Original Article

Utility of Laparoscopic Uterine Myomectomy as a Treatment for Infertility with No Obvious Cause Except for Uterine Fibroids

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Abstract

Objectives: Uterine fibroids are capable of causing infertility, but there are no definite criteria for which laparoscopic uterine myomectomy (LM) is known to be beneficial. To investigate the usefulness of LM, we examined pregnancy rates in patients with infertility with no obvious cause except for the presence of uterine fibroids.

Materials and Methods: We retrospectively reviewed the clinical records at Suzuki Memorial Hospital between June 2010 and August 2014. We found 60 eligible patients (LM group, 46; non-LM group, 14). The criteria for performing LM were a maximal fibroid diameter of 40 mm or more or the presence of >4 fibroids.

Results: The duration of infertility before the first visit was significantly longer in the LM group; although there was no significant difference in the mean patient age and body mass index. Pregnancy was achieved in 45.7% of patients (21/46) in the LM group and 28.6% (4/14) in the non-LM group. There were no pregnancies in patients with >10 fibroids. The postoperative pregnancy rate in the LM group was comparable to previously reported pregnancy rates.

Conclusions: Our criteria for performing LM in patients with no obvious cause for infertility except for uterine fibroids seem appropriate, especially when the fibroids are large and the number of fibroids is between 4 and 9. However, our results suggest that the effectiveness of LM is low in patients with 10 or more uterine fibroids.

Keywords: Infertility, laparoscopic myomectomy, pregnancy outcome, uterine fibroid

Introduction

Uterine fibroids are benign tumors found in about 20% of women over 35 years of age.[1] The influence of uterine fibroids on fertility is still controversial,[2,3] but there is indirect evidence supporting a negative effect such as infertility, abortion, and premature birth: approximately 50% of women who have not previously conceived become pregnant after myomectomy.[3] Thus, surgical treatment for uterine myoma is considered therapeutic for patients hoping to achieve pregnancy. However, a recent comprehensive review concluded that the benefits of myomectomy had not been revealed consistently except in patients undergoing myomectomy for submucosal fibroids >2 cm or for fibroids that distort the endometrium.[4] As a consequence, guidelines for the management of fibroids in patients with infertility are not currently available.

The feasibility and safety of laparoscopic uterine myomectomy (LM) have been confirmed by several previous studies.[5-7] As it is less invasive and causes fewer adhesions than laparotomy, LM is the treatment of choice for uterine myomas when patients desire future childbearing. However, the effects of LM on subsequent pregnancy have not been fully evaluated.

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Currently, each institution sets their own criteria for LM as a treatment for infertility in patients for whom no obvious cause except uterine fibroids has been determined, taking into account patient age, infertility duration, and number and size of fibroids. To investigate the usefulness of LM as treatment for infertility, we retrospectively examined the pregnancy rates and outcomes in infertile patients with uterine myoma who underwent LM compared with those who did not have the procedure.

Materials and Methods

Inclusion and exclusion criteria

The Institutional Review Board of Suzuki Memorial Hospital (SMH; Iwanuma city, Miyagi, Japan) approved the study protocol. All patients gave written consent for surgery after receiving complete information on the procedure, including the possible complications of general anesthesia, laparoscopy, and myomectomy. We retrospectively reviewed the clinical records from the outpatient department of SMH between June 2010 and August 2014. A total of 60 patients with no obvious cause for infertility except for uterine fibroids were included in the study. All couples underwent a comprehensive infertility evaluation before surgery, including basal body temperature, ultrasonographic examination, ovulation studies, hysterosalpingography, diagnostic hysteroscopy, and semen analysis. Patients with only submucosal myomas or who had anesthetic contraindications to laparoscopy were excluded from the study. Patients with additional infertility factors were also excluded from the study. Forty-six patients with intramural or subserous fibroids exceeding 4 cm in diameter or numbering >4 underwent LM (LM group), and 14 patients underwent observation (non-LM group).

Perioperative management and follow-up

Treatment with a gonadotropin-releasing hormone agonist was not mandatory before surgery. It was used in patients who had a long waiting period (2–3 months) before surgery could be performed. Patients in the LM group were advised to wait 3 months after surgery before trying to conceive. We generally observed patients for an additional 3 months with the expectation of a natural pregnancy. If a patient did not achieve pregnancy by 6 months after LM, we recommended assisted reproductive technology (ART), including artificial insemination with the husband's semen or *in vitro* fertilization.

Operative technique

All myomectomies were performed under general anesthesia. A 10-mm laparoscope was inserted through an umbilical incision and connected to a video monitor. After securing the intraabdominal field of view using two subcutaneous steel wires to lift lower abdominal wall, an additional three incisions were made in the suprapubic area: 5- or 12-mm ports were placed in each iliac fossa, and a 5-mm port was placed in the midline. A wound retractor was inserted through the umbilical port, and gasless laparoscopic surgery was performed. After injection of 100-fold diluted vasopressin into the myoma surface, an incision was made through the uterine wall using monopolar electrosurgical scissors. The fibroid was removed using either a morcellation device or by blunt dissection. Bleeding was coagulated using bipolar diathermy. The defect was closed with one or two layers of intramyometrial suture, using 0-polyglactin in an interrupted or continuous manner. If the endometrial cavity was exposed, a three-layer closure was performed. After suturing the uterine wall, fibrin spray was used on the serosa of the uterus to prevent the formation of adhesions.

Statistical analysis

Student's *t*-test was used for comparing the LM group with the non-LM group. In all cases, $P < 0.05$ was considered to be statistically significant. The normality of the data was evaluated by examining the skewness and kurtosis of scatter plots and histograms for each of the surgical outcomes.

Results

The characteristics and outcomes of both groups are listed in Table 1. Our group performed LM when the maximum fibroid diameter was 40 mm or more or when the number of myomas was 4 or more [Figure 1]. There were no significant differences in patient age and body mass index between the groups. The duration of infertility before the presentation was significantly longer in the LM group ($P = 0.037$). The pregnancy rate was 45.7% in the LM group and 28.6% in the non-LM group; this was not statistically different. The mean number of fibroids per patient was 5.3 ± 5.0 and 1.3 ± 0.6 in the LM group and non-LM group, respectively [Table 1]. When the number of fibroids was three or fewer, the pregnancy rate was 45.5% in the LM group and 28.6% in the non-LM group [Table 1]. In this subset of patients, LM was significantly superior to observation as treatment for infertility. More importantly, when the number of fibroids was between 4 and 9, the pregnancy rate in the LM group increased to 64.7% (11/17). There were no pregnancies in

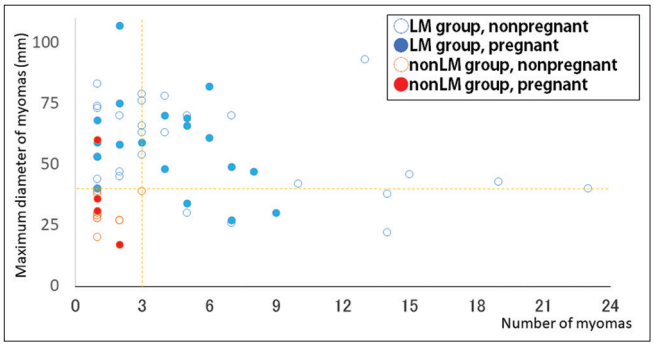

Figure 1: Scatter plot of maximum diameter and number of myomas

Table 1: Comparison of laparoscopic uterine myomectomy group and nonlaparoscopic uterine myomectomy group

	LM group (n=46)		Non-LM group (n=14)		P
Age (years)	37.1±3.3		37.1±3.8		0.971
BMI	22.1±2.9		23.2±3.8		0.519
Infertility period before first visit (m)	55.8±44.0		44.1±26.5		0.037
Pregnancy rate (%)	45.7 (n=21)		28.6 (n=4)		0.095
Number of myomas	5.3±5.0	Pregnancy rate (%)	1.3±0.6	Pregnancy rate (%)	
1-3	22	10 (45.5)	14	4 (28.6)	0.045
4-9	17	11 (64.7)	0	-	N/A
10-	7	0	0	-	N/A
Maximum diameter (mm)	57.2±18.6	Pregnancy rate (%)	32.0±9.9	Pregnancy rate (%)	
10-39	7	3 (42.8)	13	3 (23.0)	0.25
40-69	25	13 (52.0)	1	1 (100)	0.1
70-99	13	3 (23.0)	0	-	N/A
100-	1	1 (100)	0	-	N/A
Location of largest myoma					
Intramural	35		12		
Subserosal	5		2		
Both	6		0		

BMI: Body mass index, LM: Laparoscopic uterine myomectomy, N/A: Not available

patients with >10 myomas (n = 7). The mean size of the largest fibroid was 57.2 ± 18.6 mm and 32.0 ± 9.9 mm in the LM group and non-LM group, respectively [Table 1].

The comparison between pregnant and nonpregnant patients in the LM group is shown in Table 2. The mean age of pregnant patients was 35.8 years, significantly younger than nonpregnant patients (mean age, 38.1 years; P = 0.021). There was no significant difference in the duration of infertility, number of myomas, maximum myoma size, or operative time.

The outcome of pregnancies occurring in the LM group and the non-LM group is shown in Table 3. The average interval between LM and pregnancy was 10.2 months, and about half of pregnancies were achieved using ART. All pregnancies in the non-LM group were achieved naturally. Spontaneous abortions were observed in three patients (14%) in the LM group and one patient (25%) in the non-LM group. The 13 women (62%) who delivered by cesarean after LM were assessed for pelvic adhesions, but there was no report of severe pelvic adhesions.

Discussion

The study confirms that LM is feasible and may be considered for select infertility patients. Previous studies report an overall pregnancy rate between 33% and 58% in patients who undergo LM for infertility.[7-9] Although there is no clear causal relationship between uterine myoma and infertility, more than half of patients undergoing myomectomy conceive within 1 year.[8] The average interval between LM and pregnancy is 10.2 months in our study, comparable to the interval reported elsewhere (7.5 − 13.9 months).[9-11] Although Samejima *et al*. demonstrate that myomectomy benefits especially those patients who do not have additional infertility factors,[10] we did not find a statistically significant difference in pregnancy rates between our LM and non-LM groups. While the literature does not show that a clear correlation has been found between the characteristics of removed fibroids and the rate of conception,[12,13] our results show that LM seems to be superior to observation when the number of fibroids is between one and nine. However, the effectiveness of LM is seemingly low in patients with >10 uterine myomas.

The patients in the LM group who achieved pregnancy show no significant difference from those who were not able to get pregnant in the duration of infertility, number of removed fibroids, the maximum size of fibroids, operative time, and the location of largest fibroid; only patient age is significantly different. These results are compatible with those of another study reporting that younger age is an advantageous factor for pregnancy if there is no male factor or endometriosis present.[10] A significantly increased pregnancy rate was observed in patients who underwent resection of submucosal fibroids >2 cm.[14] However, no clear correlation between pregnancy rate and tumor diameter is observed regarding the subserosal and intramural fibroid.

There is no clear standard for how long patients should use contraception after LM. At our center, we recommend that patients wait 3 months after LM to attempt conception. Darwish *et al*. reported that wound healing is usually completed within 3 months.[15] While the recommended contraceptive periods vary, we feel that it is reasonable to wait for 2–3 months after LM to allow for restoration of the uterine myometrium.

Uterine rupture during pregnancy or labor is a rare but serious complication associated with myomectomy; the risk is reportedly 0.6%.[11] Several procedural factors concerning uterine rupture after LM have been reported, such as thermal

Table 2: Comparison of pregnant or nonpregnant cases in the laparoscopic uterine myomectomy group

	Pregnant (*n*=21)	Nonpregnant (*n*=25)	*P*
Age (years)	35.8±2.7	38.1±3.4	0.021
Duration of infertility before first visit (m)	44.5±34.1	65.7±49.3	0.111
Number of myoma removed	3.8±2.5	6.6±6.0	0.053
Maximum diameter (mm)	56.9±18.2	57.4±18.9	0.93
Operative time (min)	119.8±28.2	140.5±43.5	0.064

LM: Laparoscopic uterine myomectomy

Table 3: Pregnancy details in the laparoscopic uterine myomectomy and the nonlaparoscopic uterine myomectomy group

	LM group (*n*=21)	Non-LM group (*n*=4)
Natural pregnancy	11	4
ART	10	0
Interval from LM (m)	10.2±6.7	N/A
Natural delivery	1	2
C/S	13	1
Abortion	3	1
Unknown	4	0

ART: Assisted reproductive technology, C/S: Cesarean section, LM: Laparoscopic uterine myomectomy, N/A: Not available

damage from bipolar coagulation,[16] inadequate multilayer closure,[17] and the use of continuous suturing methods.[18] There are several other factors related to the healing process of the myometrium. We use electrical devices carefully to minimize thermal damage to the myometrium, and we try to suture the myometrium in layers. We saw no serious side effects, including uterine rupture, in our study.

This study has several limitations. First, this is a retrospective study, not a randomized trial. Second, we had a small sample size; therefore, further large-scale studies are recommended to validate our results.

Conclusions

Our study shows that pregnancy is achieved in 45.7% of infertile patients undergoing LM, and at least 67% of those pregnancies result in delivery. The pregnancy rate at our institute after LM is comparable to the general pregnancy rate after LM. Our results are encouraging in terms of achieving fertility by LM, especially for patients with fibroids and otherwise unexplained infertility. Randomized controlled trials are now required to more accurately determine fertility rates and pregnancy outcomes after either LM or observation.

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Conflicts of interest

There are no conflicts of interest.

References

1. Merrill RM. Hysterectomy surveillance in the United States, 1997 through 2005. Med Sci Monit 2008;14:CR24-31.
2. Khalaf Y, Ross C, El-Toukhy T, Hart R, Seed P, Braude P, *et al.* The effect of small intramural uterine fibroids on the cumulative outcome of assisted conception. Hum Reprod 2006;21:2640-4.
3. Mas A, Tarazona M, Dasi Carrasco J, Estaca G, Cristobal I, Monleon J. Updata approaches for management of uterine fibroids. Int J Womens Health 2017;9:607-17.
4. Brady PC, Stanic AK, Styer AK. Uterine fibroids and subfertility: An update on the role of myomectomy. Curr Opin Obstet Gynecol 2013;25:255-9.
5. Seracchioli R, Rossi S, Govoni F, Rossi E, Venturoli S, Bulletti C, *et al.* Fertility and obstetric outcome after laparoscopic myomectomy of large myomata: A randomized comparison with abdominal myomectomy. Hum Reprod 2000;15:2663-8.
6. Bernardi TS, Radosa MP, Weisheit A, Diebolder H, Schneider U, Schleussner E, *et al.* Laparoscopic myomectomy: A 6-year follow-up single-center cohort analysis of fertility and obstetric outcome measures. Arch Gynecol Obstet 2014;290:87-91.
7. Daraï E, Dechaud H, Benifla JL, Renolleau C, Panel P, Madelenat P, *et al.* Fertility after laparoscopic myomectomy: Preliminary results. Hum Reprod 1997;12:1931-4.
8. Sudik R, Hüsch K, Steller J, Daume E. Fertility and pregnancy outcome after myomectomy in sterility patients. Eur J Obstet Gynecol Reprod Biol 1996;65:209-14.
9. Soriano D, Dessolle L, Poncelet C, Benifla JL, Madelenat P, Darai E, *et al.* Pregnancy outcome after laparoscopic and laparoconverted myomectomy. Eur J Obstet Gynecol Reprod Biol 2003; 108:194-8.
10. Samejima T, Koga K, Nakae H, Wada-Hiraike O, Fujimoto A, Fujii T, *et al.* Identifying patients who can improve fertility with myomectomy. Eur J Obstet Gynecol Reprod Biol 2015; 185:28-32.
11. Koo YJ, Lee JK, Lee YK, Kwak DW, Lee IH, Lim KT, *et al.* Pregnancy outcomes and risk factors for uterine rupture after laparoscopic myomectomy: A single-center experience and literature review. J Minim Invasive Gynecol 2015;22:1022-8.
12. Smith DC, Uhlir JK. Myomectomy as a reproductive procedure. Am J Obstet Gynecol 1990;162:1476-9.
13. Vercellini P, Maddalena S, De Giorgi O, Pesole A, Ferrari L, Crosignani PG, *et al.* Determinants of reproductive outcome after abdominal myomectomy for infertility. Fertil Steril 1999; 72:109-14.
14. Varasteh NN, Neuwirth RS, Levin B, Keltz MD. Pregnancy rates after hysteroscopic polypectomy and myomectomy in infertile women. Obstet Gynecol 1999;94:168-71.
15. Darwish AM, Nasr AM, El-Nashar DA. Evaluation of postmyomectomy uterine scar. J Clin Ultrasound 2005;33:181-6.
16. Cobellis L, Pecori E, Cobellis G. Comparison of intramural myomectomy scar after laparotomy or laparoscopy. Int J Gynaecol Obstet 2004;84:87-8.
17. Parker WH, Einarsson J, Istre O, Dubuisson JB. Risk factors for uterine rupture after laparoscopic myomectomy. J Minim Invasive Gynecol 2010;17:551-4.
18. Fujimoto A, Morimoto C, Hosokawa Y, Hasegawa A. Suturing method as a factor for uterine vascularity after laparoscopic myomectomy. Eur J Obstet Gynecol Reprod Biol 2017;211:146-9.