# Clinical evaluation of three methods in the treatment of adenomyosis

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#### Summary

Objective: To evaluate the efficacy of three methods in the treatment of adenomyosis (ADM). Materials and Methods: Retrospective analysis of the clinical data of 180 patients with ADM diagnosed in the First Affiliated Hospital of Xinjiang Medical University from 2010 January to 2013 January, including 75 cases of hysterectomy (Group A), 30 cases underwent ultrasound guided radiofrequency ablation (group B), and 75 cases of gonadotropin releasing hormone (GnRH) conservative drug treatment (Group C). Results: Hysterectomy is an effective treatment, but the patients will lose reproductive function, and may lead to premature ovarian failure. GnRH drugs are not exact, long course of treatment, the price is expensive, and the side effect is important. radiofrequency ablation has little side effect, hospitalization time is short, less treatment cost, will not change the ovarian blood supply, does not affect ovarian function, for patients with fertility requirements, and uterine aspiration and retention can be used as the preferred method of treatment. Conclusion: Ultrasound guided radiofrequency ablation treatment of uterine adenomyosis, as a minimally invasive technique to preserve the uterus, and radiofrequency ablation is expected to be new targeting ways for ADM, to make up the deficiency of existing treatment methods, maintain the retention period uterine endocrine function and endometrial shedding, maintain the patients physiological and psychological balance, and prevent reproductive tract infection, and is expected to become the safe, effective new way of treatment of ADM.

Key words: Adenomyosis; Radiofrequency ablation; Surgery; GnRH.

#### Introduction

Adenomyosis (ADM) is the invasion of functional endometrial glands and stroma in the myometrium by benign lesions caused by a variety of pathogenic factors, heavy menstruation, and obvious dysmenorrhea are the main clinical features, mostly occurring at 40 years of age or older and seriously affects the health and quality of life in women. The incidence is significantly increase in recent years and has became a worldwide gynecological problem [1, 2]. Previously there was medical treatment and surgical treatment, but its high cost and the larger adverse effects, relapse rate after treatment, increased recurrence rate in conservative surgery, and with the presence of radical surgery, there was risk of loss of fertility and some patients had poor results. Radiofrequency ablation of ADM is a minimally invasive technique to retain the uterus, can be repeated with effective treatment, and is a simple operation with easy application. This study retrospectively analyzed 180 cases of uterine ADM patients from January 2010 to January 2013 in the present hospital, with three different lines of treatment and follow-up, and are reported below.

## Material and Methods

The clinical and pathological diagnosis of ADM of 180 fertile patients, between ages 29 to 52 (mean 41.08) years. All patients had clinical symptoms of varying degrees, as dysmenorrhea, increased menstrual flow, menstruation, lower abdominal pain dur-

ing menstruation, etc., a history of two to 15 (mean  $(6\pm2.8)$  years. Patients were without menopausal symptoms, without coagulation disorders, liver and kidney dysfunction, hypertension, diabetes, and coronary heart disease history. According to the different treatment groups of patients: 1) hysterectomy group A: 75 cases, 2) radiofrequency ablation group B: 30 patients, and 3) GnRH drugs conservative group C: 75 cases. All patients were followed up.

Before and after treatment patients were followed up every time to understand the following items: 1) dysmenorrhea rating: adoption of internationally accepted Visual Analogue Scale (VAS) recording, the scale  $1 \sim 10$ , 0 representing no pain and 10 being the most severe pain, 2) menstrual flow rates: the use of menstrual blood loss figure fPBAC) score, according to Higham *et al.* [3] using the standard monthly PBAC score more than 100 points considered menstrual flow > 80 mL, was diagnosed as menorrhagia, 3) B ultrasonic examination: vaginal B-ultrasound discovered uterine size, lesion size, anterior and posterior wall thickness, uterine size (by a long ellipsoid volume formula) = 0.523 × diameter × anterior posterior diameter × diameter [4], and 4) detection before and after treatment with a month of hemoglobin, E2, and CA125.

In June after treatment, the shape and size of the uterus returned to normal and the clinical symptoms disappeared; after radiofrequency ablation the total volume of uterus or ectopic lesions reduced and more than 20% of clinical symptoms improved. After radiofrequency treatment within six months, the total volume of uterus and morphology or the ectopic lesions of myometrium showed no significant change and there was no improvement or worsening in clinical symptoms [5]. Total efficiency = (cure + improved) / total number of cases.

SPSS 17.0 software was utilized for statistical analysis of measurement data to meet the parametric test conditions, analyze variance, and those that did not meet the parametric test conditions rank sum test. The data was counted by utilizing the  $\chi^2$  test (test level  $\alpha = 0.05$ ). A p < 0.05 was considered statistically significant.

Table 1. — *Comparison of the treatment effect among the three groups.* 

|                                 | A group (n=75) | B group (n=30) | C group (n=75) | $\chi^2$ | p       |
|---------------------------------|----------------|----------------|----------------|----------|---------|
| Number of cured patients        | 75(100.0)      | 20(66.7)       | 0              | 160.565* | < 0.001 |
| Number of patients who improved | 0              | 9(30.0)        | 44(58.7)       |          |         |
| Effective treatment             | 75(100.0)      | 29(96.7)       | 44(58.7)       | 77.849▲  | < 0.001 |
| Non effective treatment         | 0              | 1(3.3)         | 31(41.3)       |          |         |

<sup>\*</sup> Number of radiofrequency ablation for the cure group, surgical treatment group, and the conservative treatment group of three methods, improving the number of inactive persons.

Table 2. — Comparison of three groups according to age, length of hospital stay and expenses.

|                   | A group (n=75)     | B group (n=30)   | C group (n=75)     | $F/\chi^2$ | p       |
|-------------------|--------------------|------------------|--------------------|------------|---------|
| Age               | 42.12±5.16         | 37.33±4.25       | 41.55±4.86         | 10.831     | < 0.001 |
| Stay in hospital  | 11.00 (5.00)       | 2.00(1.00)       | 7.00 (6.00)        | 71.010     | < 0.001 |
| Hospital expenses | 16326.21 (5172.60) | 2920.00 (170.00) | 10230.00 (9774.02) | 79.943     | < 0.001 |

Age of variance test, length of stay, and hospital expenses rank test, α 0.05

#### Results

At one-year follow-up in group A (hysterectomy group) after treatment, 75 cases were cured and the ADM rate was 100% (75/75). Radiofrequency ablation in group B after treatment, 20 cases were cured, was effective in 29 cases and ineffective in one case. In group with ADM treatment, the efficiency was 96.7% and the cure rate was 66.7%. GnRH drugs in conservative group C after treatment was effective in 44 cases, ineffective in 31 cases, and the treatment efficiency was 58.7%. In the three groups of patients treated, the difference was statistically significant (p < 0.001), group A treatment efficiency > group B > group C.

All patients received one month to one year follow-up; 95 cases postoperatively had complete disappearance of dysmenorrhea, menstrual flow was significantly reduced, changed daily menstrual pads not more than three times, menstruation lasted 2~5 days, with no positive signs in pelvic examination. Fifty-three cases had less complaint of dysmenorrhea than before, 18 cases showed no significant change in dysmenorrhea, and three cases showed an increase, and 11 cases had recurrence, as shown in Table 2.

In group A, the hysterectomy operation time was  $101.8 \pm 34.1$  minutes, and mean blood volume  $200 \pm 75$  mL. In the radiofrequency ablation group B, the operation time was  $18 \pm 8$  minutes and blood loss was less than 10 ml. GnRH drugs in patients with conservative treatment in group C of one to nine-pin, a total of 32 patients underwent anti-drug add-on therapy. The above data in group B compared with radiofrequency ablation hysterectomy group A had a shorter operative time with less blood loss.

Selecting treatment time: after one week the menstrual bleeding stopped (abnormal uterine bleeding was excluded after endometrial lesions). Preoperative cleansing enema and moderate bladder filling were done. There were patients who required to have their IUD removed before surgery. Uterine shape was palpated with a spatula in

lithotomy position. Needle electrode (radiofrequency ablation) equipment BBT-RF-C-type machine was utilized, with intravenous anesthesia, dynamic ultrasound monitor, and the needle electrode was guided through the vagina into the cervix thickening of the myometrium (ectopic foci). Power parameters were selected according to the product manual, with settings of 25~40 W. The entire cross-section of the ultrasonic probe and needle electrode slitting position were always ensured that they were positioned in the middle of the diseased tissue. Complete solidification after radiofrequency ablation of diseased tissue automatically indicated to stop. The B-longitudinal and transverse planes showed hyperechoic circular light group, gradually expanded to cover the entire thickened myometrium (ectopic foci), hypoechoic area without internal lesions indicated successful treatment before the end of treatment.

The total hysterectomy group was hospitalized for 11.00 ± 5.00 days, the radiofrequency ablation group B total hospitalized for  $2.00 \pm 1.00$  days, and the GnRH drugs conservative total hospitalized group C for  $7.00 \pm 6.00$  days. Three groups of patients hospitalized for a total time of treatment difference was statistically significant ( $p \le$ 0.001), i.e. hysterectomy group A hospital stay > group C > group B. Group B radiofrequency ablation group showed the hospitalization shortest time. Group A hysterectomy group hospitalization cost was  $16326.21 \pm 5172.60$  Yuan, radiofrequency ablation group B was  $2920.00 \pm 170.00$ Yuan, and the GnRH drugs conservative group C it was  $10230.00 \pm 9774.02$  Yuan. The three groups regarding hospital costs significantly compared with patients (p =<0.001), i.e. hysterectomy A group of hospital costs > group C > group B, indicating that the treatment costs were the least in the radiofrequency ablation group B patients

A standard indicator for the diagnosis of anemia in patients with hemoglobin and hemoglobin changes in men-

A Comparison group for the effective number of radiofrequency ablation, surgical treatment group, and the conservative treatment group of the two methods, ineffective compare the ratio of the number.

Table 3. — Comparison of the groups before and after treatment of hemoglobin, E2, CA125, tumor size, and anterior and posterior wall thicknesses.

| Posterior wattrittenite                   | */ =-:          |        |              |                 |              |             | ~ */ ==:        |        |         |
|---|-----------------|--------|--------------|-----------------|--------------|-------------|-----------------|--------|---------|
|   | A group *(n=75) | Z      | p            | B group *(n=30) | Z            | p           | C group *(n=75) | Z      | p       |
| Hemoglobin                                |                 |        |              |                 |              |             |                 |        |         |
| Before treatment                          | 106.00 (34.00)  | -5.233 | < 0.001      | 103.50 (16.25)  | -3.731       | < 0.001     | 104.00 (12.00)  | -6.171 | < 0.001 |
| After treatment                           | 118.00 (22.00)  |        |              | 109.00 (18.50)  |              |             | 110.00 (15.00)  |        |         |
| Before and after                          | 8.00 (15.00)    |        |              | 5.00 (11.25)    |              |             | 3.00 (9.00)     |        |         |
| treatment (after-before)                  | 0.00 (15.00)    |        |              | 3.00 (11.23)    |              | 3.00 (3.00) |                 |        |         |
| CA125                                     |                 |        |              |                 |              |             |                 |        |         |
| Before treatment                          | 67.15 (64.20)   | -7.525 | < 0.001      | 67.22(61.00)    | -3.950       | < 0.001     | 68.92(60.70)    | -6.741 | < 0.001 |
| After treatment                           | 12.00 (14.00)   |        |              | 42.00 (43.75)   |              |             | 42.00 (45.00)   |        |         |
| Before and after treatment (after-before) | -47.00 (54.30)  |        |              | -3.35 (12.48)   |              |             | -10.00 (23.50)  |        |         |
| E2  |                 |        |              |                 |              |             |                 |        |         |
| Before treatment                          | 79.00 (85.00)   | -7.295 | < 0.001      | 62.50 (51.88)   | -0.025       | 0.0980      | 56.00 (67.50)   | -7.229 | < 0.001 |
| After treatment                           | 14.00 (10.00)   |        |              | 62.50 (51.00)   |              |             | 12.00 (12.00)   |        |         |
| Before and after                          | -64.00 (87.30)  |        |              | 0 (0.90)        |              |             | -41.00 (55.00)  |        |         |
| treatment (after-before)                  |                 |        |              |                 |              |             |                 |        |         |
| Anterior wall                             |                 |        |              |                 |              |             |                 |        |         |
| Before treatment                          | 2.80 (2.10)     | -7.526 | < 0.001      | 2.00 (1.63)     | -4.787       | < 0.001     | 2.00 (1.40)     | -0.170 | 0.865   |
| After treatment                           | 0 (0)           |        |              | 0 (0.50)        |              |             | 2.00 (1.40)     |        |         |
| Before and after                          | -2.80(2.20)     |        | -1.85 (1.70) |                 | -0.10 (0.40) |             |                 |        |         |
| treatment (after-before)                  | -2.60(2.20)     |        | -1.03 (1.70) |                 |              |             | -0.10 (0.40)    |        |         |
| Posterior wall                            |                 |        |              |                 |              |             |                 |        |         |
| Before treatment                          | 3.00 (1.70)     | -7.521 | < 0.001      | 2.80 (1.75)     | -4.785       | < 0.001     | 3.10 (1.70)     | -0.359 | 0.720   |
| After Treatment                           | 0(0)            |        |              | 0 (0.53)        |              |             | 3.10 (1.30)     |        |         |
| Before and after                          | -3.00 (1.70)    |        |              | -2.70 (1.43)    |              |             | -0.10 (0.60)    |        |         |
| treatment (after-before)                  | -3.00 (1.70)    |        | -2.70 (1.43) |                 |              |             | 0.10 (0.00)     |        |         |
| Tumor size                                |                 |        |              |                 |              |             |                 |        |         |
| Before treatment                          | 31.00 (71.00)   | -7.525 | < 0.001      | 25.50 (44.18)   | -4.782       | < 0.001     | 15.54 (17.90)   | -2.416 | 0.016   |
| After treatment                           | 0 (0)           |        |              | 0 (3.28)        |              |             | 14.72 (17.97)   |        |         |
| Before and after treatment (after-before) | -31.00 (71.00)  |        |              | -25.50 (38.43)  |              |             | -0.95 (5.08)    |        |         |
| * Three ground are median (i              |                 | .:     | .:           | - 44 0.05       |              |             |                 |        |         |

<sup>\*</sup> Three groups are median (interquartile range), said paired signed rank test,  $\alpha$  0.05

strual flow are the most significant change for anemia. Serum CA125 ovarian tumor-associated antigen is the epithelial surface antigen from the body cavity, mainly expressed in the endometrium, cervix, fallopian tube, and peritoneal tissue. Ectopic endometrial secretion of CA125, its value, and the severity of the patient's condition were positively correlated to reflect more sensitive treatment of ADM. This study also demonstrated the presence of clinical symptoms in patients with CA125 before and after treatment. After treatment, patients were followed for serum CA125 levels which decreased significantly, suggesting that abdominal surgery can be effectively treated with radiofrequency ablation of ectopic endometrium.

In group A hysterectomy, Hb, E2, CA125, adenomyosis lesion size, anterior, and posterior wall thickness were comparatively statistically significant (p < 0.001); in group C after GnRH conservative medical therapy, radiofrequency ablation group B before and after treatment serum E2 had showed significant difference (p > 0.05). It was suggested that radiofrequency ablation under ultrasound guidance did not change the ovarian blood supply, did not affect ovarian function, and serum E2 before and after treatment in both groups, the difference was statistically significant (p < 0.005).

0.001). Instructions may affect ovarian function, as shown in Table 3.

Group A hysterectomy included 15 cases with early menopausal symptoms, decreased quality of life, and ten patients with varying degrees of pelvic floor disorders. Radiofrequency ablation group B had no short-term complications in all patients; only a few patients complained of occasional lower abdominal pain after surgery. GnRH drugs after conservative treatment of 29 patients in group C had hot flashes, night sweats, fatigue, and other symptoms; one patient had chills, insomnia, and chest tightness, there was one case of back pain, bilateral knee pain, one with vaginal dryness, lower abdominal pain, This shows that radiofrequency ablation had fewer incidences of complications in group B after treatment.

## **Discussion**

ADM is clinically a gynecological disease, and progressive dysmenorrhea, dyspareunia, pelvic pain, and irregular menstruation and infertility are the clinical manifestations. In recent years, its incidence is rising gradually [6, 7], and the incidence for age gradually reduces, with the average

age of this group of patients being 41.81-years-old. The function of uterus is not only to contain the fetus but it is also one of the endocrine organs, especially the uterine endometrium itself, has a variety of endocrine function, it can secrete hormones, enzymes, proteins, and has an immune function among other factors; this endocrine function is important in regulating uterine function, physiological balance, and body coordination aspects of reproductive role. It cannot be easily removed for benign uterine diseases and should be reasonable treatment option.

ADM treatment can include medical therapy and surgical treatment, but the result of medical therapy is not so good. Surgical treatment has good results [8]; in the past ADM patients would no longer have reproductive demands and most advocated hysterectomy resection [9]; this would not only bring about the risks and pain, but would also lead to pelvic organ prolapse after early menopause, ovarian blood flow decrease, and damage after long-term complications caused by pelvic floor anatomy [10]. Currently women are at 40 years of age, and still have the desire to retain their uterus, while the majority desire to improve quality of life which also requires menstruation. 2009 Guidelines for treatment of endometriosis clarify that the drugs of choice are oral contraceptives, high progesterone, testosterone derivatives, and GnRHa of four categories [11], GnRH-a inhibit pituitary release of gonadotropins, thereby suppressing ovarian secretion of estradiol and progesterone; but because of the long course of treatment, slow, expensive, and side effects, and is likely to cause long-term application of vasomotor symptoms and can lead to bone loss, thus limiting the long-term clinical application [12, 13].

Radiofrequency ablation is a thermal destruction technology, mainly using a radiofrequency current through the high heat generated during biological process, local tissue coagulation, and necrosis. Currently, radiofrequency ablation is a new minimally invasive therapy, under the guidance of superconducting technology for precise positioning of uterine adenomyosis, includes small area of incision, less influence on the body, less bleeding, shorter operative time, shorter hospital stay, less pain, quick recovery, repeatability, etc., and it meets the common needs of both doctors and patients. It enables to retain the uterus, but also achieve therapeutic purposes, while avoiding hysterectomy or affecting long-term drug therapy. Another advantage of ultrasound-guided radiofrequency ablation is the direct removal of the lesion and retaining the normal myometrium and endometrium, postoperative bleeding is periodically maintained to retain the endocrine function of uterus, maintaining patient physiological and psychological balance, it has no impact on sexual life, in addition, it retains endometrial periodic shedding of the cervix, vagina, and maintains acid-base balance to prevent bacterial infections which has a very good result for the aforementioned desires.

This study showed that (1) at one-year follow-up, group

A hysterectomy after treatment, 75 cases were cured and the group adenomyosis rate was 100% (75/75). In the radiofrequency ablation group B after treatment, 20 cases were cured, was effective in 29 cases, and ineffective in one case. In the ADM group treatment, efficiency was 96.7%, and the cure rate was 66.7%. GnRH drugs conservative group C after treatment, showed effective in 44 cases, ineffective in 31 cases, and the treatment efficiency was 58.7%. In the three groups of ADM disease, treatment difference was statistically significant (p < 0.001), group A treatment efficiency > group B > C group. (2) All patients received one month to one-year follow-up; 95 cases of dysmenorrhea symptoms completely disappeared after surgery and significantly reduced menstrual flow. Fifty-three cases of dysmenorrhea symptoms improved, 18 cases of dysmenorrhea showed no significant change, while in three cases it increased, and 11 cases had recurrence. (3) Group A hysterectomy operation time was  $101.8 \pm 34.1$  minutess with a mean blood volume of  $200 \pm 75$  mL. In the radiofrequency ablation group B, the operation time was 18 ± 8 minutes and blood loss was less than 10 ml. GnRH drug with conservative treatment group C of one to nine-pin, with a total of 32 patients underwent anti-drug add-on therapy. The above data can be drawn in group B compared with radiofrequency ablation hysterectomy group A, with a shorter operative time and less blood loss. (4) Group A total hysterectomy hospitalization was  $11.00 \pm 5.00$  days, in the radiofrequency ablation group B total it was  $2.00 \pm 1.00$ days, and in the GnRH conservative total hospitalized group C it was  $7.00 \pm 6.00$  days. In the three groups of patients hospitalized for a total time of treatment, the difference was statistically significant ( $p \le 0.001$ ), i.e. hysterectomy group A hospital stay > group C > group B; group B patients with radiofrequency ablation showed the shortest hospitalized time. Group A hysterectomy group hospitalization costs were  $16326.21 \pm 5172.60$  Yuan, in the radiofrequency ablation group B they were 2920.00  $\pm$ 170.00 Yuan, and in the GnRH conservative group C they were  $10230.00 \pm 9774.02$  Yuan; three groups of hospital costs significantly compared to patients ( $p \le 0.001$ ), i.e. hysterectomy A group of hospital costs > group C > group B. The treatment of patients with radiofrequency ablation group B had the lowest costs. (5) Group A hysterectomy group, hemoglobin, E2, CA125, adenomyosis lesion size, and anterior and posterior wall thicknesses were statistically significant (p < 0.001) in group C after GnRH conservative medical therapy, while in the radiofrequency ablation B group before and after treatment, serum E2 was not significantly different (p > 0.05). It can be stated that ultrasound-guided radiofrequency ablation of ovarian blood supply does not change and does not affect ovarian function. (6) Group A hysterectomy included 15 cases of patients that had early menopause symptoms, decreased quality of life, and ten patients with varying degrees of pelvic floor disorders. Radiofrequency ablation group B

had no short-term complications in all patients and only a few patients complained of lower abdominal pain after surgery occasionally. GnRH after conservative treatment of 29 patients in group C had hot flashes, night sweats, fatigue, and other symptoms; one patient had chills, insomnia, chest tightness, one case of back pain, and bilateral knee pain. One case had vaginal dryness, lower abdominal pain, etc. and the symptoms of add-on therapy after in-ceased. This shows that radiofrequency ablation has fewer incidences of complications i -group B after treatment. Group A hysterectomy larger than radiofrequency ablation treatment group B, described that hysterectomy is an effective treatment, but permanent loss of reproductive function may lead to premature ovarian failure [14], affecting the quality of life, causing pelvic floor organ prolapse, and other longterm complications. GnRH drug efficacy is not plausible, as treatment takes time, is slow, expensive, has side effects, is likely to cause long-term vasomotor symptoms, may lead to bone loss, and may need to undergo anti-drug add-on therapy which ultimately increases the economic burden on patients. Among the three groups, radiofrequency ablation treatment group had fewer side effects, shorter operative time, less blood loss, shorter hospitalization, less expenses of treatment, did not effect ovarian blood supply or ovarian function, had a less complication rate; fertility requirements and the desire to retain the uterus in patients proved it to be the preferred method of treatment.

In summary, a simple treatment with GnRH drugs has high cost, inaccurate efficacy, is easy to relapse, treatment is lengthy, has side effects, requires to add anti-treatment. If a hysterectomy is performed, vital organs and female reproductive function will be lost, but women will also have early menopause and even undergo premature aging. If the patient has the desire to retain the uterus, radiofrequency ablation is available, it has low cost, does not affect ovarian and endocrine function, and can retain the uterus and cyclical shedding of the endometrium, which maintains the patient's physiological and psychological balance while preventing infections of reproductive tract. For comprehensive clinical treatment of uterine benign diseases we require a minimally invasive surgical technique, with small incision, having less influence on body, shorter hospital stay, faster recovery, repeatability, etc., and can be able to retain the uterus, but also be very effective for therapeutic purposes, while avoiding hysterectomy or long-term impact on women's physical and mental health medications, which can be widely recommended. In short, the advantages of radiofrequency ablation can be summarized as follows: 1) locate and secure treatment, evaluate the patent system and qualitative and quantitative controls to ensure safe treatment, 2) minimally invasive treatment ensures compact self-curing treatment through the vagina and cervix, and does not damage any other organs, 3) quantitative control, tool patented technology, and output power tracking control can effectively control the scope of ectopic foci which are solidified, 4) qualitative control of fibroid tissue impedance index as a measure of them can reach more thorough solidification degree, 5) visual effects, completely cut pedicle coagulation, 6) immunological and biological thermal effects can enhance immune function, thereby inhibiting residues and small fibroids grow. Ultrasound-guided radiofrequency ablation combined with GnRH effect may be better, it can preserve the uterus as a minimally invasive technique, and it is expected to become a safe and effective treatment of ADM in the future.

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