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Original article

Recurrence of uterine myoma after laparoscopic myomectomy: What are the risk factors?

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ABSTRACT

Objective: Uterine myoma is a common gynecologic disease. Myomectomy is selected to preserve the uterus, and with recent advances in laparoscopic technology, laparoscopic myomectomy (LM) has become a common treatment. However, myoma can recur after LM, and to date, reports on post-LM recurrence rates and risk factors have been inconsistent. This retrospective study examines post-LM recurrence rates and the possible risk factors for recurrence.

Materials and Methods: Between 1995 and 2010, 250 patients who underwent LM at a single institution were followed from the postoperative sixth month to the fifth year semiannually for recurrence by ultrasound/magnetic resonance imaging (MRI). Mean age, body mass index (BMI), preoperative gonadotropin-releasing hormone agonist (GnRHa) therapy, surgical time, blood loss, number of removed myomas, and largest myoma diameter were compared between patients with recurrence and those without. Recurrence rates were also investigated by individual risk factors, including patient age, GnRHa therapy, number of removed myomas, and largest tumor diameter.

Results: Cumulative post-LM recurrence rates were 15.3%, 43.8%, and 62.1% at postoperative years 1, 3, and 5, respectively. There were significant differences in surgical time, blood loss, and number of removed myomas between patients with recurrence and those without. Analysis of risk factors revealed significant correlation between recurrence rates and patient age, number of myomas, and myoma size.

Conclusion: Risk of post-LM recurrence increases over time. Risk factors are age, myoma size, and number of tumors. Particular attention to recurrence is required for patients with uterine myomas of $\geq$10 cm diameter, with numerous myomas, and those age 35 years or older.

Introduction

Myoma is a common gynecologic disease occurring in 20% of females at the age of 30 years and older and 40% at the age of 40 years and older.[1,2] Myomectomy is the surgical option selected to preserve the uterus. Recently, laparoscopic myomectomy (LM) has become a procedure of choice because it is less invasive. However, myoma can recur after LM as after open surgery. Rossetti et al[3] have reported recurrence rates of 23% in open surgery and 27% in laparoscopic surgery; there was no statistically significant difference between these rates. Yoo et al[4] have reported recurrence rates of 11.7%, 36.1%, 52.9%, and 84.4%, respectively, at 1, 3, 5, and 8 years after LM.[4] They also reported that recurrence was less frequent in patients with two or fewer myomas, myomas of a size comparable to 13 weeks' gestation, patients with no postoperative deliveries, and patients younger than 35 years.[4] They concluded that age, number of tumors and size, presence of pelvic disease, and postoperative parity were risk factors for recurrence. Nezhut et al[5] have reported recurrence rates of 31.7% and 51.4% in 3 and 5 years, respectively, and Fedele et al[6] have reported a recurrence rate of 51% at 5 years.

Overall, the results of studies on post-LM recurrence remain inconsistent, and no study to date has thoroughly evaluated the individual risk factors that may contribute to recurrence. Following is a report of a retrospective investigation of recurrence rates and possible risk factors for post-LM recurrence of myoma. This study included a greater number of recurrent cases than has previously been available.

Materials and methods

A total of 334 patients underwent laparoscopic myomectomy at a single hospital between January 1995 and December 2010.

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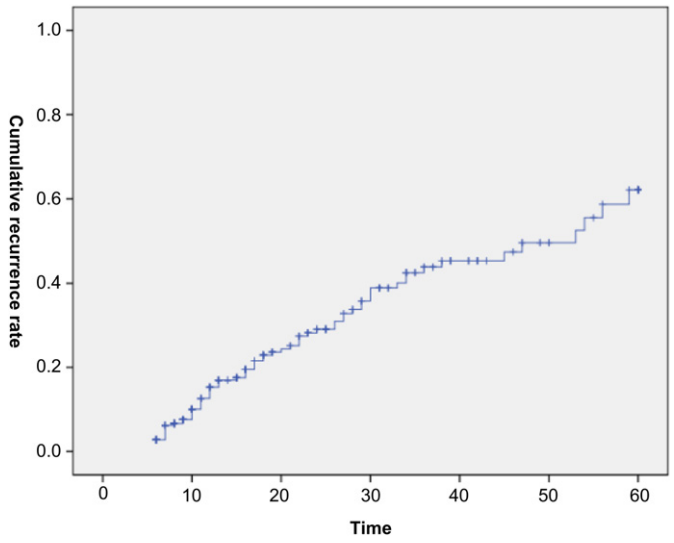

Fig. 1. Cumulative recurrence rates after laparoscopic myomectomy (post-LM recurrence rates) were 15.3 ± 2.5%, 43.8 ± 4.5%, and 62.1 ± 6.7% at postoperative years 1, 3, and 5, respectively.

Of these, 250 were followed from the sixth month to the fifth year postoperatively, during which they were checked for recurrence semiannually by methods including ultrasound and magnetic resonance imaging (MRI). Recurrence was confirmed when a myoma with a diameter of 1 cm or larger was detected by ultrasound or MRI.

Post-LM recurrence and repeat surgery rates were investigated as well as the cumulative recurrence rates at 1, 3, and 5 years postoperatively. The patients were divided in two groups, recurrent and nonrecurrent, and potential risk factors for recurrence, including mean age, body mass index (BMI), preoperative gonadotropin releasing hormone agonist (GnRHa) therapy, surgical time, blood loss, number of removed myomas, and the largest myoma diameter were compared. Recurrence rates were then compared between each of the following subgroups: GnRHa therapy group versus non-GnRHa group; group with one enucleated myoma versus group with two or more enucleated myomas; group of age 35 years or older versus group younger than 35 years; and group with the largest myoma diameter ≥10 cm versus diameter <10 cm.

The patients with recurrence were subdivided into three groups depending on recurrence time: <1 year, ≥1 year and <3 years, and ≥3 years and <5 years. The number of cases and mean myoma diameter at recurrence were compared among the groups.

Surgical technique

With a uterine manipulator inserted, a pneumoperitoneum needle was inserted through the umbilicus, and the pneumoperitoneum was accessed by the closed method. Subsequently, the first trocar was inserted through the umbilicus and the laparoscope was inserted. The second and third trocars were placed in the left and right lower abdomen, and the fourth trocar was placed on the left side of the umbilicus. The size of the trocars was 5 mm except for the fourth, which was 12 mm for the retrieval of myomas and intracorporeal suturing. To reduce blood loss, vasopressin diluted 100-fold was locally injected through the surface of myomas.[7,8] The myometrium was incised with an ultrasonic knife and the myomas were grasped, pulled, and enucleated with a borer. The uterine incision was closed in two to three layers with 1-Vicryl suture on a CT-1 needle (Johnson & Johnson). Enucleated myoma nodules were then retrieved from the body with a morcellator. The surgery was completed after hemostasis was confirmed, the intraperitoneal cavity was washed, and a Seprafilm (genzyme) hyaluronic acid/carboxymethylcellulose membrane was applied to the incision sites.[9]

Table 2
Recurrence rates by risk factor.

Risk factor		*p* value
Age <35 y	Age ≥35 y	
18.8% (range: 16–85)	35.2% (range: 58–165)	<0.01
BMI < 25	BMI ≥ 25	
28.0% (range: 60–214)	38.9% (range: 14–36)	n.s.
Without GnRHa	With GnRHa	
26.9% (range: 49–182)	36.8% (range: 25–68)	n.s.
Number of myomas = 1	Number of myomas ≥2	
23.0% (range: 26–113)	35.0% (range: 48–137)	0.04
Myoma diameter <10 cm	Myoma diameter ≥10 cm	
28.1% (range: 66–235)	53.5% (range: 8–15)	0.04

BMI = body mass index; GnRHa = gonadotropin-releasing hormone agonist; n.s. = no significant difference.

Statistical analyses

The Kaplan-Meier method was used for evaluating the cumulative recurrence rates. For a comparison of the rates between the two groups, a Chi-square test was performed. Results were statistically significant when $p < 0.05$.

Results

There were 74 patients who had recurrent myomas during the postoperative study period, for an overall recurrence rate of 29.6% (74 of 250). The repeat surgery rate was 2.4% (6 of 250). The cumulative recurrence rates were 15.3%, 43.8%, and 62.1% at postoperative years 1, 3, and 5, respectively (Fig. 1). The comparison between the recurrence and nonrecurrence groups is shown in Table 1. There was no significant difference in mean age (37.5 years vs. 36.1 years); mean BMI (22.1 vs. 21.3); administration of GnRHa (33.8% vs. 24.4); or the mean largest myoma diameter (7.0 cm vs. 6.6 cm). There were significant differences in the mean surgical time and mean blood loss (176 minutes vs. 151 minutes

Table 1
Comparison of results between the recurrence and nonrecurrence groups.

	Overall	Recurrence group	Nonrecurrence group	*p* value
	n = 250	*n* = 74	*n* = 176	
Age (y) (range)	36.6 ± 5.1 (26–51)	37.5 ± 4.6 (27–46)	36.1 ± 5.0 (26–51)	n.s.
Body mass index (kg/m^2) (range)	21.4 ± 3.0 (16.4–35.7)	22.1 ± 3.4 (16.6–32.9)	21.3 ± 3.1 (16.4–35.7)	n.s.
GnRH (%) (range)	27.2 (68/250)	33.8 (25/74)	24.4 (43/176)	n.s.
Surgical time (min) (range)	155 ± 60 (65–422)	176 ± 62 (80–422)	151 ± 59 (65–405)	<0.01
Blood loss (mL) (range)	183 ± 210 (9–1250)	249 ± 258 (10–1250)	156 ± 174 (9–800)	<0.01
Number of myomas (range)	3.1 ± 3.5 (1–31)	3.7 ± 3.4 (1–16)	2.7 ± 3.4 (1–31)	0.03
Largest diameter (cm) (range)	6.8 ± 2.5 (1.5–14.8)	7.0 ± 2.1 (2.4–12.1)	6.6 ± 2.4 (1.5–14.8)	n.s.

GnRH = gonadotropin-releasing hormone; n.s. = no significant difference.

Table 3
Number of recurrence cases and mean myoma diameter at recurrence in the three recurrence groups.

Recurrence time	<1 y	≥1 y and <3 y	≥3 y and <5 y	Total
Number of cases (%)	28 (37.8)	38 (51.4)	8 (10.8)	74
Mean diameter at recurrence (cm) ± standard deviation	2.2 ± 1.1	2.2 ± 1.3	2.4 ± 1.0	2.2 ± 1.2

and 249 mL vs. 156 mL), and in the mean number of enucleated myomas (3.7 vs. 2.7).

Table 2 summarizes the recurrence rate by risk factor. No significant difference was found in the recurrence rate after administration of GnRHa therapy (36.8% vs. 26.9%). Significant differences in post-LM recurrence rates were confirmed between patients with two or more myomas and those with single lesions (35.8% vs. 23.0%) and between patients who were age 35 years and older and those who were younger than 35 years (35.2% vs. 18.8%). Patients in whom the largest enucleated myoma was ≥10 cm also had a significantly higher rate of recurrence than those with myomas <10 cm diameter (53.5% vs. 28.1%).

Table 3 summarizes the number of recurrence cases and the mean myoma diameter at recurrence in the three recurrence groups. The number was 28 (37.8%), and the mean diameter was 2.2 cm in the group with recurrence in <1 year, 38 (51.4%) and 2.2 cm in the group ≥1 year and <3 years, and 8 (10.8 %) and 2.4 cm in the group ≥3 years and <5 years.

Discussion

LM is less invasive and as safe as open myomectomy.[3,10–14] LM is increasingly performed in our facility because it is less invasive. However, there have been few studies of post-LM recurrence rates. This study has investigated overall recurrence rates and the potential risk factors for recurrence. The cumulative recurrence rate was 62.1% at 5 years postoperatively. This rate is comparable to 5-year recurrence rates reported previously. Although post-LM recurrence is frequent, the repeat surgery rate in the current study was only 2.4%, which indicates that most of the recurrent myomas are small and asymptomatic, therefore requiring no further intervention.

Among the potential risk factors for recurrence, surgical time, blood loss, and the number of enucleated myomas were significantly higher in the patients with recurrence than in the non-recurrence group. Previous studies have also reported that a larger number of enucleated myomas is associated with a higher recurrence rate. The larger volumes of blood loss and longer surgical times suggest that the surgical procedures were challenging, likely due to the presence of large or numerous myomas. Thus, larger number and larger size of myomas are thought to be related to the higher recurrence rates in these patients.

Regarding the individual risk factors, the recurrence rate was significantly higher in the group with two or more enucleated myomas, in patients age 35 years and older, and in cases where the diameter of the largest myoma was ≥10 cm. Obesity and preoperative GnRHa therapy did not affect the recurrence rates. GnRHa is administered preoperatively in some instances to reduce the size of myomas. Reductions of myoma volumes by approximately 40% can be expected after four to six courses of GnRHa administration.[15] However, preoperative GnRHa therapy has been reported to have a significantly higher rate of postoperative recurrence (37.5% vs. 14.8%).[3] It is proposed that this is because the shrunken myomas may be overlooked at the time of surgery and left in the uterus. Although particularly small myomas may become indistinct after GnRHa therapy, and the possibility of overlooked myomas cannot be denied, the current study investigates the risk of recurrence without consideration of the correlation between overlooked myomas and postoperative recurrence. The authors of the current study have previously found that GnRHa therapy does not increase the risk of postoperative myoma recurrence if all myomas confirmed preoperatively by MRI were enucleated, and this study, in which a greater number of cases was evaluated, has again demonstrated that preoperative GnRHa therapy does not increase the risk of postoperative recurrence after LM.[16]

In conclusion, the rate of recurrence of myoma after LM increases over time. The risk factors related to recurrence are patient age, myoma size, and number of tumors. Particular attention to the increased risk of recurrence is required for patients with uterine myoma >10 cm, numerous myomas, and in patients who are 35 years or older.

Conflicts of interest

The authors declare that they have no conflicts of interest related to this study.

References

1. Henderrickson ME, Kempson RL. *Surgical Pathology of the Uterine Corpus*. Philadelphia, PA: WB Saunders; 1980.
2. Parsons L, Sommers SC. *Gynecology*. 2nd ed. Philadelphia, PA: WB Saunders; 1978.
3. Rossetti A, Sizzi O, Soranna L, et al. Long-term results of laparoscopic myomectomy: recurrence rate in comparison with abdominal myomectomy. *Hum Reprod*. 2001;16:770–774.
4. Yoo EH, Lee PI, Huh CY, et al. Predictors of leiomyoma recurrence after laparoscopic myomectomy. *J Minim Invasive Gynecol*. 2007;14:690–697.
5. Nezhat FR, Roemisch M, Nezhat CH, Sedman DS, Nezhat CR. Recurrence rate after laparoscopic myomectomy. *J Am Assoc Gynecol Laparosc*. 1998;5:237–240.
6. Fedele L, Parazzini F, Luchini L, Mezzopane R, Tozzi L, Villa L. Recurrence of fibroids after myomectomy: a transvaginal ultrasonographic study. *Hum Reprod*. 1995;10:1795–1796.
7. Fletcher H, Frederick J, Hardie M, Simeon D. A randomized comparison of vasopressin and tourniquet as hemostatic agents during myomectomy. *Obstet Gynecol*. 1996;87:1014–1018.
8. Frederick J, Fletcher H, Simeon D, Mullings A, Hardie M. Intramyometrial vasopressin as a haemostatic agent during myomectomy. *Br J Obstet Gynaecol*. 1994;101:435–437.
9. Diamond MP. Reduction of adhesions after uterine myomectomy by Seprafilm membrane (HAL-F): a blinded, prospective, randomized, multicenter clinical study. Seprafilm Adhesion Study Group. *Fertil Steril*. 1996;66:904–910.
10. Mais V, Ajossa S, Guerriero S, Mascia M, Solla E, Melis GB. Laparoscopic versus abdominal myomectomy: a prospective, randomized trial to evaluate benefits in early outcome. *Am J Obstet Gynecol*. 1996;174:654–658.
11. Seracchioli R, Rossi S, Govoni F, et al. Fertility and obstetric outcome after laparoscopic myomectomy of large myomata: a randomized comparison with abdominal myomectomy. *Hum Reprod*. 2000;15:2663–2668.
12. Cagnacci A, Pirillo D, Malmusi S, Arangino S, Alessandrini C, Volpe A. Early outcome of myomectomy by laparotomy, minilaparotomy and laparoscopically assisted minilaparotomy. A randomized prospective study. *Hum Reprod*. 2003;18:2590–2594.
13. Benassi L, Marconi L, Benassi G, Accorsi F, Angeloni M, Besagni F. Minilaparotomy vs laparotomy for uterine myomectomies: a randomized controlled trial. *Minerva Ginecol*. 2005;57:159–163.
14. Alessandri F, Lijoi D, Mistrangelo E, Ferrero S, Ragni N. Randomized study of laparoscopic versus minilaparotomic myomectomy for uterine myomas. *J Minim Invasive Gynecol*. 2006;13:92–97.
15. Friedman AJ, Barbieri RL, Benacerrag BR, Schiff I. Treatment of leiomyomata with intranasal or subcutaneous leuprolide, a gonadotropin-releasing hormone agonist. *Fertil Steril*. 1987;48:560.
16. Kotani Y, Shiota M, Umemoto M, Tobiume T, Shimaoka M, Hoshiai H. Efficacy of preoperative gonadotropin-releasing hormone agonist therapy for laparoscopic myomectomy. *Asian J Endosc Surg*. 2009;2:24–28.