cesarean sections had a significant influence on the uterine arteries Doppler between 20–24 and 28–34 weeks of gestation. Previous cesarean section was an independent predictor of postpartum hemorrhage and APGAR score at the 5 th minute < 7. Pregnancy-associated arterial hypertension and number of previous deliveries influenced the risk of composite neonatal outcome, but not the presence of previous cesarean section alone.

Supplementary Material

- **Table S1.** Influence of the presence of a previous cesarean section and placenta location on the pulsatility index (PI) of the uterine arteries Doppler, according to gestational age at the time of ultrasound examination.
- **Table S2:** Association between confounders (diabetes mellitus during pregnancy, pregnancy-associated arterial hypertension, number of previous deliveries and body mass index), and adverse maternal/perinatal outcomes.

Conflict of Interest

The authors declare that they have no conflict of interest.

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