ORIGINAL RESEARCH

Maternal and Neonatal Outcomes of Placenta Previa with and without Coverage of a Uterine Scar: A Retrospective Cohort Study in a Tertiary Hospital

Jiaming Rao [1]
Dazhi Fan [1]
Zixing Zhou[1]
Xin Luo[1]
Huiting Ma [1]
Yingchun Wan[1]
Xiuyin Shen[1]
Dongxin Lin [1]
Huishan Zhang[1]
Yan Liu[2]
Zhengping Liu [1,2]

[1]Foshan Fetal Medicine Institute, Affiliated Foshan Maternity & Child Healthcare Hospital, Southern Medical University (Foshan Maternity & Child Healthcare Hospital), Foshan, Guangdong, 528000, People's Republic of China; [2]Department of Obstetrics, Affiliated Foshan Maternity & Child Healthcare Hospital, Southern Medical University (Foshan Maternity & Child Healthcare Hospital), Foshan, Guangdong, 528000, People's Republic of China

Correspondence: Zhengping Liu; Yan Liu
Foshan Fetal Medicine Institute and Department of Obstetrics, Affiliated Foshan Maternity & Child Healthcare Hospital, Southern Medical University (Foshan Maternity & Child Healthcare Hospital), Renminxi Road 11, Foshan, Guangdong, 528000, People's Republic of China
Tel +86 757 82969878
Fax +86 757 82969772
Email liuzphlk81@outlook.com; liuyan20102011@163.com

Background: To compare the maternal and neonatal outcomes of placenta previa (PP) with and without coverage of a uterine scar in Foshan, China.

Methods: A retrospective cohort study comparing all singleton pregnancies with PP was conducted at a tertiary, university-affiliated medical center from 1 January 2012 to 31 April 2017 in Foshan, China. Demographic, clinical and laboratory data were extracted from electronic medical records (EMRs). Maternal and neonatal outcomes of PP with and without coverage of a uterine scar were compared by statistical method.

Results: There were 58,062 deliveries during the study period, of which 726 (1.25%) were complicated PP in singleton pregnancies and were further classified into two groups: the PP with coverage of a uterine scar group (PPCS, n=154) and the PP without coverage of a uterine scar group (Non-PPCS, n=572). Overall, premature birth (<37 weeks, 67.5% vs 54.8%; *P*=0.019), cesarean section (100% vs 97.6%; *P*=0.050), intraoperative blood loss >1000 mL (77.9% vs 16.0%; *P*<0.001) or >3000mL (29.9% vs 3.0%; *P*<0.001), bleeding within 2-24 hours after delivery (168.2±370.1 ml vs 49.9±58.4 ml; *P*<0.001), postpartum hemorrhage (48.7% vs 15.7%; *P*<0.001), transfusion (34.6% vs 16.1%; *P*<0.001), hemorrhage shock (7.8% vs 1.9%; *P*<0.001), hysterectomy (2.6% vs 0.5%; *P*=0.019), fetal distress (35.7% vs 12.1%; *P*<0.001) and APGAR score at 1 min (15.2% vs 7.1%; *P*=0.002) had a significant difference between PPCS group and Non-PPCS group. After grouping by whether complicated with placenta accreta spectrum disorders (PASD), we found that PPCS was significant associated with more intraoperative blood loss >1000mL, intraoperative blood loss >3000mL, bleeding within 2–24 hours after delivery and fetal distress than the Non-PPCS group.

Conclusion: The PPCS group had poorer maternal and neonatal outcomes than the Non-PPCS group after grouping by whether pregnancies complicated with PASD or with different placental positions.

Keywords: placenta previa, placenta accreta spectrum disorders, pregnancy outcomes, uterine scar, hysterectomy, cesarean section

Plain Language Summary

Placenta previa is particularly dangerous when covering a uterine scar (PPCS). PPCS, also called pernicious placenta previa (PPP), one of the most dangerous types of PP and defined as when the placenta overlies a uterine scar that may or may not with accreta. The incidence

of PPCS has increased correspondingly with the increase of cesarean section in China and often leads to unexpected bleeding during delivery and increased risk for peripartum hysterectomy.

This study investigated risk factors and maternal and neonatal outcomes in women with PPCS and Non-PPCS in a Chinese cohort. As the rate of CS increases with China's universal two children policy, the rate of PP, especially PPCS, will most likely increase as well. Women with PPCS were more likely to have some poorer maternal and neonatal outcomes than the Non-PPCS group even after grouping by whether pregnancies complicated with PASD or with different placental positions. Health care providers should be aware of possible complications of PPCS to provide proper counseling to their patients.

Introduction

Placenta previa (PP) is defined as implantation of the placenta in the lower uterine segment overlying the endocervical os, and it is known as an important cause of serious fetal and maternal morbidity and mortality.[1,2] PP is associated with an increased risk of bleeding, blood transfusion, postpartum anemia, hysterectomy, septicemia, thrombophlebitis and maternal death.[3–5] A population-based study[6] noted that 44.4% of patients with PP delivered before 37 weeks of gestation, 16.9% of these delivered before 34 weeks of gestation, and neonatal mortality rates were increased by threefold to fourfold.

The reported incidence for PP was higher in Asia (1.2%) and lower in Europe (0.36%), North America (0.29%) and sub-Saharan Africa (0.27%).[7] Our previous research[8] showed that the incidence of PP was between 0.93% and 2.01% in mainland China. Several factors[2,5,8–10] increase the risk for PP, including prior cesarean delivery, prior surgical abortion, advancing maternal age, multiparity, multiple pregnancy, and assistive reproductive technology. Although the etiology of placenta previa remains indeterminate, there appears to be a link between endometrial damage and uterine scarring and subsequent placenta previa, which is an important and common cause of the occurrence of the PP. Certainly, Women who have undergone one or more cesarean section are at greater risk for subsequent placenta disorders, and there is a dose–response relationship between the number of prior cesarean sections and subsequent PP and PASD.

In general, PP is subdivided into three categories according to the position of the placenta and the cervix: complete previa, marginal previa, and partial previa. However, PP is particularly dangerous when covering a uterine scar (PPCS). PPCS, also called pernicious placenta previa (PPP), one of the most dangerous types of PP, was proposed by Chattopadhyay et al[11] and defined as when the placenta overlies a uterine scar that may or may not with accreta. The incidence of PPCS has increased correspondingly with the increase of cesarean section in China and often leads to unexpected bleeding during delivery and increased risk for peripartum hysterectomy.[9,12,13]

A large number of previous studies have reported the clinical outcomes and associated risk factors of PP,[5,10,11,14–17] and only a few reports have focused on comparing PPCS and Non-PPCS.[9,12,13] Information about these conditions is important so that women with a specific type of PP can be appropriately counseled regarding their outcomes and clinical care providers can be appropriately prepared for their deliveries. Thus, the specific objective of this study was to investigate the maternal and neonatal outcomes of women with PPCS and Non-PPCS in a Chinese cohort.

Materials and Methods
Study Design and Population

A retrospective cohort study comparing pregnancies with PP with and without coverage of a uterine scar was conducted over 24 weeks. This hospital was a tertiary university-affiliated medical center with a stable number of approximately 13,000 deliveries per year, which accounted for approximately 10% of the city's deliveries and provided care for the region's obstetrical population, especially those with complicated pregnancies. There were 58,062 pregnancies who delivered a liveborn or a stillborn infant of at least 24 gestational weeks at our hospital during the period of January 2012 to March 2017, and 726 women who had complicated PP with a singleton pregnancy were included for further study (Figure 1). All data were retrospectively analyzed from the electronic medical records, surgical records and anesthetic records. Exclusion criteria included multiple pregnancies, misdiagnosis or fetal malformation; not delivering in the study hospital and no archive in the hospital electronic system; or loss of information regarding placental position.

PP is defined as implantation of the placenta in the lower uterine segment in advance of the fetus, including complete placenta previa, partial placenta previa and marginal placenta previa. Low-lying placenta previa was excluded in our study because of its different clinical management.[18] In this study, the patients with PP were divided into two groups: the placenta previa with coverage of a uterine scar group (PPCS group, n=154 cases) and the placenta previa without coverage of a uterine group (Non-PPCS group, n=572 cases). PPCS was defined as PP where the placenta covered a uterine
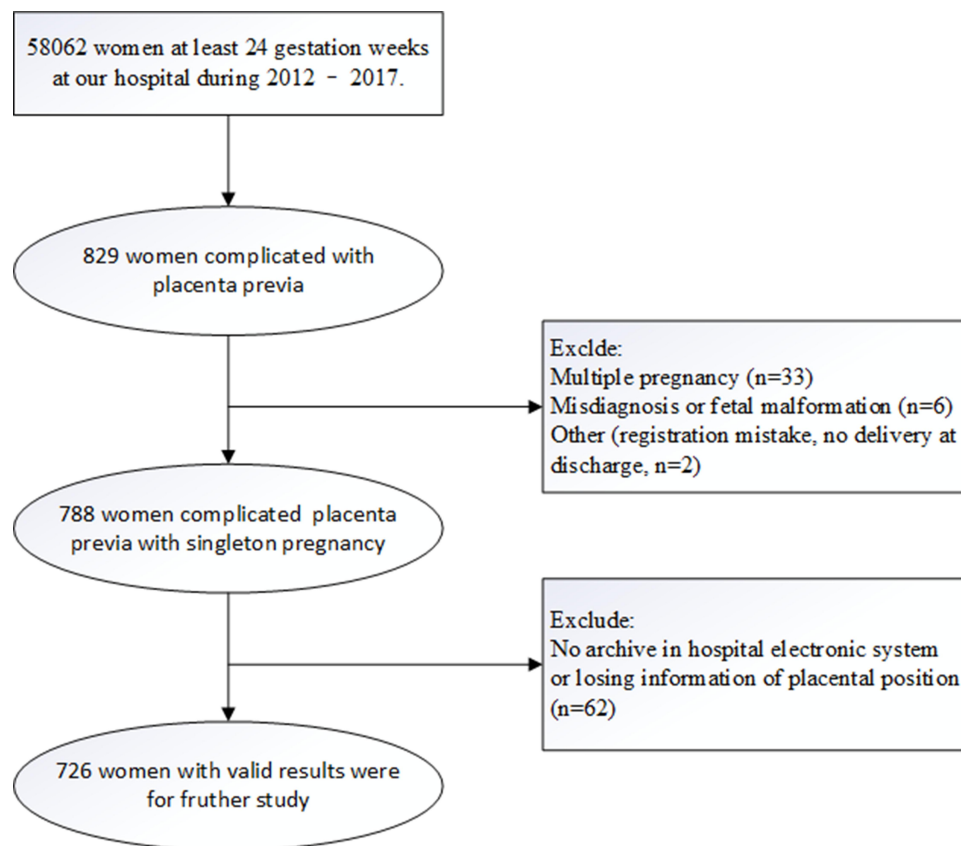
Figure 1 Flow chart of the study population.

scar in the lower uterine segment. Non-PPCS was defined as PP where placenta did not cover a uterine scar in the lower uterine segment. The placental position was divided into 3 groups: anterior, posterior, and ante-posterior or laterally positioned. The placental position was evaluated in a transverse cross-section by ultrasound or MRI, in which the maximum placental area was depicted. Anterior placenta is a placenta dominantly attached to the anterior wall of the uterus, and a posterior placenta is a placenta dominantly attached to the posterior wall of the uterus. The other placentas were defined as ante-posterior or laterally positioned.

All types of PP or AIP were diagnosed by experienced obstetricians, based on serial transvaginal or transabdominal ultrasonographic scans or MRI, and confirmed at the time of delivery and pathological results. Detailed diagnostic criteria have been reported in our previous studies.[19]

Definitions
Clinical and laboratory data were extracted from electronic medical records. The following clinical characteristics were evaluated in all patients: maternal age, BMI, gestational weeks, race/ethnicity, parity, prior CS, mode of delivery,

in vitro fertilization and embryo transfer (IVF-ET) or not, diseases associated with pregnancy (gestational diabetes mellitus, hypertension disorder complicating pregnancy). To compare maternal and neonatal outcomes, gestational weeks, mode of delivery (vaginal, CS), postpartum hemorrhage, postpartum anemia, hysterectomy, infant weight, intrauterine death, fetal distress, Umbilical cord blood pH, Apgar score at 1 min, and Apgar score at 5 min were compared in the groups. We calculated gestational age on the basis of the actual delivery date in the medical record. PPH was diagnosed according to blood loss of more than 500 mL for vaginal deliveries and more than 1000 mL for cesarean delivery by the American College of Obstetricians and Gynecologists (ACOG).[20] Postpartum anemia was defined as a hemoglobin concentration of <110 g/L (6.8 mmol/L) according to WHO.[21] HDCP (systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥ 90 mmHg, with or without proteinuria) can be classified into five groups: (1) gestational hypertension, (2) preeclampsia, (3) eclampsia, (4) superimposed preeclampsia on chronic hypertension and (5) chronic hypertension in pregnancy preeclampsia.[22] GDM was diagnosed when one of the following conditions was met: (1) fasting plasma glucose ≥ 5.1

mmol /L two or more times; (2) two or more test results equal to or above the following values after a 75 g-load OGTT: fasting, 5.1 mmol/L; 1-hour, 10.0 mmol/L; 2-hour, 8.5 mmol/L. The prediction and diagnosis of fetal distress lacks a single indicator during the prenatal and delivery stages, and we are able to make a diagnosis based on a comprehensive assessment of the following observations:: (1) early stage tachycardia >160 bpm; during severe hypoxia <120bpm; CST shows late deceleration, variable deceleration; fetal heart rate <100 bpm, with frequent late decelerations indicating severe fetal hypoxia, may lie intrauterine any moment; (2)And/or meconium stained amniotic fluid; (3)And/or reduced or absent fetal movement; (4) And/or umbilical cord blood pH < 7.2.

Statistical Analysis

Categorical data were reported as numbers and percentages (%), and descriptive data were expressed as the means ± standard deviations (SD). Boxplots describe the amount of bleeding between groups by using the median, the upper quartile, and the lower quartile. The 95% confidence intervals or interquartile range were calculated and presented. Statistical significance was calculated using the χ^2 test or Fisher's exact test for differences in qualitative variables and the Mann–Whitney U-test or t-test for differences in continuous variables. Statistical analyses were performed with the Statistical Package for Social Science Version 22.0 (SPSS Inc, Chicago, IL, USA) and R (3.4.1). Two-tailed P values <0.05 were considered statistically significant.

Ethics Approval and Informed Consent

The study was approved by the Human Subjects Committee of the Southern Medical University Affiliated Maternal & Child Health Hospital of Foshan. To ensure patient privacy, our data did not include the patient's name, phone number, home address, or other sensitive information. Informed consent is waived because research is based on EMRs and all information is processed anonymously. This study was conducted in accordance with the Declaration of Helsinki.

Results

There were 58,062 pregnant women who delivered a liveborn or a stillborn infant of at least 24 gestational weeks at our hospital during the period of January 2012 to March 2017, and 726 women had complicated PP with a singleton pregnancy and were identified for further data review (Figure 1). Of these 726 women, 152 (20.9%) had PPCS and 574 (79.1%) had Non-PPCS.

The clinical characteristics of the groups are shown in Table 1. The mean age of individuals with pregnancies complicated with PP was 31.71 ± 5.25 years old, the mean BMI was 26.06 ± 3.11, and the mean number of gestational weeks was 35.70 ± 2.46 weeks. Most of the women were Han Chinese (98.6%), 31.5% were primipara and 8.3% had a pregnancy with IVF-ET. PPCS was significantly associated with advanced maternal age, higher than average BMI, greater parity and prior CS compared with Non-PPCS. There were no significant differences in gestational weeks, IVF-ET, HDCP and GDM between the two groups.

PPCS was significantly associated with a higher proportion of total PASD (46.8% vs 12.6%, P< 0.001) and placenta increta or percreta (37.7% vs 5.6%) compared to Non-PPCS. The PPCS group was dominated by anterior placentas (46.8%), followed by ante-posterior or laterally positioned (33.8%) and posterior placentas (19.5%), while the Non-PPCS group was dominated by posterior placentas (56.3%), followed by ante-posterior or laterally positioned (21.9%) and anterior placentas (21.9%) (Table 2).

In pregnancies complicated with PASD (n=144, Table 3), the PPCS group was associated with poor maternal outcomes for intraoperative blood loss (3000 [1500, 4500] mL vs 700 [400, 1500] mL, P<0.001, Figure 2) and bleeding within 2–24 hours after delivery (220.1 ± 436.4mL vs 65.5±114.2 mL, P=0.008) than the Non-PPCS group. The PPCS group was associated with a higher incidence of intraoperative blood loss> 1000 mL (90.3% vs 40.8%, P<0.001), intraoperative blood loss> 3000 mL (52.8% vs 16.9%, P<0.001) and higher fetal distress (36.1% vs 18.1%, P=0.015) than the Non-PPCS group. There was no significant association between the PPCS group and the Non-PPCS group in the rates of gestational weeks, mode of delivery, postpartum hemorrhage, hemorrhagic shock, postpartum anemia, hysterectomy, intrauterine death, umbilical cord blood and APGAR score at 1 min and 5 min.

In pregnancies not complicated with PASD (n=582, Table 3), the PPCS group was associated with poor maternal outcomes for intraoperative blood loss (1100 [800, 1750] mL vs 400[300, 600] mL, P<0.001, Figure 2), bleeding within 2–24 hours after delivery (118.9±289.9 vs 47.7±45.1 mL, P<0.001). The PPCS group was associated with a higher incidence of intraoperative blood loss> 1000 mL (67.1% vs 12.5%, P<0.001), intraoperative blood loss> 3000 mL (9.8% vs 1.0%, P<0.001), postpartum hemorrhage (68.3% vs 15.2%, P<0.001), transfusion (30.5% vs 13.6%, P<0.001) and higher fetal distress

Table 1 Comparison of Baseline Characteristics of Patients with PPCS and Non-PPCS

Characteristics	Total (n=726)	PPCS (n=154)	Non-PPCS (n=572)	*P value*
Maternal age mean ± SD, y	31.71±5.25 [16–48]	32.50±4.88 [21–43]	31.48±5.33 [16–48]	0.027*
Maternal BMI[a] mean ± SD	26.06±3.11 [17.31–39.96]	26.49±3.35 [19.44–38.05]	25.93±3.03 [17.31–39.96]	0.041*
Gestational weeks mean ± SD	35.70±2.46 [28–41]	35.72±2.25 [28–41]	35.84±2.39 [28–41]	0.530
Race/ethnicity (%)				0.925
Han Chinese	716(98.6)	152(98.7)	564(98.6)	
National minority	10(1.4)	2(1.3)	8(1.4)	
BMI at delivery (%)				0.327
<24	183(25.2)	32(20.8)	151(26.4)	
24 to 28	365(50.3)	80(51.9)	285(49.8)	
>28	178(24.5)	42(27.3)	136(23.8)	
Parity (%)				<0.001*
1	229(31.5)	0(0)	229(40.0)	
2	401(55.2)	126(81.8)	275(48.1)	
3	85(11.7)	25(16.2)	60(10.5)	
≥4	11(1.5)	3(1.9)	8(1.4)	
Prior CS (%)				<0.001*
No	482(66.4)	0	482(84.3)	
Yes	244(33.6)	154(100)	90(15.7)	
IVF-ET (%)				0.059
No	666(91.7)	147(95.5)	519(90.7)	
Yes	60(8.3)	7(4.5)	53(9.3)	
HDCP				0.078
No	704(97.0)	146(94.8)	558(97.6)	
Yes	22(3.0)	8(5.2)	14(2.4)	
GDM				0.785
No	604(83.2)	127(82.5)	477(83.4)	
Yes	122(16.8)	27(17.5)	95(16.6)	

Notes: Data are mean±SD (independent *t*-test) or n (%) (x^2 test); *P < 0.05. Percentages do not total 100% owing to missing data.
Abbreviations: n, number of observations; SD, standard deviation; [a]BMI at delivery, body mass index at delivery; HDCP, hypertensive disorder complicating pregnancy; GDM, gestational diabetes mellitus; CS, cesarean section; IVF-ET, in vitro fertilization and embryo transfer.

Table 2 Comparison of PASD and Placenta Position in Patients in the PPCS and Non-PPCS Groups

PASD	Total (n=726)	PPCS (n=154)	Non-PPCS (n=572)	*P value*
With PASD	144(19.9)	72(46.8)	72(12.6)	<0.001*
Placenta accreta	54(7.5)	14(9.1)	40(7.0)	
Placenta increta or percreta	90 (12.4)	58(37.7)	32(5.6)	
Placenta position				<0.001*
Anterior	197(27.1)	72(46.8)	125(21.9)	
Posterior	352(48.5)	30(19.5)	322(56.3)	
Ante-posterior or laterally positioned	177(24.4)	52(33.8)	125(21.9)	

Notes: Percentages do not total 100% owing to missing data. *P < 0.05

(35.4% vs 11.2%, *P*<0.001) than the Non-PPCS group. There was no significant association between the PPCS group and Non-PPCS group in the rates of gestational weeks, mode of delivery, hemorrhagic shock, postpartum anemia, hysterectomy, intrauterine death, umbilical cord blood and Apgar score at 1 and 5 min.

Table 3 Comparison of Pregnancy Outcomes with and without PASD in Patients with PPCS and Non-PPCS

Maternal/Neonatal Outcomes	All (n=726)		P-value	With PASD (n=144)		P-value	Without PASD (n=582)		P-value
	PPCS (n=154)	Non-PPCS (n=572)		PPCS (n=72)	Non-PPCS (n=72)		PPCS (n=82)	Non-PPCS (n=500)	
Maternal									
Gestational weeks			0.019*			0.630			0.315
28–36	102(67.5)	312(54.8)		53(74.6)	48(67.6)		49(61.3)	264(53.0)	
37–39	46(30.5)	240(42.2)		16(22.5)	21(29.6)		30(37.5)	219(44.0)	
> 40	3(2.0)	17(3.0)		2(2.8)	2(2.8)		1(1.3)	15(3.0)	
Mode of delivery			0.050*			-			0.125
Vaginal	0	14(2.4)		0	0		0	14(2.8)	
Cesarean section	154(100.0)	558(97.6)		79(100.0)	72(100.0)		87(100.0)	486(97.2)	
Intraoperative blood loss> 1000 mL	120(77.9)	91(16.0)	<0.001*	65(90.3)	29(40.8)	<0.001*	55(67.1)	62(12.5)	<0.001*
Intraoperative blood loss> 3000 mL	46(29.9)	17(3.0)	<0.001*	38(52.8)	12(16.9)	<0.001*	8(9.8)	5(1.0)	<0.001*
Bleeding within 2 hours after delivery, mL	34.7±89.7	28.5±58.8	0.353	44.4 ±113.1	19.9±44.6	0.109	25.6±59.7	29.8±60.5	0.607
Bleeding within 2–24 hours after delivery, mL	168.2 ±370.1	49.9±58.4	<0.001*	220.1 ±436.4	65.5±114.2	0.007*	118.9 ±289.9	47.7±45.1	<0.001*
Postpartum hemorrhage	75(48.7)	90(15.7)	<0.001*	19(26.4)	14(19.4)	0.322	56(68.3)	76(15.2)	<0.001*
Transfusion	53(34.6)	92(16.1)	<0.001*	28(39.4)	24(33.3)	0.448	25(30.5)	68(13.6)	<0.001*
Hemorrhagic shock	12(7.8)	11(1.9)	<0.001*	10(13.9)	4(5.6)	0.091	2(2.4)	7(1.4)	0.480
Postpartum anemia	39(23.5)	172(30.1)	0.250	19(26.4)	30(41.7)	0.053	20(24.4)	142(28.4)	0.453
Hysterectomy	4(2.6)	3(0.5)	0.019*	4(5.6)	2(2.8)	0.404	0	1(0.2)	0.685
Neonatal									
Infant weight, g			0.916			0.616			0.826
<1500	6(3.9)	23(4.1)		2(2.8)	1(1.4)		4(4.9)	22(4.4)	
1500–2500	35(22.9)	145(25.6)		17(21.8)	21(29.6)		18(22.0)	124(25.0)	
2500–4000	111(72.5)	396(69.8)		51(71.8)	49(69.0)		60(73.2)	347(70.0)	
>4000	1(0.7)	3(0.5)		1(1.3)	0		0	3(0.6)	
Intrauterine death	0(0)	4(0.7)	0.298	0(0)	0(0)	-	0	4(0.8)	0.416
Fetal distress	55(35.7)	69(12.1)	<0.001*	26(36.1)	13(18.1)	0.015*	29(35.4)	56(11.2)	<0.001*
Umbilical cord blood pH	7.17±0.78	7.25±0.45	0.212	7.24±0.12	7.26±0.10	0.442	7.12±1.00	7.25±0.48	0.157
APGAR <7at 1 min	23(15.2)	40(7.1)	0.002*	17(24.6)	9(12.9)	0.075	6(7.3)	31(6.3)	0.715
APGAR <7at 5 min	4(2.6)	16(2.8)	0.877	1(1.4)	1(1.4)	0.992	3(3.7)	15(3.0)	0.769

Notes: Data are mean±SD (independent t-test) or n (%) (x^2 test) or Fisher's Exact Test.; *P < 0.05. Percentages do not total 100% owing to missing data.
Abbreviations: n, number of observations; SD, standard deviation; PASD, placenta accreta spectrum disorder; PPCS, placenta previa with coverage of a uterine scar.

In pregnancies complicated with PASD and different placenta position (Anterior, Posterior and Ante-posterior or laterally positioned, n=144, Table S1), the PPCS group was associated with higher intraoperative blood loss > 1000 mL (94.4% vs 57.1%, P=0.001), intraoperative blood loss > 3000 mL (55.6% vs 28.6%, P=0.048) than

the Non-PPCS group in anterior placenta; the PPCS group was associated with higher intraoperative blood loss > 1000 mL (77.8% vs 23.1%, P=0.003), intraoperative blood loss > 3000 mL (44.4% vs 3.8%, P=0.003), bleeding within 2–24 hours after delivery (199.0±161.4 vs 58.41 ±72.04%, P=0.005) than the Non-PPCS group in posterior
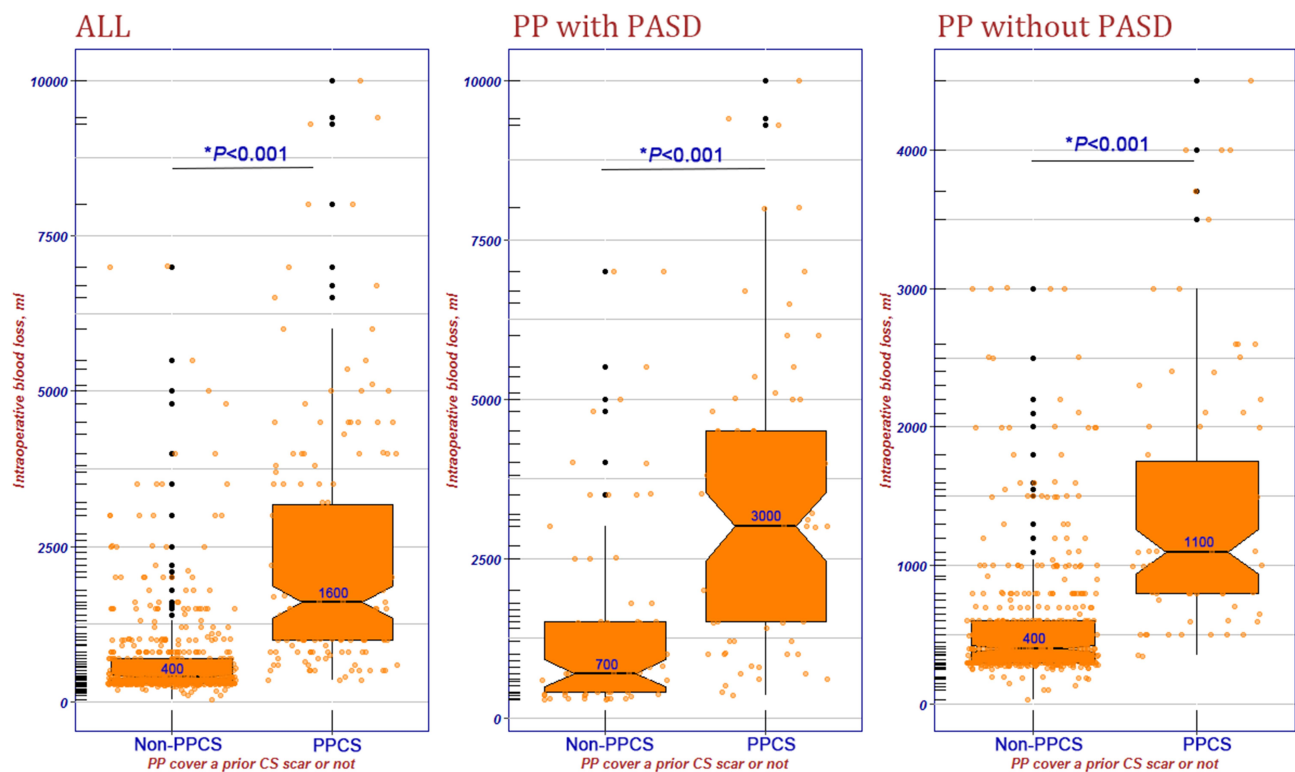
Figure 2 Box plots of intraoperative blood loss in the PPCS and Non-PPCS groups of women with and without PASD. *Using *t*-test for differences between Non-PPCS group and PPCS group.

placenta; the PPCS group was associated with higher intraoperative blood loss > 1000 mL (88.9% vs 45.8%, *P*=0.001), intraoperative blood loss > 3000 mL (51.9% vs 20.8%, *P*=0.022) and APGAR <7 at 1 min (29.6% vs 0, *P*=0.004) than the Non-PPCS group in Ante-posterior or laterally positioned placenta.

In pregnancies not complicated with PASD and different placenta position (Anterior, Posterior and Ante-posterior or laterally positioned, n=582, Table S2), the PPCS group was associated with higher intraoperative blood loss > 1000 mL (66.7% vs 25.5%, *P*=0.001), intraoperative blood loss > 3000 mL (13.9% vs 3.9%, *P*=0.037), bleeding within 2–24 hours after delivery (69.5±82.6 vs 44.0±33.7, *P*=0.018) and postpartum hemorrhage (75.0% vs 29.1%, *P*<0.001) than the Non-PPCS group in anterior placenta; the PPCS group was associated with higher intraoperative blood loss > 1000 mL (71.4% vs 8.2%, *P*<0.001), bleeding within 2–24 hours after delivery (121.3±165.6 vs 49.4±51.6, *P*<0.001), postpartum hemorrhage (66.7% vs 9.5%, *P*<0.001), transfusion (23.8% vs 8.5%, *P*=0.021) than the Non-PPCS group in posterior placenta; the PPCS group was associated with higher intraoperative blood loss > 1000 mL (64.0% vs 12.0%, *P*<0.001),

bleeding within 2–24 hours after delivery (196.6±510.5 vs 45.5±32.2, *P*=0.005) and postpartum hemorrhage (60.0% vs 17.8%, *P*<0.001) than the Non-PPCS group in Ante-posterior or laterally positioned placenta.

Discussion
Principal Findings of This Study

Prior studies have shown that PP was significantly associated with a range of adverse outcomes for both mothers and neonates; however, comparisons of PP with and without coverage of a uterine scar were rarely reported. Thus, the aim of our study was to investigate the maternal and neonatal outcomes of PPCS and Non-PPCS in a Chinese cohort. This large retrospective cohort study of 726 women with PP between January 2012 and March 2017 found that the PPCS group had poorer maternal and neonatal outcomes for intraoperative blood loss, postpartum hemorrhage, and higher hospitalization expenses than the Non-PPCS group, even after being grouped according to whether they were complicated with PASD and placenta position.

A survey of maternal and child health in Asia by the WHO showed that the rate of cesarean section in China was 46.2% in

2010, which is the three times (15%) of the WHO's recommended upper limit.[23] Another study[24] recently found that the cesarean section rate rose from 28.8% in 2008 to 34.9% in 2014. However, this proportion varies widely in the 31 provinces of China from 4% to 62.5% in 2014. The high cesarean delivery rate is associated with an increased risk of placenta previa in subsequent pregnancies since the risk of PP rises as the number of prior cesarean sections increases. Besides, China's family planning policy has been in place for more than three decades, and most couples have been restricted to only one child since 1980. Therefore, many pregnant women have had a primary cesarean section due to the popularity of caesarean sections and increased safety as well as social factors on account of only one child being allowed. Rising primary cesarean delivery rates strongly affect maternal mortality rates due to the increase of placenta previa and accreta after multiple cesareans. Placental accreta is a serious obstetrical complication and its management is challenging, with more difficult surgical operations and higher hysterectomy rates.[25,26] With the rapid growth of the aging population, China relaxed its more than three-decade-old family planning policy and allowed a couple to have two children (Universal two-child policy) in 2016. Hence, it is conceivable that there will be more multipara with a scarred uterus and PPCS in the future in China, which will pose a huge challenge to health care providers.

PP diagnosed in early pregnancy may not persist in late pregnancy and near term. PP is suspected and diagnosed in approximately 5% of pregnancies between 15 and 16 weeks,[27] and almost 90% of PP resolves to a normal position by term,[28] which may be explained by the elongating of the uterus and the gradually rising position of the placenta away from the cervix with increasing gestational age. However, such a mechanism will be interfered with if the placenta is covered in uterine scarring from a prior CS such that the placenta cannot move normally. The effects of a previous cesarean section were obvious, and the placenta was unlikely to "migration" in the presence of a hysterectomy scar. Moreover, our data showed that nearly half (46.8%) of PPCS pregnancies combined with PASD, suggesting that we should do detailed prenatal examination, including ultrasound and MRI when we find this condition in clinical practice, to determine the likelihood of placenta implantation, location and depth of placenta accreta.

The correlation between gestational age and different types of placenta previa remains controversial. Some studies reported no differences in gestational age at delivery of infants born to mothers with different types of placenta previa.[17,29] However, more studies agreed that premature delivery was more frequent in women with complete placenta previa,[18,30] but the comparison of preterm birth rates between infants with mothers with PPCS and Non-PPCS is rarely reported. We found that there is no statistic significant difference between PPCS and Non-PPCS in mean gestational weeks, but the PPCS have the higher proportion of gestational weeks <37 the Non-PPCS (67.5% vs 54.8%).

Some studies have addressed whether types of placenta previa are associated with the severity of symptoms in mothers and neonates, but data aimed at understanding PPCS were insufficient. Our results show that women with PPCS had a higher rate of intraoperative blood loss, postpartum hemorrhage, transfusion, and hysterectomy and that the infants born to women with PPCS had lower Apgar scores at 1 min. Specifically, women in the PPCS group are at an approximately 3-fold (48.7% vs 15.7%) increased risk of postpartum hemorrhage, and 5-fold (2.6% vs 0.5%) increased risk of hysterectomy than women in the Non-PPCS group. Additionally, the presence of accreta is often the factor that determines a change in clinical management and outcome. We divided the subjects into an PASD group and non-PASD group and found that obstetric hysterectomy was performed in 5.6% and 0 of the women with PPCS and Non-PPCS, respectively, in the PASD group, while it was performed in 0% and 0.2% of the women with PPCS and Non-PPCS, respectively in the non-PASD group. Prior studies simply compared the hysterectomy rates between the two PASD groups but did not perform subgroup analysis based on the type of placenta implantation. Nevertheless, our results showed that the proportion of women with hysterectomy was lower than that reported in most other studies. Ling Li[12] reported that the hysterectomy rate was 8.47% in women with PPCS and 0% in women with Non-PPCS. Another study[13] in China reported hysterectomy rates were 11.9% (12/101) and 0.8% (3/369) in women with PPCS and Non-PPCS, respectively. However, there is also a report of a very low hysterectomy rate from Israel, which stated that only 1.2% of mothers with PP underwent a -hysterectomy.[31] One possible and important reason for the low hysterectomy rate in our study is that obstetricians in our hospital use a random placenta margin incision[32] (also calledan Ar's incision), and we have found it may be a potentially valuable surgical procedure to control intraoperative and postoperative bleeding in pregnancies with complete placenta previa. We believe that retaining the uterus is of great significance to young women who desire

to preserve fertility, so it is acceptable to have an increased risk of postpartum hemorrhage and transfusion in women with PPCS if we can preserve the uterus.

There was no significant difference in IVF-ET between the PPCS and Non-PPCS groups in our study because IVF-ET is a potential confounding factor, both HDCP and diabetes or GMD of clinical outcomes. Studies have shown that women who conceived with assisted reproductive technology (ART) procedures had an increased incidence of placenta previa regardless of the type of ART procedure.[33,34] The mechanism for the development of the relationship between IVF-ET and PP is uncertain. One explanation is that ART procedures, maternal factors associated with sterility or a combination of both may increase the risk of PP in ART pregnancies. Varying theories have been developed around the effects of hormones on the endometrium, the effects of embryo transfer and the effects of changes in uterine contraction wave patterns.[35]

Strengths and Limitations of the Study

This is one of the largest studies investigating risk factors and clinical outcomes for PPCS and Non-PPCS placenta previa from a single medical center. The largest strength of this study is that the large sample size allowed us to study the association of PPCS and Non-PPCS and maternal and neonatal outcomes. However, there are several potential limitations to this study. First, despite this hospital being the largest maternity and child health care hospital in Foshan, selection bias is likely because this is a single-center study and this is a retrospective review that relied on medical documentation and a database. Second, although we used ultrasound or MRI to distinguish between the front and back walls of the placenta, the division is not very precise since we did not measure the area of the anterior or posterior placenta walls. Larger studies are needed to determine the safety and efficacy of interventional radiology before this technique can be recommended for routine management of placenta implantation.[36] Therefore, this study does not use the following procedures: intraoperative internal iliac artery and/or postoperative uterine artery embolization and internal iliac artery or abdominal balloon occlusion. It would be prudent to compare hospitals at different levels or in different regions due to the presence of different surgical instruments, surgical procedures, hemostasis procedures, surgical physician levels, and anesthetics. Finally, we only reported whether pregnant women had a previous cesarean section, and did not reported

the specific number of previous cesarean sections, which may have lost some of information. All of these potential limitations should be considered when interpreting the results of this study.

Conclusion

In conclusion, we investigated risk factors and maternal and neonatal outcomes in women with PPCS and Non-PPCS in a Chinese cohort. As the rate of CS increases with China's universal two children policy, the rate of PP, especially PPCS, will most likely increase as well. Women with PPCS were more likely to have some poorer maternal and neonatal outcomes than the Non-PPCS group even after grouping by whether pregnancies complicated with PASD or with different placental positions. Health care providers should be aware of possible complications of PPCS to provide proper counseling to their patients.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

JR designed and implemented the study, conducted data analysis and write the manuscript; FD, ZZ, LX, MH, WY, SX, LD and ZH designed the statistical analysis and help with data analysis; FD helped with analysis plan and result interpretation; LY and LZ designed the study and developed the manuscript. All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Disclosure

The authors have no conflicts of interest relevant to this article.

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