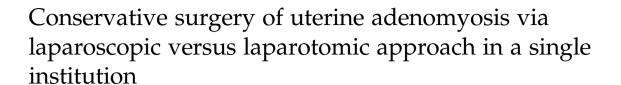
doi:10.1111/jog.13658

J. Obstet. Gynaecol. Res. 2018



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Abstract

Aims: To evaluate the surgical outcomes of both approach methods (laparoscopy vs laparotomy) and to suggest the proper surgical approach according to type of uterine adenomyosis (focal vs diffuse).

Methods: We retrospectively analyzed 224 cases of uterine adenomyomectomy, 116 laparotomic and 108 laparoscopic, performed between July 2011 and June 2016 by a single surgeon (Y. S. K.). In all 224 cases, the surgeon had used transient occlusion of the uterine artery (TOUA). Surgical outcomes included weight of specimen, operating time, estimated blood loss and intraoperative injury to other organs. Postoperative clinical outcomes included symptom improvement (dysmenorrhea, menorrhagia and others) and recurrence.

Results: All patients in the laparoscopic group had been diagnosed with focal uterine adenomyosis, and most in the laparotomic group (85.3%) had been diagnosed with diffuse type. The largest lesion diameters were 6.48 cm in the laparotomic group and 4.34 cm in the laparotomic group. Operation time and estimated blood loss were 116.12 min and 222.67 mL in the laparotomic group and 75.09 min, respectively, and 155.33 mL in the laparoscopic group. There was no case of laparotomic conversion in patients with laparoscopic adenomyomectomy.

Conclusion: Conservative surgery is effective to reduce the symptoms of adenomyosis regardless of approach method. For near-complete excision of adenomyosis, the diffuse type is recommended to be treated with laparotomic adenomyomectomy, and focal lesions less than 5 cm can be treated with laparoscopic conservative surgery.

Key words: adenomyosis, conservative surgery, laparoscopy, laparotomy.

Introduction

Adenomyosis is defined as the presence of endometrial tissue within the myometrium. It presents with a wide range of clinical symptoms that include heavy menstrual bleeding, dysmenorrhea and recurrent abortion, and it might be associated with subfertility. Medical therapies include continuous use of oral contraceptive pills, high-dose progestins, selective estrogen/progesterone receptor modulators,

levonorgestrel-releasing intrauterine devices, aromatase inhibitors, danazol and gonadotropin receptor hormone agonists. All therapeutic strategies are only temporarily effective, and conception is impossible during the treatment period; moreover, some patients are refractory to the medical treatments.¹ The most effective surgical treatment has been limited to hysterectomy in patients with uterine adenomyosis. However, the growing popularity of late childbearing has increased the demand for uterus-conserving treatment

Received: September 28 2017.

Accepted: March 20 2018.

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as a way of preserving fertility. Recently, a few studies have reported on conservative surgery in patients with uterine adenomyosis.

Although uterus-conserving surgery for adenomyosis has been increasing along with information on and interest in both patients and gynecology surgeons, no study has presented the outcomes of conservative surgery in patients with adenomyosis by type and approach method at a single institution using one surgical technique.

In the present study, we present patient characteristics and the surgical outcomes of laparoscopic and laparotomic adenomyomectomy performed by a single surgeon following the same procedure.

Based on the 224 adenomyomectomy operations, we introduce the efficacy and safety of the surgical technique under stable operative conditions with less bleeding by transient occlusion of the uterine artery (TOUA). Furthermore, we present practical guidelines for conservative surgery in patients with uterine adenomyosis by type and surgical approach.

Methods

We retrospectively analyzed 224 patients with uterine adenomyosis who underwent adenomyomectomy with TOUA between July 2011 and June 2016 by a single surgeon (Y. S. K.); the adenomyosis had been preoperatively diagnosed primarily with transvaginal ultrasonography. The ethical committee of Ulsan University Hospital approved the study File No. 2013-09-621 and File No. 2013-08-618 on 5th December 2014. The indication for conservative surgical treatment of adenomyosis was refractory symptoms in patients who wanted to preserve their fertility. The surgeon performed laparotomic adenomyomectomy for the diffuse type of uterine adenomyosis and for adenomyotic lesions of more than 5 cm in maximal diameter for focal adenomyosis. When excising the lesion, we preserve the endometrium at a minimum 5 mm depth for restoring endometrial blood flow after the surgery. Most of the patients had received three consecutive injections of gonadotropin-releasing hormone agonist (GnRHa) at 1-month intervals after the surgery. Five months after the third GnRHa injection, when menstruation had returned, patients completed a standardized questionnaire in the outpatient clinic. Then, we followed up the patients in the outpatient clinic at 6-month intervals.

The patients rated dysmenorrhea using an 11-point scale (0 = no pain, 10 = worst pain imaginable) and menorrhagia using the Mansfield-Voda-Jorgensen menstrual bleeding scale. We calculated symptom improvement as the decline ratio (%) of the difference between initial and postoperative symptoms 7 months after each surgery. We defined complete remission (CR) as 100% symptom improvement, partial remission (PR) as >30% improvement and stable disease as $\le 30\%$ improvement. We also defined recurrence as relapse of adenomyotic lesion by ultrasonography with relapse of related menstrual symptoms.

We described laparotomic adenomyomectomy with TOUA and laparoscopic adenomyomectomy in previously published reports.^{2–4} Surgical outcomes included weight of excised lesion, operation time, estimated blood loss, any injury to nerves or uterine vessels and hysterectomy conversion.

We used Statistical Package for Social Sciences (SPSS, Inc.) for the statistical analyses. Data are expressed as mean \pm standard deviation (SD) or absolute number (%) and considered P < 0.05 statistically significant.

Results

The mean ages of the patients were 42.09 ± 4.73 years in the laparoscopic group and 37.49 ± 4.78 years in the laparotomic group; the parity was statistically different between the two groups. Although dysmenorrhea was more frequent than menorrhagia, the most frequent symptom was the combination of both. All patients with diffuse-type uterine adenomyosis had received laparotomic adenomyomectomy TOUA. The diameters largest lesion were 6.48 ± 2.15 cm in the laparotomic group 4.34 ± 1.04 cm in the laparoscopic group, and there was a statistically significant difference between the two groups (Table 1).

During the last year of the study period, we began measuring the excised specimen weights because we considered this a valuable objective parameter for evaluating surgical outcomes of adenomyomectomy. The total number of specimens we weighed was 70, 40 in the laparotomic group and 30 in the laparoscopic group. There was a significant difference between the two groups (mean weights: 108.29 and 32.73 g in the laparotomic and laparoscopic groups, respectively). Estimated blood

Table 1 Preoperative characteristics of patients

Characteristics	Laparotomy ($n = 116$)	Laparoscopy ($n = 108$)	<i>P</i> -value
Age (year, mean \pm SD) (median) (range)	$37.49 \pm 4.73 (37) (26-48)$	42.09 ± 4.78 (42) (27–53)	< 0.001
Parity (mean \pm SD) [†]	0.6 ± 0.80	1.71 ± 0.84	< 0.001
Nulliparity	68 (58.62%)	13 (12.04%)	
Multiparity	48 (41.38%)	95 (87.96%)	
Major symptom			0.072
Menorrhagia	10 (8.6%)	13 (12.0%)	
Dysmenorrhea	36 (31.0%)	36 (33.3%)	
Combined [‡]	69 (59.5%)	52 (48.2%)	
Others	1 (0.9%)	7 (6.48%)	
Type of adenomyosis			< 0.001
Diffuse	99 (85.3%)	0 (0%)	
Focal	17 (14.29%)	108 (100%)	
Location of adenomyosis			< 0.001
Anterior	19	32	
Posterior	51	60	
Fundal	8	16	
Whole uterus	38	0	
Maximal size of adenomyosis (cm, mean \pm SD)	6.48 ± 2.15	4.34 ± 1.04	< 0.001

†Number of deliveries; ‡Combined, mixed symptoms of menorrhagia and dysmenorrhea; Data are expressed as mean \pm standard deviation or absolute numbers (%). SD, standard deviation.

loss was 222.67 ± 231.15 mL in the laparotomic adenomyomectomy with TOUA group and 155.33 ± 116.25 mL in the laparoscopic adenomyomectomy with TOUA group, and that difference was significant as well (P = 0.006). In the laparoscopic group, there was no case of conversion from laparoscopic to laparotomic adenomyomectomy. In both groups, there was no case of conversion from adenomyomectomy to hysterectomy (Table 2).

Dysmenorrhea improved in 99.99% of patients (CR: 30.12%; PR: 69.88%), and menorrhagia was relieved in 85.34% (CR: 14.67%; PR: 70.67%) in the laparotomic group. In the laparoscopic group, dysmenorrhea improved in 96.92% of patients (CR: 52.38%; PR: 45.24%), and menorrhagia was relieved in 82.05% (CR: 17.95%; PR: 64.10%).

During the mean 16.59 months of follow-up after laparotomic adenomyomectomy with TOUA and 13.37 months after laparoscopic adenomyomectomy

with TOUA, there was recurrence in 10 (8.62%) patients in the laparotomic group and 11 (10.2%) in the laparoscopic group. There were no significant differences in symptom improvement or recurrence rate between the two groups (Table 3). Of the 21 patients with recurrence, 3 ultimately received hysterectomies, 31 months after laparotomic adenomyomectomy for 1 patient and 34 and 49 months after laparoscopic adenomyomectomy for 2 patients.

We had 14 cases of conception after adenomyomectomy, 12 in the laparotomic group and 2 in the laparoscopic group. Of the 14 pregnancies, 5 were by in vitro fertilization, and 9 were natural. Three patients miscarried in the first trimester due to missed abortions. The 11 deliveries were by caesarean at a mean gestational age of 36.4 weeks, and one case was a twin delivery. There was no case of uterine rupture in the present study (Table 4).

Table 2 Comparison of surgical outcomes of adenomyomectomy with transient occlusion of uterine arteries (TOUA)

Characteristic	Laparotomy	Laparoscopy	<i>P</i> -value
Weight of specimen (g) ^{†‡}	$108.29 \pm 104.35 (n = 40)$	$32.73 \pm 18.15 (n = 30)$	< 0.001
Operating time (min)	116.12 ± 4.0	75.09 ± 3.9	< 0.001
Estimated blood loss (mL) ^{†§}	222.67 ± 231.15	155.33 ± 116.25	0.006
Combined Endometriosis (%)	37/116 (31.9%)	12/108 (11.1%)	< 0.001

 \dagger Mean \pm standard deviation; \ddagger In the laparotomic and laparoscopic cases, the weight of 40 and 30 specimens, respectively; \$(preoperative hemoglobin level) – (postoperative hemoglobin level); if the hemoglobin level is higher than preoperative value, it was not counted. Hb, Hemoglobin.

Table 3 Symptom follow-up 7 months after adenomyomectomy with transient occlusion of uterine arteries (TOUA)

	Laparotomy		Laparoscopy		<i>P</i> -value		
Follow-up period (month)	16.59 ± 10.12		13.37 ± 13.13		0.045		
Symptom improvement [†]	CR	PR	SD	CR	PR	SD	
Dysmenorrhea (%)	25 (30.12)	58 (69.88)	0 (0)	22 (52.38)	19 (45.24)	1 (2.38)	0.816
Laparotomy $n = 83$							
Laparoscopy $n = 42$							
Menorrhagia (%)	11 (14.67)	53 (70.67)	11 (14.6)	7 (17.95)	25 (64.10)	7 (17.95)	0.833
Laparotomy $n = 75$							
Laparoscopy $n = 39$							
Relapse rate	1	0/116 (8.62%))	1	1/108 (10.2%))	0.606
Period until relapse (month)	17.4 ± 9.57		19.55 ± 9.80		0.618		
Only symptomatic	2		4				
Only sonographic	6		5				
Symptomatic and sonographic		2			2		
Eventual hysterectomy		$\overset{-}{1^{\ddagger}}$			2 [§]		
Complication		1^{\P}			$1^{\dagger\dagger}$		

†Symptom improvement was calculated by the decline ratio (%) of the difference between initial symptom and postoperative symptom 7 months after the date of operation. Dysmenorrhea was checked on an 11-point numerical scale (0 = no pain, 10 = the pain is as bad as can be). Menorrhagia was evaluated using the Mansfield-Voda-Jorgensen (MVJ) menstrual bleeding scale; ‡The patient received laparotomic hysterectomy 31 months later after adenomyomectomy because of recurrence; §One patient received hysterectomy 34 months later, and the other patient received hysterectomy after 49 months because of recurrent dysmenorrhea. In those two cases, laparoscopic vaginal hysterectomy was performed; ¶Small bowel perforation; ††Superficial inferior epigastric artery bleeding on the trocar site. Data are expressed as mean ± standard deviation or absolute numbers (%). CR, complete remission (100% of symptom improvement rate); PR, partial remission (>30% of symptom improvement rate); SD, stable disease (≤30 of symptom improvement rate).

Table 4 Fertility outcomes after adenomyomectomy

	Laparotomy	Laparoscopy
Conception	11	1
By ART	5	_
By natural	6	1
Missed abortion	3	_
Delivery	7	_
Mean gestational age [†]	36 + 4 weeks	_

†Mean gestational age at the time of delivery of eight delivered cases.; Data compiled until 31 December 2016. ART, Artificial reproductive technology.

Discussion

Conservative surgery for uterine adenomyosis has aimed to excise adenomyosis lesions as completely as possible while restoring the uterine architecture and endometrial function. However, there are some limitations with any conservative adenomyomectomy, including degree of excised lesion, method of uteroplasty, successful preservation of the endometrium for fertility and intraoperative complication risks (mainly heavy bleeding). Because of the obscure architectural boundary between the normal myometrium and adenomyosis lesions, complete excision of the lesions is different from usual uterine repair after myomectomy. Uteroplasty after adenomyomectomy is challenging because the consistency of the remaining myometrium

adjacent to the adenomyosis is hard, which makes restoration difficult.

There is no standard treatment of adenomyosis in women who wants to preserve fertility. The surgical approach is considered more invasive than medical treatment, but adenomyomectomy is the inevitable choice for medical refractory patients who want to get pregnant. Recently, Yones et al. reviewed diverse techniques and clinical results of conservative surgery for adenomyosis. The results showed that excision of adenomyosis is effective for symptom control such as menorrhagia and dysmenorrhea and most probably for adenomyosis-related infertility,5 although the relationship between infertility and uterine adenomyosis is in debate.⁶ Detailed surgical skill is essential to alleviate concerns about perioperative complications, such as profuse bleeding,⁷ and peripartum complications, which include placenta accreta, uterine atony and uterine rupture that can induced by myometrial defects.^{8,9} Conservative surgical technique is classified as complete excision of adenomyosis, cytoreductive surgery/ partial adenomyomectomy. 10 There is no proven technique that secures the best clinical and reproductive performance. Our technique is complete excision, and the strategy for complete excision of adenomyosis should be as complete as possible while preserving normal myometrium. Even if it is the focal type or diffuse type of adenomyosis, choosing the appropriate surgical technique is the most important part to reduce complication and achieve better outcomes.

The proper surgical strategy, laparotomic or laparoscopic, should be planned according to the type of uterine adenomyosis (diffuse vs focal) because, in our experience, successful conservative adenomyomectomy via laparoscopic approach in the diffuse type might be impossible. In the present study, the surgeon performed laparotomic adenomyomectomy with TOUA in all cases of diffuse-type uterine adenomyosis; the surgeon selected the approach method based on whether or not the patients intended to have children because of zero parity due to secondary infertility related to the adenomyosis. There is a technical difference between laparoscopic and laparotomic adenomyomectomy.^{3,4}

Complete lesion excision and uteroplasty to restore the normal uterus has been shifting to laparotomic adenomyomectomy for patients with focal-type uterine adenomyosis and maximum lesion diameter of 5 cm and for single women and virgins. This shifting to laparotomic adenomyomectomy was based on the surgeon's decision to increase the degree of surgical completeness.

There has been increasing interest in conservative surgical treatment in patients with uterine adenomyosis, including surgical and practical guidelines for selecting the approach method and surgical strategy by type of adenomyosis and counseling about pregnancy. We presented 224 cases of conservative adenomyomectomy by a single surgeon via laparoscopy and laparotomy and showed the data for each group according to type of adenomyosis and approach type; we also showed the data on comparisons between the two groups.

In both of the groups, TOUA was used to reduce intraoperative heavy bleeding and obtain a stable operation field.¹¹ The present study showed that TOUA is a useful technique for safely performing operations with expected heavy bleeding such as conservative adenomyomectomy because estimated blood loss and operation time might be comparable or even superior. In addition, the benefit of TOUA is the restoration of uterine arterial flow just after adenomyomectomy. In TOUA, uterine arteries are clipped temporarily, not permanently ligated, which does not affect the uterine blood supply related to ovarian and endometrial function. It has been reported that the permanent interruption of uterine arterial flow can lead to endometrial and ovarian dysfunction that could induce subfertility. 11-14

The efficacy and feasibility of TOUA adenomyomectomy should be evaluated continuously to determine the effectiveness of this technique in terms of symptom relief, successful pregnancy and delivery of healthy infants based on long follow-up periods and with more patients. In this study, for all cases of focal-type uterine adenomyosis, the surgeon performed laparoscopic adenomyomectomy; the mean maximum lesion diameter was 4.34 ± 1.04 cm. Laparoscopic adenomyomectomy limits the ability to perform uteroplasty without dead space in the excised defective uterine bed and to approximate the edges of the remaining myometrium and endometrium. In our surgeon's experience and in the present study, this limitation could not be overcome when the maximum lesion diameter was greater than 5.0 cm. Therefore, in spite of the focal type, laparotomic adenomyomectomy can be recommended for uterine adenomyosis with lesions of more than 5 cm in maximum diameter.

When making decision for the surgery, consultation is needed for those who want to become pregnant regarding the fact that conservative surgery might result in additional risk of peripartum complications, and there is lack of data about reproductive outcomes. Saremi et al. reported that 30% of 70 patients who attempted pregnancy achieved a clinical pregnancy and 16 deliveries, and Kishi et al. reported a rate of 31.4% who tried to become pregnant after conservative surgical treatment. 15,16 We had 14 cases of conception after adenomyomectomy, 12 in the laparotomic group (Table 1) and 2 in the laparoscopic group; of the 14 pregnancies, 5 were by in vitro fertilization, and 9 were natural. Three patients miscarried in the first trimester due to missed abortions; these patients had histories of recurrent abortions, and thus, factors other than adenomyosis could have affected their miscarriages. The 11 deliveries were caesarean, with a mean gestational age of 36.4 weeks, and one case was a twin delivery (Table 4). One of the concerns after adenomyomectomy is the heightened possibility of uterine rupture, a catastrophic obstetrical complication after uterine surgery. There are eight known cases of uterine rupture after adenomyomectomy, six following laparoscopic surgery and two following laparotomies.^{8,9} However, there was no case of uterine rupture in our cases. This might reflect the efficacy of our conservative surgery with TOUA, which reduces tissue death from intraoperative bleeding by using electrocautery, which can cause defects in the uterine wall and loss of tensile strength by

inducing necrosis of the myometrium and permanent ligation of both uterine arterial flows. Another unique aspect of our conservative surgery is our layer-bylayer suturing during uteroplasty.

Our technique of complete excision shows outstanding symptom improvement and other surgical outcomes. However, fertility and delivery outcomes require longer study periods and more patients. Longer-term results should document successful pregnancies and deliveries after surgical treatment of adenomyosis.

To the best of our knowledge, this is the first study to compare conservative adenomyomectomy via laparotomic and laparoscopic approaches for both types of uterine adenomyosis by a single surgeon. It is more helpful to evaluate surgery outcomes without bias toward specific surgical techniques. On the contrary, there could be selection bias because a surgeon's experience determines the approaching method.

Because the standard procedure for adenomyomectomy is not yet established, treatment for adenomyosis should be individualized, and conservative surgery would be one of the choices for the women who are refractory to medical treatment. When planning conservative surgery for adenomyosis, deliberate preoperative evaluation is required for choosing laparoscopy or laparotomy by type of uterine adenomyosis and patients' desire to bear children. Our comparison data could be useful for selecting the proper conservative surgery in patients with uterine adenomyosis according to disease type.

Acknowledgments

None.

Disclosure

All authors declare that they have no conflicts of interest or conflicting financial ties.

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