



Robot-Assisted Laparoscopic Myomectomy versus Abdominal Myomectomy for Large Myomas Sized over 10 cm or Weighing 250 g

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Purpose: Here, we compared the operative and perioperative outcomes between robot-assisted laparoscopic myomectomy (RALM) and abdominal myomectomy (AM) in patients with large (>10 cm) or heavy myomas (>250 g).

Materials and Methods: We included 278 patients who underwent multi-port RALM (n=126) or AM (n=151) for large or heavy myomas in a tertiary care hospital between April 2019 and June 2020. The t-test, chi-square, Bonferroni's test, and multiple linear regression were used.

Results: No differences were observed in age, body mass index, parity, or history of pelvic surgery between the two groups. Myoma diameters were not different (10.8±2.52 cm vs. 11.2±3.0 cm, $p=0.233$), but myomas were lighter in the RALM group than in the AM group (444.6±283.14 g vs. 604.68±368.35 g, respectively, $p=0.001$). The RALM group had a higher proportion of subserosal myomas, fewer myomas, fewer large myomas over >3 cm, lighter myomas, and longer total operating time. However, the RALM group also had shorter hospital stay and fewer short-term complications. Estimated blood loss (EBL) was not different between the two groups. The number of removed myomas was the most significant factor (coefficient=10.89, $p<0.0001$) affecting the EBL.

Conclusion: RALM is a feasible myomectomy technique even for large or heavy myomas. RALM patients tend to have shorter hospital stays and fewer postoperative fevers within 48 hours. However, RALM has longer total operating time.

Key Words: Fertility, open abdomen techniques, robotic surgical procedures, uterine myomectomy

INTRODUCTION

Uterine myoma is the most common benign gynecologic tumor in reproductive-aged women.^{1,2} Patients with symptomat-

ic myomas who are unresponsive to medical treatment, myomas compressing the adjacent organs, or myomas associated with subfertility are candidates for hysterectomy or myomectomy. Myomectomy is the fertility-preserving surgical option. However, the original myomectomy surgical technique, abdominal myomectomy (AM), is associated with larger abdominal incision, more postoperative pain, more analgesic use, longer hospital stay, and higher risk of postoperative pelvic adhesion compared to minimally invasive surgery (MIS).³⁻⁵ Therefore, MIS techniques, such as laparoscopic myomectomy (LM) and robot-assisted laparoscopic myomectomy (RALM), have been replacing AM in a broader number and variety of cases. In many countries, including Korea, there has been a trend toward the increased use of RALM.⁵⁻⁷

The use of RALM has several advantages. First, it uses the Endowrist technology, which allows the articulation of instruments

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by up to 540° as well as easier intracorporeal suturing. This is in contrast to LM, which only permits limited multiple-layered intracorporeal myometrial suturing, even by the most experienced laparoscopic surgeons. Second, RALM may be considered in complex surgical cases for which traditional laparoscopy is not indicated. Longer skin incisions, higher risk of pelvic adhesions, higher pain scores, and longer hospital stays could all be avoided by preventing the conversion of traditional laparoscopy to abdominal surgery. In a large multicenter study of 32118 abdominal, vaginal, laparoscopic, and robotic hysterectomy surgeries performed by three high-volume surgeons in nine centers for 21 months, the robotic hysterectomy cohort had higher rates of adhesions, uteri >250 g, and morbid obesity, as well as longer hospital stays. However, there were no significant differences in intraoperative complications among groups.⁸

However, RALM also has its disadvantages. First, it is a costly technique.⁹⁻¹² Second, it has been reported that RALM is associated with longer operating times compared to AM and LM, especially in early reports.^{12,13} It is expected that large myomas require even longer operating times. However, the operating time might be shortened with surgical experience and increased proficiency.¹⁴ To reduce intrapersonal variation, it is important to conduct investigations with short study periods.

Despite the global trend toward the use of MIS techniques, AM is still the first choice for large, multiple myomas, as well as in women with pelvic adhesions or a history of previous abdominal surgery or peritonitis. It remains unclear whether RALM is suitable for this type of tumor. Therefore, in this study, we investigated the feasibility and safety of RALM for large or heavy myomas by comparison with AM.

MATERIALS AND METHODS

Study design and patients

In this retrospective study, we enrolled all patients undergoing RALM or AM between April 1, 2019, and June 30, 2020 at our hospital. Myomectomy was performed by fellowship-trained, minimally invasive gynecologic surgeons with over 15 years of surgical experience. A total of six surgeons performed RALM and eight surgeons performed AM. A hybrid RALM technique¹⁵⁻¹⁷ was not used, not even in patients with very large dominant myomas (20 cm) or multiple myomas (>30) requiring removal.

The inclusion criterion was having either a large myoma (over 10 cm in size) or a heavy myoma (over 250 g in weight). After applying the inclusion criterion, we excluded six cases of single-site RALM for homogeneity and exact comparisons. We finally included 126 cases of multi-port RALM (61.1%) of the 206 cases of RALM and 151 (70.8%) of the 213 cases of AM. The decision on the surgical type, RALM or AM, was made after counseling the patients regarding the size and number of myomas, and based on future pregnancy plans, desire in preserving the uterus, the patient's preference, and cost.

We obtained the following data from each patient's chart: age, marital status, gravidity, parity, body mass index (BMI), and history of previous abdominal surgery, including Caesarean section. The diameter of the dominant myoma, defined as the longest diameter of the dominant myoma, was measured on preoperative ultrasound images. For more accurate measurements, magnetic resonance images were used when available [n=127, n=66 (52.4%) in RALM and n=61 (40.4%) in AM]. Myomas were categorized into subserosal or other types, including intramural, submucosal, and intraligamentary myomas.

We also obtained the following surgery-related data: surgical approach (RALM or AM), concomitant surgery, total operating time from skin incision to closure, estimated blood loss (EBL), number of removed myomas, conversion rate to laparotomy, blood transfusion, and adjacent organ injury. Data on perioperative outcomes, including the weight of the removed myomas, duration of hospital stay, postoperative fever, readmission within 30 days, and postoperative complications (e.g., reoperation, postoperative transfusion, deep vein thrombosis or pulmonary embolism, bowel obstruction, ileus, and sepsis), were also collected.

This retrospective study was approved by the Institutional Review Boards for Human Research of our center (2020-0633). Written informed consent was waived due to the retrospective nature of this study.

Statistical analysis

To compare continuous variables between RALM and AM, we used the Student's t-test. To compare the proportions of categorical variables between the two groups, we used the chi-square tests. In addition to single-variable analysis, multiple linear regression was used to identify the factors that were significantly related to EBL in the RALM and AM groups after adjusting for possible confounding factors. All computations were performed with R, a language and environment for statistical computing (R Foundation for Statistical Computing, Vienna, Austria).¹⁸

RESULTS

Patient baseline characteristics

Patient demographics and baseline characteristics did not differ significantly between the RALM and AM groups (all $p > 0.05$) (Table 1). The proportion of subserosal myomas was higher in the RALM group (28/126, 22.2%) than in the AM group (10/151, 6.6%). The mean maximal diameter of the dominant myoma was smaller in the RALM group (10.8±2.52 cm) than in the AM group (11.2±3.03 cm). The proportion of multiple myomas was not different between the RALM group (82/126, 65.1%) and the AM group (109/151, 72.2%). The median number of myomas sized over 3 cm was smaller in the RALM group (1) than in the AM group (2). The mean weight of the removed myomas was available in 103 cases of RALM and 117 cases of AM, and was

significantly lighter in the RALM group [444.6±283.14 (97–1425) g vs. 604.68±368.35 (10.5–1800) g, respectively].

Comparison of single variables between RALM and AM

We performed statistical analysis of 16 single variables [type of

Table 1. Patient Baseline Characteristics

Characteristics	RALM (n=126)	AM (n=151)	p value
Age (yr)	38.06±5.90	38.09±5.64	0.966
BMI (kg/m ²)	23.05±4.05	23.46±4.20	0.408
Married	51 (40.4)	58 (38.4)	0.491
Nulligravidity	97 (76.9)	128 (91.4)	0.448
Parity [median (range)]	0 [0–3]	0 [0–3]	0.166
Previous pelvic surgery			
Caesarean section	10 (7.9)	12 (7.9)	1
Other pelvic surgery	13 (10.3)	29 (19.2)	0.063
Concomitant surgery	6 (4.8)*	8 (5.2) [†]	0.969

AM, abdominal myomectomy; BMI, body mass index; RALM, robot-assisted laparoscopic myomectomy.

Data are expressed as mean±standard deviation or n (%) unless otherwise stated.

*Including unilateral ovarian cystectomy (n=2), unilateral ovarian cystectomy with unilateral salpingectomy (n=2), cervical mass excision (n=1), and transobturator midurethral sling surgery (n=1), [†]Including unilateral ovarian cystectomy (n=4), bilateral ovarian cystectomy (n=2), and unilateral salpingophorectomy (n=2).

myoma, maximal myoma diameter, weight of the removed myomas, number of removed myomas, multiple myomas, number of large myomas sized over >3 cm, total operating time, EBL, pre- and postoperative hemoglobin (Hb) level, changes between pre- and postoperative Hb, transfusion rate, number of transfused packs, massive transfusion (transfusion of >10 units of packed red blood cells), duration of hospital stay, and perioperative complications] to determine whether the observed values of these variables were significantly different between the RALM and AM groups. Since there were many variables in the test, we applied the Bonferroni’s multiple testing correction to avoid false-positive results. The cut-off p value for significance was 0.05/16=0.003. Among the 16 variables, seven showed significant differences in their means or proportions between the RALM and AM groups. The variables that had significant results were the type of myoma, number of removed myomas, myoma weight, total operating time, preoperative Hb levels, duration of hospital stay, and perioperative complications. Total operating time showed the most significant result ($p=1.71 \times 10^{-13}$), followed by duration of hospital stay ($p=8.74 \times 10^{-13}$) (Table 2).

Intraoperative outcomes

Total operating time was longer in the RALM group [164.33±71.62 (63–500) min] than in the AM group [108.75 ± 32.06 (49–

Table 2. Comparison of Patients in RALM and AM Groups

Variable	RALM (n=126)	AM (n=151)	p value
Type of main myoma			7.96×10 ⁻⁴
Subserosal	28	10	
Other*	89	141	
Maximal myoma diameter (cm)	10.8±2.52	11.2±3.03	0.233
Number of myomas [median (range)]	3 [1–34]	4 [1–50]	3.51×10 ⁻⁵
Number of myomas sized >3 cm [median (range)]	1 [1–10]	2 [1–10]	9.37×10 ⁻³
Multiple myomas	82 (65.1)	109 (72.2)	0.294
Weight of the removed myomas (g) [†]	444.6±283.14	604.68±368.35	0.001
Total operating time (min) [‡]	164.33±71.62	108.75±32.06	1.71×10 ⁻¹³
Estimated blood loss (mL)	368.4±256.76	297.15±178.95	0.009
Preoperative Hb (g/dL)	12.69±1.38	12.16±1.67	0.005
Postoperative Hb (g/dL)	9.09±1.72	8.93±1.83	0.446
Difference of Hb (g/dL)	3.6±1.85	3.23±1.45	0.073
Transfusion	34 (27.0)	53 (35.1)	0.202
Number of transfused packs [median (range)]	0 [0–17]	0 [0–10]	0.147
Massive transfusion >10 packs	1 (0.8)	2 (1.3)	1
Duration of hospital stay (days)	2.68±1.95	4.13±0.79	8.74×10 ⁻¹³
Postoperative complications	33 (26.1)	82 (54.3)	5.16×10 ⁻⁶
Fever (within 48 h)	23 (18.2)	60 (39.7)	1.68×10 ⁻⁵
Fever (after 48 h)	8 (6.3)	18 (11.9)	
Bleeding	1 (0.8)	3 (2.0)	
Other complications	1 (0.8)	1 (0.7)	

AM, abdominal myomectomy; Hb, hemoglobin; RALM, robot-assisted laparoscopic myomectomy.

Data are expressed as either n, n (%) or mean±standard deviation unless otherwise stated.

*Including intramural, submucosal, intraligamentary, and cervical myomas, [†]Data were available in 108 cases of RALM and 117 cases of AM, [‡]Time from skin incision to skin closure.

221) min]. EBL was comparable between the two groups [368.4±256.76 (30–1500) mL in the RALM group versus 297.15±178.95 (20–1000) mL in the AM group]. Pre- and postoperative Hb levels were also comparable between the two groups (12.69±1.38 g/dL and 9.09±1.72 g/dL in the RALM group vs. 12.16±1.67 g/dL and 8.93±1.83 g/dL in the AM group). Hospital stays were shorter in the RALM group (2.68±1.95 days) than in the AM group (4.13±0.79 days). The RALM group (26.1%) had fewer complications compared to the AM group (54.3%) (Table 2).

Short-term complications

Postoperative complications were significantly fewer in the RALM group than in the AM group. The difference was caused by fewer cases of postoperative fever within 48 h of operation in the RALM group. Considering the routine postoperative course, patients were discharged after 2 days for RALM and after 4 days for AM in our hospital; postoperative fever within 48 h of operation extended the hospital stay, causing a delayed discharge. Among patients with postoperative fever within 48 h of operation, 11 out of 23 patients in RALM were discharged after a mean of 1.09 days (10 patients discharged 1 day later, on postoperative day 3; and one patient discharged 2 days later, on postoperative day 4). In the AM group, 7 out of 60 patients were discharged after a mean of 1.71 days (five patients discharged 1 day later, on postoperative day 5; and one patient discharged 2 and 5 days later each, on postoperative days 6 and 9). Other complications occurred in one out of 132 cases in the RALM group (0.8%, hemoperitoneum causing reversible acute kidney injury), and in one out of 151 cases in the AM group (0.7%, both leg pain and diarrhea) (Table 2).

Results of multiple linear regression analysis

To identify the factors significantly associated with EBL and apply this analysis result to prepare and manage other risk factors for postoperative anemia, we performed multiple linear regression analysis. We selected the variables possibly associated

with EBL based on the results of single-variable analysis and our previous knowledge. The variables included concomitant surgery, age, BMI, history of pelvic surgery, type of myoma, maximal myoma diameter, number of large myomas (>3 cm in size), weight of the removed myomas, total operating time, and type of surgery (RALM or AM). The number of removed myomas was the most significant factor (coefficient=10.89, $p<0.0001$). Myoma total weight and type of surgery were also significant factors ($p<0.0001$). The coefficients of these variables were all positive, which indicated that EBL increased with an increase in variables (Table 3).

DISCUSSION

This retrospective study showed that RALM for large or heavy myomas was associated with greater blood loss and longer total operating time compared to AM; however, transfusion rate was not different. RALM was also associated with shorter hospital stays and fewer short-term complications. In multiple linear regression analysis, the number of removed myomas was the most important factor for EBL. Therefore, surgeons should be ready to manage other risk factors associated with postoperative anemia when performing RALM for multiple large or heavy myomas. A recent Cochrane review concluded that preoperative iron supplements accompanied by preoperative gonadotropin-releasing hormone agonist (vasopressin) injection should be thoroughly considered in these cases.^{19–21} However, the maximal myoma diameter was not associated with EBL in our study. Therefore, we can consider RALM for large myomas (over 10 cm in size).

In terms of the comparison between RALM and AM, a retrospective study published in 2007 (shortly after the introduction of RALM) showed that RALM ($n=29$) had a lower mean EBL (195.7 mL vs. 354.7 mL, $p<0.05$), shorter hospital stays (1.48 days vs. 3.62 days, $p<0.05$), longer operating times (231.38 min vs. 154.41 min, $p<0.05$), and higher cost compared to AM ($n=29$).⁹ In 2011, Barakat, et al.²² published another earlier retrospective study comparing the short-term surgical outcomes of RALM ($n=89$), LM ($n=93$), and AM ($n=773$). They showed that AM (126 min, $p<0.001$) had shorter operating time compared to LM (155 min) or RALM (181 min), even though the mean diameter of myomas removed by AM (7.7 cm) and RALM (7.5 cm) was significantly larger than that of myomas removed by LM (6.7 cm). In 2018, Wang, et al.²³ reported a meta-analysis of AM, LM, and RALM. They showed significantly lower EBL (68.2 to 138.42 vs. 85.3 to 420, $p=0.02$), lighter postoperative bleeding (2 vs. 10, $p=0.03$), and fewer intraoperative complications (30 vs. 46, $p=0.009$) with RALM ($n=773$) compared to LM ($n=1079$). In our study, we only included large and heavy myomas undergoing RALM and AM. We also observed longer operating times in RALM, confirming the results of previous literature. In terms of hospital stay and short-term perioperative complications,

Table 3. Factors Associated with Estimated Blood Loss

Variable	Coefficient (95% CI)	<i>p</i> value
Concomitant surgery	4.8638 (-139.4534–149.1809)	0.947
Age	0.5351 (-4.3064–5.3766)	0.829
BMI	-4.1849 (-10.7532–2.3834)	0.213
History of pelvic surgery	-10.2104 (-77.9457–57.5248)	0.768
Type of myoma	72.0538 (-3.6627–147.7702)	0.064
Maximal myoma diameter	2.9149 (-8.7947–14.6244)	0.626
Number of myomas	10.9193 (5.1201–16.7185)	$2.85\times 10^{-4*}$
Number of myomas sized >3 cm	5.7571 (-14.0963–25.6105)	0.570
Weight of the removed myomas	0.1435 (0.0438–0.2432)	$5.23\times 10^{-3*}$
Total operating time	0.4454 (-0.0723–0.963)	0.093
Type of surgery	96.3153 (29.9995–162.6311)	$4.85\times 10^{-3*}$

BMI, body mass index; CI, confidence interval.

* $p<0.05$ by multiple linear regression analysis.

our study also showed that RALM was associated with shorter hospital stay and fewer short-term complications compared to AM. Regarding pregnancy outcomes, a long-term, 15-year follow-up study in 2016 reported no difference in the spontaneous pregnancy rate, abortion rate, live birth rate, and bleeding during delivery between RALM (n=25) and AM (n=81).²⁴

In terms of MIS for large myomas, a recent study published in 2017 analyzed the cases of three high-volume centers and reported the complications of MIS (n=221, 100 cases of RALM and 116 cases of LM) and AM (n=29) for large, numerous myomas performed over 44 months.²⁵ The authors compared the cases (with complications) and the controls (without complications), and also compared the results with previously published data on MIS myomectomy. The authors concluded that MIS for large, numerous myomas is feasible, and that the complications were not different from those of MIS for smaller, fewer myomas.²⁵

In our study also showed that 126 RALM for large (sized over 10 cm) or heavy (weighing over 250 g) myomas is feasible, and 28 cases were RALM in cases with five or more myomas. There were two cases of 10 myomas and three cases each of 15 myomas, 30 myomas, 34 myomas; therefore, numerous myomas are not necessarily a contraindication of RALM.

Another recent study published in 2018 also compared RALM for large myomas (sized over 10 cm) (n=32, mean weight of 446.5 g) with RALM for myomas smaller than 10 cm (n=42, mean weight of 288.1 g). They concluded that RALM for large myomas is a feasible and safe surgical option with acceptable operation time (263.4 min vs. 219.1 min, $p=0.02$) and low risk of complications, as our result showed lower complication rates.¹⁴ In 2015, Cheng, et al.²⁶ also reported the outcomes of RALM for complex myomas, which were defined as more than two myomas, large myomas (sized over 8 cm), or preexisting pelvic adhesions. The mean myoma diameter was 7.3 cm, with a mean weight of 367.4±317.7 (10–1070) g, and EBL was 235.7 mL. There were 5 (23.8%) cases of transfusion, zero case of conversion to open surgery, and only one complication of wound cellulitis. The authors concluded that RALM is a safe and effective method to treat complex myomas.²⁶ Similarly, our results demonstrated a 27.2% transfusion rate, and no case of conversion to open surgery in larger (> 10 cm) and heavier (444.6±283.14 g) myomas.

This study had several strengths. First, to our knowledge, this study included the largest number of large or heavy myomas (126 in the RALM group and 151 in the AM group) to compare the operative and perioperative outcomes between RALM and AM. Second, the relatively short study period (15 months) in the current study can preclude intrapersonal variation in surgical experiences. Third, the homogeneous surgical skills and experiences of our surgeon, with over 15 years of gynecologic surgery in a high-volume center, could also help reduce interpersonal variation.

However, this study also had some limitations. First, this was

not a randomized controlled study. Secondly, the perioperative follow-up duration was short (within the first 30 postoperative days). However, the primary objective of this study was to compare the operative and perioperative outcomes to assess the feasibility of using RALM instead of AM in large or heavy myomas. Third, we only included cases performed within the most recent 15 months. This cannot exclude selection bias; therefore, further research comparing RALM and AM for large or heavy myomas over a longer period will be needed. The difference in learning curves between RALM and AM may also affect study results; therefore, we intended to include cases that were treated by surgeons who have mastered the new procedure. Finally, there was a lack of data regarding the preoperative use of a gonadotropin-releasing hormone agonist or selective progesterone receptor modulator, history of uterine artery embolization, and use of perioperative medical agents to decrease blood loss, such as tranexamic acid, misoprostol, vasopressin, or oxytocin. However, these factors were also not considered in previous retrospective studies comparing RALM and AM.

In conclusion, our findings suggest that RALM is a feasible and safe surgical option for large or heavy myomas, and is comparable to AM. To determine which is the best surgical option for myomectomy of large or heavy myomas, further well designed, large-scale, randomized controlled trials of RALM, LM, and AM are needed. These should include cases performed by several groups of surgeons with a similar level of surgical experience using a few elements.

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AUTHOR CONTRIBUTIONS

Conceptualization: Sa Ra Lee. **Data curation:** Sa Ra Lee. **Formal analysis:** Sa Ra Lee and Eun Sil Lee. **Funding acquisition:** Sa Ra Lee and Eun Sil Lee. **Investigation:** Sa Ra Lee, Young-Jae Lee, Shin-Wha Lee, Jeong Yeol Park, Dae-Yeon Kim, Sung Hoon Kim, Yong-Man Kim, Dae-Shik Suh, and Young-Tak Kim. **Methodology:** Sa Ra Lee, Eun Sil Lee, and Sung Hoon Kim. **Supervision:** Sung Hoon Kim. **Validation:** Young-Tak Kim. **Visualization:** Eun Sil Lee. **Writing—original draft:** Sa Ra Lee, Eun Sil Lee. **Writing—review & editing:** Sa Ra Lee and Eun Sil Lee. **Approval of final manuscript:** all authors.

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