CLINICAL RESEARCH

e-ISSN 1643-3750 © Med Sci Monit, 2018; 24: 4659-4666 DOI: 10.12659/MSM.907404

Published: 2018.07.06		Embolization (UAE) vers Cesarean Scar Pregnand (LCSPDS) in Treatment of Pregnancy	sus Laparoscopic cy Debridement Surgery of Cesarean Scar
Authors' Contribution: Study Design A Data Collection B Statistical Analysis C Data Interpretation D Manuscript Preparation E Literature Search F Funds Collection G	BD 1 AC 2 EF 1 EF 1	Junhong Guo Jiangtao Yu Qing Zhang Xiaojie Song	 Department of Obstetrics and Gynecology, Wuhan Children's Hospital (Wuhar Maternal and Child Healthcare Hospital), Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, P.R. China Department of Obstetrics and Gynecology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, Zhejiang, P.R. China
Correspondin Source of	g Author: f support:	Xiaojie Song, e-mail: songxiaojie333@163.com Departmental sources	
Back Material/N	rground: Aethods:	The present study aimed to compare the clinical eff laparoscopic cesarean scar pregnancy debridement se ean scar pregnancy (CSP). A retrospective analysis was performed on 87 CSP pa ed 87 cases, 51 were treated with UAE and 36 were se erative blood loss, operation time, length of hospital compared.	ficacy and safety of uterine artery embolization (UAE) vs. surgery (LCSPDS) in the treatment of patients with cesar- atients from March 2012 to February 2017. For the includ- treated with LCSPDS. The operation success rate, intraop- l stay, perioperative complications, and β -HCG level were
Conc	Results: clusions:	For the UAE group, 41 patients underwent successful a group were successfully treated, with no case of peri traoperative blood loss, and length of hospital stay w days, respectively. In the LCSPDS group, the operation stay were 85.45±30.02 min, 108.56±54.12 mL and 7. the UAE group was significantly longer than in the LC UAE and LCSPDS each have their own advantages a vidualized surgical programs based on specific patier forming complete utarine cavity curattage	surgeries (80.4% success rate), and 36 cases in the LCSPDS ioperative death. In the UAE group, the operation time, in- were 82.23 ± 45.21 min, 112.58 ± 68.54 mL, and 12.56 ± 3.03 on time, intraoperative blood loss, and length of hospital .65 \pm 2.48 days, respectively. The length of hospital stay for CSPDS group (P<0.05). nd disadvantages in treating CSP. Thus, appropriate indi- nt circumstances are needed to avoid indiscriminately per-
MeSH Ke	ywords:	Cesarean Section • Pregnancy Complications, Car	diovascular • Uterine Artery Embolization
Full-t	ext PDF:	https://www.medscimonit.com/abstract/index/idAr	t/907404
			1 Z7

Clinical Efficacy and Safety of Uterine Artery



MEDICAL SCIENCE

MONITOR

Received: 2017.10.04 Accepted: 2018.02.01

Background

Cesarean scar pregnancy (CSP) is a special type of ectopic pregnancy where the embryo implants in a cesarean section scar on the lower anterior uterine wall [1,2]. The continuous increase in the cesarean deliveries rate has led to increased CSP incidence. The trophoblastic cells of a CSP-induced fertilized egg implant on a uterine scar, which contains an increased amount of fibrous tissue and is a weak point on the muscle wall, and the risk of uterine rupture, bleeding, or other adverse events increases significantly. At present, there is still no unified and standardized treatment guideline for CSP due to the lack of high-quality, randomized clinical trials and the low incidence rate. However, there is a consensus that the pregnancy should be terminated as soon as it is confirmed. Generally, the treatment procedure selection was made according to general condition of the patient, such as whether she had developed massive hemorrhage, the hCG level, the size and location of the embryo, and the depth of the embryo invasion according to ultrasound examination. Generally, laparoscopic surgery can be considered for those who have a lesion convex to the abdominal cavity. However, for patients with a large embryo that has a rich blood supply, a high hCG level (>100 000 IU/L) is recommended when first receiving UAE to block the blood supply, and then combined laparoscopy or laparoscopy vaginal surgical treatment is performed.

Patients with CSP are generally young and are expected to have high uterine integrity with a high chance of re-pregnancy [3]. Thus, bilateral uterine arterial infusion embolization is currently used to treat CSP [4–6]. Nawroth et al. [7] successfully applied uterine arterial embolization (UAE) combined with conservative medical treatment to manage CSP, and they reported that only UAE can effectively be substituted for hysterectomy to prevent pelvic hemorrhage. In the present study, we retrospectively analyzed 51 CSP patients treated with UAE in our hospital in recent years and compared them with CSP patients treated with LCSPDS. We also explored the advantages and disadvantages of these 2 procedures.

Material and methods

Patients

Retrospective analysis was performed on 87 CSP patients admitted in Wuhan Children's Hospital (Wuhan Maternal and Child Healthcare Hospital) from March 2012 to February 2017. Among these cases, 51 were treated with UAE and 36 were treated with LCSPDS. The inclusion criteria were: (1) all patients were clinically diagnosed with CSP and confirmed by color Doppler ultrasound or magnetic resonance imaging (MRI), (2) clinical data were complete, and (3) the patients were treated with UAE or LCSPDS. The exclusion criteria were: (1) CSP diagnosis was unclear, (2) other treatment methods were used, and (3) the clinical and follow-up data were incomplete. The indication criteria for patients who received UAE were: (1) patients had CSP II or III disease; (2) patients had high risk of developing intraoperative hemorrhage as determined by comprehensive assessment by the medical team.

Generally, the treatment strategy was selected according to the severity of the disease, such as myometrial thickness. In the UAE group, most patients had CSP III or CSP II disease and no patients had CSP I disease. However, more than half of the patients had CSP I disease in the LCSPDS group (Table 1).

Diagnosis of CSP

The following points are the diagnostic criteria for uterine CSP: (1) amenorrhea or vaginal bleeding, (2) hematuria with positive β -human chorionic gonadotropin (HCG), and (3) ultrasound findings confirming the diagnosis. These ultrasound findings include the lack of gestational tissue in the uterine cavity and cervical canals, the presence of gestational sac or mixed mass at the anterior wall of the uterine isthmus at the lower uterine incision scar, decreased amount of normal uterine muscle tissue between the uterus and the bladder, and thinned uterine muscle between the gestational sac and bladder [for cervical isthmus pregnancy]) (Figure 1). For equivocal ultrasound results, MRI can be used to determine the location of embryonic implantation and assess the depth of intrusive growth from the gestational sac to the muscular layer (Figure 2).

UAE surgery process

The surgery was performed using a Philips V5000 digital subtraction angiography machine with routine disinfectant towels and local anesthesia. Through the Seldinger technique, the right femoral artery was percutaneously punctured, a 5F arterial catheter sheath was placed, and a 5F Robert catheter guided by a super smooth guide wire was employed for bilateral uterine artery selective intubation [8,9]. Then, 15-20 ml of iohexol was injected into the iliac arteries. Radiography confirmed that the catheter was placed at the opening of the left uterine artery through the guide wire after the left iliac arteries and left uterine arteries were opened. Next, high-pressure uterine arteriography confirmed that the target vessel was the left uterine artery. Embolization was then performed with gelatin sponge particles. When embolization was finished, mild intravascular reflux ensued, and the catheter was pulled to the iliac internal iliac artery opening to apply high-pressure angiography. After no development was observed at the left side of the uterine artery trunk and branch, the climbing technique was used to treat the right internal iliac artery (Figure 3). A 15-min compression and a compression bandage were applied Table 1. The general characteristics of the 2 groups.

Characteristics	UAE (n=51)	LCSPDS (n=36)	χ²/t	Р
Age-y (mean ±SD)	32.21±5.68	31.56±5.02	0.55	0.58
Times of pregnancy [n, (%)]				
2	45 (88.3)	32 (88.9)		
>2	6 (11.7)	4 (11.1)		
Gestational weeks (mean ±SD)	7.81±1.32	7.66±1.30	0.53	0.60
Abortion history [n, (%)]				
Positive	12 (23.5)	10 (27.8)		
Negative	39 (76.5)	26 (72.2)		
WBC-10º/L (mean ±SD)	8.56±2.33	7.98±2.54	1.10	0.27
β-HCG-mIU/ml (mean ±SD)	3896.80±874.52	3905.45±778.57	0.05	0.96
Progesterone-ng/ml (mean ±SD)	18.22±3.21	17.89±3.33	0.47	0.64
E2-pg/ml (mean ±SD)	388.56±45.21	369.87±50.23	1.81	0.07
FSH-mIU/ml (mean ±SD	2.87±0.74	2.74±0.68	0.83	0.41
Abdominal and gynecological surgeries history [n, (%)]			0.08	0.77
Positive	2 (3.9)	1 (2.9)		
Negative	49 (96.1)	35 (97.1)		
Myometrial thickness [n, (%)]			55.51	0.00
CSP I	0 (0.0)	25 (69.4)		
CSP II	25 (49.0)	11 (30.6)		
CSP III	26 (51.0)	0 (0.0)		
Number of prior cesarean deliveries [n, (%)]			0.27	0.60
1	47 (92.2)	32 (88.9)		
≥2	4 (7.8)	4 (11.1)		
Crown-rump length (cm)	1.43±0.12	1.45±0.13	0.74	0.46

to the puncture point as postoperative routine and 6 h afterward at the right lower limb break. Eventually, the patients were able to perform out-of-bed activities 24 h after the operation. After the selective bilateral uterine arterial infusion embolization, the patients were closely observed for blood β -HCG level decline and gestational sac blood supply changes. Then, 3–7 days after surgery, complete curettage of the uterine cavity under B-ultrasound monitoring was performed.

LCSPDS surgery process

Each patient was induced by tracheal intubation anesthesia. Then, a 10-mm trocar was used for umbilical puncture, two 5-mm trocars for the left lower abdominal punctures, and a 5-mm trocar for the right lower quadrant puncture. Intracervical pressure of 12–14 mmHg was maintained, and the abdomen was explored. Blunt and sharp separation of the uterine lower segment and bladder adhesions was performed, and the uterine and bladder peritoneum was opened to the peritoneal fold. The bladder was pushed aside, and 6 U of pituitary hormone was injected into the lower uterine wall. The lower uterine scar was cut with a unipolar electric hook. The lesion was removed, and the scar was pruned. Finally, 0/1 absorbent lines were employed to suture the myometrium continuously [10].

Statistical analysis

The statistical analysis was made with SPSS17.0 software, the measurement data are expressed as $\overline{\chi}\pm$ s, and the comparison between groups was made based on the *t* test of the sample mean. The enumeration data are expressed with a relative number, and the comparison between groups was made based on the χ^2 test. P<0.05 was considered as a statistically significant difference.



Figure 1. Transvaginal sonography of uterine incision pregnancy (Transvaginal ultrasonography showed mixed masses in the lower segment of the anterior wall of the uterus, white arrow).

Success rates

Among the 51 cases in the UAE group, 41 underwent successful surgeries (80.4% success rate). The remaining 10 unsuccessful cases included 5 cases of open abdominal laparotomy hysterectomy, 3 cases of LCSPDS operation, and 2 cases of open abdominal uterine incision scar lesion removal. All 47 cases in the LCSPDS group were successful, with no case of perioperative death.

Comparison of operation time, intraoperative blood loss, and length of stay

The operation time, intraoperative blood loss, and length of stay were 82.23±45.21 min, 112.58±68.54, and 12.56±3.03 days, respectively in the UAE group. For the LCSPDS group, the operation time, intraoperative blood loss, and length of stay were 85.45±30.02 min, 108.56±54.12 mL, and 7.65±2.48 days, respectively. The length of stay for the UAE group was significantly

longer than those of the LCSPDS group (P<0.05). However, the operation time and intraoperative blood loss were not significantly different between the 2 groups (P>0.05) (Table 2).

Plasma β -HCG comparison

The 1-week postoperative plasma β -HCG level was 286.32±189.65 mlu/ml in the UAE group and 56.23±33.56 mlu/ml in the and LCSPDS group, and the difference was statistically significant (P<0.05) (Figure 4).

Complications

In the UAE group, 5 cases of postoperative fever, 2 cases of nausea, 1 case of vomiting, and 1 case of Scr/BUN increase were noted (17.6% overall complication rate). In the LCSPDS group, 4 cases of fever, 4 cases of nausea, 3 cases of vomiting, and 1 case of AST/ALT/GGT increase were observed (33.3%



Figure 2. Magnetic resonance imaging (MRI) of uterine incision pregnancy (Scar defect of anterior wall of uterus, white arrow; Intrauterine yolk sac, red arrow).

overall complication rate). However, the difference between the 2 groups was not statistically significant (P<0.05) (Table 3).

Discussion

CSP is considered a special type of ectopic pregnancy. Previously, China's births were dominated by natural childbirth and included low cesarean section rates and low CSP incidence. However, in the last 10 years, with the yearly increase in cesarean section rates and initiation of China's second child policy, CSP incidence has significantly increased [11].

CSP must be treated immediately after diagnosis. The pregnancy must also be terminated at once because of the increasing risk of fatal bleeding with continued CSP. The principle of uterine CSP treatment is to rapidly terminate pregnancy while excluding the gestational sac and maximally preserving the patient's fertility [6,12]. Different individual clinical treatment programs should be developed on the basis of specific patient circumstances, including age, underlying diseases, past childbearing experience, future childbearing desires, and number of CSP weeks. Once CSP is diagnosed, the patients should first be assessed for preoperative risk; uterine surgery or labor induction should not be performed haphazardly to avoid fatal bleeding. To date, no uniform specifications and corresponding treatment guidelines are available for treating CSP. Most studies suggest that controlling bleeding, removing the lesion, and preserving the patient's reproductive function are the main treatment safety principles for CSP patients [10,13,14]. The current CSP treatment methods include drug therapy, drug therapy + uterine surgery, laparoscopic/laparoscopic total hysterectomy, uterine incision scar pregnancy foci removal under laparoscopy, vaginal uterine incision scar pregnancy lesions + uterine muscle wall repair, and selective UAE [10,15-17]. However, selecting the appropriate treatment method for CSP is most important for the whole treatment plan. A suitable treatment procedure can reduce the risk of developing hemorrhea, shorten the time of hospitalization, and save medical resources. At present, most studies [18-20] indicate that CSP patients with severe CSP II or CSP III should receive UAE treatment, which can significantly decrease the risk of developing intraoperative hemorrhage. Recently, Cali et al. [21] evaluated a new ultrasonic sign in assessment of the relationship between the gestational sac of a CSP and the endometrial line (the COS). They found that COS may help to determine whether a CSP



Figure 3. Angiograph of uterine artery embolization (A, D: Intraoperative iliac arteriography; B, E: Intraoperative arteriography of uterus artery; C, F: Uterine artery embolization).

Table 2. The operation time, blood loss and hospital stay comparison between the 2 groups ($\overline{\chi}\pm s$).

Group	Operation time (min)	Blood loss (ml)	Hospital stay (days)
UAE (n=51)	82.23±45.21	112.58±68.54	12.56±3.03
LCSPDS (n=47)	85.45±30.02	108.56±54.12	7.65±2.48
t	0.41	0.32	8.74
Р	0.68	0.75	<0.0001

will progress towards a less severe form of morbidly adherent placenta (MAP), amenable to postnatal treatment, and successful pregnancy outcome. This is practicable and useful for CSP treatment selection.

In 2008, Gonsalves et al. reported successfully using UAE to treat uterine fibroids [22]. In the following years, the method

has improved and become an important minimally invasive technique for conservative treatment. UAE technology continues to improve and is widely used in treating postpartum hemorrhage, placenta previa, uterine incision scar pregnancy, and other gynecological diseases. In recent years, with the increasing incidence of uterine CSP, UAE has been broadly used in treating CSP. Nawroth et al. [7] first reported successfully





technology is safe and effective and can cause minimal injury to the patients' normal organs during uterine CSP treatment.

In the present study, we used a retrospective method to compare the clinical efficacy and safety of UAE vs. LCSPDS in treating CSP. No significant difference was found between UAE and LCSPDS in terms of preoperative and intraoperative blood loss or perioperative complications. However, the UAE group in our study stayed significantly longer in the hospital than the LCSPDS group did. The UAE group required a longer operation time, which is related to the repeat complete uterine cavity curettage after the patients received UAE. Compared with LCSPDS patients, the UAE patients did not undergo surgical pelvic agitation and hence avoided the risk of pelvic organ adhesions.

Table 3. The incidence of	perioperative	complications	comparison	of the 2	groups [n	, (%)].
---------------------------	---------------	---------------	------------	----------	-----------	---------

Group	Fever	Nausea	Vomiting	AST/ALT/GGT elevated	Scr/BUN elevated
UAE (n=51)	5 (9.8)	2 (3.9)	1 (1.96)	0 (0.00)	1 (1.96)
LCSPDS (n=36)	4 (11.11)	4 (11.11)	3 (8.33)	1 (2.78)	0 (0.00)

Table 4. The advantages and disadvantages of UAE and LCSPDS.

Treatment	Advantages	Disadvantages
UAE	1) Significantly decreases the intraoperative hemorrhage risk; 2) Reduces the risk of hysterectomy	1) Increase in cost of hospitalization; 2) Radiation exposure for patients and health care providers
LCSPDS	1) Complete removal of pregnancy lesions and repair scar incision; 2) Quickly and significantly decreases the β -HCG level; 3) Avoids recurrence of CSP	 Potential risk of developing massive hemorrhage; Not suitable for CSP II/III patients; 3) Not suitable for emergency CSP

using uterine artery embolization combined with drug treatment in managing CSP. Their findings showed that combining uterine artery embolization and drug treatment for CSP is safe and effective. They also believed that the method is the only alternative to hysterectomy for controlling pelvic bleeding.

Previous studies have shown the following advantages of UAE in treating uterine CSP [23,24]. (1) Embolizing the uterine artery can directly block the uterine blood circulation, cause ischemia and hypoxia in local lesions, and deprive embryos of blood supply to achieve mechanical necrosis. (2) The blood flow is blocked; hence, vaginal blood flow is rapidly controlled to reduce blood loss. (3) Blocking the uterine blood flow may also reduce bleeding during the complete curettage of the uterine cavity and help avoid traumatic open abdominal surgery. As a result, the organic integrity and fertility of young patients are retained. (4) The gelatin sponge is absorbed 14–21 days after embolization and is absorbed completely by 3 months, and does not affect reproductive organ functions. Clearly, the

LCSPDS involved higher surgical trauma and required general anesthesia, which is also accompanied by risks. The advantages and disadvantages of these 2 treatment procedures are described in Table 4.

Conclusions

Laparoscopic surgery is generally applied for the outer convex type of CSP; this procedure enables intra-abdominal visualization and stoppage of bleeding under direct vision. Most CSP patients suffer from adhesions between the lower uterine segment and the bladder; thus, the technical requirements are higher for laparoscopic instruments and surgeons.

Conflict of interest

None.

References:

- 1. Matyszkiewicz A, Jach R, Nocun A et al: [Cesarean scar pregnancy.] Ginekol Pol, 2015; 86(10): 791–98 [in Polish]
- 2. Zahalkova L, Kacerovsky M: Cesarean scar ectopic pregnancy. Ceska Gynekol, 2016; 81(6): 414–19 [in Czech]
- 3. Fylstra DL: Ectopic pregnancy within a cesarean scar: A review. Obstet Gynecol Surv, 2002; 57(8): 537–43
- Cao S, Zhu L, Jin L et al: Uterine artery embolization in cesarean scar pregnancy: Safe and effective intervention. Chin Med J, 2014; 127(12): 2322–26
- Chen H, Zhou J, Wang H et al: The treatment of cesarean scar pregnancy with uterine artery embolization and curettage as compared to transvaginal hysterotomy. Eur J Obstet Gynecol Reprod Biol, 2017; 214: 44–49
- Bayoglu Tekin Y, Mete Ural U et al: Management of cesarean scar pregnancy with suction curettage: A report of four cases and review of the literature. Arch Gynecol Obstet, 2014; 289(6): 1171–75
- Nawroth F, Foth D, Wilhelm L et al: Conservative treatment of ectopic pregnancy in a cesarean section scar with methotrexate: A case report. Eur J Obstet Gynecol Reprod Biol, 2001; 99(1): 135–37
- Wozniak S, Pyra K, Kludka-Sternik M et al: Uterine artery embolization using gelatin sponge particles performed due to massive vaginal bleeding caused by ectopic pregnancy within a cesarean scar: A case study. Ginekol Pol, 2013; 84(11): 966–69
- 9. Qi F, Zhou W, Wang MF et al: Uterine artery embolization with and without local methotrexate infusion for the treatment of cesarean scar pregnancy. Taiwan J Obstet Gynecol, 2015; 54(4): 376–80
- Wang YL, Su TH, Chen HS: Laparoscopic management of an ectopic pregnancy in a lower segment cesarean section scar: A review and case report. J Minim Invasive Gynecol, 2005; 12(1): 73–79
- 11. Qiao B, Zhang Z, Li Y: Uterine artery embolization versus methotrexate for cesarean scar pregnancy in a Chinese population: A meta-analysis. J Minim Invasive Gynecol, 2016; 23(7): 1040–48
- Birge O, Karaca C, Arslan D et al: Medical management of cesarean scar pregnancy at advanced age: Case report and literature review. Clin Exp Obstet Gynecol, 2016; 43(1): 140–42
- 13. OuYang Z, Yin Q, Xu Y et al: Heterotopic cesarean scar pregnancy: Diagnosis, treatment, and prognosis. J Ultrasound Med, 2014; 33(9): 1533–37

- 14. Sugawara J, Senoo M, Chisaka H et al: Successful conservative treatment of a cesarean scar pregnancy with uterine artery embolization. Tohoku J Exp Med, 2005; 206(3): 261–65
- Lian F, Wang Y, Chen W et al: Uterine artery embolization combined with local methotrexate and systemic methotrexate for treatment of cesarean scar pregnancy with different ultrasonographic pattern. Cardiovasc Intervent Radiol, 2012; 35(2): 286–91
- Liu W, Shen L, Wang Q et al: Uterine artery embolization combined with curettage vs. methotrexate plus curettage for cesarean scar pregnancy. Arch Gynecol Obstet, 2016; 294(1): 71–76
- Hasegawa J, Ichizuka K, Matsuoka R et al: Limitations of conservative treatment for repeat Cesarean scar pregnancy. Ultrasound Obstet Gynecol, 2005; 25(3): 310–11
- Hong Y, Guo Q, Pu Y et al: Outcome of high-intensity focused ultrasound and uterine artery embolization in the treatment and management of cesarean scar pregnancy: A retrospective study. Medicine (Baltimore), 2017; 96: e7687
- Ma Y, Yang C, Shao X: Efficacy comparison of transcatheter arterial embolization with gelatin sponge and polyvinyl alcohol particles for the management of cesarean scar pregnancy and follow-up study. J Obstet Gynaecol Res, 2017; 43: 682–88
- Sun YY, Xi XW, Yan Q et al: Management of type II unruptured cesarean scar pregnancy: Comparison of gestational mass excision and uterine artery embolization combined with methotrexate. Taiwan J Obstet Gynecol, 2015; 54: 489–92
- 21. Cali G, Forlani F, Timor-Tritsch IE et al: Natural history of Cesarean scar pregnancy on prenatal ultrasound: the crossover sign. Ultrasound Obstet Gynecol, 2017; 50(1): 100–4
- 22. Gonsalves C: Uterine artery embolization for treatment of symptomatic fibroids. Semin Intervent Radiol, 2008; 25(4): 369–77
- 23. Kwasniewska A, Stupak A, Krzyzanowski A et al: Cesarean scar pregnancy: Uterine artery embolization combined with a hysterectomy at 13 weeks' gestation – a case report and review of the literature. Ginekol Pol, 2014; 85(12): 961–67
- 24. Zhang B, Jiang ZB, Huang MS et al: Uterine artery embolization combined with methotrexate in the treatment of cesarean scar pregnancy: Results of a case series and review of the literature. J Vasc Intervent Radiol, 2012; 23(12): 1582–88