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1	Laparoscopic Resection Verses Transvaginal Resection in the			
2	Management of Exogenous Cesarean Scar Pregnancy			
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7 Abstract

⁸ Background: Caesarean scar pregnancy (CSP) is a rare but potentially life-threatening

⁹ complication for women of reproductive age with a previous caesarean birth the incidence of

¹⁰ CSP has exponentially risen over the past two decades, due to an increasing rate of caesarean

¹¹ delivery. Because of the rarity of the condition, the majority of CSPs are case reports or small

12 case series reported in the literature, and no universal treatment guidelines has been

13 established yet.Objective: To compare the safety and efficacy of laparoscopic resection and

¹⁴ transvaginal resection as treatment options for cesarean scar pregnancy (CSP).

15

16 Index terms— exogenous caesarean scar pregnancy, laparoscopic resection, transvaginal resection.

¹⁷ **1 I. Introduction**

aesarean scar pregnancy (CSP) or caesarean scar ectopic pregnancy is a rare but potentially life-threatening 18 type of ectopic pregnancy where the gestational sac implants in a previous caesarean scar. The first case of 19 CSP was described by Larsen and Solomon in 1978. [1] The incidence of CSP being reported over the past two 20 decade has increased exponentially and is expected to rise due to the increasing rates of caesarean section (CS) 21 being high as 40-50% and some hospitals up to 70%. [2] The Estimated incidence of CSP is 1:1800-1:2,226 in 22 all Pregnancies, 0.45% in pregnancy after caesarean performed worldwide, improved diagnostic techniques and 23 increased physician awareness. The frequency of CS worldwide is about 15%, but in China the rate is as delivery, 24 and 6.1% in ectopic pregnancy after caesarean delivery. [3] Early and timely diagnosis is mandatory to prevent 25 life-threatening complications like uterine rupture, massive haemorrhage or other serious consequences. 26

Vial et al. [4] classified CSP into two subtypes based on findings on transvaginal sonographic imaging. Endogenous CSP (CSP type I) is characterized by the implantation of the gestational sac at the cesareanscar site followed by inward growth towards either the cervical isthmus space or the uterine cavity. Exogenous CSP (CSP type II) results from the deep implantation of the gestational sac into a cesarean scar defect with an outward growth that infiltrates the uterine myometrium creating a bulge from the uterine serosal layer.

Our study retrospectively analyzed the clinical data of 19 patients with exogenous CSP (type II CSP) treated in our hospital in the past five years. We analyzed and compared the outcomes, safety and efficacy of laparoscopic resection and transvaginal resection of exogenous CSP by evaluating the intraoperative blood loss, the time for serum betahuman chorionic gonadotropin (beta-HCG) to return to normal, duration of hospital stay, and resolution of the mass and return of menstruation.

³⁷ 2 II. Materials and Methods

38 3 a) Patients

A retrospective comparative study was adopted. Between January 2013 and June 2017, 19 patients with
exogenous CSP admitted at First Affiliated Hospital of Nanjing Medical University were enrolled in this study.
The inclusion criteria were; (1) a history of cesarean delivery; (2) a history of amenorrhea and a positive urine

42 pregnancy test; (3) a color Doppler transvaginal ultrasound indicating a Cesarean scar pregnancy based on the

43 diagnostic criteria stipulated by Godwin et al. [5];(i).Empty uterus and cervical canal; (ii). Development of the 44 gestational sac or fetal pole with or without cardiac activity or identification of a mixed-echo mass in the anterior

⁴⁵ part of the caesarean scar;(iii).Very thin myometrium ??1-3mm) or an absence of healthy myometrium between

the bladder wall and the sac/mass; and (iv). The gestational sac or mixed-echo mass being located toward either

47 the cervicoisthmic space or the uterine cavity in CSP-I, or the infiltration of the gestational sac or mixed-echo

48 mass into the myometrium and/or forming a bulge from the uterine serial layer in CSP-II; (v). High velocity

49 with low impedance peritrophoblastic vascular flow clearly surrounding the sac in Doppler examination; (4)

postoperative pathology report indicating implantation or the presence of chorionic villi in the myometrium; (5)
 Patient not a referral from a peripheral facility due to failed treatment for CSP.

This study was approved by the ethics committee of First Affiliated Hospital of Nanjing Medical University.

All patients in this study were thoroughly informed of the potential risks and complication, benefits and curative

54 effects of the surgeries and other alternatives and signed a written consent. The 16 patients were managed

⁵⁵ by laparoscopic resection of the CSP while 3 patients who declined laparoscopic surgery were managed by the

56 transvaginal approach.

57 4 b) Preoperative Evaluation

Data collected from all patients included maternal age, presenting symptoms, gravidity, parity, gestational age based on last menstrual period (LMP) or Ultrasound dating, number of previous Caesarean deliveries, the time interval between the last caesarean delivery and current CSP, initial preoperative serum ?-HCG, and transvaginal ultrasound findings (size of gestational sac/mass, relationship with anterior uterine myometrium, presence or absence of cardiac activity). Routine preoperative preparations were done, complete blood cell count, liver and renal function test, urinalysis, coagulation panel, and electrocardiography (ECG) were performed to rule out any

64 contraindication for surgery. Vaginal cleaning was done a day before surgery.

⁶⁵ 5 c) Surgical Methods

66 6 i. Laparoscopic resection

The patients assumed a lithotomic position, under general anesthesia. The operation field was sterilized, CO2 67 pneumoperitoneum was created conventionally, a laparoscope was inserted to visualize the anterior wall of the 68 uterus, the bladder, and for the presence of adhesion. Adhesiolysis was performed, the peritoneum between the 69 bladder and the uterus was dissected, and the bladder pushed downwards appropriately, bilateral occlusion of 70 71 ascending branches of uterine arteries was performed. Under laparoscopic monitoring the pregnancy mass was 72 suctioned till it significantly reduced in volume, then the lesion and the scar tissue which is distinguishable from normal myometrium of the uterus was excised. The uterine defect was closed up in two layers using continuous 73 sutures, and hemostatis was achieved. The uterine artery occlusion was the relieved to restore uterine blood 74 flow. An abdominal drainage tube was left in situ. Hysteroscopy was then done to visualize the uterine cavity, 75 the scar site and the patency of fallopian tube osmium. The operation was completed and patients reversed from 76 anaesthesia 77

ii. Transvaginal resection Patients were placed in a lithotomic position then put under general anesthesia. 78 The operation field was cleaned and draped. The bladder was emptied using a metal catheter. The vagina and 79 cervix were exposed using a vaginal retractor. The anterior vaginal fornix was exposed by tenaculum attached 80 to the upper lip of the cervix and pulled downwards. Normal saline was injected into the cervicovaginal space. 81 The pressure from the injected solution separated the bladder and cervix. A transverse incision was made 2 82 cm above to the clamped site; the bladder was dissected and pushed away through the cervicovaginal gap till 83 vesicoperitoneal fold, where the peritoneum was punctured and a vaginal retractor placed. A boggy area was 84 detected by a probe and considered as a scar pregnancy lesion. A transverse incision was made at the cesarean 85 section scar, where a bulge and purple bluish discoloration associated with pregnancy tissue could be visualized; 86 sometime villi could be visualized as well. The scar tissue and the pregnancy tissues were removed using an ovum 87 forceps through the incision, followed by suction to evacuate the uterine cavity. The incision was then closed in 88 two layers by a continuous lock stitch under the guidance of the detecting probe. After examining the bladder to 89 rule out any trauma during surgery, the peritoneum was sutured to ensure there was no active bleeding. Finally, 90 the vaginal wall was closed by a continuous locking suture, 3 pieces of iodine gauzes were left in situ to be removed 91 92 24 hours later after the surgery. In both the laparoscopic or transvaginal groups, an indwelling urine catheter was put to monitor urine output and was removed 48 hours postoperatively. 93

Successful treatment was regarded as a patient fully recovered, a steady decline in vaginal bleeding, serum beta HCG levels returning down to normal, the disappearance of the CSP mass, no severe complications, uterus preserved, and no need for additional treatment. Intraoperative blood loss, length of hospital stay, serum beta-HCG levels, and postoperative complication were recorded.

98 7 iii. Follow up

Patients were discharged based on the following criteria: no chief complaint, no fever, the vaginal bleeding stopped or decreased to less than normal menstrual bleeding, normal or steadily decline of beta HCG level, no CSP mass on transvaginal ultrasound or the size of mass decreased. After discharge from the hospital, all patients were
 followed up every week for 3 to 6 months. Serial measurements of serum beta HCG was done every week till
 normal. The first return of the menstrual cycle was recorded. Transvaginal ultrasound screening was carried out
 to determine if there were residual pregnant tissues within the uterine scar tissues every two weeks.

¹⁰⁵ The patients were advised to take on a suitable method of contraception for at least one year.

¹⁰⁶ 8 iv. Statistical Methods

We used SPSS 24.0 software for statistical analysis of the data. All data are represented as mean \pm standard deviation (SD). The independent sample ttest was used for intergroup comparison. A p value (P<0.05) was considered statistically significant.

110 9 Results

From January 2013 to June 2017, 19 patients diagnosed with exogenous CSP were managed in our gynecology 111 ward. During the same period, 212 cases of Endogenous CSP were admitted in our hospital. The clinical 112 characteristics of the patients according to the type of surgery are provided in Table 1. All the patients had a 113 history of low-segment cesarean deliveries, and their ages ranged from 22-44 years (33.05 ± 6.20 years) .3 patients 114 had a history of 2 Cesarean deliveries while the rest of the 16 had one prior cesarean delivery. The preoperative 115 serum beta HCG level was 710-156,452 IU/L. The interval between the last caesarean delivery and current CSP 116 was 5.94 ± 4.03 years (0.7-22) years), 6 cases had a fetal cardiac activity present on ultrasound. The thickness of 117 the myometrium from the seros to the gestational sac, as measured on ultrasound was 1.0mm-5.0mm, and the 118 119 largest diameter ranged from 10mm-40mm

Of the 19 patients with an exogenous CSP, 3 received Transvaginal resection of the CSP with the operation completed successfully. For the other 16 patients, we conducted laparoscopic resection, 4 patients received bilateral uterine artery remobilization before surgery due to a large amount of vaginal bleeding on admission. All were successful, and none of them required secondary treatment.

The postoperative Transvaginal color Doppler ultrasound reexaminations did not reveal any significant mass at the uterine isthmus. For both groups the intraoperative blood loss, the duration of hospital stay, the time for the serum beta HCG to return to normal, time for complete resolution of CSP mass and resumption of menstruation between the two groups showed no statistically significant difference (P>0.05). (Table 2). The pathological report of the lesion tissues taken from the 19 patients revealed chorionic villi in the myometrium, consistent with the preoperative diagnosis of CSP. The success rate in both groups was 100% with no postoperative complication.

130 10 Discussion

In 1978, Larsen and Solomon first reported one case of scar pregnancy and proposed the concept of scar pregnancy after caesarean section. [1]Until 2001, there were 19 cases of scar pregnancy reported in 2 case reports and by 2011 the number of cases described in the literature was 751, showing a rapid increase in the incidence of this type of pregnancy which can be attributed to the increasing number of caesarean deliveries being done, improved diagnostic tools and increased physician knowledge and awareness of the condition. [6]. Due to the relatively lower incidence, there has been no universal standard method of treatment of CSP. Classification using ultrasonography provided the basis for the management of patients.

The exact etiology of CSP is unknown but it has been suggested that a shortage of blood supply at a low uterine segment after cesarean delivery may result in insufficient fibrosis and repair hence forming uterine scar dehiscence or small-scar defects and later CSPs. [7] Such defects can also develop from the trauma of other uterine surgery for such as curettage, myomectomy, metroplasty, hysteroscopy and even manual removal of placenta. [8,9] Better suturing techniques of the cesarean incision may help prevent CSP.

CSP can occur in any woman of child bearing age with a previous caesarean delivery. The age reported in literature ranges between 20-45 years old, and the gestational age at presentation is 5-16 weeks. [3,9] In this study the age of the 19 patients was 22-44 years old, and the gestational age was 4-14 weeks, which is consistent with literature. No positive correlation between the number of Caesarean sections and the risk of CSP has been shown. Rotas et al reviewed 112 cases of which 52% had a history of one CS, 36% had a history of 2 CS, 12% had 3 or more previous CS, suggesting that the number of previous is not related to the risk of CSP. [10] Our study found 16 patients (84.2%) had a history of 1 CS and 3 patients (15.8%) had 2 previous CS.

CSP often presents with symptoms of irregular vaginal bleeding and /or abdominal pain or discomfort, but a 150 few are asymptomatic and CSP is found incidentally on routine first trimester Ultrasound. A number of cases are 151 misdiagnosed as a spontaneous abortion of an intrauterine pregnancy, or after medical abortion or curettage done 152 153 for abnormal vaginal bleeding. In this study all patients had a history of amenorrhea, no cases were misdiagnosed, 154 52.6% of patients presented with irregular vaginal bleeding, 15.7% with both vaginal bleeding and abdominal pain, and 31.5% were asymptomatic. Routine transvaginal ultrasonography is therefore recommended in early 155 pregnancy for patients who have previously undergone a cesarean delivery to rule out CSP. The Transvaginal 156 ultrasonography is the standard first line diagnostic tool with a diagnostic accuracy as high as 86.4% reported 157 combined with detailed patient history. [10] The Ultrasound diagnosis criteria for endogenous CSP proposed 158 includes an empty uterine cavity, empty cervical canal, gestational sac seen at either the uterine isthmus or 159

the anterior uterine wall, and myometrial tissue depression detected between the gestational sac and bladder 160 wall. [4,5] Magnetic resonance imaging(MRI), hysteroscopy, or laparoscopy can be considered when ultrasound 161 imaging is inconclusive or equivocal in order to reduce the misdiagnosis rate. It is notable that MRI is a costly 162 163 diagnostic technique and that this must often be taken into account in clinical environment. Ultrasonography has the advantages of being non-invasive, simple, and cheap. [11,12,13] The pathological examination done in 164 this study confirmed the accuracy of using ultrasonography for diagnosis. 165

Medical 11 166

Expectant management is not recommended as it is associated with poor outcome including hysterectomy. 167 [14] The currently available therapeutic options reported in the literature include medical therapy such as 168 injecting embyrocides(such as kalium chloratum) into the gestational sac, and systematic or local administration 169 of methotrexate (MTX), uterine artery embolization (UAE), hysteroscopic resection, laparotomic resection, 170 laparoscopic resection or more recently transvaginal resection. [6] Treatment should be individualized for every 171 case of CSP after adequate preoperative assessment based on the gestational age, viability of fetus, myometrial 172 173 defects, and presenting symptoms and physicians experience.

Surgical excision of CSP has the highest cure rate, and is not only effective in termination of pregnancy but also 174 allows repair of scar defects while avoiding risk of hysterectomy caused by complications such as massive bleeding 175 176 and uterine perforation during curettage and preserve fertility of the patient so as to avoid occurrence of repeat CSP. ??15,16,} The gestational sac that grows toward the urinary bladder (exogenous CSP) has a higher risk 177 for massive hemorrhage than the gestational sac that grows toward the uterine cavity (endogenous CSP). So for 178 most patients in which the gestational sac grew toward the urinary bladder in most literature reports underwent 179 surgical excision. Since the first report in 1978, laparotomy, laparoscopy, hysteroscopy or transvaginal excision of 180 CSP and repair of the uterine defect have been reported successfully. After resection of CSP and repair of the scar 181 through laparotomy, the serum beta HCG can be return to normal in 1-3 weeks after operation and it can reduce 182 183 risk of uterus rupture and recurrence of CSP. However, laparotomy is associated with larger surgical wounds, long 184 hospital stay and more postoperative pain and adhesion formation. It is usually used in emergencies in patients with unstable hemodynamic and actively bleeding. [3] In recent years, with the development and improvement 185 of minimally invasive technology, more physicians in China and abroad are using laparoscopic and transvaginal 186 techniques in the treatment of CSP. Minimally invasive surgery has well established advantages of a smaller 187 surgical wound, less postoperative pain, a shorter hospital stay, quicker recovery, and better aesthetic results. 188 [16,17] Since 2012, our hospital has taken the lead in exploring laparoscopy and transvaginal surgery in the 189 190 province, 16 cases successfully treated with laparoscopy and 3 cases with transvaginal approach, the operations were smooth and intraoperative blood loss was minimal $(159.38\pm155.54 \text{ and } 76.67\pm40.41 \text{ respectively})$ and there 191 192 were no postoperative complications. After the operation, the serum beta HCG decrease was satisfactory, minimal 193 or no pregnancy tissue remained, and the results were satisfactory. However, laparoscopic surgery is expensive 194 and is highly demanding for surgeons .Our experience is that:1.We should know the indications for operation: CSP patients with transvaginal colour Doppler ultrasound findings sgowing no gestational sac in the uterine 195 196 cavity but the CSP mass bulging externally at the anterior wall of the lower uterine segment <5mm from serous layer and the echo of the gestational sac in the anterior wall of the lower segment of uterus is rich in blood 197 flow signals; 2. Avoid instrumental manipulation of the uterine cavity before operation, so as to reduce massive 198 bleeding caused by instrumentation; 3. Temporarily occluding the blood flow of both uterine arteries, so as 199 to reduce blood supply to the lesion and hence reducing massive bleeding during the operation. Some studies 200 have used mifepristone administered preoperatively in order to reduce intraoperative blood loss and enhance 201 202 apoptosis and necrosis of the trophocytes or intraoperative local injection of oxytocin or injection of vasopressin 203 with satisfactory results. [15,16]; 4. Open the vesico-uterine peritoneal fold, push the bladder downwards to avoid both bladder injury during the surgical procedure and subsequent difficulties when suturing the uterine 204 incision. Under laparoscopic monitoring, suction the pregnancy mass till it has significantly reduced in volume, 205 then the lesion and the scar tissue which is clearly distinguishable from normal myometrium of uterus is excised; 206 The uterus should be sutured in two layers so as to prevent recurrence of CSP and preserve reproductive 207 5. function; 6. After resection and repair of scar lesions, the uterine artery occlusion is relieved, uterine blood flow 208 is restored, and uterine function preserved. 209

Transvaginal approach is relatively simple in experienced hands. However there are limitation in gestation age, 210 amount of bleeding, gestational sac location, difficulty in cervical exposure and a small operation field. [17].Our 211 experience is; 1. The gestational age <90days, the gestational sac diameter <5cm, <5mm from the serosal layer, 212 213 the position of the gestational sac is low and the cervix is easily exposed; 2. Intraoperative injection of oxytocin 214 into the cervix helps reduce bleeding during the operation: 3. Normal saline is injected into the cervico-vaginal 215 gap, the pressure from the injected normal saline fully separates the bladder and cervix; 5. The incision is closed 216 by a continuous locking stitch under the guidance of the detecting probe, carefully repairing the anterior wall of the uterus, to avoid scar incision diverticulum and small sinus formation. 217

Our study was limited by the sample size and the lack of multicenter data, and lack of follow up on future 218 reproductive outcomes. In the future, we will conduct a prospective, randomized, controlled study with more 219 patients to make up for these deficiencies. 220 V.

221

222 **12** Conclusion

For patients with CSP is early, timely, and clear diagnosis is key, and individualized treatment that should be implemented in accordance with the gestational age, hemodynamic stability of the patient, serum beta HCG levels, and ultrasound and MRI findings. Laparoscopic resection and transvaginal resection are the most reasonable approach for managing exogenous CSP because of the deep implantation of the mass into the myometrium and very thin myometrium between the gestational sac and the bladder, hence high risk of rupture with other treatment modalities. They both have a comparable high success rate, thorough lesion clearance, fewer complications, and a shorter time to beta HCG levels returning to normal. However, both require accumulated patient experiences and surgical techniques are necessary before broad application.

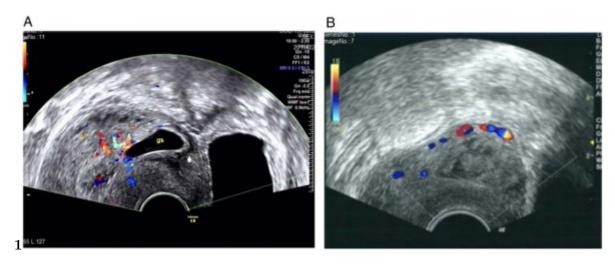


Figure 1: Fig. 1 :

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Figure 2: E

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Characteristics	laparoscopic group	Transvaginal	Р	
	aparoscopic Sroup	group	value	
		Stoup	?	
Maternal age (years)	$33.23{\pm}5.07$	$33.03 {\pm} 5.00$	0.993	
Gravidity	$4.01{\pm}1.5$	$4.10{\pm}1.48$	0.509	
Abortion	$1.74{\pm}1.38$	1.90 ± 1.40	0.387	
Gestational age (days)	$49.25 {\pm} 5.59$	$44.67 {\pm} 6.11$	0.2149	
Number of previous cesarean deliveries				
1	13	3		
2	3	0		
Time interval between previous CS and present CSP (ye	ars) 5.92 ± 3.71	$6.33 {\pm} 4.23$	0.467	
Initial level of serum ?-HCG (IU/L)	44995 ± 41966	43211 ± 42751	0.389	
Largest diameter of CSP mass (mm)	27.87 ± 13.76	$29.01{\pm}14.09$	0.285	
Abbreviations: CSP, cesarean scar pregnancy; CS, cesarean sections; ?-HCG, beta human chorionic gonadot				
2 Data presented as mean + SD (range) or number (percentage) unless indicated otherwise				

? Data presented as mean \pm SD (range) or number (percentage) unless indicated otherwise

? Student t test

Figure 3: Table 1 :

 $\mathbf{2}$

Variable

[Note: Abbreviations: CSP, cesarean scar pregnancy; ?-HCG, beta human chorionic gonadotropin. ? Data is given as mean \pm SD (range) or percentage unless indicated otherwise ? Student t test IV.]

Figure 4: Table 2 :

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233 .2 Conflict of interest

234 None.

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