

# Investigation and Analysis of Influencing Factors of Moderate to Severe Pain After Uterine Artery Embolization in Patients with Cesarean Scar Pregnancy

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**Objective:** To investigate the occurrence and influencing factors of moderate to severe pain in patients with cesarean scar pregnancy (CSP) after uterine artery embolization (UAE).

**Methods:** Ninety-eight patients with CSP who underwent UAE in gynecology department of the Fujian Medical University Union Hospital from January 2017 to December 2020 were enrolled, and the specialty data in patients were collected for pain assessment with the adoption of the numerical rating scale (NRS).

**Results:** Moderate to severe pain occurred in 36 patients after surgery, and the interquartile of time to the first onset of postoperative pain in patients was 3.04 (1.75, 7.40) hours. The number of pregnancies, number of miscarriages, human chorionic gonadotropin (HCG) before curettage, duration of medication before UAE, and hemorrhage after UAE were not significantly correlated with the occurrence of moderate to severe pain after UAE ( $P > 0.05$ ). The volume of gestational sac and days of gestation were responsible for the occurrence of moderate to severe pain after UAE ( $P < 0.05$ ), with the former being the main influencing factor, and these explained 8.3% of the total variance.

**Conclusion:** Moderate to severe pain occurred commonly in patients with CSP undergoing UAE. In clinical care of patients with CSP who are going to undergo UAE, data concerning the volume of gestational sac and days of gestation should be considered for anticipatory pain assessment, and interventions should be implemented as early as possible to reduce the pain and improve the experience of care.

**Keywords:** cesarean scar pregnancy, uterine artery embolization, moderate to severe pain, research

## Introduction

In recent years, with the liberalization of the second-child policy in China, the cesarean delivery rate has been increasing, leading to a significant increase in the incidence of cesarean scar pregnancy (CSP).<sup>1</sup> CSP refers to a special type of ectopic pregnancy in which the fertilized egg implants in the uterine incision scar resulting from a previous cesarean delivery, but with a time-limited definition of early pregnancy.<sup>2</sup> CSP is one of the long-term complications of cesarean delivery.<sup>3</sup> Some literature also refers to this as “post-cesarean uterine scar pregnancy” or “scar pregnancy.”

The occurrence of CSP often causes massive vaginal hemorrhaging and uterine rupturing in the late stage, making it one of the more difficult abnormal pregnancies

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to manage clinically.<sup>4</sup> Moreover, because the embryo is implanted in the cesarean incision scar located in the lower uterine segment, the weak muscle wall tissue of the uterine scar area is easily penetrated during the growth and development of the fetal sac (implantation therein).<sup>5</sup> Coupled with the lack of contractility of the cesarean incision scar, the broken blood vessels in patients with CSP cannot be closed naturally during abortion or curettage, and fatal massive hemorrhaging may occur. It has been reported that uterine artery embolization (UAE) has less bleeding than other surgical treatments.<sup>6</sup>

Pain is one of the main factors of surgical stress, which can aggravate insulin resistance, delay patients' early postoperative activities, increase the incidence of postoperative complications, prolong hospital stay, and may develop into chronic pain and reduce patients' postoperative quality of life. Pain management is an important content of ERAS.<sup>7</sup> One of the main challenges of UAE is the management of postoperative pain,<sup>8</sup> which has an incidence of 92.7%, including 29.0% of severe pain,<sup>9</sup> and which is mainly correlated with vasospasm caused by repeated irritation of the vessel wall or prolonged stay in the vessel of catheters and guidewires.<sup>10</sup> Therefore, it is of great significance to be familiar with and master the factors of pain in patients undergoing UAE and properly foresee the implementation of intervention measures to improve the overall quality of patients during hospitalization and improve treatment satisfaction. UAE is widely adopted for patients with various gynecological and obstetric conditions, such as adenomyosis,<sup>11</sup> postpartum hemorrhage,<sup>12</sup> and CSP.<sup>13</sup>

Patients were placed in a flat position and routinely disinfected and covered with aseptic hole towels. After local anesthesia, the right femoral artery was punctured to place the catheter sheath, and the catheter was delivered and cannulated to the bilateral uterine arteries respectively. Then 50 mg of Methotrexate (MTX), gelatin sponge granules, and gelatin sponge strips were injected via the left and right uterine arteries and embolized to them for flow blockage. After bilateral UAE, the uterine capillaries are still open, and the blood supply to the uterus is maintained through the capillaries and the surrounding collateral vessels, thereby avoiding ischemic and necrotic uterus.<sup>14</sup>

UAE for the treatment of CSP is safe and reliable. The present study aims to investigate the occurrence of moderate to severe pain in patients with CSP after UAE in Fujian Medical University Union Hospital, and then to provide a reference for the purposeful implementation of

the necessary interventions on the influencing factors to reduce the pain, enhance the comfort of hospitalization, and improve the medical experience for patients.

## Materials and Methods

### Study Subjects

In the present study, a retrospective analysis was used to select 98 patients with a maximum age of 45 years, a minimum age of 21 years, and an average age of  $33.16 \pm 5.05$  years who experienced pain after UAE for CSP in the Fujian Medical University Union Hospital from January 2017 to December 2020 as the study population. The minimum gestation period was 35 days and the maximum was 96 days, with an average of  $51.73 \pm 11.50$  days.

The diagnostic criteria of CSP referred to the ultrasound diagnostic criteria of CSP first proposed by Godin et al<sup>15</sup> ① No evidence of intrauterine pregnancy; ② No evidence of pregnancy in the cervical canal; ③ Pregnancy sac visible in the anterior wall of the uterine isthmus; ④ Defective uterine muscle tissue between the gestational sac and the bladder; ⑤ Amenorrhea.

The inclusion criteria were as follows: ① Patients with CSP confirmed by ultrasound or magnetic resonance image (MRI); ② Patients with a previous history of cesarean section; ③ Patients with significantly elevated  $\beta$ -HCG, which was consistent with weeks of menopause.

The exclusion criteria were as follows: ① Patients with cervical pregnancy; ② Patients with intrauterine pregnancy; ③ Patients with previous UAE for CSP; ④ Patients with pain caused by other diseases at the time of admission.

### Study Methods

#### Specialty Data Collection

Specialty data that might affect patient pain were included as factors in the present investigation, including the number of pregnancies, the number of miscarriages, days of gestation, duration of medication before UAE, HCG before curettage, the volume of the gestational sac, and hemorrhage after UAE. The volume of the gestational sac referred to the first color ultrasound findings on admission, hemorrhage after UAE was estimated by weighing, and the remaining data were obtained from the medical records, laboratory test results, and medical prescriptions for the patient.

#### Evaluation Indicators

The numerical rating scale (NRS)<sup>16</sup> was adopted for the evaluation of patient pain after UAE. A scale of 0 to 10 was

used to represent different degrees of pain. The grading standards were as follows: 0 for no pain, 1 to 3 for mild pain, 4 to 6 for moderate pain, 7 to 9 for severe pain, and 10 for critical pain. The time of pain onset referred to the period between the end of the UAE and the onset of pain back on the ward.

## Statistic Analysis

The SPSS 23.0 software was adopted for data processing. Measurement data that satisfied the normal distribution were expressed as means and standard deviations, and those that failed to satisfy the normal distribution were expressed as medians. Countable data were expressed as percentages and number of cases, with the adoption of the  $\chi^2$  test. Multiple linear regression analysis was used, and those statistically significant indicators in the univariate analysis were introduced for further analysis of the independent factors influencing the development of moderate to severe pain after UAE in patients with CSP.  $P < 0.05$  was considered statistically significant.

## Results

1. The time and frequency of pain occurrence were analyzed in 36 patients with moderate to severe postoperative pain,

and the results showed that 25 patients (69.44%) had one occurrence of pain, 8 patients (22.22%) had two occurrences, and 3 patients (3.33%) had three or more occurrences. The time to the first onset of pain was calculated, and the results showed that the interquartile of the time to the first onset of pain in patients after surgery was 3.04 (1.75, 7.40) hours.

2. Univariate analysis of the occurrence of moderate to severe postoperative pain in patients with CSP undergoing UAE was conducted, and the results suggested that the number of pregnancies, number of miscarriages, HCG before curettage, duration of medication before UAE, and hemorrhage after UAE were not significantly correlated with the occurrence of moderate to severe pain after UAE ( $P > 0.05$ ). Both the volume of gestational sac and days of gestation were responsible for the occurrence of moderate to severe pain ( $P < 0.05$ ), as shown in Table 1.

3. Multivariate linear regression analysis was conducted with the nature of the pain as the dependent variable and the two statistically significant single factors in the univariate analysis as independent variables, ie, the volume of gestational sac and days of gestation. The results revealed that the volume of the gestational sac was the main influencing factor for the occurrence of

**Table 1** The Analysis of Factors Influencing Postoperative Pain in Patients with Cesarean Scar Pregnancy Who Received Uterine Artery Embolization (n=98)

Related Factors		Moderate to Severe Pain (n=36, %)	Mild Pain+No Pain (n=62, %)	$\chi^2$	P-value
The number of pregnancies	2	4 (11.1)	3 (4.8)	2.800	0.247
	3	6 (16.7)	18 (29.1)		
	>3	26 (72.2)	41 (66.1)		
The number of miscarriages	0	7 (19.4)	10 (16.1)	0.592	0.898
	1	14 (38.9)	24 (38.7)		
	2	9 (25.0)	14 (22.6)		
	>2	6 (16.7)	14 (22.6)		
The days of gestation	≤84	33 (91.7)	62 (100.0)	5.330	0.021
	>84	3 (8.3)	0		
The time of curettage after intervention (hours)	≤24	23 (63.9)	44 (71.0)	0.528	0.468
	>24, ≤48	13 (36.1)	18 (29.0)		
	>48	0	0		
The HCG before curettage (IU/mL)	≤50,000	16 (44.4)	36 (58.1)	1.696	0.193
	>50,000	20 (55.6)	26 (41.9)		
The volume of hemorrhage (mL)	≤100	35 (97.2)	58 (93.5)	0.635	0.426
	>100	1 (2.8)	4 (6.5)		
The volume of the gestational sac (cm <sup>3</sup> )	≤18	29 (80.6)	61 (98.4)	9.660	0.002
	>18	7 (19.4)	1 (1.6)		

moderate to severe pain after UAE ( $P < 0.05$ ), which explained 8.3% of the total variance, as shown in Table 2.

## Discussion

### Moderate to Severe Pain Was Common in Patients with CSP After UAE

For women who have had a cesarean section, a high level of caution should be exercised for the occurrence of CSP in a second pregnancy, and early intervention is necessary once the diagnosis is confirmed.<sup>17</sup>

The main principle of UAE for the treatment of CSP and postpartum hemorrhage<sup>3,18</sup> is the intravascular injection of embolic material to directly cut off the blood supply to the target area of the uterine artery, resulting in ischemic necrosis of the lesion or embryonic tissue. Intravascular infusion of MTX increases the local drug concentration and enhances the embryo-killing effect. It has been reported in the literature that there is also a correlation between pain after UAE and factors such as embolization material, level of embolization, type of disease, and drugs used during the embolization.<sup>19</sup>

Among the 98 patients investigated in the present study, 36 cases had moderate to severe pain, an incidence of 36.7%, similar to the incidence of 35.2% reported by Armstrong et al,<sup>20</sup> which suggests that moderate to severe pain commonly occurs in patients with CSP after UAE. Post-UAE pain is acute pain that may develop into chronic pain in approximately 10% to 50% of patients if not treated promptly.<sup>21</sup>

Results in the present study revealed that 25.55% of cases had experienced two or more onsets of moderate to severe

pain after UAE, and the time for the first occurrence of pain was around 3 hours. When patients returned to the ward after surgery, nursing staff should focus on the chief complaint of patients about 3 hours after surgery and timely intervention. Therefore, it was necessary to provide patients with effective and scientific pain care, ask them about the pain in a timely manner, communicate with them before the onset of pain, inform them about the operation of UAE, together with discussing the cause, nature, and location of the pain.

Patients should be instructed correctly to divert their attention, and learn self-suggestion, self-relaxation, and other methods to ensure they could cooperate with treatment with a positive attitude to improve the pain threshold, tolerance, and reduce the occurrence of chronic pain. In case of the occurrence of moderate to severe pain, patients should be treated with non-steroidal drugs as prescribed by the doctor, actively informed of the possible side effects, and the efficacy of the drugs should be observed. Patients should be advised to treat the pain correctly to relieve it and improve comfort. Based on the theory of accelerated rehabilitation surgery, bilateral lumbar block can be used for patients with high pain risk, which can not only effectively reduce pain, but also reduce the demand for analgesic drugs.<sup>22</sup> A prospective study report pointed out that injection of lidocaine into uterine artery can reduce the pain after UAE and promote the rehabilitation of patients.<sup>23</sup> Therefore, appropriate preventive treatment can be taken timely according to the needs of patients to reduce the postoperative pain.

**Table 2** Multivariate Linear Regression Analysis of the Factors Influencing Postoperative Pain in Patients with Cesarean Scar Pregnancy Who Received Uterine Artery Embolization

Independent Variable	Non Standardized Coefficient	Standardization Coefficient Beta	t-value	P-value	95% Confidence Interval		Adjusted R-Square value	F-value	P-value
					Lower Limit	Upper Limit			
Constant (quantity)	2.356		8.259	0	1.789	2.922	0.083	5.387	0.006
Gestational sac volume	-0.478	-0.271	-2.241	0.027	-0.901	-0.055			
The days of gestation	-0.200	-0.071	0.590	0.556	-0.873	0.473			

## The Volume of the Gestational Sac and Days of Gestation Were the Influencing Factors in the Development of Moderate to Severe Pain in Patients with CSP After UAE

The results in Table 1 show that there exists a strong correlation between the volume of the gestational sac, the days of gestation, and the development of moderate to severe postoperative pain in patients. The multivariate linear regression analysis in Table 2 demonstrates that the volume of the gestational sac was the main influencing factor for the development of moderate to severe pain ( $P < 0.05$ ). Since the isthmus of the uterus is thinner and less elastic due to previous scarring in patients with CSP, early intervention is needed to terminate the pregnancy once the gestational sac implants in this area, and there is always a risk of hemorrhage and uterine rupture as the gestational week increases.<sup>24</sup> In patients with CSP, the volume of the gestational sac increases as the gestational week increases, and the blood circulation and the load on the organism gradually increase, intensifying the postoperative pain even when treated with UAE. This was consistent with the results reported by Liang Ning.<sup>25</sup>

To reduce the occurrence of moderate to severe postoperative pain in patients with CSP who underwent UAE, medical staff should consider the volume of the gestational sac and choose the best time to provide treatment that could improve the postoperative comfort of the patients.

In summary, patients with CSP who underwent UAE were prone to develop moderate to severe postoperative pain. The incidence was 36.7%, 69.44% of whom had only one pain. The volume of the gestational sac and days of gestation were the main factors influencing the occurrence of moderate to severe pain, with the volume of the gestational sac being the main influencing factor. Three hours after embolization was the peak period for the occurrence of moderate to severe pain. However, there were some limitations in the present study. The thickness of the scar was not collected, other factors that might cause pain in patients were not considered, and whether the number of c-sections had an effect on pain was not collected, which could be included in future studies.

In clinical care of patients with CSP who were to receive UAE, pain evaluation should be assessed in advance, taking the volume of the gestational sac and the days of gestation into account. Interventions should be implemented early to reduce pain and improve the health care experience for patients.

## Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki (as was revised in 2013). The study was approved by Ethics Committee of the Fujian Medical University Union Hospital. Written informed consent was obtained from all participants.

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## Disclosure

The authors declare that they have no competing interests.

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