

Appendix 1

All surgical procedures, including suction curettage, hysteroscopy, laparoscopy and laparotomy were performed by well-trained gynecologic surgeons. Except for laparotomy, surgery was performed under general anaesthesia with the woman in dorsolithotomy position, and 6 units of pituitrin diluted in 20 mL saline were injected into 3 and 9 points of the cervix before dilatation.

1.1 The routine surgical procedures of suction curettage in treatment of cesarean scar ectopic pregnancy

Suction curettage was the basic surgical step before subsequent hysteroscopic resection or laparoscopic excision. For suction curettage $\pm$ hysteroscopy group, suction curettage was performed under ultrasound guidance, and for hysteroscopy + laparoscopic monitoring/excision group, suction curettage was performed under laparoscopic monitoring. Suction curettage was performed with a negative pressure of 400–450 mmHg gently. It was wisely to aspirate decidua in the uterine cavity at first, then gestational tissue at the caesarean scar was aspirated avoiding the excess pressure against the anterior wall. After suction, it was necessary to check the villi and embryonic tissue in the container.

1.2 The routine surgical procedures of hysteroscopic treatment of cesarean scar ectopic pregnancy

Operative hysteroscopy was performed after curettage not only to evaluate whether products of conception at the uterine scar site have been removed completely, but also to remove residual products by hysteroscopic electrotomy if necessary. Uterine distension was achieved using 5% mannitol solution with a pressure < 100 mmHg. The intervention began by an overview of the uterine cavity. The endometrial cavity was empty and a cesarean scar diverticulum/defect (CSD) could be seen at the scar of the anterior wall of the uterus. Sweeping the decidua basalis from the uterine wall with the loop resectoscope gently is more than enough without causing hemorrhage. Hysteroscopic electrotomy in an 80W monopole current would play a role if dense adhesion or implantation of conception products exists, but the depth should be very shallow to avoid uterine perforation. If necessary, blood vessels were coagulated in a 100W coagulation current. It is noteworthy that lower abdomen compression at upper symphysis pubis by the assistant is usually helpful to expose the deep top of the CSD to make sure no residue of conception products,

1.3 The routine surgical procedures of laparoscopic treatment of cesarean scar ectopic pregnancy

Laparoscopy should be established before suction curettage and hysteroscopic procedure for better surveillance, in order to prevent inadvertent myometrial perforation and monitor

conditions of the myometrial layer between the gestational sac and bladder. Then, suction

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curettage removal of CSEP in a short time can induce uterine contractions to help reduce blood loss during subsequent hysteroscopic removal of the conception products completely. Moreover, if the conception products could not be removed completely by hysteroscopy, or the anterior myometrial layer is absent or thin-appearing with outward bulge or retraction, or massive hemorrhage occurred, laparoscopic excision of the conception products and repair of CSD was recommended.

In the laparoscopy repair group, the routine surgical procedures were as follows: (1) the peritoneum was opened between the bladder and the uterus, and the bladder was pushed down carefully; (2) the scar was exposed, and a visible convex mass was observed, or the muscle layer of the scar was thin or perforated; (3) curettage was performed under laparoscopic guidance to remove the remaining conceptus tissue; (4) the scar on the uterus was incised and trimmed; (5) the myometrial incision was sutured with continuously for the first layer with a synthetic, absorbable suture; (6) horizontal transverse mattress suture was used for the second layer; and (7) the peritoneum between the bladder and the uterus was sutured continuously for the third layer.

1.4 The routine surgical procedures of transvaginal excision of cesarean scar ectopic pregnancy

Transvaginal hysterotomy was an alternative novel surgical approach for management of CSEP type IIb and IIIa. The routine surgical procedures were as follows: (1) after a pair of vaginal retractors was placed into the vagina, the cervix was grasped and manipulated with an

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Allis clamp. Adrenaline solution (1.5µg/mL;10–20mL) was injected submucosally for hydrodissection and hemostasis before an incision was made at the anterior cervicovaginal junction; (2)the bladder was dissected away until the anterior peritoneal reflection was identified; (3)the CSP mass was identified as a bluish bulge located in the anterior wall of the lower uterine segment; (4) a transverse incision was made on the lower margin of the most prominent area of the bulge; (5) ectopic pregnancy tissue was removed with sponge forceps or suction through the incision on the uterus isthmus, Thorough curettage was done through the incision or cervical canal; (6) the edges of the incision were trimmed with scissors to remove all of the scar tissue; (7) the myometrial incision were closed with continuous locking sutures with 2-0 absorbable sutures for the first layer, and horizontal transverse mattress suture was used for the second layer;(8)the vaginal incisions were closed with continuous locking sutures.

1.5 The routine surgical procedures of laparotomic treatment of cesarean scar ectopic pregnancy

Surgery was performed under general anaesthesia with the woman in horizontal-supine position. The routine surgical procedures were as follows: (1) to prevent life-threatening bleeding, 6 units of pituitrin diluted in 20 mL saline were injected into lower uterine segment first;(2)then the bladder was pushed aside carefully; (3) for temporary occlusion of the bilateral uterine arteries as vascular pretreatment, a rubber tourniquet was passed through the avascular zone on both sides of the broad ligament and temporarily tied around the uterine isthmus; (4)a transverse incision was made on the lower margin of the most prominent area of the bulge; (5)

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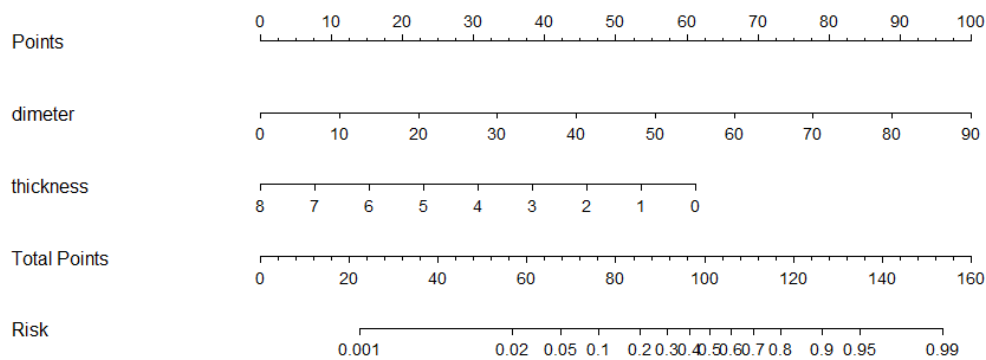
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pregnancy tissue was removed with sponge forceps or suction through the incision on the uterus isthmus; (6) the edges of the incision were trimmed with scissors to remove all of the scar tissue; (7) the myometrial incision were closed with continuous sutures with 2-0 absorbable sutures for the first layer, and horizontal transverse mattress suture was used for the second layer;(8)after the uterine incision was sutured, the vascular band was released, and the uterine arteries were recanalized; (9)the peritoneum between the bladder and the uterus was sutured continuously for the third layer. For permanent arterial inclusion, the bilateral uterine or internal iliac arteries were exposed and then double ligated with 1-0 nonabsorbable sutures.

Appendix 2. The nomogram model for predicting hemorrhage during a cesarean scar pregnancy surgical procedure. The nomogram can be applied by the following procedures: (1) obtain the points corresponding to each predictor; (2) the sum of the points is recorded as the total score; and (3) the predicted risk corresponding to the total score is the probability of intraoperative blood loss ≥ 300 mL during the cesarean scar pregnancy surgical procedure.

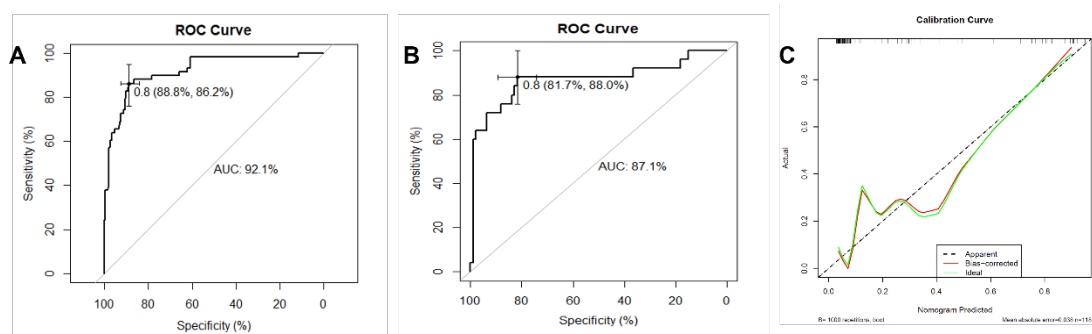


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Appendix 3. Receiver operating curves and calibration plots. Modeling group, area under the curve (AUC) of the risk assessment model is 0.92 (95% CI: 0.879–0.963) (A); validation group, AUC of the risk assessment model is 0.87 (95% CI 0.77–0.97) (B); calibration plots of the nomogram model in the validation group for predicting hemorrhage during cesarean scar pregnancy operation (C). Calibration curves were applied to evaluate the calibration of the models. The *horizontal axis* is the predicted probability provided by the model, and the *vertical axis* is the observed incidence of intraoperative blood loss ≥ 300 ml. The *45° line* is the actual probability. When the prediction probability of model is closer to the 45° line, the prediction model has better calibration power.



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Appendix 4. Values of Anterior Myometrium Thickness and Average Diameter of the Gestational Sac or Mass Based on Different Anterior Myometrium Thickness Level in Predicting Hemorrhage During Cesarean Scar Ectopic Pregnancy Surgical Resection

Variables	AUC (95%CI)	Sensitivity (95%CI, %)	Specificity (95%CI, %)	LR+ (95%CI)	LR- (95%CI)	Cut off Value (95%CI, mm)
Anterior myometrium thickness (mm)	0.84(0.79-0.90)	75.9(62.8-86.1)	88.4(83.3-92.3)	6.5(4.4-9.7)	0.3(0.2-0.4)	1.3(1.2-1.5)
Anterior myometrium thickness >1mm	0.77 (0.66-0.89)	76.2(52.8-91.9)	66.0(58.8-72.7)	2.2(1.6-3.1)	0.4(0.2-0.8)	2.8(2.0-3.0)
Average diameter of gestational sac/mass (mm) when thickness 1-3mm	0.80(0.69-0.91)	68.4(43.4-87.4)	79.4(70.0-86.9)	3.3(2.0-5.4)	0.4(0.2-0.8)	33.8 (22.5-50.5)
Average diameter of the gestational sac/mass (mm) when thickness ≤1mm	0.88(0.80-0.97)	75.7(58.8-88.2)	87.5(67.6-97.3)	6.1(2.1-17.7)	0.3(0.2-0.5)	50.3 (49.5-60.5)

CI: confidence interval; LR+, positive likelihood ratio; LR-, negative likelihood ratio;

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Appendix 5. Baseline Characteristics of Patients With Cesarean Scar Ectopic Pregnancy in the New Classification Group

Group	I	II		III		P	Total
	(n=168)	IIa(n=170)	IIb(n=53)	IIIa(n=119)	IIIb(n=54)		
Age (years)	34(29.3,37)	33(29,36)	35(31,38)	33(30,37)	33(30.8,36)	0.467	33(30,37)
Gravidity (number)	4(3,4)	4(3,4)	4(3,5)	4(3,5)	3(2,4)	0.253	4(3,5)
Para (number)	1(1,2)	2(1,2)	1(1,2)	2(1,2)	1 (1,2)	0.668	2(1,2)
Previous CS (number)	1(1,2)	2(1,2)	1(1,2)	1(1,2)	1(1,2)	0.140	1(1,2)
Time interval since last CS (years)	5(3,7)	4(2,7)	6(4,8) ^a	5(2.6,7.0)	4(2,6) ^b	0.011	4(2.8,7)
Gestational age (days)	51(4560.8)	48(43,54)	60(51,75.5)	56(49,66)	72(60,84.5)	<0.001^c	53(46,64)
Di (mm)	17.8(11.4,25.0)	17.0(13.0,21.5)	34.7(31.8,42.7)	32.0(25.0,39.0)	55.5(50.8,63.6)	<0.001^d	23.5(15.7,34.0)
Th (mm)	4.5(3.8,5.0)	2.4(2.0,2.8)	2.0(1.7,2.2)	0.5(0.5,0.5)	0.5(0.5,0.5)	<0.001^e	2.1(0.5,3.5)
Serum β-HCG levels (mIU/ml)	18856.0 (4066.0,47583.0)	29463.0 (12567.0,52368.0)	53320.0 (2170.0,121383.5)	51583.0 (3651.0,107209.0) ^f	13420.0 (1929.3,66498.0)	0.004	28240.5(6250.3,62628.5)
Duration of vaginal bleeding (d)	2(0,9)	2(0,8)	5(0,15)	7(0,20)	14(2.8,38.8)	<0.001^g	3(0,13)
Gestational sac/mass with Ultrasound							
Gestational Sac	154(91.7)	160(94.1)	42(79.2)	82(68.9)	22(40.7)	<0.001^h	460(81.6)
Gestational Mass	14(8.3)	10(5.9)	11(20.8)	37(31.1)	32(59.3)		104(18.4)
Fetal cardiac activity							
negative	109(64.9)	81(47.6)	24(45.3)	65(54.6)	40(74.1)	0.001ⁱ	319(56.6)
positive	59(35.1)	89(52.4)	29(54.7)	54(45.4)	14(25.9)		245(43.4)
Uterine arteriovenous fistula							
negative	162(96.4)	164(96.5)	50(94.3)	116(97.5)	33(61.1)	<0.001^j	525(93.1)
positive	6(3.6)	6(3.5)	3(5.7)	3(2.5)	21(38.9)		39(6.9)
Previous treatment							
failure							
negative	145(86.3)	144(84.7)	39(73.6)	85(71.4)	23(42.6)	<0.001^k	436(77.3)
positive	23(13.7)	26(15.3)	14(26.4)	34(28.6)	31(57.4)		128(22.7)

Di, average diameter of gestational sac/mass;Th, anterior myometrium thickness.

a, $P<0.05$ vs. the IIa group.

b, $P<0.05$ vs. the IIb group.

c, $P<0.05$ between any two groups except the IIIa vs IIb group and IIIb vs IIb group.

d, $P<0.05$ between any two groups except the IIa vs I group, IIIa vs IIb group and IIIb vs IIb group.

e, $P<0.05$ between any two groups except the IIb vs IIa group and IIIb vs IIIa group.

f, $P<0.05$ vs. the I group.

g, $P<0.05$ between any two groups except the IIa vs I group ,IIb vs I group, IIb vs IIa group, IIIa vs IIb group, IIIb vs IIIa group.h, $P<0.005$ between any two groups except the IIa vs I group ,IIb vs I group, IIIa vs IIb group.

i, $P<0.005$ between the IIa vs I group, IIIb vs IIa group and IIIb vs IIb group.

j, $P<0.005$ between the IIIb vs I group, IIIb vs IIa group, IIIb vs IIb group, and IIIb vs IIIa group.

k, $P<0.005$ between the IIIa vs I group, IIIa vs IIa group, IIIb vs I group, and IIIb vs IIa group, and IIIb vs IIb group.

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Appendix 6. Detailed Information About the Cases With Changed Surgical Planning Before or During the Procedure

Case No.	Age	GA (days)	Th (mm)	Di (mm)	Type	First-line surgical strategy recommended	Surgical planning changed	Reasons for changing surgical planning	Operation duration (min)	Blood loss (ml)	β-HCG return to normal (4 weeks)
1	30	42	3.5	18.7	I	Suction curettage + Hysteroscopy under ultrasound guidance	Switching to Suction curettage + Hysteroscopy under Laparoscopic monitoring during operation	founding the anterior uterine wall bulged outward under ultrasound surveillance during operation	45	20	Yes
2	30	64	4	63	I	Suction curettage + Hysteroscopy under ultrasound guidance	Switching to Suction curettage + Hysteroscopy under Laparoscopic monitoring before operation	Needing to guide the excision of uterine septum at the same time	200	500	Yes
3	29	49	2.8	11	Ila	Suction curettage + Hysteroscopy under ultrasound guidance	Switching to Suction curettage + Hysteroscopy + Laparoscopic excision during operation	Founding the anterior uterine wall bulged outward under ultrasound surveillance During operation	65	100	Yes
4	33	76	1.2	25	Ila	Suction curettage + Hysteroscopy under ultrasound guidance	Switching to Suction curettage + Hysteroscopy +Laparoscopic excision during operation	Founding the anterior uterine wall bulged outward under ultrasound surveillance during operation	80	200	Yes
5	36	50	0.5	40.5	IIla	Laparoscopic excision	Switching to Emergency laparotomic excision Before operation	Before operation on admission, presenting massive bleeding	90	1000	Yes
6	38	44	0.5	26	IIla	Laparoscopic excision	Switching to Emergency laparotomic excision Before operation	Before operation on admission, presenting massive bleeding	110	1000	Yes
7	42	57	0.5	47	IIla	Laparoscopic excision	Switching to Emergency laparotomic excision Before operation	Before operation on admission, presenting massive bleeding, with a history of previous treatment failure at the local maternity care facilities	165	100	Yes
8	44	68	0.5	48.7	IIla	Laparoscopic excision	Switching to Emergency laparotomic excision Before operation	Before operation on admission, presenting massive bleeding, with a history of previous treatment failure at the local maternity care facilities	115	100	Yes
9	31	95	0.5	71.2	IIlb	Laparoscopic excision after UAE or Laparotomic excision	Switching from Laparoscopic excision to Laparotomic excision during operation	Massive hemorrhage occurred during operation	180	400	Yes
10	27	116	0.5	74	IIlb	Laparoscopic excision after UAE or Laparotomic excision	Switching from Laparoscopic excision to Laparotomic excision during operation	Massive hemorrhage occurred during operation, with a history of previous treatment failure at the local maternity care facilities	140	1200	Yes
11	32	72	0.5	72	IIlb	Laparoscopic excision after UAE or Laparotomic excision	Switching from Laparoscopic excision to Laparotomic excision during operation	Massive hemorrhage occurred during operation	145	3000	Yes
12	32	94	0.5	62.7	IIlb	Laparoscopic excision after UAE or Laparotomic excision	Switching from Laparoscopic excision to Laparotomic excision during operation	Massive hemorrhage occurred during operation, with a history of previous treatment failure at the local maternity care facilities	140	800	Yes

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