Observational Study

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A comparison between laparoscopy and hysteroscopy approach in treatment of cesarean scar pregnancy

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Abstract

The aim of the study was to compare the efficacy of laparoscopy and hysteroscopy for the treatment of cesarean scar pregnancy (CSP) and analyze the clinical factors associated with successful selection for hysteroscopic or laparoscopic treatment of CSP.

We retrospectively studied 112 cases of CSP that were treated by laparoscopy and/or hysteroscopy in our hospital from December 2014 to December 2017. In total, 72 of these patients underwent ultrasound-guided curettage and hysteroscopic resection without uterine scar defect repair. Fourty of these patients underwent laparoscopic resection and repair of the uterine scar defect. We analyzed the different clinical variables between the 2 groups and identified the clinical factors which could predict the need for the laparoscopic repair of uterine scar defect. Results showed that laparoscopy and hysteroscopy were safe ways to treat CSP, and no patient underwent hysterectomy. The β-hCG level in both of the 2 groups decreased to normal 4 to 8 weeks after surgery. There were significant differences between the hysteroscopy group and laparoscopy uterine scar repair group in terms of days of amenorrhea, gestational sac diameter, myometrial thickness, operation time, intraoperative blood loss, and hospitalization duration ($P < .05$). Logistic regression analysis showed that the days of amenorrhea, gestational sac diameter and myometrial thickness were independent risk factors for CSP treated by minimally invasive surgery, which were also shown by ROC curve analysis to be predictors of the need for the repair of the uterine scar defect, with optimal cutoffs of 52.50 days, 3.25 cm, and 2.05 mm, respectively; and the areas under their corresponding ROC were 0.721, 0.851, and 0.927, respectively.

We conclude that laparoscopy and hysteroscopy are safe and efficient minimally invasive procedures for the treatment of CSP. The days of amenorrhea, gestational sac diameter and myometrial thickness may be key factors associated with successful selection for hysteroscopic or laparoscopic treatment of CSP.

Abbreviations: β-hCG = β-human chorionic gonadotropin, AUC = area under the curve, CSP = cesarean scar pregnancy, DIC = disseminated intravascular coagulation, MTX = methotrexate, RCT = randomized controlled trial, ROC = receiver operating characteristic, UAE = uterine artery embolization.

Keywords: cesarean scar pregnancy, hysteroscopy, laparoscopy, operative treatment

1. Introduction

Cesarean scar pregnancy (CSP) is a rare type of ectopic pregnancy and involves embryo implantation at the site of a cesarean scar, which is located completely outside the uterus and is surrounded by myometrium and fibrous tissue.[1] CSP can cause serious complications, including abnormal placentation, uterine rupture, and life-threatening hemorrhage; CSP can even be fatal.[2,3] The latest data indicate that CSP incidence is in the range from 1:2500 to 1:8000.[4] In recent years, the cesarean section rate has increased, especially after the two-child policy was implemented in China in 2015.[5] The harm of CSP to women has gradually been revealed. The widespread use of early transvaginal sonography may lead to better detection and diagnosis of CSP.

The available treatment options include uterine suction curettage, local resection through laparotomy, laparoscopy, hysteroscopy, uterine artery embolization (UAE), methotrexate (MTX), and even hysterectomy. Uterine suction curettage as a primary treatment for CSP is not recommended due to the high risk of hemorrhage, which may become life-threatening and even require emergency laparotomy or hysterectomy.[6] If treatment is delayed, CSP can evolve into placenta accreta or uterine rupture.[7] However, it is difficult to identify the optimal management strategy because there is no universal consensus on the best treatment modality. Accurately assessing the risk factors of patients before treatment is very important for clinicians seeking to choose a reasonable treatment plan.

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With the development of gynecological minimally invasive surgery, there are obvious advantages in the surgical treatment of CSP. The aim of the study was to compare the efficacy of laparoscopy and hysteroscopy for the treatment of CSP and to assess the factors associated with successful selection for hysteroscopic or laparoscopic treatment of CSP.

2. Materials and methods

2.1. General information

This observational study was carried out retrospectively with 112 CSP patients who underwent minimally invasive surgery (hysteroscopy with or without combined laparoscopic repair of the defect) at the Qilu Hospital of Shandong University (Shandong, China) between December 2014 and December 2017. Written informed consent was obtained from each patient, and the study was approved by the Ethics Committee of Qilu Hospital of Shandong University (Approval number: 2016039). Data of the CSP patients were obtained from their electronic medical records.

The diagnostic criteria for CSP were as follows: a history of cesarean section; an elevated serum concentration of β-human chorionic gonadotropin (β-hCG) (>10.00 IU/L); and fulfillment of the following ultrasound standards: no fetal parts in the uterine cavity or cervix, development of the gestational sac in the anterior portion of the lower uterine segment, a thin myometrial layer between the gestational sac/placenta and bladder (range from discontinuous myometrium to less than half of myometrium), and the presence of a rich vascular pattern in the area of the cesarean scar.[4],[8],[9],[10]

The exclusion criteria were as follows: cervical pregnancy; uterine isthmus gestation; inevitable abortion; incomplete abortion; and gestational trophoblastic disease. Patients who underwent treatment with MTX or UAE followed by surgery were excluded.

Criteria of selecting surgical methods for CSP patients in our clinical work:

1. myometrial thickness ≥3 mm, ultrasound-guided curettage and hysteroscopy.
2. 1 mm < myometrial thickness <3 mm, Hysteroscopy was performed first, and whether to add laparoscopic defect repair was determined according to the intraoperative situation.
3. myometrial thickness ≤1 mm, hysteroscopy and laparoscopic defect repair.

2.2. Case retrieval and allocation

Through electronic case retrieval, the patients diagnosed as CSP and treated by minimally invasive surgery were selected. Among all 112 patients, 72 patients who underwent ultrasound-guided curettage and hysteroscopy without repair of the defect were classified as the hysteroscopy group; 40 patients who needed repair of the defect under laparoscopy in addition to hysteroscopic surgery were classified as the laparoscopy repair group. 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;
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 and hysteroscopic guidance to remove the remaining conceptus tissue;
4. the scar on the uterus was incised and trimmed; and
5. the scar was sutured with absorbable sutures (Fig. 1).

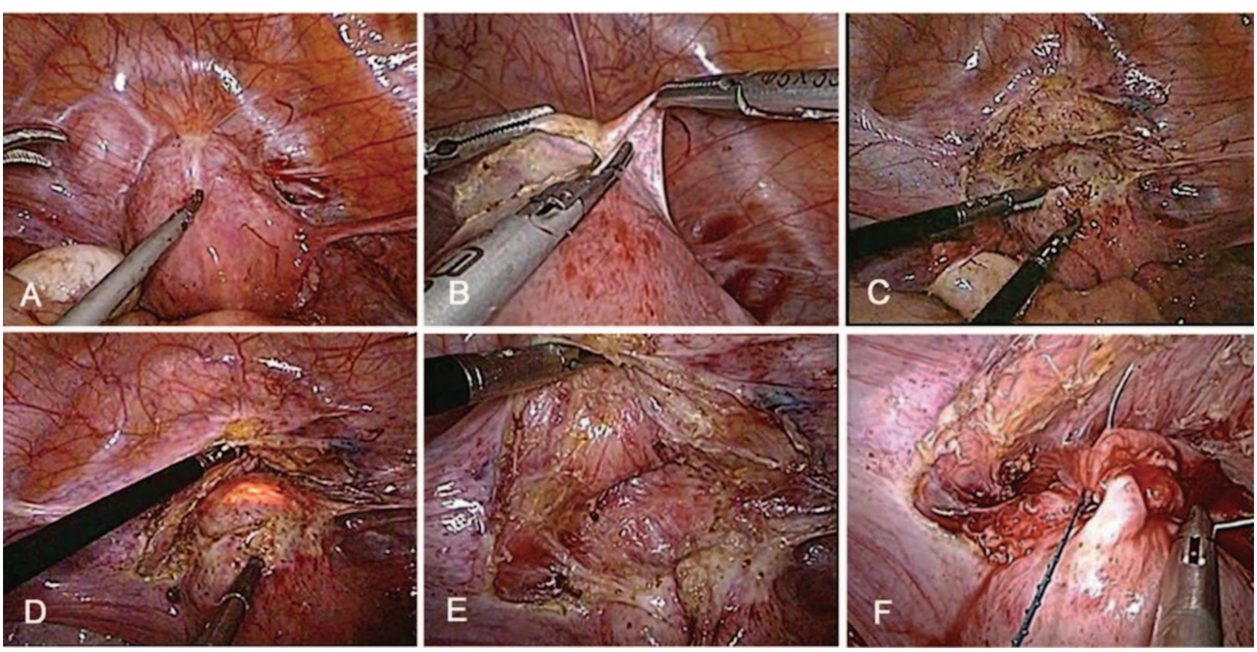

Figure 1. Laparoscopic images of the operation. (A) CSP mass. (B) The peritoneum is opened between the bladder and the uterus. (C) The bladder is pushed down, and the uterine cesarean section scar is exposed. (D) The light transmittance test was positive in the weak part of the muscle tissue when the conceptus tissue was removed under hysteroscopy. (E) When uterine suction curettage was performed, the weak part of the muscle tissue was obviously depressed. (F) When the mass was cleared, the scar defect was sutured with a synthetic, absorbable, barbed suture.

Laparoscopy and hysteroscopy were performed by fellowship-trained minimally invasive gynecological surgeons. The tissue samples were collected and sent for pathological examination. After being discharged, the patients were asked to return for outpatient visits every 2 weeks for the monitoring of their serum β-hCG level and ultrasounds until they were cured.

2.3. Clinical characteristics analysis

The following variables were included: age; time since last cesarean section; number of pregnancies; number of cesarean sections; number of induced abortions; days of amenorrhea; gestational sac diameter (average value); β-hCG level; myometrial thickness; cardiac activity in the gestational sac (fetal heartbeat) operation time; intraoperative blood loss; and hospitalization duration.

2.4. Statistical analysis

SPSS 17.0 (SPSS Inc, Chicago, IL) statistical software was used for the data analysis. Single-variable analysis was performed by *t* tests, and the Chi-Squared (χ^2) test was performed for categorical variables. Variables that were significantly different between the groups were entered into the logistic regression model to identify risk factors associated with the severity of CSP and predictors of the choice of surgical procedure. Receiver operating characteristic (ROC) curve analysis was used to identify the optimal cutoff values of the variables in order to summarize the indications for laparoscopic scar repair. The optimal cutoff values was defined by the point on the ROC curve with the minimum distance between the 0% false-positive rate and the 100% true positive rate, and the highest value of the area under the curve (AUC). Differences with $P<.05$ were considered statistically significant.

3. Results

3.1. The efficacy of laparoscopy and hysteroscopy for the treatment of CSP

Among the included patients, 107 (95.5%) were successfully treated without any complications, 2 underwent conversion to laparotomy, and 3 experienced intraoperative blood loss >1000 ml. There were no cases of uncontrolled intraoperative bleeding or hysterectomy. The factors that needed to be monitored after the operation were vaginal bleeding, the β-hCG level, and the size of the mass in the cesarean scar. Most of the patients experienced only slight vaginal bleeding for 4 to 5 days after the operation. At 4 to 8 weeks after the surgery, the β-hCG level decreased to normal. Color Doppler ultrasonography showed that the uterine scar defect was significantly improved in the laparoscopy repair group.

3.2. Comparison of the different clinical variables between the 2 groups

Patients in the 2 groups showed no significant difference in age ($P=.718$), time from the last cesarean ($P=.194$), number of pregnancies ($P=.238$), number of cesarean sections ($P=.399$), number of induced abortions ($P=.789$), or β-hCG level ($P=.241$). However, there were significant differences between the laparoscopy repair and hysteroscopy groups in the days of amenorrhea ($P=.000$), gestational sac diameter ($P=.000$), operation time ($P=.000$), intraoperative blood loss ($P=.000$), and hospitalization duration ($P=.000$). Both the days of amenorrhea and gestational sac diameter were significantly larger in the laparoscopy repair group than in the hysteroscopy group ($P<.05$). The average operation time in the laparoscopy repair group was 108.00 minutes, which was significantly longer than that in the hysteroscopy group. The average intraoperative blood loss in the laparoscopy repair group was 305.75 ml. However, the average blood loss in the hysteroscopy group was only 22.64 ml. Meanwhile, the hospitalization duration in the hysteroscopy group was significantly shorter than that in the laparoscopy repair group (Table 1).

The myometrial thickness and fetal heartbeat were categorical variables, and they were analyzed by the χ^2 test. The χ^2 test was performed according to whether the myometrial thickness was less than 3 mm in the 2 groups. Statistical analysis showed that there was a significant difference in muscular thickness between the 2 groups ($\chi^2=37.113$, $P=.000$). In the laparoscopy repair group, the majority of patients had a muscle thickness less than 3 mm. In contrast, in the hysteroscopy group, most of the patients had a muscle thickness greater than or equal to 3 mm. The χ^2 test was performed according to whether there was a fetal heartbeat in the 2 groups. The results showed no significant difference ($\chi^2=0.479$, $P=.489$) (Table 2).

3.3. Logistic regression analysis to identify risk factors

Multivariate logistic regression analysis was applied to identify the risk factors that could predict the necessity for the

Table 1

Clinical characteristics of patients in 2 groups of CPS patients.

Characteristic	Laparoscopy repair Group (n=40)	Hysteroscopy Group (n=72)	*P* value
Age (y)	33.60±4.77	33.26±4.67	.718
Time from last cesarean (y)	5.93±3.76	4.92±3.99	.194
Number of pregnancy	4.28±1.20	3.94±1.52	.238
Number of cesarean section	1.38±0.59	1.47±0.58	.399
Number of induced abortion	1.80±1.11	1.74±1.26	.789
Days of amenorrhea (d)	59.38±13.83	49.78±8.09	.000*
Gestational sac diameter (cm)	3.73±1.41	2.08±1.02	.000*
β-hCG level (IU/L)	42463.80±52887.83	31945.50±24990.22	.241
Operation time (m)	108.00±39.20	25.00±13.87	.000*
Intraoperative blood loss (ml)	305.75±376.84	22.64±19.25	.000*
Hospitalization duration (d)	8.65±3.15	5.24±3.31	.000*

* $P<.05$.

Gestational sac diameter (cm): the average diameter of gestational sac.

Table 2

Chi-Squared test analysis of variable factors in 2 groups of CSP patients.

Variable	Laparoscopy repair Group (n=40)	Hysteroscopy Group (n=72)	χ^2	*P* value
Myometrial thickness			37.113[#]	.000[*]
<3 mm	38	24		
≥3 mm	2[**]	48		
Fetal heatbeat			0.479	.489
Yes	14	30		
No	26	42		

[*] *P*<.05.
[**] Expected count less than 5.
[#] Continuous correction.

laparoscopic repair of uterine scars. As shown in Table 3, the days of amenorrhea (B=0.073; OR=1.076; *P*=.044), gestational sac diameter (B=0.810; OR=2.240; *P*=.002), and myometrial thickness (B=−3.251; OR=0.039; *P*=.000) were independent factors correlated with the severity of CSP. The days of amenorrhea days and gestational sac diameter were positively correlated with the severity of CSP. In contrast, the myometrial thickness was negatively correlated with the severity of CSP. The β-hCG level and fetal heartbeat were not independently correlated with CSP (Table 3).

3.4. ROC curve analysis to identify optimal cut-off values

ROC curve analysis was used to evaluate the optimal cut-off values for the following variables to summarize the indications for laparoscopic scar repair: days of amenorrhea, gestational sac diameter, β-hCG level, and myometrial thickness. The areas under the ROC curves (AUCs) for the days of amenorrhea, gestational sac diameter, β-hCG level, and myometrial thickness were 0.721 (*P*=.000, 95% CI: 0.618–0.823), 0.851 (*P*=.000, 95% CI: 0.771–0.930), 0.459 (*P*=.468, 95% CI: 0.329-–0.588), and 0.927 (*P*=.000, 95% CI: 0.878–0.976), respectively (Fig. 2). For the days of amenorrhea, the optimal cut-off was 52.5 days, with a sensitivity of 0.725 and specificity of 0.667. For the gestational sac diameter, the optimal cutoff was 3.25 cm, with a sensitivity of 0.700 and specificity of 0.903. For the myometrial thickness, the optimal cutoff was 2.05 mm, with a sensitivity of 0.950 and specificity of 0.806. In addition, the AUC was higher for the myometrial thickness than gestational sac diameter and days of amenorrhea (0.927>0.851>0.721) (Table 4).

4. Discussion

In the present study, we retrospectively analyzed 112 patients diagnosed with CSP and treated with minimally invasive surgery. We found that hysteroscopy and laparoscopy were safe and efficient minimally invasive treatment methods for CSP. Moreover, the days of amenorrhea, gestational sac diameter and myometrial thickness may be factors associated with the successful selection hysteroscopic or laparoscopic treatment of CSP, and these 3 factors played importment part in predictting the need for uterine scar defect repair under laparoscopy.

4.1. The efficacy and complications of minimally invasive surgery for CSP

To date, no standardized treatment for CSP has been established. The therapeutic options are medical, surgical, or a combination of both. In recent years, experience with the management of CSP has increased, and more patients with CSP are treated by minimally invasive surgery. However, the best choice of surgical approach, efficacy, and correlated risk factors remain inconclusive.

In our present study, hysteroscopy and laparoscopy were shown to be effective methods for the treatment of CSP. There were no cases of hysterectomy among the 112 patients. No serious complications occurred after the operation. This is consistent with a previous study. Kanat-Pektas et al[11] performed a systematic review to determine the efficacy and safety of different primary treatment modalities in the management of CSP, and their findings suggested that hysteroscopy and laparoscopic hysterotomy were safe and efficient surgical procedures that could be adopted as primary treatment modalities for CSP. Another systematic review study found that additional treatment was required in 17% of patients undergoing hysteroscopic resection of CSP and that the laparoscopic open excision and repair of the defect were associated with a high success rate (97.1%) and no major complications.[12] One recent study assessed the efficacy and safety of treatment options for CSP and revealed that the laparoscopic, vaginal, and open excision and repair of the defect were associated with high success rates (>96%) and a low risk of hemorrhage (≤4%).[13] It seems that laparoscopy is more effective than hysteroscopy in treating

Table 3

Results of multivariate logistic regression analysis.

	B	Wals	Sig.	OR	95% C.I.
Days of amenorrhea (d)	0.073	4.037	.044[*]	1.076	1.002−−1.156
Gestational sac diameter (cm)	0.810	9.689	.002[*]	2.249	1.350−3.746
β-hCG level (IU/L)	0.000	1.067	.302	1.000	1.000−1.000
Myometrial thickness (mm)	−3.251	14.825	.000[*]	0.039	0.007−0.203
Fetal heartbeat	0.436	0.377	.539	1.547	0.385−6.225

[*] *P*<.05.
95% CI = 95% confidence interval, OR = odds ratio.

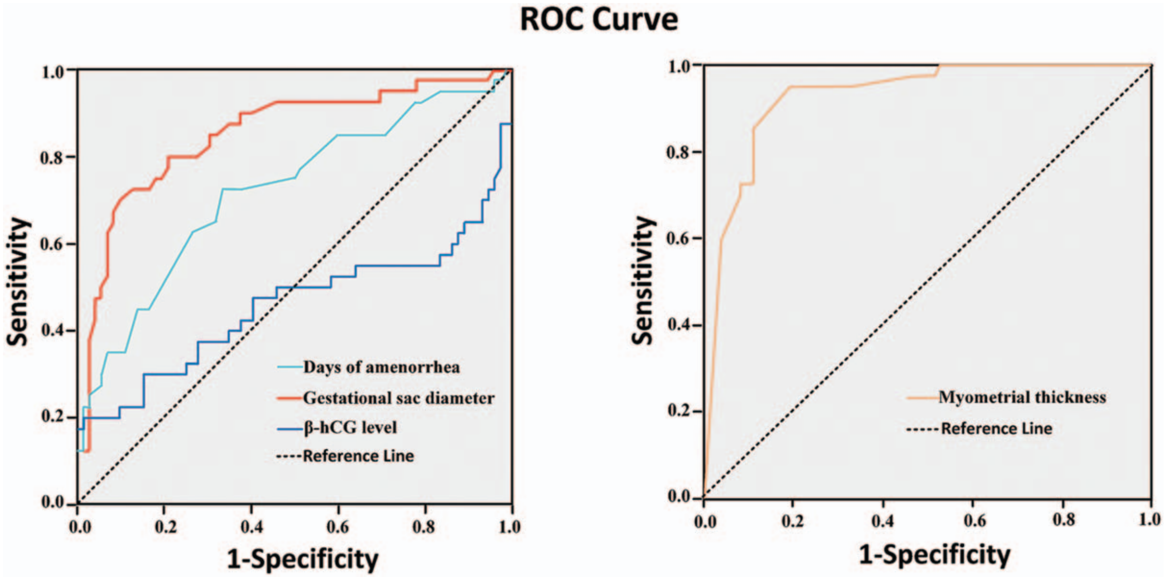

Figure 2. ROC curve analysis was used to assess risk factors that could predict laparoscopic scar repair, including days of amenorrhea, gestational sac diameter, β-hCG level, and myometrial thickness. The AUCs for the days of amenorrhea, gestational sac diameter, β-hCG level, and myometrial thickness were 0.721, 0.851, 0.459, and 0.927, respectively.

CSP, but if every CSP patient is treated with laparoscopy, there may be over treatment. This raises the issue of when to choose hysteroscopic surgery only and when to add laparoscopy. Appropriate preoperative diagnosis and evaluation, the identification of high-risk cases, and the application of reasonable judgment in accordance with the corresponding surgical indications form the basis for reducing complications.

4.2. The clinical characteristics of CSP patients treated by hysteroscopy or laparoscopy

Studies have suggested that the patients age at pregnancy, gestational age, β-hCG level, gestational sac or CSP mass size, myometrial thickness, and peritrophoblastic perfusion were independent risk factors for CSP.[14,15] Are the above risk factors also risk factors of minimally invasive surgery for CSP? Which factors are associated with successful selection for hysteroscopic or laparoscopic treatment of CSP? In the past, we also speculated that the number of pregnancies, number of cesarean sections, number of induced abortions, and time from last cesarean section were all related to the choice of surgical methods for CSP.

In order to solve the problem, we compared the clinical characteristics of patients who were successfully treated with hysteroscopy alone with those who needed laparoscopy to repair scar defects. Our results showed that there were no significant differences in age, time from the last cesarean, number of pregnancies, number of cesarean sections, number of induced abortions or β-hCG level between the 2 groups. However, there were significant differences between the 2 groups in the number of days of amenorrhea and gestational sac diameter (Table 1). In addition, there were significantly more days of amenorrhea and a larger gestational sac diameter in the laparoscopic repair group than in the hysteroscopic resection group. This may suggest that the earlier the CSP is treated, the simpler the operation, while the later the treatment is, the more complex the operation. Our results suggest that CSP should be treated as early as possible. Some gynecologists believe that the β-hCG level and fetal heartbeat are also influential factors in the treatment of CSP. However, in our study there were no significant differences in these 2 clinical variables between the hysteroscopic resection group and the laparoscopic repair group. In contrast, the difference in myometrial thickness between the 2 treatment groups was statistically significant.

These results suggested that days of amenorrhea, gestational sac diameter, and myometrial thickness might be factors associated with successful selection of minimally invasive surgery for CSP.

4.3. The risk factors for CSP treated by minimally invasive surgery: when does a uterine scar defect need to be repaired?

Logistic regression analysis was further used to confirm the risk factors associated with the laparoscopic repair of uterine scars.

Table 4

Cutoff values of the risk factors which could predict laparoscopic scar repair.

Risk factors	Cutoff	Sensitivity	Specificity	AUC	*P* value	95% CI
Days of amenorrhea (d)	52.50	0.725	0.667	0.721	.000*	0.618–0.823
Gestational sac diameter (cm)	3.25	0.700	0.903	0.851	.000*	0.771–0.930
β-hCG level (IU/L)	93857.50	0.200	0.986	0.459	.468	0.329–0.588
Myometrial thickness (mm)	2.05	0.950	0.806	0.927	.000*	0.878–0.976

* $P < .05$.
95% CI = 95% confidence interval.

The results show that the days of amenorrhea, gestational sac diameter, and myometrial thickness are independent risk factors, and these 3 factors are closely related to the choice of surgical method. The days of amenorrhea and gestational sac diameter are positively correlated with the severity of CSP. In contrast, the myometrial thickness is negatively correlated with the severity of CSP. This means that more amenorrhea days, a larger gestational sac diameter, and a thinner myometrial layer all indicate a higher risk of CSP.

In recent years, there have been many studies involving CSP risk factors. One study investigated the risk factors associated with excessive intra-operative hemorrhage during an evacuation operation and found that gestational age, β-hCG level, size of the gestational sac, thickness of the myometrial layer and presence of peritrophoblastic perfusion might be associated with excessive intra-operative hemorrhage during the suction evacuation of CSP.[15] Another study found that the number of previous cesareans, the myometrial thickness, and the risk class were specific significant risk factors in complications occurrence.[16] One study conducted by Yan Ma also found that both the menolipsis time and maximum diameter can be used to predict the risk of intraoperative bleeding for CSP.[17] However, there are few reports about the risk factors of minimally invasive surgery for CSP so far. Our study identified gestational sac diameter and myometrial thickness as risk factors for hysteroscopic or laparoscopic treatment of CSP, and explored the predictors of the need for uterine scar defect repair.

When does a uterine scar defect need to be repaired? To avoid overtreatment and provide appropriate surgical treatment, our study further screened for factors associated with defect repair. ROC curve analysis found that the days of amenorrhea, gestational sac diameter, and myometrial thickness were closely related to the repair of the uterine defect. ROC analysis further showed that the optimal cutoff values for the days of amenorrhea, gestational sac diameter, and myometrial thickness were 52.5 days, 3.25 cm, and 2.05 mm, respectively. This means that if the number of days of amenorrhea days is greater than 52.5 days, the gestational sac diameter is more than 3.25 cm, and the myometrial thickness is less than 2.05 mm, then in addition to curettage and hysteroscopy, laparoscopic repair of the uterine defect may be necessary.

4.4. The limitations of our study

The main limitations of the present study were as follows: First, this was a retrospective study. Because of insufficient information, such as data on peritrophoblastic perfusion, some clinical variables were not statistically analyzed. Second, there was a lack of long-term follow-up data, such as the outcome of the next pregnancy and the probability of recurrent CSP. We suggest that prospective, randomized, large-sample, multi-center randomized controlled trials (RCTs) are needed.

5. Conclusion

Hysteroscopy and laparoscopy are safe and efficient minimally invasive procedures that can be adopted as treatment methods for CSP. The days of amenorrhea, gestational sac diameter, and myometrial thickness may be factors associated with the successful selection hysteroscopic or laparoscopic treatment of CSP. For CSP patients with >52.50 days of amenorrhea, a gestational sac diameter >3.25 cm, and a myometrial thickness <2.05 mm, laparoscopic repair of the uterine defect may be necessary, in addition to curettage and hysteroscopy. These results provide a basis for the accurate evaluation of CSP patients before minimally invasive surgery and may reduce the risk of uncontrollable intraoperative bleeding, uterine scar perforation and a second surgery.

Author contributions

Conceptualization: Baoxia Cui.
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Writing – review & editing: Baoxia Cui.

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