A prediction model for the efficacy of transvaginal repair in patients with cesarean scar diverticulum: An evidence-based proposal for patient selection

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Abstract

Objective: To establish a prediction model to help the doctor determine which patients are more suitable for transvaginal repair based on the prediction model. **Design:**All enrolled patients underwent CSD repair performed by a single team. All women in this study had a follow-up clinic visit at 6 months to record their menstruation and measure multiple parameters of the CSD by MRI. **Setting:**Retrospective study **Sample:** This study included 1015 women who underwent transvaginal repair of cesarean scar diverticulum (CSD) at Xinhua Hospital and Shanghai First Maternity & Infant Hospital between June 2014 and May 2021. **Main outcome measures:** CSD patients are categorized as having optimal healing when the menstruation duration is no more than 7 days and the thickness of residual myometrium(TRM) is no less than 5.39 mm after vaginal repair. The final nomogram is constructed to predict surgical outcomes based on pre- and postoperative variables. **Results:** The key factors determining optimal healing are the timing of cesarean section; menstrual cycle; CSD length, width, depth, and the myometrial layer thickness of the lower uterine segment. With the prediction model, scores are given to each parameter according to the statistics. Total scores range from 0 to 25 points with a cutoff point of 16.5. Predicted that transvaginal repair achieves optimal healing when a score greater than 16.5 points. Uterine position and preoperative TRM are the key factors affecting postoperative TRM. The width of the CSD and the thickness of the lower uterine segment are the key factors affecting postmenstrual abnormal uterine bleeding ($P<0.01$). **Conclusions:** We establish a prediction model system for the first time that may predict the repair effect of CSD and can potentially be useful in future clinical trials to determine which patients should be repaired or other treatment options.

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Abstract

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To establish a prediction model to help the doctor determine which patients are more suitable for transvaginal repair based on the prediction model.

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Main outcome measures:

CSD patients are categorized as having optimal healing when the menstruation duration is no more than 7 days and the thickness of residual myometrium(TRM) is no less than 5.39 mm after vaginal repair. The final nomogram is constructed to predict surgical outcomes based on pre- and postoperative variables.

Results:

The key factors determining optimal healing are the timing of cesarean section; menstrual cycle; CSD length, width, depth, and the myometrial layer thickness of the lower uterine segment. With the prediction model, scores are given to each parameter according to the statistics. Total scores range from 0 to 25 points with a cutoff point of 16.5. Predicted that transvaginal repair achieves optimal healing when a score greater than 16.5 points. Uterine position and preoperative TRM are the key factors affecting postoperative TRM. The width of the CSD and the thickness of the lower uterine segment are the key factors affecting postmenstrual abnormal uterine bleeding ($P<0.01$).

Conclusions:

We establish a prediction model system for the first time that may predict the repair effect of CSD and can potentially be useful in future clinical trials to determine which patients should be repaired or other treatment options.

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Keywords: Prediction model system, cesarean scar diverticulum, transvaginal repair, treatment options, reproductive function reconstruction

Introduction

In 1995, Morris first identified a poorly muscular healing scar on the uterine incision, now called the previous cesarean scar defect (CSD), of patients who developed postmenstrual abnormal uterine bleeding(PAUB) after a cesarean section (C-section) (Figure 1A-1C). The incidence of CSD ranges from 50% to 84% in random populations of women with a history of cesarean section1.

Because many scholars consider that reducing the rate of the cesarean section can reduce the occurrence of CSD, CSD has not received widespread attention. However, women with CSD suffer from a series of symptoms, all of which affect the patient's quality of life. PAUB can affect a couple's sex life and the couple's relationship. It can also cause genital tract inflammation, vulva pruritus, and chronic abdominal pain2,3. Additionally, with the implementation of China's three-child policy, women of childbearing age who have a history of C-section will face subsequent pregnancy, and research has shown that CSD size and the TRM are significantly correlated with subsequent infertility, it also significantly reduces the success rate of frozen embryo transfer4-5. It has also shows that CSD is associated with cesarean scar pregnancy, placenta previa with placenta accreta, and even uterine rupture6,7.

The treatment approaches for CSD are usually divided into durgs and surgery, but there are no treatment guidelines. Drugs mainly include oral contraceptives, which can improve the symptom of PAUB during medication, but it may relapse after stopping drugs8. Common surgical procedures can be broadly categorized as reconstructive surgery and surgery for improved PAUB symptoms. Reconstructive surgical techniques, such as laparoscopic(LP)and vaginal repair(VR), involve isthmocele resection and resuture. Surgery for improving PAUB symptoms, such as hysteroscopic electroresection (HP), HP involves the removal of the fibrous tissue flap from the bottom of the defect and cauterizes the remaining scar tissue by using a wire loop9-11. Hysteroscopic resection surgery can improve PAUB symptoms but will lead to thinning of the myometrial tissue around the CSD, increasing the risk of the subsequent pregnancy12. In patients with severe pelvic adhesions, attempt to repair the CSD through vaginal surgery may be difficult in entering the abdomen, leading to the risk of bladder injury or surgical failure. We use vaginal repair assisted by single-port laparoscopy to reduce the risk of bladder injury (Figure 1D, E, F). Therefore, a good preoperative evaluation can help to formulate a more suitable treatment to improve prognosis. It is particularly important to recognize that not all diverticula require surgery and that not all surgeries can improve the diverticulum.

Our surgical team has treated more than 1500 CSD patients from 17 provinces and cities across China, Australia, and the United States since 2013. More than 1200 cases of CSD through VR have been successfully carried out, and it is the largest CSD treatment cohort known nationally and internationally. Our previous study screened 607 women with a history of C-section by transvaginal ultrasound(TVS) and found that when the mean TRM is more than 5.39 mm, these women without PAUB symptoms (menstrual durations less than 7 days) 14. This TRM size is similar to that of Glavind's study, whose research shows the TRM of 5.8 mm will be helpful for symptom control post-operatively13. According to this result, we define a menstruation duration of no more than 7 days and a TRM of no less than 5.39 mm after vaginal repair as optimal healing.

Our previous studies indicated that CSD disappeared in 64.52% of CSD patients after VR and that 60.0% of patients reached [?]7 days of menstruation15. However, the factors affected healing were not defined, so a model for predicting the outcome of repair surgery is urgently needed. This study retrospectively analyzed 1015 cases of transvaginal repair of CSD to develop a prediction model for the first time. The findings of this study will be used to form an evidence-based proposal for patient selection.

Methods

Patient Cohort and Data Collection

A total of 1015 patients were initially enrolled, and 940 patients were involved in the final analysis. Patients enrolled between June 2014 and May 2017 underwent scar defect repair in Shanghai First Maternity & Infant Hospital, and those enrolled between May 2017 and May 2021 underwent repair in Xinhua Hospital (The enrolled subjects were not replicated with the previous articles published by our team). All VR surgeries were performed by a single doctor. Seventy-five patients were lost to follow-up at 3 or 6 months after CSD repair. According to the results of our previous studies, the scar stabilizes 3 months after CSD repair surgery, and there is no change after 6 months[16]. Therefore, we used MRI measurements of CSD at 6 months postoperative, in combination with a statistical analysis of age, uterine position, number of C-sections, the timing of cesarean section(selective or emergency operation), menstrual cycle, menstrual period and CSD size before and after repair surgery. According to the analysis results, the key factors determining the prognosis of diverticulum repair were identified, and the scoring model was established (eFigure 1 in the Supplement).

This study was approved by the Ethics Committee of Xinhua Hospital Affiliated with Shanghai Jiao Tong University School (XHEC-H-2018-002) of Medicine and Shanghai First Maternity & Infant Hospital affiliated with Tongji University (KS1512). All patients signed written informed consent to participate in this study.

Surgical Procedures

The surgical techniques are described in detail in our previous publication[15], and the most important steps of the procedure are summarized below.

At a distance of 0.5 cm below the site of the reflexed vesica-cervical area, an anterior incision was made from the 3 o'clock to the 9 o'clock position using an electric knife. After entry into the abdominal cavity and complete exposure of the cervix, the location of the uterine defect was determined, and the thickness of the lower uterine segment of the CSD could be gauged through contact with the surgeon's index finger and sounding. The CSD tissue was resected, the incision tissues were trimmed to healthy myometrium with dissecting scissors, and the incision was closed with a double layer of 1–0 absorbable interrupted sutures. All operations were performed by the same surgeon with extensive vaginal surgical experience.

Statistical Analysis

In the analyses, β coefficients and ORs are presented as estimates of effect, and the reported statistical significance levels were all two-sided, with statistical significance set at 0.05. Statistical analysis was conducted with R software (3.5.1; R Foundation for Statistical Computing) and SAS version 9.4 (SAS Institute Inc., Cary, NC).

A descriptive analysis of patients and a demographic comparison between the suboptimal healing group and the optimal healing group were performed. The distributions of the baseline characteristics of the patients are represented by the mean ± SD or as a number (n) with a percentage (%). Differences between groups were assessed as follows: t-test and ANOVA were used for continuous variables and multiple comparisons, and the $\chi 2$ test was used for categorical variables.

Multivariate linear regression was used to assess the association between CSD parameters and optimal healing, CSD parameters and menstrual improvement, and CSD parameters and TRM after adjustment for potential confounding variables.

These patients were randomly divided into two cohorts: a training cohort (634, 70%) and an internal validation cohort (306, 30%). After multivariable logistic regression analysis, clinical candidate predictors were applied to develop an individualized prediction model by using the training cohort. Forward and backward stepwise regression was applied by using the likelihood ratio test with Akaike's information criterion as the stopping rule. To provide a quantitative tool for prediction, we built nomograms based on multivariate logistic analysis of the training cohort. We selected the point that yielded the highest Youden's index (i.e., specificity + sensitivity - 1) on the receiver operating characteristic (ROC) curve of the training set as the optimal cutoff value and used it to calculate which score combination for every patient represented the sum of scores for each risk factor.

Calibration curves were plotted to assess the calibration of the nomogram using the Hosmer-Lemeshow test. To quantify the discrimination performance of the nomogram, Harrell's C-index was measured. The nomogram was subjected to bootstrapping validation (1,000 bootstrap resamples) to calculate a relatively corrected C-index. We also evaluated the nomogram using the area under the curve (AUC) of the ROC with a 95% confidence interval (95% CI). Internal validation was carried out using data from 306 patients. Decision curve analysis was performed to determine the clinical usefulness of the nomogram by quantifying the net benefits at different threshold probabilities.

Results

1. Patient characteristics

The characteristics of the patients are summarized in Table 1. The median age of the study patients was 33 years (range: 22 to 44 years). The median duration of menstruation before and after C-sections were 6.13±1.10 and 13.37±3.64 days, respectively. The median TRM measured via MRI before VR was 2.73 ± 1.82 mm. The measurement data, namely, length, width, and depth of the CSD via MRI, were 8.96±3.95 mm, 14.33±8.12 mm, and 6.40±2.96 mm, respectively (eTable 1 in the Supplement). Of these women, 33.19% (312/940) achieved optimal healing(TRM[?]5.39mm and durations of menstruation [?]7 days).

2. Association between optimal healing and the clinical characteristics of the patients or the measurement data of CSD by univariate analysis.

The thickness of the muscular layer of the lower segment of the uterus in the optimal healing group was significantly lower than that in the suboptimal healing(TRM¡5.39mm or durations of menstruation ¿7 days) group (20.63+-25.23 vs. 32.15+-28.27, $p < 0.05$). The width of the CSD via MRI of the optimal group was 13.39+-7.98 mm, which was significantly lower than that of the suboptimal healing group (14.80+-8.15 mm) (eTable 2 in the Supplement).

3. Association between menstruation duration or TRM and the clinical characteristics of the patients and the measurement data of CSD by univariate analysis.

Interestingly, we find that the thickness of the muscular layer of the lower segment of the uterus in the menstruation [?]7 days group is significantly lower than that in the menstruation >7 days group (22.67+-26.88 vs. 31.77+-27.84, $p < 0.05$). The width of the CSD via MRI of the menstruation [?] 7 days group is 13.27+-8.14 mm, which is significantly lower than that of the menstruation>7 days group (14.99+-8.04 mm). 47.61% (409/859) of the patients from the TRM[?]5.39 mm group has an anterior position of the uterus and only 23.46% (19/81) of patients from the TRM<5.39 mm group had an anterior position of the uterus. When TRM is[?]5.39 in postoperative, the TRM is thicker in preoperative (2.79+-1.87 vs. 2.16+-0.93, $p < 0.05$) (eTable 3 in the

Supplement).

4. Multivariable linear regression models for the association of CSD parameters and optimal healing/menstrual improvement/TRM

The multiple linear regression results based on the entire sample are presented in

Table 1. There is a significant negative association between CSD width and myometrial

layer thickness of the lower uterine segment in the optimal healing group. Additionally,

there is a significant positive association between the length and depth of the CSD in

the optimal healing group. However, there is no significant association between CSD

width and TRM improvement; however, a significant positive association between

CSD depth and TRM is observed, and the uterine position is significantly associated with TRM improvement. Even so, the width of the CSD is significantly associated with menstrual improvement. Additionally, there is a significant positive association

between menstrual cycle duration and CSD length or depth in favor of menstrual

improvement.

5. A prediction model for the optimal healing of CSD

Multivariable logistic regression analysis is used to assess the individualized

prediction model, and the final nomogram bases on logistic regression analysis in the

training cohort is built. Both the thickness and width of the CSD via MRI are negatively associated withoptimal healing ($p<0.05$). CSD depth,CSD length,the menstrual cycle after cesarean section, and the timing of surgery in the cesarean section was positively associated with optimal healing ($p < 0.05$). The model derived from the estimated β-regression coefficients of twelve variables is developed as a nomogram (Figure 2A, eTable 4 in the Supplement). The calibration curve of the nomogram shows adequate agreement between observation and prediction in the training cohort and internal validation cohort (Figure 2C-2E). The Hosmer-Lemeshow test returned a nonsignificant value ($P = 0.419$ in the training cohort, $P = 0.963$ in the internal validation cohort). This result represent no departure from a perfect fit. The C-index for the prediction model is 0.790 for the training cohort. The calibration curve depicted the calibration of the model in terms of the agreement between the observed outcome of optimal healing and the predicted risk of optimal healing. Furthermore, the prediction nomogram yielded a C-index of 0.823 according to internal validation of the nomogram. The decision curve analysis for the nomogram is presented in Figure2B.The net benefit is comparable within this range based on the nomogram. With the nomogram model, we can provide patient treatment recommendations.

6. The predictive score model

The predictive score of each predictor is assigned by dividing the beta coefficient from the logistic regression model by 0.20 (eTable 5 in the Supplement). Thickness is given the highest score of 9.0, and CSD length is given the lowest score of 0.5. The menstrual cycle after C-sections is given a score of 3.0. CSD width is given a score of 6.0, and the timing of surgery in the cesarean section is given a score of 4.0. Total scores range from 0 to 25 points with a cutoff point of 16.5 (Table 2). When the score [?]16.5, the patient can be predicted to achieve optimal healing. This suggests that we can improve the surgical protocol or change the treatment plan if the score is ¡16.5.

Discussion

In our previous study, we published a nomogram for the preoperative prediction of surgical treatment efficacy for CSD. We referred to Glavind's studies that defined the class A healing group as having a TRM no less than 5.8 mm after vaginal repair[13]. Only 167 patients were included in the training cohort. Due to the limited number of cases, previous research only identified risk factors for failure to achieve class A healing[17]. Our study has improved the shortcomings and built the prediction model system.

Our research shows the timing of C-sections, the menstrual cycle, and the length, width, depth, and thickness of the lower uterine segment of the CSD can predict whether CSD repair surgery can achieve optimal healing. The results are similar to Liu's research, which shows that the number of C-sections, a trial of labor (elective or urgent C-sections), C-section interval, and uterine position were independent risk factors for CSD[18]. Interestingly, we find that elective C-section surgery is a risk factor for CSD, but they respond better to repair surgery when CSD occurs. We think that the reason for this may be the trial process of myometrial stretching and contraction is a protective factor for wound healing; however, there may be potential biological mechanisms that lead to suboptimal healing in patients who develop CSD after the trial process such that conditions are not conducive to healing of the incision when the CSD is repaired.

We also find that when the menstrual cycle is greater than 26 days, optimal healing is more easily achieved after surgery. This means that patients with long menstrual cycles (>26 days) have better surgical outcomes, which is consistent with our previous finding that oral contraceptives or GnRHa can improve menstrual conditions. We think GnRHa can prolong the menstrual cycle or reduce the menstrual volume to a certain extent, so patients with a long menstrual cycle can heal relatively well after surgery. It is possible that chronic inflammation caused by menstrual stimulation can hurt wound healing. Additionally, our results show that a CSD width of greater than 13.8 mm will influence surgical efficacy, particularly the improvement of postoperative menstruation. Previous case studies found that CSD repair with a CSD width [?]18.85 mm had a poor prognosis[15], which was consistent with the index in our prediction model.

On the other hand, we find that not all patients sought to achieve optimal healing by treatment. Some patients may only expect to improve menstrual conditions, while others will expect to increase the TRM to reduce the risk of pregnancy but do not care much about PAUB. Therefore, we also discuss the factors that can improve menstruation or increase TRM merely. The results show that the posterior uterus or TRM [?]2.79 mm is the independent correlation factor for TRM improvement. However, CSD width [?]13.27 mm or the thickness of the lower uterine segment [?]22.67 mm preoperatively can predict PAUB symptom improvement.

Many studies have confirmed that the presence of a CSD might increase the risk of subsequent cesarean scar pregnancy. One study showed that repair surgery both reduced the incidence of cesarean scar pregnancy and increased the number of live deliveries[19]. This finding reflects complete correction of the CSD by suturing, which strengthens the uterine wall and promotes either complete or partial healing of the uterine scar after surgery. Therefore, for patients with subsequent pregnancy requirements, the recommendation is to evaluate whether optimal healing can be achieved or whether TRM can be improved after surgery by a prediction model.

We hope to use the prediction model to enable more appropriate treatment options for patients with CSD. We recommend vaginal repair surgery as the first choice when the score is [?] 16.5 because this approach is less damage, lower cost, and a shorter hospital stay. When the score is less than 16.5 suggests that the patient will have difficulty achieving optimal healing through vaginal repair. In this case, when the patient has no desire for a subsequent pregnancy, hysteroscopic resection surgery can be recommended. Hysteroscopic resection is considered the least invasive among the possible operations; however, hysteroscopy may have the potential risk for decreased resistance of the residual myometrial tissue at the level of the repair and may lead to uterine rupture during subsequent pregnancy[20-22]. Therefore, hysteroscopic surgery is not recommended for patients with pregnancy intentions. Additionally, the TRM should not be less than 3 mm, given the anticipated risk of perforation or bladder injuries[23-24]. For patients with a score¡16.5 without pregnancy requirements, younger patients can be recommended to use oral contraceptives or an intrauterine device (IUD). The levonorgestrel intrauterine system may have a role in the safe and effective management of PAUB in patients with CSD. The study shows that after 1 year of treatment, 22 patients (78.6%) reported an improvement in symptoms with the levonorgestrel intrauterine system. The mean duration of menstruation is 18 and 5 days before and after treatment, respectively[25]. This is a good choice for patients who just want to improve their menstruation.

If the score is less than 16.5 and the preoperative residual muscle layer is less than 2.16 mm, but the patient has a strong desire to become pregnant, she should be fully informed of the possibility of a poor outcome before surgery. If the patient has a history of multiple operations and abdominal adhesions are considered preoperatively, pelvic adhesion decomposition can be performed by a single-port laparoscope that can be released to restore the normal anatomical structure, and then vaginal surgery can be performed to avoid excessive anterior or posterior flexion of the uterus, which may be helpful to improve postoperative recovery. Adding oral contraceptives or GnRHa to prolong menstruation after surgery may also help to improve the prognosis. We have demonstrated the effectiveness of GnRHa in another study, and the article has been submitted (data unpublished, under review).

Our study is the first prediction model performed in China to assess the surgical efficacy of CSD. The major strength of our study is determining which patients with CSD should be repaired or other treatment options according to the score. Several limitations should be considered when interpreting the results of this study. First, this is a retrospective study, which has inherent biases. Second, this study comes from a single institution, and the nature of the database is a strength. Although consistency in surgical techniques is ensured, there are limitations in patient selection. Third, alternative treatment options and their effectiveness should be further validated. In addition, our study requires an external validation cohort to make the results more convincing, and the inclusion of such information is planned in our future studies.

Conclusions

In conclusion, the use of the CSD scoring prediction model may be important to evaluate the potential outcome of a patient with CSD, and doctors can estimate the surgical efficacy for individual patients. Optimal healing is easier to achieve when the score is [?] 16.5. In turn, patients should be considered for other treatment plans, such as oral contraceptives, an IUD, or surgery combined with drug treatment. More importantly, it will be helpful to eliminate factors that may cause poor healing rather than performing surgery immediately.

Author Contributions:

Xipeng wang ,Jun Zhang and Xingchen Zhou had full access to all of the data in the

study and take responsibility for the integrity of the data and accuracy of the data

analysis.

Study concept and design: Xipeng Wang and Jun Zhang.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Xingchen Zhou and Zhenyan Gao.

Critical revision of the manuscript for important intellectual content: Xipeng Wang

and Jun Zhang.

Statistical analysis: Zhenyan Gao

Obtained funding: Xipeng Wang

Administrative, technical, or material support: Huihui Chen; Yizhi Wang and Yujia

Yin

Study supervision: Xipeng Wang

Conflict of interest: The authors report no conflict of interest.

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in other randomized trials. Data regarding any of the subjects in the study has not been previously published unless specified. Data will be made available to the editors of the journal for review or query upon request.

References

1. Tang X, Wang J, Du Y, et al. Caesarean scar defect: Risk factors and comparison of evaluation efficacy between transvaginal sonography and magnetic resonance imaging. Eur J Obstet Gynecol Reprod Biol 2019;242:1-6. 2. Tower AM, Frishman GN. Cesarean scar defects: an underrecognized cause of abnormal uterine bleeding and other gynecologic complications. J Minim Invasive Gynecol 2013;20:562–72. 3. Tulandi T, Cohen A. Emerging manifestations of cesarean scar defect in reproductive-aged women. J Minim Invasive Gynecol 2016;23:893–902. 4. Beilei Bi, Shanshan Gao, Fan Ruan. Analysis on the clinical association of uterine scar diverticulum with subsequent infertility in patients underwent cesarean sections. Medicine 2021; 100:41 5.Ling Huang , Sunxing Huang, Yuan Yuan. Reduced pregnancy and live birth rates after in vitro fertilization in women with cesarean section scar diverticulum: A retrospective cohort study. Japan

Society of Obstetrics and Gynecology 2022;1: 146–154. 6. Cheng XY, Cheng L, Li WJ, et al. The effect of surgery on subsequent pregnancy outcomes among patients with cesarean scar diverticulum. Int J Gynecol Obstet 2018;141:212–6. 7. Zhou D, Wu F, Zhang Q, et al. Clinical outcomes of hysteroscopy-assisted transvaginal repair of cesarean scar defect. J Obstet Gynaecol Res 2020; 46 (2):279-285. 8. Setubal A, Alves J, Osorio F, et al. Treatment for uterine isthmocele, a pouchlike defect at the site of a cesarean section scar. J Minim Invasive Gynecol 2018;25(1):38–46. 9. Vervoort A, van der Voet LF, Hehenkamp W, et al.Hysteroscopic resection of a uterine caesarean scar defect (niche) in women with postmenstrual spotting: a randomised controlled trial. BJOG 2018;125(3):326–334. 10. Zhao W, Liu G, Yang Q, et al. A new method using a Foley Catheter to locate the diverticulum in laparoscopic repair of uterine cesarean scar defects. Eur J Obstet Gynecol Reprod Biol 2018;223:14–17. 11. Chen H, Wang H, Zhou J, et al. Vaginal repair of cesarean section scar diverticula diagnosed in non-pregnant women. J Minim Invasive Gynecol 2019;26(3):526–534. 12. Lagana AS, Pacheco LA, Tinelli A, et al. Optimal timing and recommended route of delivery after hysteroscopic management of isthmocele? A consensus statement from the global congress on the hysteroscopy scientific committee. J Minim Invasive Gynecol 2018;25(4):558 13. Glavind J, Madsen LD, Uldbjerg N, Dueholm M. Ultrasound evaluation of cesarean scar after single- and double-layer uterotomy closure: a cohort study. Ultrasound Obst Gyn 2013;42:207-12 14. Xingchen Zhou, Tao Zhang, Huayuan Qiao, et al.Evaluation of uterine scar healing by transvaginal ultrasound in 607 nonpregnant women with a history of cesarean section. BMC Women's Health 2021; 21:199 15. Zhou X, Yao M, Zhou J, Tan W, Wang H, Wang X. Defect width: the prognostic index for the vaginal repair of cesarean section diverticula. Arch Gynecol Obstet 2017;295(3):623-630. 16. Jieru Zhou, Min Yao,Husheng Wang, et al. Vaginal repair of cesarean section scar diverticula that resulted in improved postoperative menstruation. The Journal of Minimally Invasive Gynecology 2016;06:013 17. Yizhi Wang, Qinyi Zhu, Feikai Lin, et al. Development and internal validation of a Nomogram for preoperative prediction of surgical treatment effect on cesarean section diverticulum. BMC Women's Health 2019; 19:136 18. Songjun Liu, Linlin Chen, Guang Zhu, et al.Analysis of risk factors for cesarean scar Diverticulum. Medicine 2021, 100:17 19. Xian Ying Cheng, Li Cheng, Wen Juan Li, et al. The effect of surgery on subsequent pregnancy outcomes among patients with cesarean scar diverticulum. Int J Gynecol Obstet 2018; 141: 212–216 20. Feng YL, Li MX, Liang XQ, Li XM. Hysteroscopic treatment of postcesarean scar defect. J Minim Invasive Gynecol 2012;19(4):498–502. 21. Gubbini G, Centini G, Nascetti D, et al. Surgical hysteroscopic treatment of cesarean-induced isthmocele in restoring fertility: prospective study. J Minim Invasive Gynecol 2011;18(2):234–7 22. Api M, Boza A, Gorgen H, Api O. Should cesarean scar defect be treated laparoscopically? a case report and review of the literature. J Minim Invasive Gynecol 2015;22:1145–52. 23. Hui Shi, Jingyan He, Yunhe Gao, et al.Treatment of C-section diverticula with hysteroscopic resection in women without childbearing intention: a retrospective cohort study. BMC Women's Health 2020; 20:75 24. Abacjew-Chmylko A, Wydra DG, Olszewska H. Hysteroscopy in the treatment of uterine cesarean section scar diverticulum: a systematic review. Adv Med Sci 2017;62(2):230–239. 25. Ou YC, Chen YY, Lan KC, et al. Levonorgestrel intrauterine system for the treatment of intermenstrual spotting in patients with previous cesarean delivery scar defect. J Obstet Gynaecol Res 2022; 48(1)

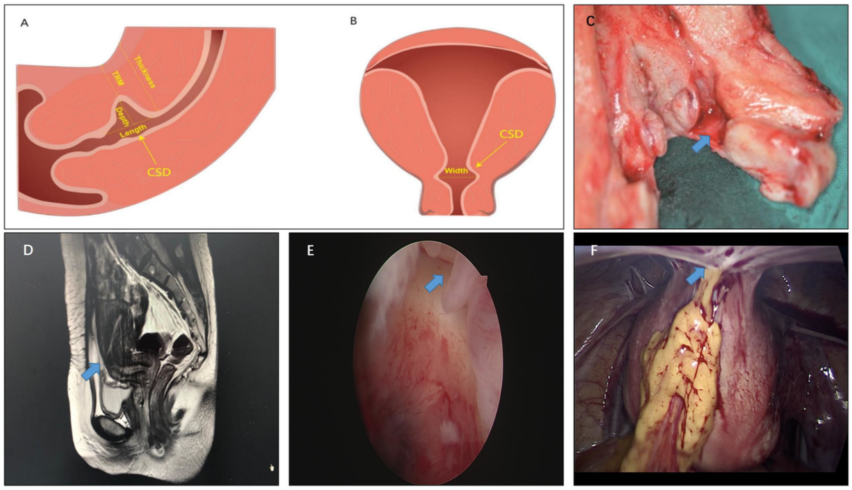
Figure legends

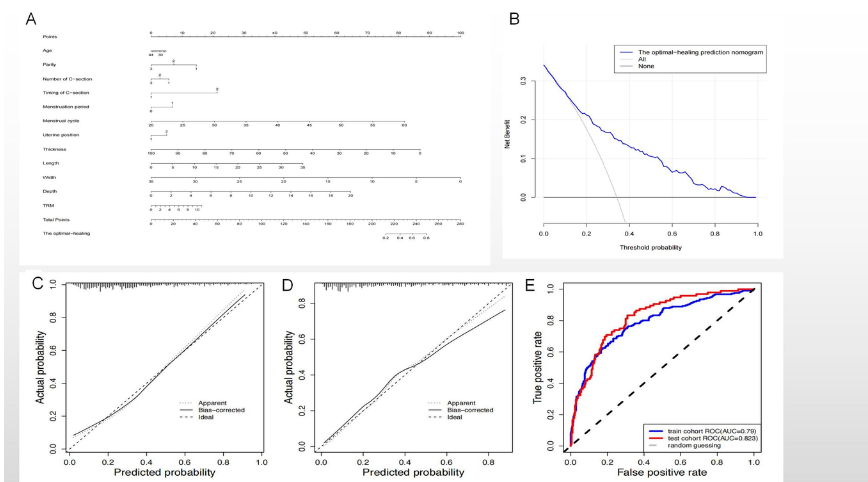
Figure 1: Simulated diagram of CSD: A: Depth, length, TRM, and thickness of the lower uterine segment (thickness) of the CSD; B: CSD width; C: Uterus opened to show the CSD; D-F: MRI, hysteroscopy and single-port laparoscopy in a representative CSD patient. The blue arrow indicates the CSD site. F: Severe pelvic adhesions were observed, and the uterus was completely adhered to the abdomen, changing the normal anatomy.

Figure 2: A: Nomogram for the prediction of optimal healing. The different variable values correspond to a point at the bottom of the figure, and the sum of the points for all the variables obtaining a total point corresponds to the probability of optimal healing at the bottom of the figure. **B:** Decision curves of the prediction model. The y-axis represents the net benefit. The blue line represents the nomogram, and the gray line represents the assumption that all CSD patients had optimal healing. The black line represents the assumption that no CSD patients had optimal healing. The higher the decision curve of the model is,

the larger the net benefit. **C-E:** Performance of the nomogram. Calibration curves of the nomogram in the training cohort (C) and internal validation cohort (D). ROC curves in the training and internal validation cohorts (E).

Supplemental figure 1: Flow chart of the study





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