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**Nomogram predicting the likelihood of live-birth rate after surgery for deep infiltrating endometriosis without bowel involvement in women who wish to conceive: a retrospective study**

Alexandra ARFI (*MD*), Sofiane BENDIFALLAH (*MD, PhD*), Emmanuelle MATHIEU D'ARGENT (*MD*), Clothilde POUPON (*MD*), Marcos BALLESTER (*MD, PhD*), Jonathan COHEN (*MD, PhD*), Emile DARAI (*MD, PhD*)

**STRUCTURED ABSTRACT**

**Objective:** To study the fertility and live birth (LB) rate in women after surgery for deep infiltrating endometriosis (DIE) without bowel involvement and to evaluate the predictive factors of LB after DIE surgery without bowel involvement.

**Study Design:** Retrospective cohort study. A total of 118 women who wished to conceive and who underwent surgery for DIE without bowel involvement were analyzed between January 2006 and December 2014. A multivariate logistic regression analysis of selected factors and a nomogram to predict the subsequent LB rate was constructed.

**Results:** Thirty-six woman had a LB (30.5%). In multivariate analysis, factors associated with a LB were: age  $\leq 30$  years ( $p = 0.0024$ ), BMI  $\leq 25$  kg / m<sup>2</sup> ( $p = 0.029$ ) and Enzian grade 1 ( $p < 0.001$ ). These factors were associated to develop a nomogram. Before and after the bootstrap sampling procedure, the predictive model had an AUC of 0.84 (95% CI, 0.82–0.86) and 0.81 (95% CI, 0.79–83), respectively, and showed a good calibration.

**Conclusions:** This work presents the originality of describing the fertility and the LB rate after surgery for DIE without bowel involvement with a predictive model. Such tools can help

clinicians to support the patient in making an informed decision about fertility treatment options, contributing to the decision-making process by defining simple risk factors of poor LB probability that can help identify good candidates for MAR.

**Keywords:** Medically assisted reproduction / endometriosis without bowel involvement / nomogram / prediction models / Live birth

1 **Introduction**

2           Deep infiltrative endometriosis (DIE) is a common gynecological pathology that affects  
3 up to 50% of infertile women (1).

4           While the association between DIE without bowel involvement and infertility is well  
5 supported throughout the literature, an absolute cause-effect relation has not been  
6 established (2). Despite the publication of international guidelines, the management of  
7 endometriosis without bowel involvement and associated infertility remain unclear (3–10).

8           To date, although several scoring systems and nomograms have been published to  
9 evaluate the PR after ICSI–IVF in infertile patients (11-13), none of them: are applicable to  
10 patients with DIE without bowel involvement and were specifically developed to determine  
11 the individual live birth probability.

12           The objective of this study was therefore to develop a nomogram for the likelihood of  
13 live-birth rate (LBR) after surgery in women with DIE without bowel involvement and who  
14 wish to conceive, and establishing an optimal threshold to optimize post-surgical decision-  
15 making.

16

17

## 18 **Materials and Methods**

19 We conducted a retrospective analysis of our database using information from  
20 women with DIE without bowel involvement who wished to conceive and who underwent  
21 surgery from January 2006 to December 2014 at Tenon University Hospital in Paris, France.

22 For each woman, the following parameters were recorded: age at surgery, body mass  
23 index (BMI), smoking status, presence of endometrioma and/or adenomyosis on magnetic  
24 resonance imaging (MRI), serum level of anti-Müllerian hormone (AMH), fertility before  
25 surgery, symptoms, previous surgery for endometriosis, type of surgery, surgical route,  
26 Enzian and ASRM scores calculated during surgery, occurrence of pregnancy (spontaneous  
27 or after medically assisted reproduction (MAR)) and obstetrical issues.

28 Patients were excluded if colorectal endometriosis was diagnosed pre-operatively during  
29 clinical examination and/or on imaging exams (MRI, pelvis ultrasound...).

30

31 Endometriosis surgery was performed by endoscopy. The first step of the surgery  
32 consisted in exploring the abdomino-pelvic cavity to exhaustively assess the endometriotic  
33 lesions and calculate the ASRM and Enzian scores. The endometrioma were treated by  
34 cystectomy when greater than 5 cm. The ureters were systematically identified before  
35 dissection and some degree of ureterolysis, either uni- or bilateral, was performed. Once the  
36 external lateral surface of the utero-sacral ligament had been fully liberated, the  
37 rectovaginal space and the homolateral pararectal fossa were opened. The utero-sacral  
38 ligaments and/or torus were removed if infiltrated. If the vaginal wall was involved, an en  
39 bloc resection including the utero-sacral ligaments and a partial colectomy was performed.

40

41 All patients underwent a first postoperative visit 4-6 weeks after surgery then once a  
42 year to evaluate fertility and obstetrical issues.

43 A nomogram was developed for the LBR in women who wished to conceive after surgery for  
44 DIE without bowel involvement. A multivariate analysis was performed using the logistic  
45 regression model and including all the factors that were statistically significant on univariate  
46 analysis or clinically relevant from the literature (8) . Missing values in the predictors were  
47 multiply imputed with chained equations (MICE) (9,10) before statistical analyses. The complexity of  
48 the model was controlled using the Akaike information criterion (11). A P-value of 0.05 was  
49 considered significant. The final model equation was then organized as a nomogram designed  
50 to calculate patient-specific probabilities of a live birth after surgery. Values for each of the  
51 model covariates were mapped to points on a scale ranging from 0 to 100, with total points  
52 obtained for each model covariate mapped to the probability of a live birth associated with  
53 the area under the receiver-operating characteristic curve (AUC) to measure the model's  
54 discriminatory power. It is generally accepted that an AUC of 1.0 indicates perfect accuracy  
55 between cases with or without a live birth, an AUC of 0.7–0.8 indicates satisfactory  
56 discrimination, values of 0.8 represent good discrimination whereas an AUC of 0.5 indicates  
57 no relationship (12). Calibration was assessed using plots that overlap the prediction model.

58 A bootstrapping technique to obtain relatively unbiased estimates (200 repetitions)  
59 was used for internal validation. The bootstrapping method is based on resampling obtained  
60 by randomly drawing data and replacing them with samples from the original dataset. It  
61 provides an estimate of the average optimism of the AUC of the receiver-operating  
62 characteristics (AUC-ROC) (13). Calibration was assessed using plots that overlapped the  
63 prediction model.

64 The optimal threshold (cut-off probability) of the nomogram in terms of clinical utility  
65 defined by the Youden Index (14), was evaluated according to the ROC curve. The sensitivity,  
66 specificity, negative predictive values (NPVs), and positive predictive values (PPVs), were  
67 estimated at this threshold.

68 The categorical and numerical variables were analyzed using the  $\chi^2$  test and the  
69 Student t test, respectively. Differences were considered significant at a P-value of .05. All  
70 analyses were performed using the R package with the Design, Hmisc, Design,  
71 Presence/absence ([http:// lib.stat.cmu.edu/R/CRAN](http://lib.stat.cmu.edu/R/CRAN)).

72

73 Prospective recording of data was approved by the French authority CCTIRS (Advisory  
74 Committee on Information Processing in Healthcare Research) CEROG 2012-GYN-10-03. All  
75 the women gave their informed consent.

76

## 77 **RESULTS**

78 During the study period, 118 women with DIE without bowel involvement who  
79 wished to conceive underwent a resection of DIE. Epidemiological and surgical  
80 characteristics of the population are summarized in Table 1. The median age of the women  
81 was 30 years (range 19-45) and 100 (84.7%) were under 30. The median age was lower in  
82 the group of patients who conceived but there were no other epidemiological differences or  
83 differences in the surgical location of DIE (Table 1). Resection of DIE was performed by  
84 laparoscopy, without laparoconversion, for all the patients. In addition to the resection of  
85 the torus (corresponding to the posterior region of the uterine cervix where the uterosacral  
86 ligaments meet, at the upper half of the posterior surface of the cervix) and utero-sacral

87 ligaments, 36 patients (30.6%) required a cystectomy for endometrioma and 24 patients a  
88 colpectomy (20.3%).

89 No difference in the ASRM score was noted between patients who conceived and  
90 those who did not (median total score: 37 versus 30, respectively ( $p=0.38$ )). The rate of  
91 patients with ASRM stage I/II and III/IV in the group of patients who conceived and those  
92 who did not were 36.1% and 35.4%, and 63.9% and 64.6%, respectively (not significant). No  
93 difference in the proportion of patients with endometriomas who required a colpectomy  
94 was noted between the groups. There were more patients with a grade 1 Enzian score in the  
95 group of patients who conceived.

96 Overall, the median time to conception after surgery was 6 months (range; 2-48) for  
97 spontaneous pregnancies and 19 months (4-48) for pregnancies following MAR. The overall  
98 PR was 39% (46/118). No stillbirths were reported. Sixteen patients (34.8%) became  
99 pregnant after MAR leading to 13 live births. Nine women had a miscarriage (six after  
100 spontaneous pregnancy and three after MAR). One woman who conceived spontaneously  
101 had an ectopic pregnancy.

102 The overall LBR was 30.5% (36/118): 47% (17/36) of live births occurred in the  
103 spontaneous pregnancy group and 53% (19/36) in the MAR group.

104

105 A BMI  $>30$  kg/m<sup>2</sup> ( $p=0.017$ ), and an AMH serum level  $>2$  ng/ml ( $p=0.0006$ ) were  
106 predictive factors for obtaining a spontaneous pregnancy compared to a MAR pregnancy  
107 (Table 2). PRs at 12 and 24 months were similar in both groups (no statistically significant  
108 difference).

109

110 In multivariate analysis, age at diagnosis, BMI and Enzian score were significantly  
111 associated with the likelihood of live birth after surgery in infertile women who had  
112 undergone surgery (Figure 1). These factors were included in the logistic regression model  
113 (Table 3). Although the AMH level was not statistically significantly associated with live birth,  
114 it was included in the construction of the predictive model due to its clinical relevance  
115 (8,15,16). The predictive model had an AUC of 0.84 (95% CI, 0.82–0.86) before the 200  
116 repetitions of bootstrap sample corrections and 0.81 (95% CI, 0.79-83) afterwards (Figure 2-  
117 A).

118 No difference was observed between the predicted probability obtained from the  
119 bootstrap correction and the actual probabilities of live birth ( $p=0.3829$ ) implying that the  
120 nomogram was well calibrated. The average difference and the maximal difference in  
121 predicted and calibrated probabilities of recurrence were 6.4% and 1.07%, respectively  
122 (Figure 2-B).

123

124 The optimal threshold in terms of statistical and clinical utility was defined by a 20%  
125 Youden index (20). At this threshold, sensitivity, specificity, positive predictive and negative  
126 predictive values of the model were 70.7%, 86.1% 92.1%, and 56.4%, respectively.

127 Applying this threshold, a subset of women of poor prognosis (i.e., the subgroup of  
128 women with a low likelihood of obtaining a live birth after surgery) was defined as those  
129 with a predicted probability of live birth under 20%. In this subset, the PR and LBR were  
130 14.2% (9/63) and 7.9% (5/63), respectively. Above the 20% threshold, the likelihood of  
131 obtaining a live birth after surgery was high with a PR and LBR at 70.9% (39/55) and 56.4%  
132 (31/55), respectively. Figure 3 highlights the cumulative LBR according to the optimal  
133 threshold ( $p<0.001$ ) for the whole population.

134

135 For women with a Youden index under 20% who conceived spontaneously, the PR and  
136 LBR were 3.4% (2/58) and 1.7% (1/58), respectively. Above the 20% threshold, the PR and  
137 LBR were 63.6% (28/44) and 50.0% (22/44), respectively. Figure 4 highlights the cumulative  
138 LBR according to the optimal threshold ( $p < 0.001$ ) for women who conceived spontaneously.

139

#### 140 **COMMENTS**

141

142 To the best of our knowledge, the nomogram we present here is the first to evaluate  
143 the individual likelihood of a live birth after surgery for DIE without bowel involvement in  
144 women who wish to conceive. Its clinical interest lies in the inclusion of readily available  
145 clinical, biological and surgical characteristics which are commonly used in practice.

146

147 As no randomized controlled trials have been published comparing first-line MAR to  
148 first-line surgery in women with DIE-related infertility without bowel involvement, fertility  
149 management strategies are mainly based on retrospective studies (17). However, the LBR  
150 and PR for infertile women who conceive spontaneously or following MAR after surgery are  
151 heterogeneously reported in literature (17). In view of these confusing data, the indication  
152 of surgery for women with DIE without bowel involvement who are considering MAR  
153 remains somewhat blurred (4). In contrast, for the subset of women for whom spontaneous  
154 conception is planned, complete removal of DIE lesions seems to be associated with a  
155 significant improvement in fertility outcome. In the present study, we specifically focused on  
156 defining predictive factors associated with LBR and PR in the sub-population of symptomatic  
157 infertile women who underwent a first surgical management for DIE without bowel  
involvement. We report an overall PR and LBR of 30.5% and 39%, respectively which is in

158 discordance with previous literature reports (17) . In their recent literature review, in the  
159 specific group of women with DIE without bowel involvement who underwent surgery,  
160 Cohen et al (17) reported an overall PR (spontaneous and MAR) of 68.5% (compared to  
161 39.8% in our study) and a spontaneous PR of 50.5% (compared to 66% in our study). These  
162 discrepancies should be interpreted with caution for the following reasons: (i) the review  
163 was based on heterogeneous studies with few details about the precise extent and location  
164 of DIE lesions, and (ii) the studies contained little information concerning the length of  
165 postoperative follow-up and the general characteristics of the patients, in particular the  
166 etiology of infertility. In the present study, 48% of the 25 patients who underwent MAR  
167 became pregnant. This PR is similar to that reported by Mounsambote et al (18) in a study  
168 comparing IVF PR in a surgical (40%) and non-surgical (41%) group for infertile patients with  
169 DIE without bowel involvement (p=1). Our PR after MAR is also similar to that reported by  
170 Capelle et al. (19) evaluating the results of IVF according to the extent of DIE and of lesion  
171 removal. However, it is difficult to compare our results with those of Capelle et al. because  
172 of the differences in the populations studied: in our series, the endometriotic lesions were  
173 always completely removed while some patients in the Capelle et al. study underwent  
174 incomplete surgery; in addition, our population only included patients with DIE without  
175 bowel involvement which was not the case for the Capelle et al. study.

176 Our clinical end-point, i.e. the likelihood of a live birth, is relevant as it is currently  
177 unclear how to best manage infertile women with DIE without bowel infiltration. The  
178 nomogram we present here should help physicians identify which women have a good  
179 chance of giving birth after spontaneous conception and which women would benefit from  
180 MAR. On this topic, the ESHRE guidelines state that the effectiveness of surgical excision of

181 deep nodular lesions before treatment by ART in women with endometriosis-associated  
182 infertility is not well established in terms of reproductive outcome (20,21). The benefit of  
183 first-line surgery is only considered in infertile women with AFS/ASRM Stage I/II  
184 endometriosis undergoing laparoscopy prior to treatment with ART. For these women  
185 complete surgical removal of endometriosis to improve the LBR is recommended, although  
186 the benefit has not been well established (22). In 2010, Adamson et al (6) published a  
187 prediction model of spontaneous pregnancy after surgery – the Endometriosis Fertility Index  
188 (EFI) – including factors such as age, length of infertility, previous pregnancy and surgical  
189 factors. The index has been externally validated three times (23–25), and supports the  
190 prognostic relevance of laparoscopic surgery in endometriosis-related infertile patients. The  
191 main limitation of the EFI score is that it is based on the AFS score and thus only considers  
192 superficial endometriosis and not DIE, which is the main clinical challenge. In contrast, our  
193 study provides an accurate and evidence-based tool to help physicians determine the  
194 likelihood of pregnancy and live birth in women with DIE-related infertility and without  
195 bowel involvement. We define according to the threshold good candidate for spontaneous  
196 conception a LBR 1.7% vs 50.0% under and above the threshold of 20 %.

197         The current study is the first to establish a correlation between the Enzian score and  
198 fertility. The recent consensus published by the World Endometriosis Society (5) on the  
199 classification of endometriosis, recommends the use of the rASRM classification and the  
200 Enzian score to standardize practice. While no study has been published to date on Enzian  
201 and fertility, the authors suggest that the Enzian score has a low predictive ability to detect a  
202 woman's response to infertility treatment. However, in the present study, we report that  
203 women who conceive after surgery were more likely to have a Grade 3 Enzian score

204 (p<0.0001). This would indicate that surgery should be recommended for women with a low  
205 score (Grade 1). In our nomogram, the Enzian score emerges as the most relevant factor  
206 influencing the probability of a live birth. Further studies are thus needed to assess the true  
207 relevance of the Enzian score as a predictive factor for fertility. In our study, the Enzian score  
208 was calculated during surgery but Di Paola et al. (31) have shown that MRI correlates with  
209 the Enzian score with an accuracy of 95% in the detection and localization of DIE, thus  
210 minimizing false negative results (4%) in patients with DIE and obtaining a good preoperative  
211 staging. Extrapolating these results, we could consider that a pre-operative MRI Enzian score  
212 should be calculated for all patients before surgery to evaluate its relevance for women who  
213 wish to conceive, using our nomogram. In the future, the use of pre-operative data will  
214 become the first step in the surgery decision process. This cannot be done with the rASRM  
215 score.

216 In light of recent advances in fertility preservation techniques (FPT), such  
217 as oocytes and ovarian tissue freezing, the options for FPT in patients suffering from  
218 endometriosis should be considered. Because of possible loss of ovarian reserve due to  
219 surgery and/or presence of endometriomas, personalized counseling should be offered to all  
220 patients with endometriosis taking into account age, extent of ovarian involvement, AMH,  
221 previous and impending surgeries for endometriosis, along with current success rates and  
222 possible risks associated with FPT (32).

223

224 The main limitation of our study is its retrospective nature and the long period of data  
225 collection. Furthermore, pre-operative assessment of AMH levels, a test which is not  
226 reimbursed by the French Health System, was not performed in all patients due to the cost.

227 This work presents the originality of describing the fertility and the live birth rate after  
228 surgery for DIE without bowel involvement with a predictive model. It aims to improve  
229 information to the patient, discuss the benefit-risk balance of surgical treatment in case of  
230 infertility.

231

#### 232 **CONTRIBUTION TO AUTHORSHIP**

233 Alexandra ARFI (AA): planner, designer, data acquisition, writer, analyser

234 Sofiane Bendifallah (SB): planner, designer, data acquisition, writer, analyser

235 Emmanuelle Mathieu d'Argent (EMDA) : analyser

236 Clotilde Poupon (CP) : data acquisition

237 Marcos Ballester (MB): analyser, critical discussion

238 Jonathan Cohen (JC): analyser, critical discussion

239 Emile Darai (ED): planner, designer, analyser

240

#### 241 **DETAILS OF ETHICS APPROVAL**

242 Prospective recording of data was approved by the French authority CCTIRS (Advisory  
243 Committee on Information Processing in Healthcare Research) CEROG 2012-GYN-10-03. All  
244 the women gave their informed consent.

## REFERENCES

1. Giudice LC, Kao LC. Endometriosis. *Lancet Lond Engl*. 2004 Nov 13;364(9447):1789–99.
2. Macer ML, Taylor HS. Endometriosis and Infertility. *Obstet Gynecol Clin North Am*. 2012 Dec;39(4):535–49.
3. Practice Committee of the American Society for Reproductive Medicine. Endometriosis and infertility: a committee opinion. *Fertil Steril*. 2012 Sep;98(3):591–8.
4. Dunselman G a. J, Vermeulen N, Becker C, Calhaz-Jorge C, D’Hooghe T, De Bie B, et al. ESHRE guideline: management of women with endometriosis. *Hum Reprod Oxf Engl*. 2014 Mar;29(3):400–12.
5. Johnson NP, Hummelshoj L, Adamson GD, Keckstein J, Taylor HS, Abrao MS, et al. World Endometriosis Society consensus on the classification of endometriosis. *Hum Reprod Oxf Engl*. 2017 Feb;32(2):315–24.
6. Jacobson TZ, Duffy JM, Barlow D, Farquhar C, Koninckx PR, Olive D. Laparoscopic surgery for subfertility associated with endometriosis. *Cochrane Database Syst Rev*. 2010 Jan 20;(1):CD001398.
7. Nowroozi K, Chase JS, Check JH, Wu CH. The importance of laparoscopic coagulation of mild endometriosis in infertile women. *Int J Fertil*. 1987 Dec;32(6):442–4.
8. Adamson GD, Pasta DJ. Surgical treatment of endometriosis-associated infertility: meta-analysis compared with survival analysis. *Am J Obstet Gynecol*. 1994 Dec;171(6):1488-1504; discussion 1504-1505.
9. Nezhat C, Crowgey S, Nezhat F. Videolaseroscopy for the treatment of endometriosis associated with infertility. *Fertil Steril*. 1989 Feb;51(2):237–40.
10. Vercellini P, Fedele L, Aimi G, De Giorgi O, Consonni D, Crosignani PG. Reproductive performance, pain recurrence and disease relapse after conservative surgical treatment for endometriosis: the predictive value of the current classification system. *Hum Reprod Oxf Engl*. 2006 Oct;21(10):2679–85.
11. Cohen J, Thomin A, Mathieu D’Argent E, Laas E, Canlorbe G, Zilberman S, et al. Fertility before and after surgery for deep infiltrating endometriosis with and without bowel involvement: a literature review. *Minerva Ginecol*. 2014 Dec;66(6):575–87.
12. Adamson GD, Pasta DJ. Endometriosis fertility index: the new, validated endometriosis staging system. *Fertil Steril*. 2010 Oct;94(5):1609–15.
13. Ballester M, Oppenheimer A, d’Argent EM, Touboul C, Antoine J-M, Coutant C, et al. Nomogram to predict pregnancy rate after ICSI-IVF cycle in patients with endometriosis. *Hum Reprod Oxf Engl*. 2012 Feb;27(2):451–6.
14. Iasonos A, Schrag D, Raj GV, Panageas KS. How to build and interpret a nomogram for cancer prognosis. *J Clin Oncol Off J Am Soc Clin Oncol*. 2008 Mar 10;26(8):1364–70.

15. Brand JP. Development, implementation and evaluation of multiple imputation strategies for the statistical analysis of incomplete data sets. [Rotterdam]: Erasmus Universiteit Rotterdam; 1999.
16. Harel O, Mitchell EM, Perkins NJ, Cole SR, Tchetgen Tchetgen EJ, Sun B, et al. Multiple Imputation for Incomplete Data in Epidemiologic Studies. *Am J Epidemiol*. 2017 Nov 20;
17. Akaike H. [Data analysis by statistical models]. *No Hattatsu Brain Dev*. 1992 Mar;24(2):127–33.
18. Harrell FE, Lee KL, Mark DB. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. *Stat Med*. 1996 Feb 28;15(4):361–87.
19. Harrell FE, Lee KL, Pollock BG. Regression models in clinical studies: determining relationships between predictors and response. *J Natl Cancer Inst*. 1988 Oct 5;80(15):1198–202.
20. Schisterman EF, Perkins NJ, Liu A, Bondell H. Optimal cut-point and its corresponding Youden Index to discriminate individuals using pooled blood samples. *Epidemiol Camb Mass*. 2005 Jan;16(1):73–81.
21. Darai E, Carbonnel M, Dubernard G, Lavoué V, Coutant C, Bazot M, et al. Determinant factors of fertility outcomes after laparoscopic colorectal resection for endometriosis. *Eur J Obstet Gynecol Reprod Biol*. 2010 Apr;149(2):210–4.
22. Morice P, Uzan C, Fauvet R, Gouy S, Duvillard P, Darai E. Borderline ovarian tumour: pathological diagnostic dilemma and risk factors for invasive or lethal recurrence. *Lancet Oncol*. 2012 Mar;13(3):e103-115.
23. Mounsambote L, Cohen J, Bendifallah S, d'Argent EM, Selleret L, Chabbert-Buffet N, et al. [Deep infiltrative endometriosis without digestive involvement, what is the impact of surgery on in vitro fertilization outcomes? A retrospective study]. *Gynecol Obstet Fertil Senol*. 2017 Jan;45(1):15–21.
24. Capelle A, Lepage J, Langlois C, Lefebvre C, Dewailly D, Collinet P, et al. [Surgery for deep infiltrating endometriosis before in vitro fertilization: no benefit for fertility?]. *Gynecol Obstet Fertil*. 2015 Feb;43(2):109–16.
25. Bianchi PHM, Pereira RMA, Zanatta A, Alegretti JR, Motta ELA, Serafini PC. Extensive excision of deep infiltrative endometriosis before in vitro fertilization significantly improves pregnancy rates. *J Minim Invasive Gynecol*. 2009 Apr;16(2):174–80.
26. Papaleo E, Ottolina J, Viganò P, Brigante C, Marsiglio E, De Michele F, et al. Deep pelvic endometriosis negatively affects ovarian reserve and the number of oocytes retrieved for in vitro fertilization. *Acta Obstet Gynecol Scand*. 2011 Aug;90(8):878–84.
27. Opøien HK, Fedorcsak P, Byholm T, Tanbo T. Complete surgical removal of minimal and mild endometriosis improves outcome of subsequent IVF/ICSI treatment. *Reprod*

Biomed Online. 2011 Sep;23(3):389–95.

28. Wei D, Yu Q, Sun A, Tian Q, Chen R, Deng C, et al. [Relationship between endometriosis fertility index and pregnancies after laparoscopic surgery in endometriosis-associated infertility]. *Zhonghua Fu Chan Ke Za Zhi*. 2011 Nov;46(11):806–8.
29. Tomassetti C, Geysenbergh B, Meuleman C, Timmerman D, Fieuws S, D’Hooghe T. External validation of the endometriosis fertility index (EFI) staging system for predicting non-ART pregnancy after endometriosis surgery. *Hum Reprod Oxf Engl*. 2013 May;28(5):1280–8.
30. Boujenah J, Bonneau C, Hugues J-N, Sifer C, Poncelet C. External validation of the Endometriosis Fertility Index in a French population. *Fertil Steril*. 2015 Jul;104(1):119–123.e1.
31. Di Paola V, Manfredi R, Castelli F, Negrelli R, Mehrabi S, Pozzi Mucelli R. Detection and localization of deep endometriosis by means of MRI and correlation with the ENZIAN score. *Eur J Radiol*. 2015 Apr;84(4):568–74.
32. Carrillo L, Seidman DS, Cittadini E, Meirow D. The role of fertility preservation in patients with endometriosis. *J Assist Reprod Genet*. 2016 Mar;33(3):317–23.

## LEGENDS FOR FIGURES AND TABLES

**Figure 1:** The probability of a live birth is calculated by drawing a line to the point on the axis for each of the following variables: age, BMI, AMH and Enzian score. The points for each variable are summed and located on the total points line. Next, a vertical line is projected from the total points line to the predicted probability bottom scale to obtain the individual probability of a live birth.

**Figure 2:** A- ROC curve of the model, B- Calibration of the nomogram to predict the LBR in women with DIE without bowel involvement surgery. The discrimination accuracy of the model was 0.84 (95% CI, 0.82–0.86). There was no difference between the predicted probabilities and the observed LBRs ( $P=0.3829$ ).

**Figure 3:** Cumulative LBR according to the optimal threshold ( $p<0.001$ ) for the overall population

**Figure 4:** Cumulative LBR according to the optimal threshold ( $p<0.001$ ) for women who conceived spontaneously

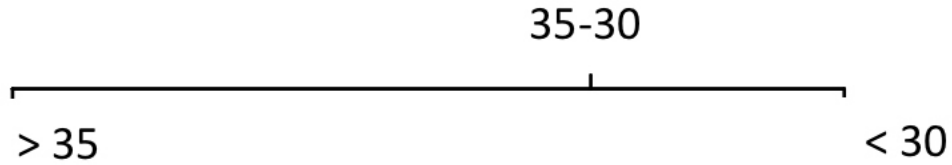
**Table 1:** Characteristics of the overall population

**Table 2:** Characteristics of the population according to the type of pregnancy

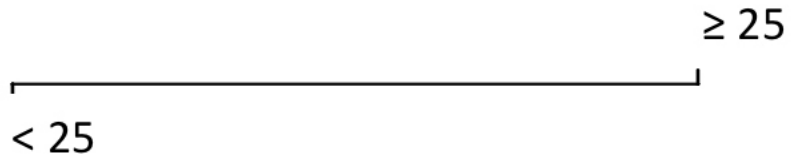
**Table 3 :** Multivariate analysis

Points 0 10 20 30 40 50 60 70 80 90 100

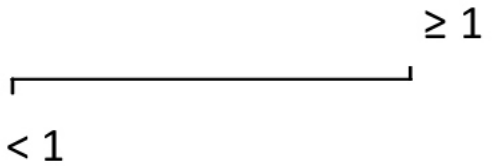
Age (years)



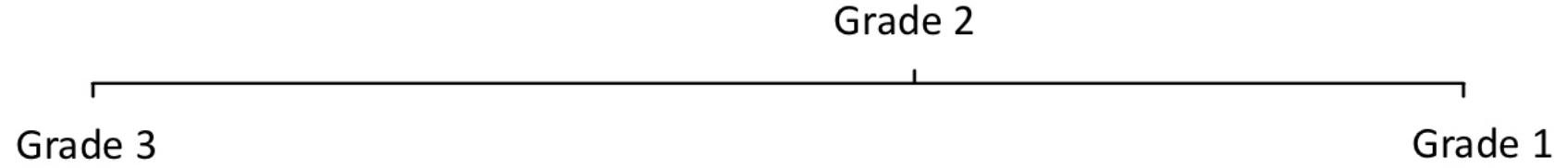
BMI (kg/m<sup>2</sup>)



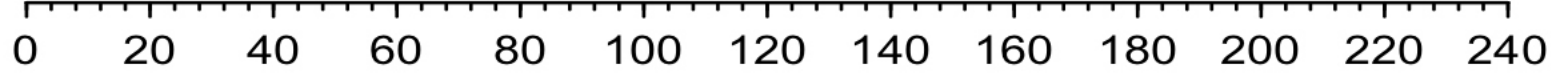
AMH serum level (ng/ml)



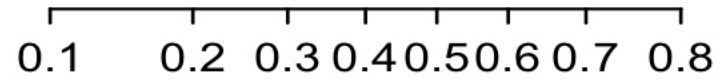
Enzian score

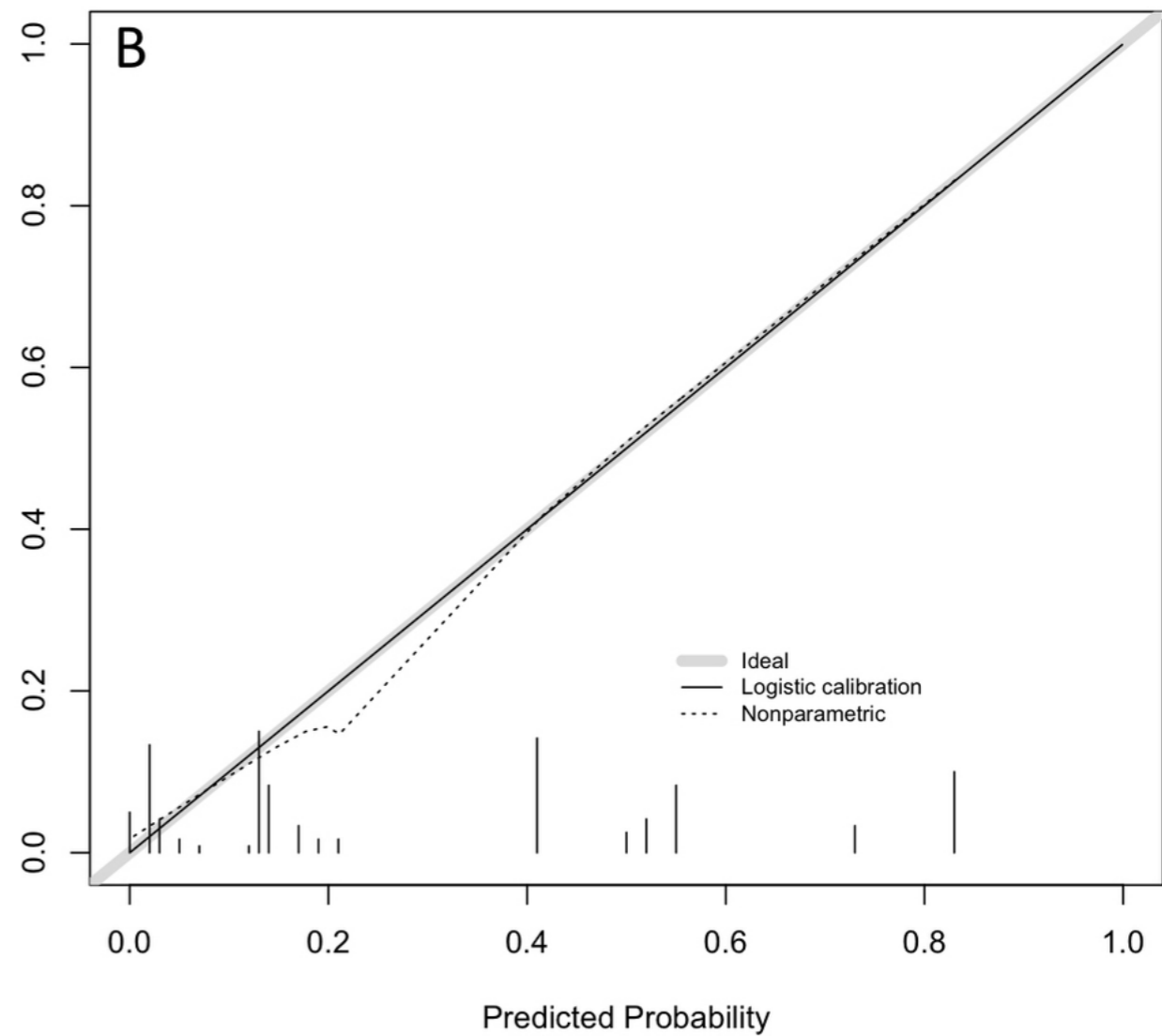
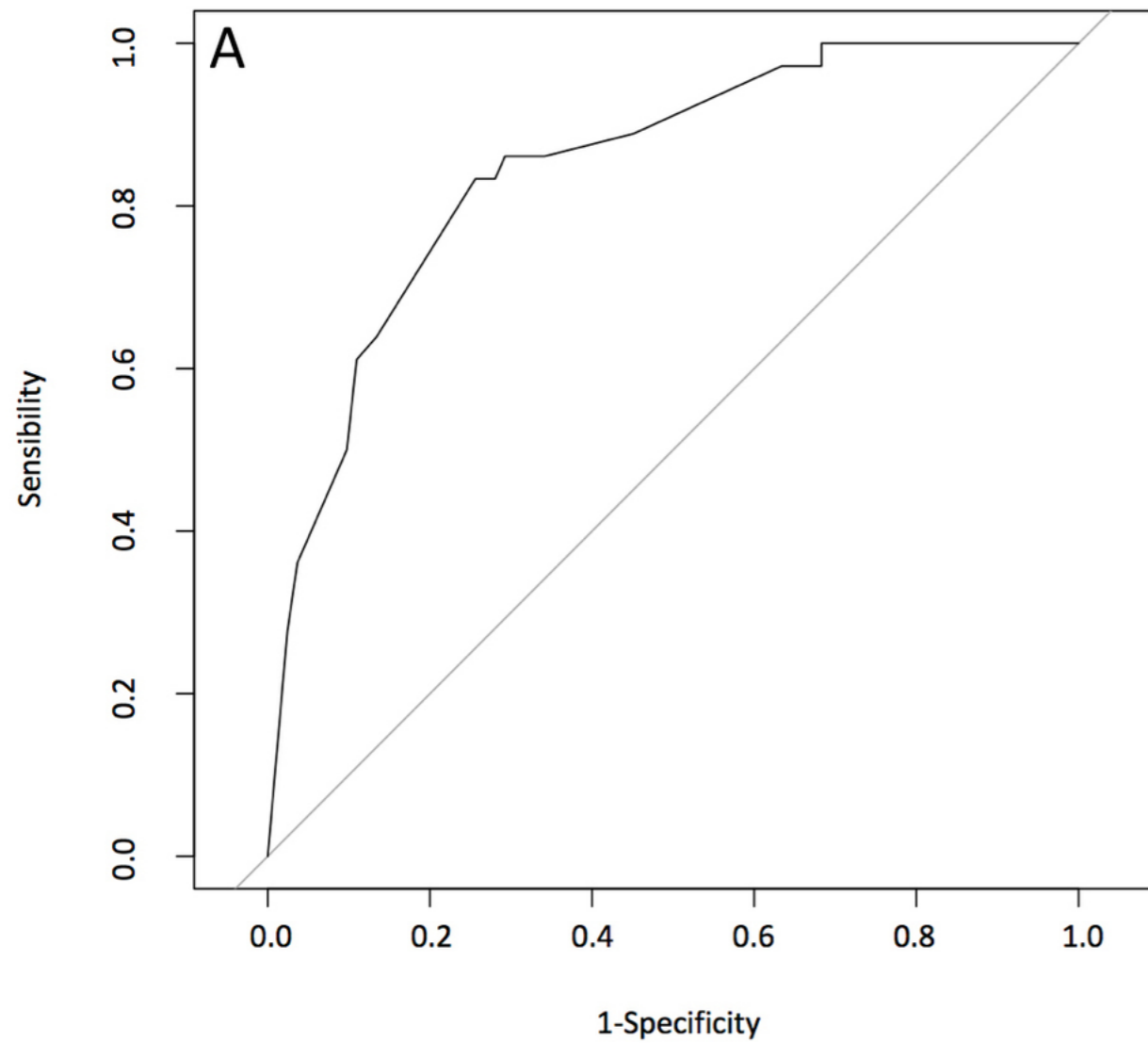


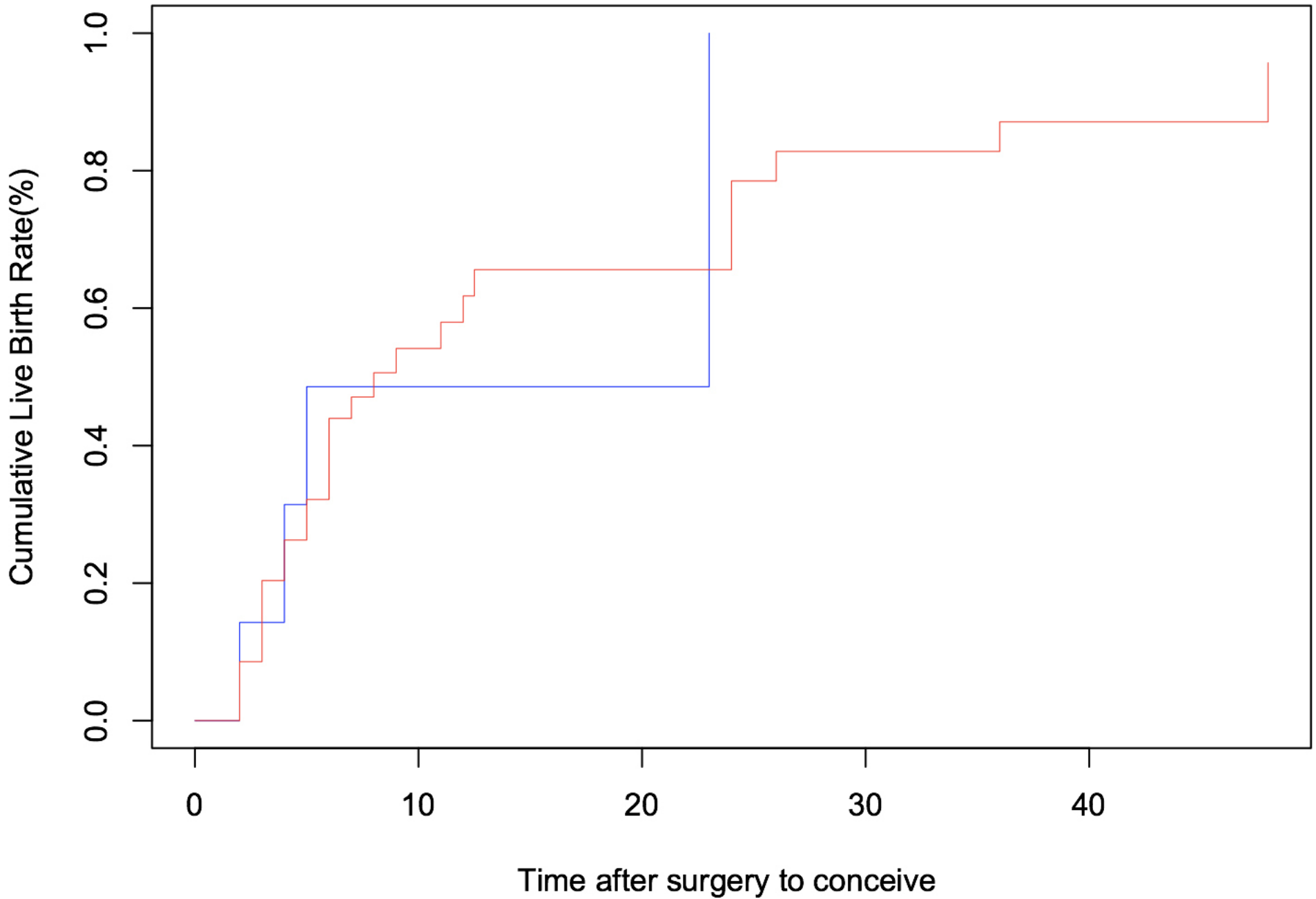
Total points

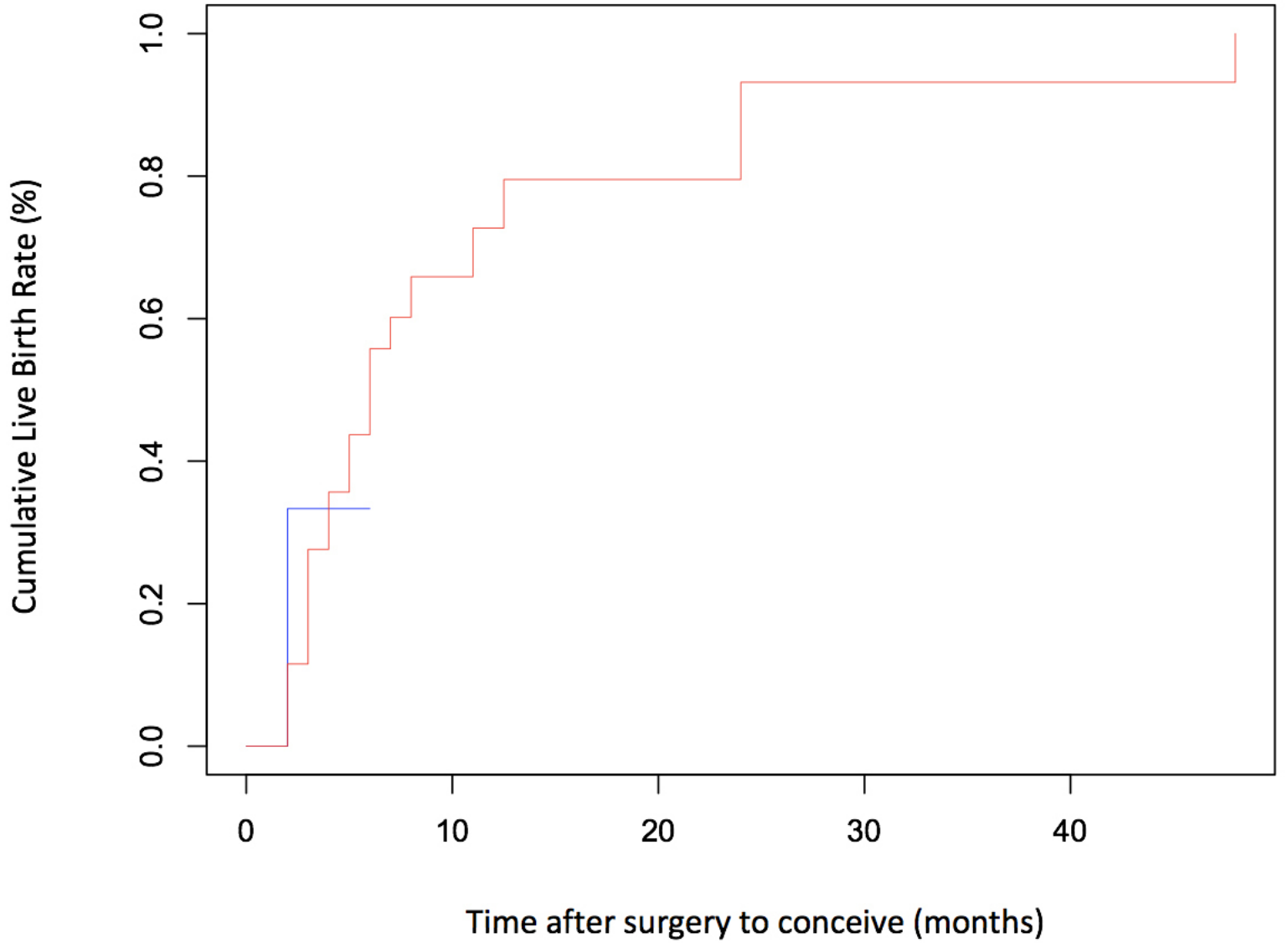


Probability of Live-Birth









**Table 1: Characteristics of the overall population**

	<b>Overall population n=118 n (%)</b>	<b>Women with no live births n = 82 n (%)</b>	<b>Women with live births n = 36 n (%)</b>	<b>P-Value<sup>b</sup></b>
<b>Mean age at diagnosis (range):</b>		30.8 (22-42)	28.6 (19-40)	
<b>Age ≤ 30 years:</b>				
- Yes	63 (53.4)	38 (46.3)	25 (69.4)	0.02
- No	55 (46.6)	44 (53.7)	11 (30.6)	
<b>BMI ≥ 25 kg/m<sup>2</sup>:</b>				
- Yes	19 (16.1)	16 (19.5)	3 (8.3)	0.15
- No	89 (75.4)	60 (73.1)	29 (80.5)	
- NA <sup>a</sup>	10 (8.5)	6 (7.4)	4 (11.1)	
<b>Smoking</b>				
- Yes	32 (27)	19 (23.2)	13 (36.1)	0.09
- No	66 (56)	50 (61)	16 (44.4)	
- NA	20 (17)	13 (15.8)	7 (19.4)	
<b>Infertility prior surgery</b>				
- Yes	66 (56)	47 (57.3)	19 (52.8)	0.65
- No	52 (44)	35 (42.7)	17 (47.2)	
<b>Prior surgery for endometriosis</b>				
- Yes	26 (22)	17 (20.7)	9 (25)	0.61
- No	92 (78)	65 (79.3)	27 (75)	
<b>MRI: adenomyosis</b>				
- Yes	17 (14.4)	10 (12.2)	7 (19.4)	0.25
- No	99 (83.9)	72 (87.8)	27 (75)	
- NA	2 (1.7)	0 (0)	2 (5.6)	
<b>Enzian score</b>				
- Grade 1	46 (39)	21 (25.6)	25 (69.5)	<0.0001
- Grade 2	27 (22.9)	19 (23.2)	8 (22.2)	
- Grade 3	45 (38.1)	42 (51.2)	3 (8.3)	
<b>ASRM score</b>				
- I/II	42 (35.6)	29 (35.4)	13 (36.1)	0.94
- III/IV	76 (64.4)	53 (64.6)	23 (63.9)	0.39
- median	/	37	30	
<b>Surgical route</b>				
- Laparoscopy	118 (100)	82 (100)	36 (100)	1
<b>Surgery resection: torus and/or utero-sacral ligaments</b>				

- Yes	82 (69.5)	60 (73.2)	22 (61.1)	0.19
- No	36 (30.5)	22 (26.8)	14 (38.9)	
<b>Surgery resection: torus and/or utero-sacral ligaments and cystectomy</b>				
- Yes	36 (30.5)	22 (26.8)	14 (38.9)	0.19
- No	82 (69.5)	60 (73.2)	22 (61.1)	

BMI: body mass index; AMH: antimullerian hormone; ASRM: american society for reproductive medicine

<sup>a</sup>NA, not available

<sup>b</sup>Univariate analysis

**TABLE 2: Characteristics of the population according to the type of pregnancy**

	<b>Spontaneous pregnancy</b>	<b>MAR pregnancy</b>	<b>p value</b>
	<b>n= 31 n (%)</b>	<b>n= 16 n (%)</b>	
<b>Age (year): ≤30</b> median, range	30 (19-41)	28.5 (22-38)	0.86
- Yes	22 (71)	10 (62,5)	0,55
- No	9 (29)	6 (37,5)	
<b>BMI (kg/m<sup>2</sup>) &gt;30</b> median, range	22 (17-29)	21 (16-30)	0.44
- Yes	0 (0)	3 (18.8)	0.04
- No	27 (87.1)	12 (75)	
- NA	4 (12.9)	1 (6.2)	
<b>Tobacco</b>			
- Yes	8 (25.8)	6 (37.5)	0.28
- No	19 (61.3)	6 (37.5)	
- NA	4 (12.9)	4 (25)	
<b>Prior surgery for endometriosis</b>	7 (22.6)	6 (37.5)	0.28
<b>AMH (ng/ml)</b> median, range	3.6 (1-6,1)	3.1 (0.48-6.7)	0.08
- <2	1 (3.2)	6 (37.5)	0.0004
- <1	0 (0)	2 (12.5)	0.03
- NA	12	7	
<b>MRI : adenomyosis</b>	5 (16.1)	4 (25)	0.46
<b>rASRM total score:</b> median, range	20 (4-124)	50 (4-114)	0.52
- Stade I, II	12 (38.7)	5 (31.2)	0.61
- Stade III, IV	19 (61.3)	11(68.8)	0.61
<b>ENZIAN score</b>			
- Grade 1	24 (77.4)	9 (56.2)	0.07
- Grade 2	6 (19.4)	3 (18.8)	
- Grade 3	1 (3.2)	4 (25)	

<b>Surgery resection: torus and/or utero-sacral ligaments</b>	22 (71)	8 (50)	0.09
<b>Pregnancy rate at 12 months</b>	24 (77.4)	9 (56.3)	0.18
<b>Pregnancy rate at 24 months</b>	29 (93.5)	12 (75)	0.25

Table 3 : Multivariate analysis

Variable	Multivariate analysis OR (95% CI)	P-value
Age (years)	Reference	
≤ 30	0.55 (0.05-5.73)	
30-35	0.14 (0.04-0.48)	0.0024
≥ 35		
BMI (kg/m <sup>2</sup> )	Reference	
≥ 25	5.1 (1.05-24.3)	0.029
< 25		
AMH (ng/ml)	Reference	
< 1	2.56 (0.21-30.7)	0.44
≥ 1		
Enzian score	Reference	
Grade 1	0.25 (0.07-0.82)	
Grade 2	0.03 (0.007-0.14)	<0.001
Grade 3		