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Uterine artery embolization *vs.* robot-assisted adenomyomectomy for symptomatic adenomyosis; efficacy and safety

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SUMMARY

Purpose: To compare the clinical efficacy and safety of uterine artery embolization (UAE) and robot-assisted adenomyomectomy (RAA) in symptomatic adenomyosis treatment.

Material and methods: From January 2018 to May 2021, 67 women with symptomatic adenomyosis underwent UAE (n = 48) or RAA (n = 19). Uterine volume reduction, variation in hemoglobin levels, pictorial blood loss assessment chart (PBAC), and symptom severity questionnaire were compared before and after the procedure. Procedure time, length of hospital stay, and decreased hemoglobin levels immediately after the procedures were also compared to assess complications.

Results: The two groups showed the similar outcomes in the mean uterine volume reduction rate and increased hemoglobin ratio at 3–6 months after the procedure. UAE, compared with RAA showed significantly shorter procedure time and length of hospital stay, and significantly smaller hemoglobin decreased ratio immediately after the procedure ($p < 0.05$). Two groups showed similar decreased ratio of the PBAC score. UAE, compared with RAA, showed significantly higher difference in symptom severity ($p < 0.05$).

Conclusion: The UAE, with similar efficacy to the RAA, is less invasive and safer than RAA in symptomatic adenomyosis treatment.

Keywords: Adenomyosis; Uterine artery embolization; Robot-assisted adenomyomectomy

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INTRODUCTION

Adenomyosis is a common benign gynecological disease characterized by ectopic endometrial tissue in the myometrium. Generally, it often appears premenopausal women who typically suffer from dysmenorrhea, menorrhagia, chronic pelvic pain, and infertility [1,2]. The standard therapy for adenomyosis is total hysterectomy; however, it is difficult to treat with hysterectomy for women who want to maintain fertility [3]. For fertility preservation in adenomyosis treatment, the first choice is medical treatment including gonadotropin-releasing hormone agonists (GnRH-a), levonorgestrel-releasing intrauterine device (LNG-IUS), oral contraceptive combined pills, progestogens and danazol [4-6]. If medical treatment does not resolve dysmenorrhea, menorrhagia or chronic pelvic pain, surgical treatment should be considered. In several surgical treatment options, adenomyomectomy is one option for women who want to preserve fertility.

Open adenomyomectomy is more effective than laparoscopic surgery for minimizing myometrium defects or hematoma [7]. However, a recent study reported that the introduction of robot-assisted laparoscopic surgery can achieve the same effect as laparotomy [8]. In addition to surgical treatment, uterine artery embolization (UAE) is a minimally invasive procedure that can reduce the size of adenomyosis and improve symptoms [9].

Therefore, the aim of the present study was to compare procedure data and operative and clinical outcomes between women with symptomatic adenomyosis who underwent robot-assisted adenomyomectomy (RAA) and those who underwent UAE.

MATERIALS AND METHODS

Patients

Between January 2018 and May 2021, 67 women with symptomatic adenomyosis underwent RAA or UAE. Each patient was sufficiently informed about all aspects of their management before the procedure, and each provided written consent. This retrospective study was approved by the Institutional Review Board.

Medical records were reviewed for demographic data, including age, body mass index (BMI), and history of prior abdominal or pelvic surgeries. Patients with acute pelvic infection, gynecological malignancy, contraindications or allergies to iodinated contrast medium were excluded.

Patients desiring to become pregnant in the future were not excluded. To determine the efficacy of the procedure, operative outcomes, including uterine volume, hemoglobin, pictorial blood loss assessment chart (PBAC), symptom severity questionnaire, procedure time, and length of hospital stay were reviewed.

Patient age ranged from 32 to 53 years (mean age, 44.2 years). None of the patient had clinical findings of menopause. All patients underwent transvaginal sonography and magnetic resonance imaging (MRI) at baseline, 1 month follow-up, 3–6 months after the procedure to evaluate the size of the uterus and extent of adenomyosis. The uterine volume was measured using MRI according to the formula for the volume of the ellipse (0.5233 × length × depth × width).

Robot-assisted adenomyomectomy (RAA)

One gynecologist performed all the RAA. Under general anesthesia, the patient was placed in the dorsal lithotomy position. The uterine mobilizer was placed vaginally in all the cases. One 12 mm trocar was placed in the umbilicus for insertion of the operative camera. Two 8 mm trocars were positioned in the right and left lower quadrants for insertion of the robotic arms. After inserting the trocar, the da Vinci Xi surgical system (Intuitive Surgical Inc., USA) was docked. Robotic instruments for the operation include penetrated bipolar forceps, harmonic, tenaculum forceps, and mega needle drivers. After the exact location of the adenomyosis was determined by visual inspection and MRI review, diluted vasopressin (vasopressin 10 IU in 100 mL of normal saline) was injected into the uterine serosa and myometrium adjacent to adenomyosis. Using a harmonic energy device, we performed a horizontal straight incision over the adenomyosis and excised the adenomyosis. After controlling for bleeding with electrocoagulation and Surgiguard gauze (Samyang Biopharm, Korea), the remaining serosa and myometrium were repaired with sutures. To prevent dead space that causes laceration or hematoma, it was sutured using a 1-0 or 2-0 monofix PDO (Samyang Biopharm, Korea) depending on the size and depth of the defect. At the end of the surgery, an anti-adhesion agent was applied to prevent adhesion, and a drainage catheter was left in the posterior cul-de-sac.

Uterine artery embolization (UAE)

The same interventional radiologist performed all patient preparation and embolization procedures, as described by Song et al. previously [10]. A unilateral femoral artery approach was performed under local anesthesia. Placing a 5.0-F RUC catheter (Cook, Bloomington, IN, USA) in the internal iliac artery, a coaxial 3-F microcatheter (Stride Hi-flow; Asahi Intecc, Osaka, Japan) was advanced distally first into the left uterine artery, followed by the right uterine artery. Embolization was performed using gelatin sponge particles (SPONGOSTAN, Johnson & Johnson, Skipton, UK). Before the embolization procedure, the gelatin sponge particles were mixed with 40 mL of 1:1 saline solution-contrast agent mixture (Iomeron; Bracco, Milano, Italy). The particle sizes were 150–560 μm initially and then changed to 560–710 μm. Complete cessation of blood flow in the proximal ascending uterine artery after 10 cardiac beats was considered the endpoint of embolization. Post-procedural pain was managed with an intravenous patient-controlled analgesia pump containing 1500 μg fentanyl sulfate and 150 mg ketorolac tromethamine, and additional nonsteroidal anti-inflammatory drugs were administered *via* intravenous injection.

Clinical follow-up

PBAC and a symptom severity questionnaire were completed before the procedure and at the 3–6 month follow-up. A PBAC was performed by described Higham JM, et al [11]. A symptom severity questionnaire was completed to assess the severity of menstrual bleeding and dysmenorrhea during and between menstrual periods on a scale from 0 (no impact) to 10 (severe impact). The scores were divided into three levels: marked improvement (difference in the score; 8–10), moderate improvement (difference in the score; 5–7), and no change (difference in the score; 4 or lower) [12].

Statistical analysis

Data were analyzed using Stata 15.1 (Stata Corporation, College Station, TX, USA). Comparisons of continuous variables across the study were analyzed using the Mann-Whitney U test. Discrete variables between groups were compared using a Pearson's chi-squared test. A two-tailed p-value of <0.05 was considered statistically significant. For the PBAC and severity score, which represent subjective scores, a 10% trimmed mean was used to provide objectivity and to remove outlier bias.

RESULTS

Of the 67 patients, 19 underwent RAA and 48 underwent UAE. **Tab. 1.** shows the characteristics of patients. No statistically significant differences in age, BMI, previous operation, and parity were found between the two groups. Uterine volume was 290.90 ± 172.91 mL in the RAA group and 425.82 ± 241.98 mL in the UAE group, and there was a statistically significant difference between the two groups (p <0.05). Furthermore, 10.53% of patients in the RAA group and 20.83% in the UAE had pure adenomyosis, with no significant difference observed in both groups.

The mean procedure time was 98.1 ± 27.6 min, and 78.3 ± 19.8 min in RAA and UAE groups. The mean ratio of hemoglobin decrease right after the procedure was 0.94 ± 0.09, and 1.01 ± 0.10 in the RAA and UAE groups. The length of hospital stay after the procedure averaged to 6.2 ± 1.8 days and 4.9 ± 1.2 days in the RAA and UAE, respectively. There were statistically significant differences in procedure time, hemoglobin decreased ratio, and length of hospital stay between the RAA and UAE groups (p <0.05, **Tab. 2.**).

Tab. 3. presents the results of follow-up outcomes at 1

Tab. 1. Characteristics of patients with symptomatic adenomyosis.

Parameters	RAA (n = 19)	UAE (n = 48)	P-value
Age	42.7 ± 5.5	44.8 ± 4.6	0.112
BMI (kg/m²)	23.5 ± 4.3	23.5 ± 3.8	0.824
Height (cm)	159.5 ± 5.0	161.0 ± 5.5	0.431
Body weight (kg)	59.5 ± 9.4	61.0 ± 10.4	0.500
Previous operation	-	-	0.903
Yes	8 (42.11)	21 (43.75)	-
No	11 (57.89)	27 (56.25)	-
Parity	1.6 ± 0.8	1.7 ± 0.9	0.688
Uterus volume	290.90 ± 172.91	425.82 ± 241.98	0.017
Type of adenomyosis	-	-	0.485
Pure adenomyosis	2 (10.53)	10 (20.83)	-
Complex adenomyosis	17 (89.47)	38 (79.17)	-

Values are presented as mean ± SD or number (%) by descriptive analysis, frequency analysis.
P-values were calculated using the Mann-Whitney U test, Pearson's chi-square test or Fisher's exact test.

Tab. 2. Postprocedure outcomes by RAA *vs.* UAE (mean ± SD).

Postprocedure Outcomes	RAA	UAE	P-value
Procedure time (min)	98.1 ± 27.6	78.3 ± 19.8	0.006
Decreased hemoglobin [a]	0.94 ± 0.09	1.01 ± 0.10	0.017
Hospital stay (day)	6.2 ± 1.8	4.9 ± 1.2	< 0.001

Values are presented as mean ± SD by descriptive analysis.
P-values were calculated using the Mann-Whitney U test.
[a]Decreased hemoglobin was calculated by dividing hemoglobin levels right after procedure by baseline.

Tab. 3. Follow-up outcomes by RAA *vs.* UAE (mean ± SD).

Follow-up Outcomes	1 month/Baseline		
	RAA	UAE	P-value
Uterine volume reduction [a]	0.57 ± 0.21	0.74 ± 0.11	< 0.001
Increased hemoglobin [b]	1.01 ± 0.09	1.13 ± 0.24	0.007
3–6 month/Baseline			
	RAA	UAE	P-value
Uterine volume reduction [a]	0.49 ± 0.16	0.50 ± 0.17	0.759
Increased hemoglobin [b]	1.09 ± 0.12	1.13 ± 0.17	0.560

Values are presented as mean ± SD by descriptive analysis.
P-values were calculated using the Mann-Whitney U test.
[a] Uterus volume change was calculated by dividing 1 month after, 3–6 months after uterine volumes by baseline uterine volumes, respectively.
[b] Decreased hemoglobin was calculated by dividing 1month after, 3–6 months hemoglobin levels by baseline levels, respectively.

month and 3–6 months after procedure. At 1 month after the procedure, the ratio of uterine volume reduction and increased hemoglobin was significantly different in both groups ($p < 0.05$). The ratio of uterine volume reduction was 0.57 ± 0.21 in RAA, greater than 0.74 ± 0.11 in UAE, and hemoglobin increased ratio was 1.01 ± 0.09 in RAA which was smaller than 1.13 ± 0.24 in UAE. At 3–6 months after the procedure, the ratio of uterine volume reduction and decreased hemoglobin had no statistically significant difference between the two groups.

Symptom improvement is demonstrated in **Tab. 4.** The PBAC score decreased after the procedure compared to baseline in both groups. However, decreased ratio had no statistically significant difference. The severity score also decreased after the procedure compared to baseline in both groups. Comparing the difference between baseline and post procedure, UAE showed a more significant decrease than RAA (6.20 ± 1.37 in RAA *vs.* 6.79 ± 1.49 in UAE, respectively, $p < 0.05$).

DISCUSSION

Our study found that UAE, which is a minimally invasive method, had a similar therapeutic effect to RAA, although there were few side effects after the procedure. Comparing the reduction in uterine size, RAA showed a greater decrease at 1 month after the procedure; however, there was no significant difference at 3-6 months after the procedure. This suggests that RAA reduces the volume of adenomyosis through resection, whereas UAE reduces the size of adenomyosis gradually through necrosis. Hemoglobin levels were similarly elevated at 1 month and 3–6 months after the procedure in both groups. UAE tended to take less time than RAA, and when comparing the amount of hemoglobin reduction before and immediately after the procedure, it was confirmed that the RAA decreased more significantly than the UAE. In addition, the hospital stay period, in which postoperative bleeding, wound recovery and surgical complications were treated, was relatively shorter in the UAE than in the RAA group.

Tab. 4. Symptom improvement outcomes (mean ± SD).

Symptom Improvement Outcomes	RAA	UAE	P-value
PBAC			
Baseline	216.88 ± 40.96	223.86 ± 44.26	0.658
Postprocedure	99.65 ± 24.93	92.64 ± 31.01	0.368
Decreased ratio[a]	0.53 ± 0.10	0.58 ± 0.13	0.076
Severity			
Baseline	8.53 ± 1.07	8.11 ± 1.35	0.367
Postprocedure	2.41 ± 0.87	1.18 ± 0.76	< 0.001
Difference[b]	6.20 ± 1.37	6.95 ± 1.39	0.025

Values are presented as 10% trimmed mean ± SD by descriptive analysis.
P-values were calculated using the Mann-Whitney U test.
[a]Percentage decrease was calculated by subtracting postprocedure score from baseline score and then dividing by baseline score.
[b]Difference was calculated by subtracting postprocedure severity score from baseline score.

Traditionally, hysterectomy is the 'gold standard' for adenomyosis that does not respond to medical treatment [4,13]. As the latest trend is moving toward uterus-preserving treatment, the number of women with adenomyosis who prefer to preserve their uterus is increasing, even though they may have already completed pregnancy [14,15]. This makes uterine-conservative surgery advance that effectively improves symptoms related to adenomyosis. However, adenomyosis often has an unclear demarcated margin and diffuse invasion into the muscle layer, so it is difficult to remove them completely. This means that the remnant adenomyosis tissue may continue to grow and relapse [16,17]. Thus, UAE that can affect the overall uterus can be an alternative.

Adenomyomectomy is one of the options for future pregnancy in women of childbearing age with symptomatic adenomyosis. Laparoscopic adenomyomectomy has disadvantages in the absence of palpation of the uterus, which makes an inaccurate assessment of the extent of adenomyosis. It has a limited range of motion, which affects the repair of myometrial defects [18]. As a result, this could increase the occurrence of myometrial defects, hematoma formation, or excessive use of electrocauterization, thus slowing the recovery of the uterus and increasing the likelihood of uterine rupture in future pregnancies. However, robot-assisted laparoscopic surgery can overcome this disadvantage [8,18]. Thus, the present study was conducted using RAA.

Several studies have reported ovarian failure in women who underwent UAE [19,20]. Some studies suggested that UAE has a negative impact on future pregnancy [21,22]. In contrast, recent studies have shown that UAE does not cause problems with ovarian function or fertility [23-25]. In terms of uterine rupture, a uterine rupture may occur more easily because RAA renders the uterine scar. However, there have been some case reports of uterine rupture after UAE; the reports suggested that UAE could cause necrosis of the myometrium, eventually leading to uterine rupture [26,27]. No large, well-designed studies on uterine rupture after UAE have been conducted. Therefore, the impact of UAE on future pregnancy requires further study.

Medical therapy for symptomatic adenomyosis is the least invasive strategy. Medical treatment is often transient, and the symptoms of adenomyosis nearly always reappear if these medications are discontinued. Some studies have reported that medical treatment after surgery provides more effective symptom control and has a lower symptom relapse rate than surgery alone [28-30]. According to a study on medical treatment before UAE for uterine myoma conducted by Kim et al., GnRH-a before UAE reduced uterine size to avoid complications such as infection, sepsis, and uterine necrosis [31]. Since GnRH-a can reduce uterine volume even in adenomyosis, the use of GnRH-a before UAE in symptomatic adenomyosis is thought to be helpful. There are insufficient studies on combination therapy of GnRH-a and UAE; thus, research on combination therapy is necessary.

The present study had some limitations. First, it did not target patients with pure adenomyosis, and the possibility that the symptoms due to myoma overlapped could not be excluded. Second, the efficacy related to pregnancy cannot be evaluated because follow-up of pregnancy before and after the procedure was not performed. Therefore, additional studies on ovarian function and fertility in patients with adenomyomsis in RAA and UAE are needed.

CONCLUSION

UAE, a minimally invasive modality, had similar treatment outcomes to RAA. In addition, it is a safe procedure with acceptable blood loss and requires a reasonably short procedure time. It is a feasible treatment modality for women with symptomatic adenomyosis who want to preserve the uterus.

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DECLARATION OF INTEREST

We certify that there are no conflicts of interest with any financial or other potential conflicts of interest.

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