Original article

The benefit of adenomyomectomy on fertility outcomes in women with rectovaginal endometriosis with coexisting adenomyosis

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Study Objective: To evaluate the effect of removal of coexisting adenomyosis on fertility outcomes in women with rectovaginal endometriosis.

Design: A retrospective cohort study.

Setting: A general hospital.

Patients: A total of 190 women who underwent laparoscopic nodule excision surgery for rectovaginal endometriosis between April 2007 and December 2012.

Interventions: Surgical excision of the rectovaginal endometriosis and coexisting uterine adenomyosis.

Measurement and main results: A total of 119 women desired postoperative pregnancy. Coexisting adenomyosis was found in 21% of the women. The overall clinical pregnancy rate was 41.2%. The only determining factor associated with a successful pregnancy was "age at surgery." Clinical pregnancy rates with or without adenomyosis were 36.0% and 42.6%, respectively. We found no significant difference in clinical pregnancy rates between the groups.

Conclusion: There is a possibility that surgical removal of coexisting adenomyosis positively effects fertility outcomes in women with rectovaginal endometriosis. However, it is also important to note that the age at surgery was a critical factor for successful pregnancy.

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Introduction

Deep rectovaginal endometriosis is one of the most severe forms of pelvic endometriosis, and its prevalence is estimated to be 5–10% of all pelvic endometriosis cases. With the recent trend toward delayed childbearing, patients with endometriosis associated subfertility show a tendency of aging and advancing in severity. This brings a range of difficulties in treatments aiming at restoring fecundity. In severe cases, adenomyosis often coexists with endometriosis and localizes at the outer myometrium without aberrations of the subendometrial myometrium (Figure 1). Recent development of image diagnostic tools like magnetic resonance imaging (MRI) has enabled preoperative diagnosis of adenomyosis. Now, the main treatment options of endometriosis associated subfertility are assisted reproductive technology (ART) and surgery. A recent article showed a higher clinical pregnancy rate of the combined treatment of surgery and subsequent in vitro fertilization (IVF) than that of surgery alone or IVF alone in women with endometriosis associated infertility.3 Regarding the determinants of fertility outcomes after surgical treatments for rectovaginal endometriosis, coexisting adenomyosis is often pointed out.4,5 However, as a recent review points out, adenomyosis was not excised in these reports.6 Thus, the effect of the removal of coexisting adenomyosis on fertility outcomes is not fully evaluated. We have performed a nodule excision surgery avoiding segmental resection in the vast majority of cases, and have routinely removed coexisting adenomyosis in all cases that MRI showed adenomyosis. We set the aim of this study on analyzing factors relating to fertility outcomes in the surgery of deep rectovaginal endometriosis, and on evaluating the effect of removal of coexisting adenomyosis.

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Materials and methods

We retrospectively compiled data of 190 women with histologically confirmed rectal endometriosis between April 2007 and December 2012. All the patients underwent surgery in the Department of Obstetrics and Gynecology, Takanohara Central Hospital, Nara, Japan. Surgical data including postoperative complications were retrieved from an operative database. Pregnancy outcomes were collected from questionnaires and/or interviews with outpatients. Among 174 women who underwent uterus conservative surgery, 119 desired postoperative pregnancies, and 116 (116/119: 99.5%) answered the questionnaire. In this study, we analyzed the 119 women that had the wish to get pregnant. Three women lost to follow-up were treated as “did not conceive”. We defined “clinical pregnancy” as the presence of a fetal heart beat at 12 weeks of gestation. All coexisting adenomyosis cases were diagnosed by preoperative MRI, and all of these were confirmed histologically. The criteria used for the definition of adenomyosis on MRI were: (1) a myometrial mass with indistinct margins of primarily low intensity with all sequences; or (2) diffuse or local widening of the junctional zone on T2 weighted images (wider than 12 mm).7–9 Furthermore, we analyzed the factors relating to clinical pregnancy by using univariable and multivariable regression analyses. The employed variables in these analyses were: age at surgery, coexisting adenomyosis, weight of adenomyosis, coexisting endometrioma, revised American Fertility Society scores, whether performing a “full thick resection” or not, and presence or not of bilateral tubal occlusions in a tubal patency test during the surgery. We defined “full thick resection” as occurrence of rectal perforations during the slicing; a partial thick resection means perforation did not occur. None of the individuals were treated preoperatively with hormonal medicines. Preoperative pain symptoms were treated with nonsteroidal antiinflammatory drugs. Postoperative hormonal drugs were prescribed in some cases who did not wish for a pregnancy. This study was approved by the Institutional Ethical Review Board of Takanohara Central Hospital on 28 November 2013 (ID 2013003), and informed consent was obtained from each of the patients.

Statistical analysis

The $\chi^2$ test was used for the comparison of groups with regard to categoric variables: the Fisher exact test was used in the case of small cell counts. Parametric and nonparametric continuous variables were compared using the Student t test and the Mann–Whitney test. A p value < 0.05 was considered statistically significant. Stepwise logistic regression analysis was used for the multivariable analysis of the factors relating to clinical pregnancy (IBM Statistics software; version 16; SPSS Inc., Chicago, IL, USA).

Surgical procedures

The patient was placed in the Trendelenburg’s position and triple puncture laparoscopic surgery was performed. We used a potassium titanyl phosphate laser device for incisions, and a bipolar device for vaporization. To superficial endometriosis, excision or vaporization was performed, and a cystectomy of ovarian endometrioma was carefully performed. Vaporization of the cyst wall was sometimes selected in cases having a history of ovarian cystectomy from the view of preservation of ovarian function. Rectovaginal endometriosis often infiltrates into the posterior wall of the uterus and the anterior wall of the rectum; the former one is often recognized as a posterior wall adenomyosis. With the use of a potassium titanyl phosphate laser device, we carefully sliced off the endometriotic nodules from both the anterior wall of the rectum and the posterior wall of the uterus. In instances having a very large nodule, we initiated the procedure by dissociation of the rectovaginal endometriotic nodules from the uterus, keeping the nodules attached to the anterior rectal wall, in the same fashion as other authors.10–12 Afterwards, the nodule was sliced off from the anterior wall of the rectum. The defected rectal wall (perforated or not) is continuously stitched with 2-0 synthetic absorbable sutures. For coexisting adenomyosis, we performed an adenomyomectomy as completely as possible in a surgical method reported earlier.13 Defected spaces were carefully obliterated with continuous stitches of 2-0 synthetic absorbable sutures to close the residual myometrium. All the surgeons performed these procedures routinely.

Results

Between 2007 and 2012, we performed 191 surgeries for deep rectovaginal endometriosis. Among them, 190 (190/191: 99.5%) cases were managed by laparoscopic nodule excision surgery with the exception of one case of segmental bowel resection operated with assistance from colorectal surgeons. Of the 174 women who selected conservative surgery, 119 desired postoperative pregnancy including five unmarried women (Table 1). Pregnancy outcomes are presented in Table 2. The median follow-up period was 24 months (range: 12–60 months). Among the 119 women who wished to conceive or were unmarried at the time of surgery, 54/119 (45.3%) became pregnant. There was no pregnancy among five unmarried women. Clinical pregnancy was found in 49/119 (41.2%) women. All the clinical pregnancy cases were conceived spontaneously or by IVF (intracytoplasmic sperm injection [ICSI]-IVF).

All 49 cases of clinical pregnancy were delivered successfully, and none of the women who underwent adenomyomectomy delivered with the use of an elective cesarean section. The median time of conception linked to clinical pregnancy was 13.7 months (range: 1–56 months). There were no obstetrical complications. Spontaneous pregnancy was found in 34/119 (28.6%) cases, and ART
pregnancy was found in 15/119 (12.6%) cases. There was no significant difference in age between the spontaneous and ART pregnancy groups. We further analyzed factors linked to clinical pregnancy with the use of univariable analysis (Table 3). “Age at surgery” was the only variable where we found significant differences between the groups. The age at surgery was also the only variable that was extracted using multivariable regression analysis for clinical pregnancy [odds ratio of 0.786 (95% confidence interval: 0.700–0.883)]. The maximum age of women succeeding in clinical pregnancy was 41 years.

Pregnancy outcomes with or without coexisting adenomyosis are presented in Table 4. Adenomyosis was found in 25/119 (21%) of women. We found significant differences between the groups in age at surgery. The age of the group with adenomyosis was significantly higher. Clinical pregnancy rates with or without adenomyosis were 36.0% and 42.6%, respectively. We found no significant difference in clinical pregnancy rates between the groups. Age distribution graphs of each group are shown in Figure 2.

Table 2
Pregnancy outcomes.

| Wish for a baby, total, n | Average age (y), range |
|--------------------------|------------------------|
| Overall pregnancy, n/n (%) | 119/119 (45.3) |
| Miscarriage, n | 4 |
| Ectopic pregnancy, n | 1 |
| Clinical pregnancy, n/n (%) | 49/119 (41.2) |
| Spontaneous pregnancy, n/n (%) | 34/119 (28.6) |
| ART pregnancy, n/n (%) | 15/119 (12.6) |

Median follow-up period: 24 months (range 12–60 months).
ART = assisted reproductive technology.

Discussion

We have routinely removed coexisting adenomyosis in nodule excision surgery for severe rectovaginal endometriosis. The major complication rate in our current study was 1% (2/190) in total, and we have not experienced persistent bowel and bladder dysfunctions following the surgery; this result is common with other surgeons applying nodule excision surgery.11,14 Nodule excision surgery was considered to be just the right treatment in cases of deep rectovaginal endometriosis.

In this study, we showed a strong negative impact of age on fertility outcomes. Age at surgery was extracted as the only determinant for clinical pregnancy, and the maximum age of women succeeding in clinical pregnancy was 41 years. Furthermore, when the women were divided into under 39 years of age and > 40 years of age groups, the clinical pregnancy rates were found to be 47.1% (48/102) and 5.9% (1/17). The decrease in the number and quality of oocytes is most commonly considered to be the cause of such a decline in pregnancy rates with advancing maternal age.15–17 Our results might imply the fact that surgical intervention cannot compensate for age-related decline in fertility.

Next, we would like to focus on the impact of coexisting adenomyosis on pregnancy outcomes. As mentioned above, we have routinely removed coexisting adenomyosis as completely as possible before surgery. As mentioned above, we have not experienced persistent bowel and bladder dysfunctions following the surgery; this result is common with other surgeons applying nodule excision surgery.11,14 Nodule excision surgery was considered to be just the right treatment in cases of deep rectovaginal endometriosis.

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As a result, coexisting adenomyosis was not deduced as a clear negative factor for clinical pregnancy, in contrast to earlier publications suggesting an adverse effect of coexisting adenomyosis on fertility outcomes when adenomyosis was not excised. In our results, the clinical pregnancy rate of women with adenomyosis appeared to be relatively lower than those without adenomyosis; however, this did not reach statistical significance. Then can we say that removal of coexisting adenomyosis improved fertility outcomes? Vercellini et al. reported that postoperative pregnancy rates when adenomyosis was not excised were around 11.9%. By contrast, the clinical pregnancy rate in the present study was 36.0%. This is rather nearer to those of generally reported postoperative pregnancy rates after surgery of severe endometriosis (30–50%). The significantly higher age could be considered as a reason for the “relatively lower clinical pregnancy rate” in the group with adenomyosis. As we showed in Figure 2, the proportion of over 35-year-olds is found to be larger in the group with adenomyosis. The difference in age distribution would bring a certain degree of difference in fertility outcomes. Although it would be inevitable that successful pregnancy rates of the women with adenomyosis could be relatively low, we believe that our present result indicates a possibility that adenomyomectomy improves fertility outcomes among those women.

Table 4

|                      | Adenomyosis + (surgery with adenomyomectomy) | Adenomyosis − (surgery without adenomyomectomy) | p       |
|----------------------|---------------------------------------------|-------------------------------------------------|---------|
| Age (y), median (range) | 37.0 (29–47)                                | 34.3 (24–48)                                    | 0.001<sup>a</sup>,<sup>b</sup> |
| Overall pregnancy, n/n (%) | 10/25 (40.0)                                | 44/94 (46.8)                                    | 0.543<sup>c</sup> |
| Clinical pregnancy, n/n (%) | 9/25 (36.0)                                 | 40/94 (42.6)                                    | 0.554<sup>c</sup> |
| Miscarriage, n | 1                                            | 3                                               | 0.842<sup>c</sup> |
| Ectopic pregnancy, n | 0                                            | 1                                               | 0.605<sup>c</sup> |

<sup>a</sup> Mann-Whitney U test.
<sup>b</sup> Significant at p ≤ 0.05.
<sup>c</sup> χ² test.

Figure 2. Age distribution graphs. Age distributions of each group are shown. The total numbers of each age range and the numbers of women that succeeded in clinical pregnancy are indicated in parallel bar graphs. Preg = pregnancy.
endometriosis typically localizes at the outer myometrium of the posterior wall keeping the junctional zone, where their sizes are, in most cases, not so extensively large, and the healthy myometrium can be seen between the adenomyosis and the endometrium. However, the deliberate consideration based on a precise diagnosis of the size and localization of each case of adenomyosis should be given for this type of surgery.

Lastly, we would like to consider the limitations of the study. Firstly, our present study was a retrospective cohort study, where patients’ selection biases should be taken into consideration. Not all women were able to determine their desire for pregnancy at the time of surgery; those who were unmarried women. We categorized those women into the “wish for baby” category. There was missing data because of several cases of lost follow-ups. These cases were treated as “did not conceive”. By this, we think we could prevent our results from giving an overestimate. Secondly, the impact of ART on pregnancy outcomes was not necessarily adequately assessed in this study. One reason considered for this was that a large number of women wished for a spontaneous pregnancy. Thus, it should be noted that our results are not enough to give conclusive evidence on the true impact of ART on pregnancy outcomes. However, it would also be a fact that the strong negative impact of age on successful pregnancy was based on the result that most women of an older age group (>40 years old) failed in successful pregnancy even after ART treatment. A well-conducted randomized study would be preferable to evaluate the true impact of adenomyosis or ART treatment on fertility outcomes.

In conclusion, our results indicate a possibility that removal of adenomyosis improves fertility outcomes among women with rectovaginal endometriosis. However, age at surgery was the critical factor for successful pregnancy. It is important to note that surgical intervention cannot compensate for age-related decline in fertility.

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