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Original Research

Predictive Nomogram for Clinical Pregnancy After *In Vitro* Fertilization/Intracytoplasmic Sperm Injection in Patients With Endometriosis: A Retrospective Cohort Study

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Abstract

Background: The aim of this study was to identify factors influencing the clinical pregnancy rate (CPR) in patients with endometriosis undergoing *in vitro* fertilization (IVF)/intracytoplasmic sperm injection (ICSI), and to construct a corresponding nomogram for prediction of pregnancy probability. **Methods:** This study analyzed clinical data from 504 patients with endometriosis who underwent IVF/ICSI treatment. Clinical pregnancy was used as the outcome variable, and univariate followed by multivariate logistic regression was performed to identify predictors and develop a prediction model. Subgroup analysis was conducted according to the results of the multivariate logistic regression and restricted cubic spline (RCS) analyses. Baseline characteristics between subgroups were balanced using propensity score matching. **Results:** Univariate and multivariate logistic regression analyses indicated that the controlled ovarian stimulation (COS) protocol (odds ratio [OR] = 1.646, 95% confidence interval [CI]: 1.055–2.570), frozen embryo transfer (FET) (OR = 1.823, 95% CI: 1.149–2.892), and patient age (OR = 0.946, 95% CI: 0.896–0.999) were independent factors associated with CPR in patients with endometriosis undergoing IVF/ICSI. The constructed prediction model demonstrated moderate predictive ability for clinical pregnancy outcomes, with area under the receiver operating characteristic (ROC) curve (AUC) values of 0.613 (95% CI: 0.553–0.673) and 0.631 (95% CI: 0.544–0.719) in the training and validation sets, respectively. RCS analysis identified three inflection points for age at 27, 31, and 37 years. Subgroup analysis further revealed that patients in the downregulation protocol and younger age groups had significantly higher pregnancy rates compared with their respective control groups. **Conclusions:** This study developed a predictive model to assist clinicians in estimating the probability of clinical pregnancy in the IVF/ICSI cycle among patients with endometriosis. For patients with sufficient time and adequate financial resources, FET is recommended to optimize pregnancy rates. For those at low risk of ovarian hyperstimulation syndrome (OHSS) and with good ovarian reserve, the use of downregulation protocols should be considered to improve endometrial receptivity. Additionally, patients with a low likelihood of natural conception are advised to pursue IVF treatment at an earlier age to mitigate the adverse effects of advanced maternal age.

Keywords: endometriosis; IVF/ICSI; clinical pregnancy rate; nomogram; assisted reproductive technology

1. Introduction

Endometriosis is a heterogeneous, hormone-dependent disease characterized by the presence and growth of endometrial tissue, including both stroma and glands, outside the uterine cavity, leading to adhesion formation and chronic inflammatory responses [1]. It affects 35% to 50% of women who experience infertility or chronic pelvic pain [2]. As a systemic inflammatory disease, endometriosis affects multiple aspects of fertility [3]. Compared with healthy individuals, patients with ovarian endometrioma (OMA) show lower anti-Müllerian hormone (AMH) levels and reduced antral follicle counts (AFC) [4]. Deep infiltrating endometriosis (DIE) induces chronic pelvic inflammation, leading to fibrosis, adhesion formation, and distortion of normal pelvic anatomy [5]. Together, these multifactorial mechanisms act synergistically to reduce female fertility and contribute to infertility.

Assisted reproductive technology (ART) is a core treatment for infertility associated with endometriosis. However, due to heterogeneity in study designs, the influence of endometriosis on IVF/ICSI outcomes remains unclear [6]. A meta-analysis by Hamdan et al. [7], which included 36 studies on ART outcomes in endometriosis between 1980 and 2014, showed that patients with endometriosis undergoing *in vitro* fertilization (IVF)/intracytoplasmic sperm injection (ICSI) had live birth rates (LBRs) similar to those without endometriosis, but significantly lower clinical pregnancy rates (CPRs) and fewer oocytes retrieved per cycle. Another meta-analysis by Yang et al. [8], including 1039 patients with OMA, found that although these patients yielded fewer oocytes and embryos, their CPRs and LBRs did not differ significantly from those without OMAs. In contrast, a study by Alson et al. [9] compared LBRs among 1040 women diagnosed with endometriosis by transvaginal Doppler ultra-

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sound undergoing their first IVF/ICSI cycle and reported a 37% reduction in LBR in patients with endometriosis compared to non-endometriosis controls. OMA appears to significantly reduce LBR among patients with endometriosis undergoing IVF/ICSI, whereas DIE does not show a similar effect. Several scoring systems, such as the revised American Society for Reproductive Medicine (rASRM) score and the Endometriosis Fertility Index (EFI), are currently used to evaluate the severity of endometriosis. However, their association with IVF outcomes remains unclear. As such, this study aims to construct a clinically applicable nomogram to predict the likelihood of clinical pregnancy after IVF/ICSI treatment in women diagnosed with endometriosis, thereby facilitating individualized treatment planning and clinical management.

2. Materials and Methods

2.1 Patients and Data Collection

This retrospective cohort study was approved by the Ethics Committee of Shenzhen People's Hospital (Approval No. LL-KY-2024114-02). Ultimately, 504 patients with endometriosis who had undergone IVF/ICSI at the Reproductive Medicine Center between January 2016 and June 2024 were included. The collected clinical data comprised the following categories: (1) general patient characteristics: age, body mass index (BMI), AFC, AMH level, basal follicle-stimulating hormone (bFSH) level, basal luteinizing hormone (bLH) level, and basal estradiol (bE2) level; (2) ART parameters: controlled ovarian stimulation protocol and type of embryo transfer, classified as either fresh embryo transfer (ET) or frozen embryo transfer (FET); and (3) pregnancy outcome, defined as the confirmation of fetal cardiac activity by color Doppler ultrasound.

The inclusion criteria were: (1) patients diagnosed with endometriosis, including ovarian endometriosis confirmed by ultrasonography, severe dysmenorrhea with ultrasonographic findings suggestive of DIE, or surgical pathology confirming endometriosis; and (2) patients experiencing regular unprotected sexual intercourse for ≥1 year without conception. The exclusion criteria were as follows: (1) concurrent adenomyosis; (2) chromosomal abnormalities in either spouse; (3) comorbid autoimmune or rheumatic diseases; and (4) a history of ovarian surgery performed for other conditions. All the patients provided written informed consent. The study flowchart is shown in Fig. 1.

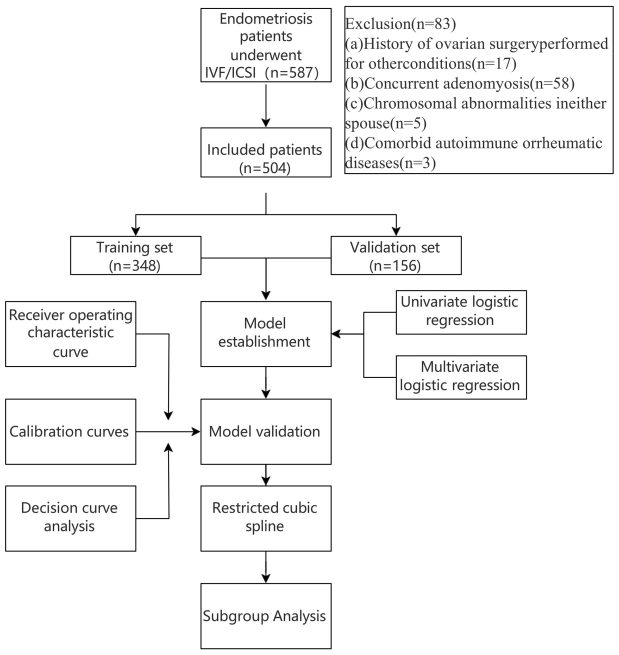


Fig. 1. Study flowchart. IVF/ICSI, *in vitro* fertilization/intracytoplasmic sperm injection.

2.2 ART Treatment Procedure

Controlled ovarian stimulation protocols were classified into two categories based on the use of pituitary downregulation: (1) downregulation protocols, and (2) non-downregulation protocols. Downregulation protocols included the long luteal phase gonadotropin-releasing hormone (GnRH) agonist (GnRH-a) protocol, the long follicular phase GnRH-a protocol, and the ultralong GnRH-a protocol. Non-downregulation protocols included the GnRH antagonist protocol, mild stimulation protocol, and progestin-primed ovarian stimulation protocol. Adequate downregulation was defined by the following criteria: Estradiol (E_2) <50 pg/mL, Luteinizing hormone (LH) <5 U/L, Follicle-stimulating hormone (FSH) <5 U/L, progesterone <1.0 ng/mL, endometrial thickness <5 mm, and antral follicles (5–10 mm in diameter) in both ovaries with no functional cysts. The treatment protocol was individualized based on each patient's specific clinical profile. Gonadotropin dosage was adjusted during the stimulation phase according to follicular growth dynamics and E_2 serum levels. When 2–3 dominant follicles measured ≥18 mm in diameter, a trigger injection was administered. Transvaginal ultrasound-guided oocyte retrieval was performed 36–38 hours after trigger. All ETs were performed by certified physicians at our center. Recombinant FSH (Puregon, N.V. Organon, Oss, North Brabant, the Netherlands) was administered at a starting dose of 150 IU and adjusted according to ovarian response. Oocyte retrieval was performed using a 17-gauge single-lumen needle (Huanhao, Shenzhen, Guangdong, China). ET was performed using a K-Soft 5000 embryo transfer catheter (Cook Medical, Bloomington, IN, USA). ICSI was indicated for severe male factor infertility, including oligoasthenoteratozoospermia or azoospermia.

2.3 Statistical Analysis

Statistical analyses were performed using SPSS (Version 27.0.1) and R software (Version 4.4.1). Data were categorized as quantitative or qualitative variables. Normality

of quantitative data was assessed using the Kolmogorov-Smirnov (K-S) test. Non-normally distributed data were summarized as median (Q1, Q3), where Q1 refers to the first quartile (25th percentile) and Q3 refers to the third quartile (75th percentile) of the dataset, and compared using the independent-samples Mann-Whitney U test. Categorical variables were described using frequencies and percentages (%). Comparisons of binary variables were performed using the Pearson chi-square test. Variables of potential significance identified in the univariate analysis were subsequently included in a multivariate logistic regression model. The overall sample was randomly divided into a training set and a validation set at a ratio of 7:3. Variables showing significant associations in the multivariate analysis were incorporated into the prediction model. The discriminative ability of the model was quantified using the area under the receiver operating characteristic (ROC) curve (AUC). Calibration curves were applied to assess the agreement between predicted probabilities and the actual observed outcomes. Restricted cubic spline (RCS) analyses were performed to examine the potential nonlinear effects of continuous variables on the outcome and to identify inflection points. Subgroup analyses were subsequently conducted based on these inflection points. Propensity score matching was conducted to balance baseline characteristics among subgroups.

3. Results

3.1 Establishment of the Nomogram

A total of 504 patients with endometriosis were included in this study. Among them, 123 were diagnosed with DIE, and 260 were diagnosed with OMA, including 66 cases of bilateral OMA. The final analysis included 348 patients in the training set and 156 patients in the validation set. The training and validation sets demonstrated comparable baseline and clinical characteristics (Table 1). Univariate logistic regression identified the following factors as statistically significant: controlled ovarian stimulation (COS) protocols, FET, age, AMH levels, AFC, number of oocytes retrieved, and number of 2-pronuclear (2PN) embryos. In contrast, no significant associations were found for surgery, presence of endometrioma, number of embryos transferred, or previous pregnancy (Table 2). Multivariate logistic regression analysis confirmed that age (odds ratio [OR] = 0.946, 95% confidence interval [CI]: 0.896–0.999), COS protocol (OR = 1.646, 95% CI: 1.055–2.570), and FET (OR = 1.823, 95% CI: 1.149–2.892) remained independently associated with the outcome (Table 3). As shown in Fig. 2, a personalized nomogram prediction model was developed to estimate the probability of pregnancy following IVF/ICSI in patients with endometriosis.

3.2 Nomogram Validation

The AUC of the training model was 0.613 (95% CI: 0.553–0.673) (Fig. 3A). In the validation set, the AUC was

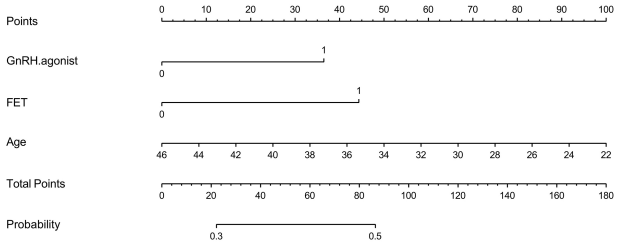


Fig. 2. Clinical nomogram model for individualized prediction of post-IVF pregnancy probability in endometriosis. IVF, *in vitro* fertilization; GnRH, gonadotropin-releasing hormone. Binary coding was adopted, with 1 denoting exposure to the corresponding intervention and 0 denoting non-exposure.

0.631 (95% CI: 0.544–0.719) (Fig. 3B). Calibration curves were used to assess the agreement between the predicted probabilities and the actual observed outcomes, indicating a good model fit (Fig. 4). Decision curve analysis (DCA) was performed to evaluate the clinical utility of the model, demonstrating that the nomogram provides favorable net clinical benefit across a reasonable range of threshold probabilities (Fig. 5).

3.3 The Impact of COS Protocols on Pregnancy Rates

Based on COS protocols, patients were divided into a pituitary suppression group and a control group. After propensity score matching for baseline characteristics, 179 patients were included in each group. A statistically significant difference ($p < 0.05$) in CPR was observed between the groups (Table 4).

3.4 Impact of the Freeze-All Strategy on CPR

Patients were categorized into a FET group and an ET group based on the ET strategy. After propensity score matching for baseline characteristics, 160 patients were included in each group. No significant difference in CPR was observed between the two groups (Table 5).

3.5 Results of RCS and Subgroup Analysis

RCS analysis ultimately identified three inflection points for patient age at 27, 31, and 37 years (Fig. 6). After matching baseline characteristics, a comparison was made between a younger age group (n = 55) and an advanced age group (n = 55). Apart from AMH levels and the proportion of patients with bilateral chocolate cysts, no statistically significant differences were observed between the two groups in terms of BMI, AFC, choice of ovarian stimulation protocol, proportion of patients with prior surgery, prevalence of endometriomas, or rate of FET. A statistically significant difference in CPR was observed between the two groups (Table 6).

Table 1. Baseline and clinical characteristics of the training and validation sets.

Characteristic	Training set (n = 348)	Validation set (n = 156)	*p*-value
Age (years)	31.00 (29.00, 34.00)	31.00 (29.00, 34.00)	0.478
BMI (kg/m^2)	21.30 (19.50, 23.50)	21.10 (19.50, 23.10)	0.451
Previous pregnancy			0.461
Yes, n (%)	41.95 (146/348)	38.46 (60/156)	
No, n (%)	58.05 (202/348)	61.54 (96/156)	
AFC (n)	10.00 (7.00, 14.00)	10.00 (6.00, 13.00)	0.301
AMH (ng/mL)	3.42 (2.06, 5.02)	2.81 (1.70, 4.84)	0.099
Surgery			0.526
Yes, n (%)	63.22 (220/348)	60.26 (94/156)	
No, n (%)	36.78 (128/348)	39.74 (62/156)	
OMAs			0.287
Yes, n (%)	50.00 (174/348)	55.13 (86/156)	
No, n (%)	50.00 (174/348)	44.87 (70/156)	
GnRH-a			0.270
Yes, n (%)	54.02 (188/348)	48.72 (76/156)	
No, n (%)	45.98 (160/348)	51.28 (80/156)	
FET			0.711
Yes, n (%)	65.80 (229/348)	64.10 (100/156)	
No, n (%)	34.20 (119/348)	35.90 (56/156)	
CPR, n (%)	56.61 (197/348)	57.05 (89/156)	0.926

BMI, body mass index; AFC, antral follicle counts; AMH, anti-Müllerian hormone; GnRH-a, gonadotropin-releasing hormone agonist; FET, frozen embryo transfer; OMAs, ovarian endometriomas; CPR, clinical pregnancy rate.

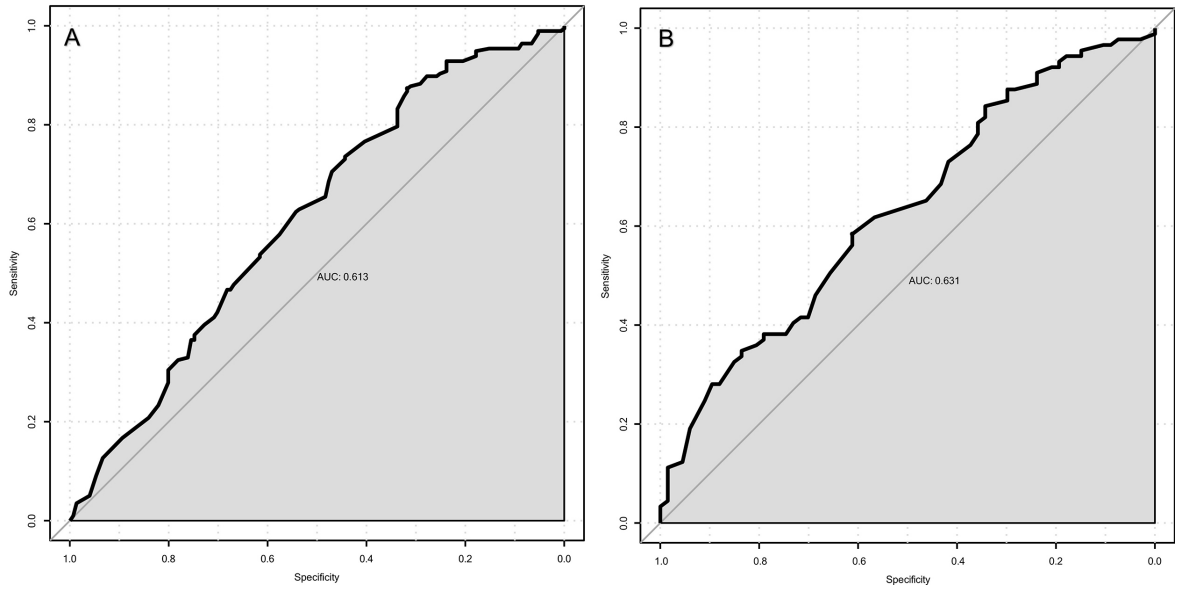


Fig. 3. Evaluation of the nomogram's predictive performance using ROC curves in the training (A) and validation (B) sets. AUC, area under the curve; ROC, receiver operating characteristic.

4. Discussion

Based on clinical data from 504 patients with endometriosis and infertility, a nomogram was constructed to estimate the probability of clinical pregnancy after IVF/ICSI. The resulting nomogram demonstrated moderate predictive accuracy and discriminative ability.

While some studies have confirmed a positive effect of surgery on postoperative natural pregnancy rates, clinical practice commonly employs the revised American So-

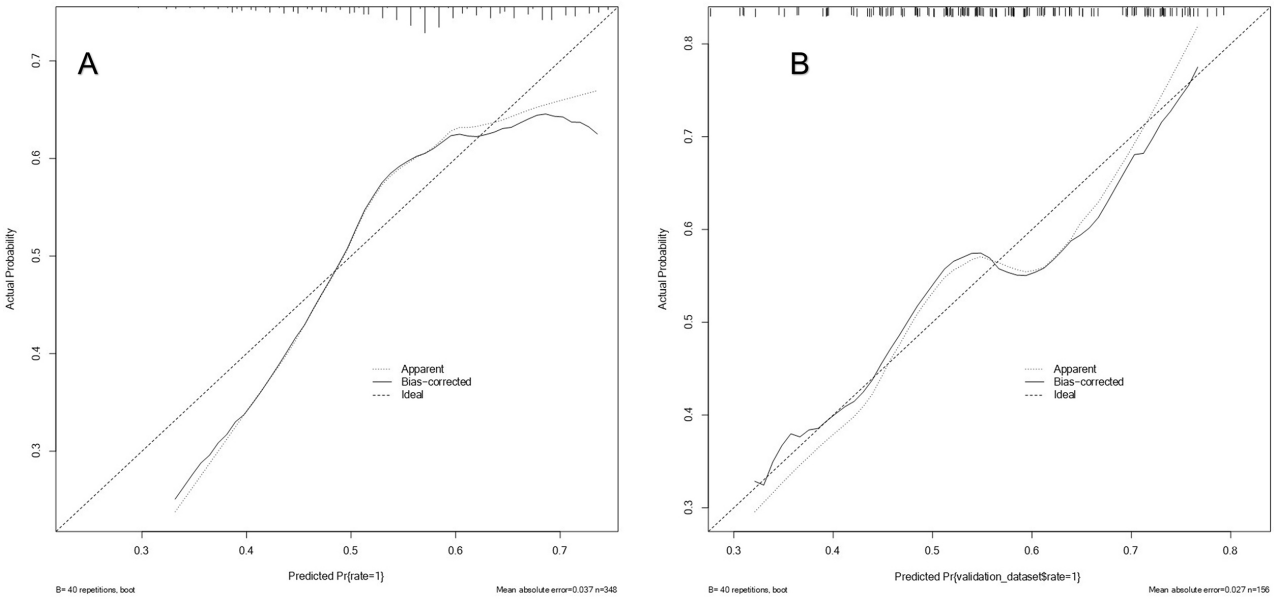


Fig. 4. Calibration curves for predicting CPR in IVF/ICSI patients with endometriosis. Calibration curves of the training set (A) and the validation set (B). CPR, clinical pregnancy rate.

Table 2. Univariate analysis of factors associated with clinical pregnancy.

Characteristic		OR	95% CI	*p*-value
GnRH-a	Yes No	1.571	1.025–2.409	0.038*
FET	Yes No	1.624	1.039–2.539	0.033*
Age (years)		0.941	0.892–0.993	0.027*
BMI (kg/m^2)		0.983	0.944–1.023	0.393
AMH (ng/mL)		1.143	1.039–1.258	0.006$^{\#}$
AFC (n)		1.053	1.013–1.095	0.009$^{\#}$
Oocytes retrieved (n)		1.057	1.026–1.089	0.001$^{\#}$
Number of 2PN embryos (n)		1.091	1.043–1.141	0.001$^{\#}$
Number of embryos transferred	Two One	1.070	0.699–1.638	0.754
Surgery	Yes No	1.037	0.665–1.618	0.872
OMAs	Yes No	1.339	0.870–2.059	0.184
Previous pregnancy	Yes No	1.515	0.985–2.329	0.058

OR, odds ratio; CI, confidence interval; 2PN, 2-pronuclear.
*$p < 0.05$, $^{\#}p < 0.01$.

Table 3. Multivariate analysis of factors associated with clinical pregnancy.

Characteristic		OR	95% CI	*p*-value
GnRH-a	Yes No	1.646	1.055–2.570	0.028*
FET	Yes No	1.823	1.149–2.892	0.011*
Age (years)		0.946	0.896–0.999	0.047*

*$p < 0.05$.

ciety for Reproductive Medicine (rASRM) score combined with the Endometriosis Fertility Index (EFI) to assess disease severity and fertility prognosis. However, the EFI is applicable only for predicting natural pregnancy rates after surgery [10]. For patients with endometriosis undergoing IVF, no widely applicable and practical scoring system is currently available. Several previous studies have attempted to develop predictive models for postoperative pregnancy outcomes following IVF, showing promising predictive performance. However, according to the latest ESHRE guidelines on endometriosis, routine surgical intervention prior to IVF is not currently recommended due to a lack of robust supporting evidence [6]. Several meta-analyses have indicated that surgery for OMAs does not improve live birth or CPRs per cycle [11,12,13]. Moreover, recent studies have reported a statistically significant decline in AMH levels after endometrioma surgery, particularly in cases of bilateral cysts [14]. As indicated by the multivariate logistic regression results, the independent factors influencing pregnancy outcomes were COS protocol, transfer strategy, and patient age. Surgical intervention failed to increase pregnancy rates ($p = 0.872$). Compared with other prediction models, the present model has a broader clinical application scope, is simpler to implement in clinical practice, and enables rapid assessment of patient status with reasonable predictive performance and calibration.

Table 4. Comparison of the CPRs of different COS protocols.

Characteristic	Pituitary suppression Group (n = 179)	Control Group (n = 179)	*p*-value
Age (years)	32.00 (29.00, 34.00)	31.00 (29.00, 34.00)	0.442
BMI (kg/m^2)	21.35 (19.98, 23.10)	21.10 (19.30, 22.90)	0.393
Previous pregnancy			0.828
Yes, n (%)	61.45 (110/179)	62.57 (112/179)	
No, n (%)	38.55 (69/179)	37.43 (67/179)	
bFSH (mIU/mL)	7.36 (6.31, 8.91)	7.78 (6.58, 9.49)	0.128
bLH (mIU/mL)	4.33 (3.37, 5.57)	4.45 (3.24, 5.98)	0.649
bE2 (pg/mL)	38.10 (26.00, 54.50)	39.00 (29.30, 54.50)	0.694
AFC (n)	10.00 (7.00, 13.00)	11.00 (6.00, 15.00)	0.608
AMH (ng/mL)	3.11 (2.27, 4.07)	2.93 (1.61, 4.90)	0.754
OMAs			0.916
Yes, n (%)	49.16 (88/179)	49.72 (89/179)	
No, n (%)	50.84 (91/179)	50.28 (90/179)	
FET			0.825
Yes, n (%)	64.25 (115/179)	65.36 (117/179)	
No, n (%)	35.75 (64/179)	34.64 (62/179)	
DIE			0.461
Yes, n (%)	26.26 (47/179)	22.91 (41/179)	
No, n (%)	73.74 (132/179)	77.09 (138/179)	
CPR (%)	64.25 (115/179)	49.72 (89/179)	0.006*

DIE, deep infiltrating endometriosis; bFSH, basal follicle stimulating hormone; bLH, basal luteinizing hormone; bE2, basal estradiol.

*$p < 0.05$.

Table 5. Comparison of CPRs between different ET strategies.

Characteristic	FET (n = 160)	ET (n = 160)	*p*-value
Age (years)	31.00 (29.00, 34.00)	32.00 (29.00, 34.00)	0.533
BMI (kg/m^2)	20.95 (19.23, 23.38)	21.00 (19.70, 23.10)	0.888
Previous pregnancy			0.255
Yes, n (%)	62.50 (100/160)	56.25 (90/160)	
No, n (%)	37.50 (60/160)	43.75 (70/160)	
bFSH (mIU/mL)	7.55 (6.25, 9.16)	7.67 (6.59, 9.10)	0.332
bLH (mIU/mL)	4.30 (3.40, 5.93)	4.13 (3.17, 5.52)	0.308
bE2 (pg/mL)	42.00 (29.93, 58.00)	40.00 (30.00, 55.00)	0.439
AFC (n)	10.00 (6.25, 14.00)	10.00 (7.00, 13.00)	0.741
AMH (ng/mL)	3.22 (2.04, 4.79)	3.25 (2.28, 4.63)	0.810
OMAs			0.736
Yes, n (%)	53.13 (85/160)	55.00 (88/160)	
No, n (%)	46.87 (75/160)	45.00 (72/160)	
GnRH-a			0.734
Yes, n (%)	57.50 (92/160)	59.38 (95/160)	
No, n (%)	42.50 (68/160)	40.62 (65/160)	
DIE			0.368
Yes, n (%)	27.50 (44/160)	23.13 (37/160)	
No, n (%)	72.50 (116/160)	76.87 (123/160)	
CPR (%)	59.38 (95/160)	51.88 (83/160)	0.177

Theoretically, FET avoids the adverse effects of non-physiological hormonal environments resulting from controlled ovarian stimulation (COS) in fresh cycles on both the embryo and the endometrium. A retrospective cohort study by Tan et al. [15], including 728 patients with histologically confirmed endometriosis undergoing their first IVF/ICSI treatment, reported similar implantation rates and CPRs between FET and fresh ET. In contrast, a meta-analysis by

Table 6. Age-stratified analysis of CPR using RCS.

Characteristic	≤27 years (n = 55)	>27years (n = 55)	*p*-value
BMI (kg/m^2)	20.20 (18.90, 21.80)	20.20 (18.90, 21.90)	0.886
Previous pregnancy			0.525
Yes, n (%)	74.55 (41/55)	69.09 (38/55)	
No, n (%)	25.45 (14/55)	30.91 (17/55)	
AFC (n)	12.00 (9.00, 17.00)	10.00 (7.00, 14.00)	0.085
AMH (ng/mL)	4.82 (2.72, 6.54)	3.39 (2.06, 5.17)	0.017*
OMAs			0.047*
Yes, n (%)	45.45 (25/55)	27.27 (15/55)	
No, n (%)	54.55 (30/55)	72.73 (40/55)	
FET			0.832
Yes, n (%)	70.91 (39/55)	72.73 (40/55)	
No, n (%)	29.09 (16/55)	27.27 (15/55)	
Surgery			0.432
Yes, n (%)	65.45 (36/55)	58.18 (32/55)	
No, n (%)	34.55 (19/55)	41.82 (23/55)	
GnRH-a			0.697
Yes, n (%)	61.82 (34/55)	58.18 (32/55)	
No, n (%)	38.18 (21/55)	41.82 (23/55)	
CPR (%)	70.91 (39/55)	50.91 (28/55)	0.032*

*$p < 0.05$.

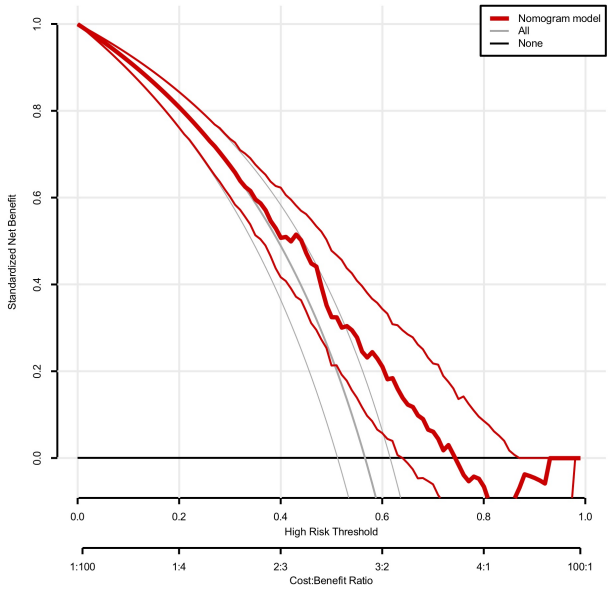


Fig. 5. Clinical decision curves of the nomogram for prediction of clinical pregnancy in endometriosis patients. The nomogram demonstrated consistently superior net benefit in DCA, confirming its clinical utility. The three curves for the nomogram model and the "All" strategy represent the point estimate (middle line) and the 95% CI (upper and lower lines) of net benefit. The solid black line represents the "None" strategy. DCA, decision curve analysis; CI, confidence interval.

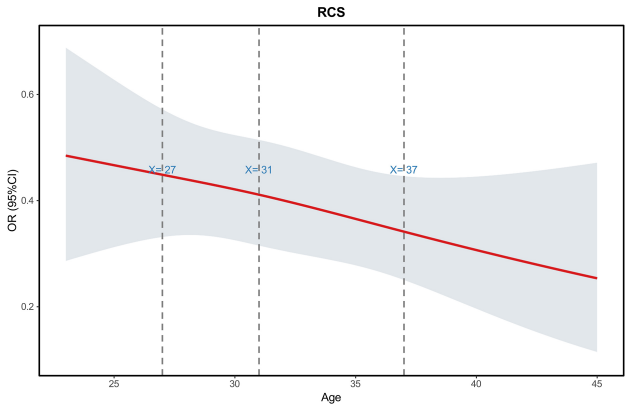


Fig. 6. RCS analysis of age in patients with endometriosis. Inflection points of the RCS curve were observed at ages 27, 31, and 37 years. RCS, restricted cubic spline. The shaded area indicates the 95% confidence interval for the fitted association derived from RCS analysis. The three vertical dashed lines at 27, 31, and 37 years correspond to the inflection points on the X-axis.

Han et al. [16], including 11 studies from various countries on ET strategies in endometriosis patients concluded that FET increased implantation rates, CPRs, and LBRs compared with fresh transfers. In the multivariate analysis, FET was identified as a significant factor. In our subgroup analysis, the CPR was higher in the FET group than in the fresh transfer group (59.375% vs. 51.875%), a trend consistent with findings from previous meta-analyses. However, this trend did not reach statistical significance, which may be attributable to the limited sample size and consequent insuffi-

cient statistical power. In summary, our findings are consistent with those reported in the meta-analysis. Therefore, for patients with sufficient time and financial resources, FET is recommended to optimize pregnancy rates.

Whether the use of GnRH-a improves endometrial receptivity and increases pregnancy rates remains a topic of ongoing debate. A Cochrane review reported that, due to limited data, current evidence is insufficient to determine the effect of GnRH-a on live birth or CPRs [17]. A meta-analysis by Cao et al. [18] found that, in randomized controlled trials, the ultralong GnRH-a protocol yielded higher CPR than the long GnRH-a protocol in patients with stage III/IV endometriosis. However, GnRH antagonist protocols offer notable advantages, such as a lower risk of ovarian hyperstimulation syndrome (OHSS), shorter treatment duration, and better patient tolerance, garnering increasing attention [19]. Propensity score matching was utilized to adjust for potential selection bias in protocol allocation, with matching based on patient age and ovarian reserve function. The results showed that the pituitary suppression group achieved a significantly higher CPR (64.25% vs. 49.72%), suggesting that, in the absence of ovarian oversuppression, the use of GnRH-a may confer clinical benefits.

Age is a critical factor influencing female fertility, presenting challenges such as reduced oocyte yield and lower pregnancy rates. RCS analysis revealed a nonlinear association between age and CPR in patients with endometriosis. After the age of 31, pregnancy rates decline more rapidly with increasing age, and this decline accelerates further beyond 37 years. Univariate logistic regression identified the number of oocytes retrieved, AMH level, AFC, and number of 2PN embryos as significant predictors; however, multivariate analysis did not demonstrate additional predictive value when combining age with AMH or AFC, suggesting that the effects of ovarian reserve markers on pregnancy rates may be mediated through age. Subgroup analysis confirmed higher CPR among younger patients. However, based on our RCS results, age exerts a substantial influence even within younger cohorts, making it difficult to establish a definitive threshold. Patients with a low probability of natural conception are advised to pursue IVF treatment at an earlier age to mitigate the adverse effects of advancing age.

Limitations

This study presents two main limitations. First, as a single-center retrospective analysis, it may be subject to selection bias. Second, the inherent heterogeneity of endometriosis, combined with variations in ovarian stimulation protocols, constrained the feasibility of robust subgroup analyses. Future studies should focus on large-scale randomized controlled trials and external validation studies to validate these findings.

5. Conclusions

In conclusion, this study developed a nomogram to assist clinicians in estimating the probability of clinical pregnancy in the first IVF/ICSI cycle in patients with endometriosis. Independent factors associated with CPRs included the COS protocols, FET, and patient age. For patients with sufficient time and financial resources, FET is recommended to maximize the likelihood of pregnancy. For patients at low risk of OHSS and with adequate ovarian reserve, downregulation protocols may be considered to improve endometrial receptivity. Patients with a low probability of natural conception should be advised to pursue IVF treatment at an earlier age to mitigate the adverse effects of advanced maternal age.

Availability of Data and Materials

Researchers may request access to the data supporting the findings of this study from the corresponding author.

Author Contributions

JZ: conceptualization, validation, writing – review & editing, supervision, project administration. GLY: investigation, resources, writing – original draft. YY: methodology, writing-review & editing. HHL: methodology, software, formal analysis, data curation, writing – original draft, writing – review & editing. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Shenzhen People's Hospital (Approval number: LL-KY-2024114-02). Written informed consent was obtained from every participant. All procedures were performed in compliance with the Declaration of Helsinki.

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Conflicts of Interest

The authors declare no conflicts of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/CEOG48399.

References

[1] Taylor HS, Kotlyar AM, Flores VA. Endometriosis is a chronic systemic disease: clinical challenges and novel innovations.

Lancet (London, England). 2021; 397: 839–852. https://doi.org/10.1016/S0140-6736(21)00389-5

[2] Burney RO, Giudice LC. Pathogenesis and pathophysiology of endometriosis. Fertility and Sterility. 2012; 98: 511–519. https://doi.org/10.1016/j.fertnstert.2012.06.029

[3] Gruber TM, Mechsner S. Pathogenesis of Endometriosis: The Origin of Pain and Subfertility. Cells. 2021; 10: 1381. https://doi.org/10.3390/cells10061381

[4] Casalechi M, Di Stefano G, Fornelli G, Somigliana E, Viganò P. Impact of endometriosis on the ovarian follicles. Best Practice & Research. Clinical Obstetrics & Gynaecology. 2024; 92: 102430. https://doi.org/10.1016/j.bpobgyn.2023.102430

[5] Grigoriadis G, Daniilidis A, Merlot B, Stratakis K, Dennis T, Crestani A, et al. Surgical treatment of deep endometriosis: Impact on spontaneous conception. Best Practice & Research. Clinical Obstetrics & Gynaecology. 2024; 93: 102455. https://doi.org/10.1016/j.bpobgyn.2024.102455

[6] Becker CM, Bokor A, Heikinheimo O, Horne A, Jansen F, Kiesel L, et al. ESHRE guideline: endometriosis. Human Reproduction Open. 2022; 2022: hoac009. https://doi.org/10.1093/hropen/hoac009

[7] Hamdan M, Omar SZ, Dunselman G, Cheong Y. Influence of endometriosis on assisted reproductive technology outcomes: a systematic review and meta-analysis. Obstetrics and Gynecology. 2015; 125: 79–88. https://doi.org/10.1097/AOG.0000000000000592

[8] Yang C, Geng Y, Li Y, Chen C, Gao Y. Impact of ovarian endometrioma on ovarian responsiveness and IVF: a systematic review and meta-analysis. Reproductive Biomedicine Online. 2015; 31: 9–19. https://doi.org/10.1016/j.rbmo.2015.03.005

[9] Alson S, Henic E, Jokubkiene L, Sladkevicius P. Endometriosis diagnosed by ultrasound is associated with lower live birth rates in women undergoing their first in vitro fertilization/intracytoplasmic sperm injection treatment. Fertility and Sterility. 2024; 121: 832–841. https://doi.org/10.1016/j.fertnstert.2024.01.023

[10] Vesali S, Razavi M, Rezaeinejad M, Maleki-Hajiagha A, Maroufizadeh S, Sepidarkish M. Endometriosis fertility index for predicting non-assisted reproductive technology pregnancy after endometriosis surgery: a systematic review and meta-analysis. BJOG : an International Journal of Obstetrics and Gynaecology. 2020; 127: 800–809. https://doi.org/10.1111/1471-0528.16107

[11] Nickkho-Amiry M, Savant R, Majumder K, Edi-O'sagie E, Akhtar M. The effect of surgical management of endometrioma on the IVF/ICSI outcomes when compared with no treatment? A systematic review and meta-analysis. Archives of Gynecology and Obstetrics. 2018; 297: 1043–1057. https://doi.org/10.1007/s00404-017-4640-1

[12] Tsoumpou I, Kyrgiou M, Gelbaya TA, Nardo LG. The effect of surgical treatment for endometrioma on in vitro fertilization outcomes: a systematic review and meta-analysis. Fertility and Sterility. 2009; 92: 75–87. https://doi.org/10.1016/j.fertnstert.2008.05.049

[13] Hamdan M, Dunselman G, Li TC, Cheong Y. The impact of endometrioma on IVF/ICSI outcomes: a systematic review and meta-analysis. Human Reproduction Update. 2015; 21: 809–825. https://doi.org/10.1093/humupd/dmv035

[14] Nankali A, Kazeminia M, Jamshidi PK, Shohaimi S, Salari N, Mohammadi M, et al. The effect of unilateral and bilateral laparoscopic surgery for endometriosis on Anti-Mullerian Hormone (AMH) level after 3 and 6 months: a systematic review and meta-analysis. Health and Quality of Life Outcomes. 2020; 18: 314. https://doi.org/10.1186/s12955-020-01561-3

[15] Tan J, Cerrillo M, Cruz M, Cecchino GN, Garcia-Velasco JA. Early Pregnancy Outcomes in Fresh Versus Deferred Embryo Transfer Cycles for Endometriosis-Associated Infertility: A Retrospective Cohort Study. Journal of Clinical Medicine. 2021; 10: 344. https://doi.org/10.3390/jcm10020344

[16] Han Y, Liu C, Liu D, Wu L, Huang W. Pregnancy outcomes in freeze-all versus fresh embryo transfer cycles of women with adenomyosis and endometriosis: a systemic review and meta-analysis. Frontiers in Endocrinology. 2025; 16: 1507252. https://doi.org/10.3389/fendo.2025.1507252

[17] Georgiou EX, Melo P, Baker PE, Sallam HN, Arici A, Garcia-Velasco JA, et al. Long-term GnRH agonist therapy before in vitro fertilisation (IVF) for improving fertility outcomes in women with endometriosis. The Cochrane Database of Systematic Reviews. 2019; 2019: CD013240. https://doi.org/10.1002/14651858.CD013240.pub2

[18] Cao X, Chang HY, Xu JY, Zheng Y, Xiang YG, Xiao B, et al. The effectiveness of different down-regulating protocols on in vitro fertilization-embryo transfer in endometriosis: a meta-analysis. Reproductive Biology and Endocrinology : RB&E. 2020; 18: 16. https://doi.org/10.1186/s12958-020-00571-6

[19] Muasher SJ, Abdallah RT, Hubayter ZR. Optimal stimulation protocols for in vitro fertilization. Fertility and Sterility. 2006; 86: 267–273. https://doi.org/10.1016/j.fertnstert.2005.09.067