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Short-Term Risk of Fibroid Recurrence After Laparoscopic Myomectomy and Its Associated Risk Factors

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Abstract

Background: Although laparoscopic myomectomy is an effective procedure for the treatment of uterine myoma, there is no clear consensus regarding its rate of recurrence and associated risk factors.
Objectives: This study aimed to investigate the recurrence rate of myoma and its risk factors after laparoscopic myomectomy.
Methods: In a historical cohort study, 172 patients who underwent laparoscopic myomectomy and had a minimum follow-up of 2 years were included. Myoma recurrence was checked semiannually by ultrasound imaging. The demographic, clinical, surgical, sonographic, and laboratory indices of the patients were compared between the recurrent and nonrecurrent groups, both in logistic regression models.
Results: The mean age of the patients was 35 ± 5.7 years (range: 18 - 47 years). Their mean follow-up time was 26.3 ± 4.2 months (range: 24 - 28). The lesion recurred in 25 (14.5%) out of 172 patients. In the univariate analysis, higher age (OR:1.111, P = 0.015), higher body mass index (OR: 1.124, P = 0.024), gonadotropin-releasing hormone (GnRH) therapy (OR = 3.83, P = 0.027), and more than 1 myoma (OR: 2.60, P = 0.032) were associated with myoma recurrence. In the multiple analysis, a higher body mass index (OR: 1.222, P = 0.003) was a significant risk factor for myoma recurrence.
Conclusions: Laparoscopic myomectomy is an effective procedure for the treatment of uterine myoma and can be used as a uterus-preserving surgical alternative in patients of reproductive age. A more radical surgical procedure might be used for patients with multiple risk factors, as revealed in the present study.

Keywords: Myoma, Fibroid, Laparoscopic Myomectomy, Recurrence, Risk Factor

1. Background

Myomas, also known as leiomyomas or fibroids, are the most common benign tumors of the female reproductive organs. They affect almost 25% of women of reproductive age and may cause clinical symptoms such as pelvic pain, heavy menstrual bleeding, and urine frequency (1). Certain types of myomas negatively impact fertility, such that fibroids are detected in 5 - 10% of infertile women (2).

The majority of myomas are asymptomatic and do not require any intervention; however, approximately 30% of myomas are symptomatic and need therapeutic intervention (3). Treatment of myomas includes pharmacological and surgical modalities. Pharmacological options contain hormonal medications such as gonadotropin-releasing hormone (GnRH) agonists and nonhormonal medications such as nonsteroidal anti-inflammatory drugs (NSAIDs). Surgical treatment is indicated if the symptom persists and the fibroid is rapidly enlarging. Myoma-related infertility and recurrent pregnancy loss could also indicate surgical intervention (4).

Hysterectomy is the definitive treatment of myomas. However, it is not an option for fertile women who wish to conceive in the future. Uterus-preserving myomectomy, either through the open or laparoscopic procedure, is the surgical option for women who want to retain their uterus (5). Although laparoscopic myomectomy is as effective as laparotomy and has lower invasiveness and less hospital stay (6), a recurrence rate of almost 50% at 5 years has been

reported following the laparoscopic myomectomy (7).

Despite the widespread use of the laparoscopic intervention, the results of studies on the rate of recurrence after laparoscopic myomectomy remain inconsistent. In addition, risk factors that contribute to recurrence after laparoscopic myomectomy are not thoroughly investigated (8).

2. Objectives

In this study, we evaluated the recurrence rate and risk factors of recurrence in a series of patients with uterine myomas treated by laparoscopic myomectomy

3. Methods

This was a historical cohort study approved by the Ethics Committee of our institute. The patients provided written informed consent to the use of their medical data for publication. Between 2011 and 2018, patients who underwent laparoscopic myomectomy for the treatment of uterine myoma and had a minimum follow-up of 2 years were included. Patients with recurrent myomas, other uterine or adnexal abnormalities such as suspected ovarian or uterine malignancy, and patients who were lost to follow-up were excluded. Finally, 172 patients were identified as eligible for this study.

Fellows of laparoscopic gynecology performed the surgeries according to the therapeutic protocol of our center and under the supervision of two attending surgeons. The patients received prophylactic antibiotics and prophylactic enoxaparin for the prevention of postoperative infection and postoperative thromboembolism, respectively. Laparoscopic myomectomy was performed as earlier described (9). In brief, three 5mm ports were placed in the lower abdomen. After the establishment of the pneumoperitoneum, the pelvic cavity was explored using a 10 mm laparoscope, and the myoma(s) were localized. Then, the uterine serosa and myometrium were incised, and the myoma was exposed. Subsequently, a 5 mm suprasymphysary port was replaced with a 10 mm port, and the myoma (s) were extracted from the surrounding myometrium through a blunt dissection using 10mm tenaculum forceps. Finally, the uterus was closed by interrupted, intracorporeal, sutures. The myoma (s) were extracted through the midline trocar after morcellation using an electric morcellator. Following extensive lavage and confirming hemostasis, an intra-abdominal drain was implemented for postoperative monitoring. The diagnosis of myoma was confirmed by histopathological examination.

Myoma recurrence was checked semiannually by ultrasound and magnetic resonance imaging (MRI) and confirmed if a myoma with a diameter of $\geq$ 1 cm was detected. The potential risk factors of recurrence evaluated in this study included demographic characteristics (e.g., age and body mass index [BMI]), clinical characteristics (e.g., the main symptom at presentation and gonadotropin-releasing hormone agonist [GnRHa] therapy), and sonographic characteristics (e.g., the type of myomas, the number of myomas, and the size of the leading myoma at its largest dimension).

3.1. Statistical Analysis

The Statistical Package for the Social Sciences v. 19.0 (SPSS Inc., Chicago, IL, USA) was used to analyze the data. Descriptive data were provided by mean and standard deviation (SD) for quantitative variables and number and percentage for qualitative variables. The quantitative variables were compared between the recurrent and nonrecurrent groups using an independent t-test. The qualitative variables were compared between the recurrent and non-recurrent groups using a chi-square test. Univariate logistic regression was performed to compute the odds ratio (OR) and the corresponding confidence interval (95% CI) for demographic and clinical variables in recurrent and nonrecurrent groups. Besides, multiple logistic regression was performed for variables with a P-value of less than 0.25. A P-value of less than 0.05 was considered significant. The sample size was calculated by the G*Power (version 3.1.9.7., USA) sample size calculator based on similar studies.

3.2. Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Tehran University of Medical Sciences (IR.TUMS.MEDICINE.REC.1400.1424).

4. Results

In this study, 172 patients with a mean age of 35.10 ± 5.56 years (range: 18-47 years) were included. The main symptoms at presentations were abnormal uterine bleeding (69, 40.1%), heavy menstrual bleeding (55, 32.0%), primary infertility (39, 22.7%), noncyclic pain (27, 15.7%), and mass (15, 8.7%). The mean follow-up time of the patients was 43.99 ± 13.25 months (range: 14 - 87 months). The lesion recurred in 25 (14.5%) out of the 172 patients.

In the univariate analysis, the mean age was significantly higher in the patients with a recurrent myoma (OR: 1.111, 95% CI: 1.021 - 1.21, P = 0.015). The mean BMI of the patients was also significantly higher in

the recurrent group (OR: 1.124, 95% CI: 1.012 - 1.248, P = 0.024). The patients' symptoms at presentation were not significantly associated with the recurrence (all P-values > 0.05; Tables 1 and 2). The lesion size was not significantly greater in the recurrent group (P = 0.12). The type of myoma was not associated with the recurrence (P = 0.566). The prevalence of GnRH in the recurrent patients (35.7 %) was more than in the nonrecurrent group (OR = 3.83, 95% CI: 1.17 - 12.60, P = 0.027). The prevalence of recurrence in patients with more than 1 myoma was higher than in patients with 1 myoma (OR: 2.60, 95% CI: 1.09 - 6.2, P = 0.032; Tables 1 and 2).

In the multiple logistic regression, the risk of recurrence rose with higher BMI (OR: 1.222, 95% CI:1.07 - 1.395, P = 0.003).

5. Discussion

We thoroughly investigated the clinical, demographic, laboratory, sonographic, and surgical risk factors of recurrence following the treatment of uterine myoma with laparoscopic myomectomy. According to our results, age, BMI, and the number of myomas were significantly higher in patients with recurrent myomas in comparison with the nonrecurrent group. In the multivariate analysis, BMI was identified as the significant risk factor for recurrence following the laparoscopic treatment of uterine myoma.

Risk factors of recurrence after laparoscopic myomectomy have been evaluated in a few other studies. Shiota et al. assessed the recurrence rate of myoma and its risk factors in 250 patients who underwent laparoscopic myomectomy. Based on their results, the cumulative recurrence rate of myoma following the laparoscopic myomectomy was 15.3%, 43.8%, and 62.1% after 1, 3, and 5 years, respectively. Age, number of myomas, and myoma size were identified as significant risk factors for recurrence. They suggested that particular attention be paid to recurrence when the diameter of the lesion is greater than 10 cm, or the patient is ≥ 35 years old (8). In the present study, the rate of recurrence was 14.5% at a mean follow-up period of 26.3 months, which was almost comparable to the aforementioned study. Age and the number of myomas were also identified as significant risk factors for recurrence after laparoscopic myomectomy. The number of myomas was identified as a significant risk factor for recurrence in the present study but not in the study by Shiota et al. (8).

Radosa et al. retrospectively reviewed the long-term risk of myoma recurrence following laparoscopic myomectomy in 224 patients. According to their results, the cumulative risk of recurrence was 4.9% at 2 years and 21.4% at 5 years. An age of 30 - 40 years and more than 1 myoma were identified as significant risk factors for recurrence after laparoscopic myomectomy (10). The rate of recurrence within 2 years was considerably higher in the present series, which could be attributed to several factors, such as the different patient characteristics.

Ming et al. evaluated the risk factors of uterine leiomyoma after myomectomy to introduce a prognostic index model for predicting the long-term risk of recurrence. In the multiple analysis, the number of myomas, residual lesions, not the submucosal type, and combined endometriosis were identified as the risk factors for recurrence after myomectomy. According to these risk factors, they introduced a prognostic model in which the high-risk group had a 4.55 times greater risk of recurrence than the low-risk group (11). In contrast to the majority of studies, the size of the myoma was not a significant risk factor for recurrence in the study by Ming et al. Although the submucosal type was associated with a lower risk of recurrence in the study by Ming et al., we did not find any significant association between the type of myoma and the risk of recurrence (11). This difference could be caused by the inclusion criteria of our study. We included patients with any number of myomas. Therefore, we only evaluated the effect of the leading myoma on the recurrence, while the patients could also have had myomas of other types whose effects were missed. Future studies that only include patients with a single myoma might better explore the association between myoma type and recurrence.

Several other studies have also investigated the risk factors of fibroid recurrence myomectomy. In most of them, age, myoma size, and the number of myomas were suggested as the risk factors for fibroid recurrence (11-15). Other risk factors, such as preoperative GnRH therapy and postoperative pregnancy, were also pointed out as risk factors for fibroid recurrence in some studies (16, 17).

Altogether, the results of the present study revealed that laparoscopic myomectomy is associated with an acceptable rate of recurrence, at least in the short term. The higher age of the patients, BMI, and the number of myomas could be used as prognostic factors of recurrence. Patients with multiple risk factors might benefit from a more radical surgical procedure to reduce the risk of recurrence.

The present study was not without limitations. The main limitations were its retrospective design and the relatively short-term follow-up. In addition, the small number of patients in some subgroups might have adversely affected the result of the statistical analysis. Therefore, future prospective studies with long-term follow-ups are required to confirm the results provided

Table 2. Comparison of Characteristics Between the Recurrent and Nonrecurrent Myoma Groups with Univariate and Multiple Logistic Regression

Variables	Univariate Odds Ratio	P-Value	Multiple Odds Ratio	P-Value
Age (y)	1.111 (1.021 - 1.21)	0.015	1.025 (0.919 - 1.142)	0.660
Body mass index (kg/m^2)	1.124 (1.012 - 1.248)	0.029	1.222 (1.07 - 1.395)	0.003
Follow-up (mo)	1.002 (0.995 - 1.01)	0.546	-	-
Myoma grade	1.001 (0.997 - 1.004)	0.810		
Marital status				
Single	1	-	-	-
Married	1.06 (0.41 - 2.73)	0.899	-	-
Symptom				
Pain and pressure	1	-	-	-
AUB and HMB	1.11 (0.40 - 3.07)	0.848	-	-
Infertility	1.57 (0.54 - 4.57)	0.407	-	-
Primary infertility				
No	1	-	-	-
Yes	0.83 (0.29 - 2.38)	0.730	-	-
Secondary infertility				
No	1	-	-	-
Yes	1.87 (0.48 - 7.33)	0.370	-	-
Fertility problem				
No	1	-	-	-
Yes	1.22 (0.49 - 3.03)	0.647	-	-
Dysmenorrhea				
No	1	-	1	-
Yes	2.05 (0.85 - 498)	0.110	1.75 (0.49 - 6.33)	0.392
Dyspareunia				
No	1	-	1	-
Yes	2.35 (0.69 - 8.08)	0.163	2.76 (0.55 - 13.80)	0.216
HMB				
No	1	-	-	-
Yes	0.80 (0.31 - 2.05)	0.645	-	-
AUB				
No	1	-	-	-
Yes	1.46 (0.62 - 3.41)	0.386	-	-
NCP				
No	1	-	-	-
Yes	0.42 (0.09 - 1.92)	0.265	-	-
Mass				
No	1	-	-	-
Yes	2.52 (0.32 - 20.11)	0.381	-	-
Gonadotropin-releasing hormone (GnRH) therapy				
No	1	-	1	-
Yes	3.83 (1.17 - 12.60)	0.027	2.49 (0.46 - 13.53)	0.292
Morcellated				
No	1	-	1	-
Morcellated	0.57 (0.23 - 1.40)	0.215	0.41 (0.14 - 1.22)	0.109
Parity				
No	1	-	-	-
Yes	0.69 (0.27 - 1.76)	0.437	-	-
Abortion				
No	1	-	-	-
Yes	1.21 (0.38 - 3.89)	0.750	-	-
Classification				
IntraMural Myoma (IMM)	1	-	-	-
SSM	2.05 (0.64 - 6.59)	0.226	-	-
SMM	0.89 (0.16 - 5.08)	0.899	-	-
IMM and SSM	1.46 (0.38 - 5.56)	0.578	-	-
Number				
1	1	-	1	-
More than 1	2.60 (1.09 - 6.2)	0.032	1.39 (0.43 - 4.43)	0.581
Size (cm)				
< 5	1		1	-
≥ 5	0.44 (0.15 - 1.27)	0.128	0.48 (0.14 - 1.65)	0.246

here.

5.1. Conclusions

Laparoscopic myomectomy is an effective procedure for the treatment of uterine myoma, with a 2-year recurrence rate of almost 14.5%. Therefore, it can be used as a uterus-preserving surgical alternative in patients of reproductive age. The patient's age, BMI, GnRH therapy, and the number of myomas could be significant risk factors for recurrence after laparoscopic myomectomy. A more radical surgical procedure might be suggested for patients with multiple risk factors to avoid the recurrence of myoma.

Footnotes

Authors' Contribution: ZA conceived and designed the evaluation and drafted the manuscript. SAP participated in designing the evaluation, performed parts of the statistical analysis, and helped to draft the manuscript. RH, BG, and BM collected the clinical data, interpreted them, and revised the manuscript. AK re-analyzed the clinical and statistical data and revised the manuscript. All the authors read and approved the final manuscript.

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Informed Consent: The patients provided written informed consent for the use of their medical data for publication.

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Table 1. Comparison of Characteristics Between Recurrent and Nonrecurrent Myoma Groups

Variables	Nonrecurrent (n = 147)	Recurrent (n = 25)	P-Value
Age (y)	34.67 ± 5.68	37.64 ± 4.02	0.013
Body mass index (kg/m^2)	24.92 ± 3.71	26.77 ± 4.14	0.024
Follow-up (mon)	187.47 ± 57.37	195.00 ± 53.99	0.549
Myoma grade	201.97 ± 135.40	210.00 ± 169.51	0.812
Marital status			0.899
Single	43 (86.0)	7 (14.0)	
Married	104 (85.2)	18 (14.8)	
Symptom			0.682
Pain and pressure	55 (87.3)	8 (12.7)	
Abnormal uterine bleeding (AUB) and Heavy menstrual bleeding (HMB)	56 (86.2)	9 (13.8)	
Infertility	35 (81.4)	8 (18.6)	
Primary infertility			0.730
No	113 (85.0)	20 (15.0)	
Yes	34 (87.2)	5 (12.8)	
Secondary infertility			0.407
No	137 (86.2)	22 (13.8)	
Yes	10 (76.9)	3 (23.1)	
Fertility problem			0.647
No	106 (86.2)	17 (13.8)	
Yes	41 (83.7)	8 (16.3)	
Dysmenorrhea			0.105
No	111 (88.1)	15 (11.9)	
Yes	36 (78.3)	10 (21.7)	
Dyspareunia			0.163
No	136 (86.6)	21 (13.4)	
Yes	11 (73.3)	4 (26.7)	
HMB			0.645
No	99 (84.6)	18 (15.4)	
Yes	48 (87.3)	7 (12.7)	
AUB			0.384
No	90 (87.4)	13 (12.6)	
Yes	57 (82.6)	12 (17.4)	
Non-cyclic Pain (NCP)			0.375
No	122 (84.1)	23 (15.9)	
Yes	25 (92.6)	2 (7.4)	
Mass			0.365
No	133 (84.7)	24 (15.3)	
Yes	14 (93.3)	1 (6.7)	
Gonadotropin-releasing hormone (GnRH) therapy			0.019
No	138 (87.3)	20 (12.7)	
Yes	9 (64.3)	5 (35.7)	
Morcellated			0.211
No	35 (79.5)	9 (20.5)	
Morcellated	110 (87.3)	16 (12.7)	
Cavity			0.133
Endometrium intact	131 (84.0)	252 (16.0)	
Endometrium opened	16 (100.0)	0 (0.0)	

Parity			0.435
No	94 (83.9)	18 (16.1)	
Yes	53 (88.3)	7 911.7)	
Abortion			0.749
No	127 (85.8)	21 (14.2)	
Yes	20 (83.3)	4 (16.7)	
Classification			0.566
IntraMural Myoma (IMM)	38 (88.4)	5 (11.6)	
SSM	37 (78.7)	10 (21.3)	
SMM	17 (89.5)	2 (10.5)	
IMM and SSM	26 (83.9)	5 (16.1)	
Number			0.028
1	104 (88.9)	13 (11.1)	
More than 1	37 (75.5)	12 (24.5)	
Size (cm)			0.127
< 5	21 (77.8)	6 (22.2)	
≥ 5	119 (88.8)	15 (11.2	