Annals of Infertility & Reproductive Endocrinology

Research Article
Published: 26 Mar, 2019

The Outcomes of Uterine Myomectomy in Infertile Patients with Uterine Leiomyomas

Masashi Yoshida and Takao Miyake*

Miyake Women's Clinic, Japan

Abstract

Background: We determined the effect of uterine myomectomy on subsequent pregnancy and delivery in infertility women with uterine leiomyoma.

Methods: Uterine interstitial and submucosal leiomyomas were observed in a total of 143 patients between 2014 and 2016. The factors compared between women who underwent myomectomy (surgical group) and women who did not (non-surgical group) were age at clinic visit, body mass index, previous pregnancy history, number of leiomyomas, maximum leiomyoma diameter, follicle stimulating hormone level on day 3 of the menstrual cycle, presence of male factors, fallopian tube factors, previous myomectomy, and assisted reproductive technology. The correlation of the abovementioned factors with chemical pregnancy was investigated by statistical analysis.

Results: Pregnancy rate in the surgical and non-surgical group was 63.0% and 39.3%, respectively, with significant difference in pregnancy rate observed based on history of myomectomy (p=0.006). Multivariate analysis using Cox's proportional hazards model showed number of leiomyomas and fallopian tube factors were related factors and no correlation with history of myomectomy was observed. The median time until chemical pregnancy was not significantly different between the groups, at 377 days in the surgical group and 419 days in the non-surgical group (p=0.706).

Conclusion: This retrospective observational study did not clarify the usefulness of uterine myomectomy in the management of patients with infertility presenting with uterine leiomyoma. However, approximately 50% of women who underwent uterine myomectomy for submucosal or interstitial leiomyomas that were either ≥ 4 cm in size or were ≥ 4 in number might become pregnant approximately 1 year postoperatively.

Keywords: Uterine leiomyomas, Uterine myomectomy, Infertile, Pregnancy, Intrapartum hemorrhage volume

OPEN ACCESS

Correspondence:
Masashi Yoshida, Miyake Women's Clinic, 1-18-5 Oyuminochuo Midori-ku Chiba, 266-0032 Chiba, Japan, Tel: 81432933500, Fax: 81432933511, E-mail: yoshida.masashi@mwclin.com

Received Date: *05 Mar 2019*
Accepted Date*: 20 Mar 2019*
Published Date*: 26 Mar 2019*

Citation:
Yoshida M, Miyake T. The Outcomes of Uterine Myomectomy in Infertile Patients with Uterine Leiomyomas. Ann Infert Rep Endocrin. 2019, 2(1): 1014.

Introduction

Uterine leiomyomas are benign tumors that affect approximately 30% of all women and may cause infertility in women who desire to have children. Uterine leiomyomas are observed in 5% to 10% of women presenting with infertility and are the sole cause of infertility in 1% to 3% of cases [1]. Indeed, uterine leiomyoma are reported to be the cause of approximately 7% of recurrent spontaneous abortions [2]. Submucosal leiomyomas and interstitial leiomyomas cause deformation of the uterine lumen and are specific types of uterine leiomyomas that might reduce fertility. However, there is still no consensus regarding the appropriateness of performing myomectomy to treat these types of leiomyomas [3-6].

The objective of this retrospective study was to determine the effect of uterine myomectomy on subsequent pregnancy and delivery in women presenting with infertility and to determine the usefulness of the procedure.

Materials and Methods

Subjects were 1,705 women who received consultation at our clinic for a chief complaint of infertility between January 2014 and December 2016. Uterine interstitial and submucosal leiomyomas were observed in a total of 143 patients, with the observation period set to last until December 2017.

The basic indications for uterine myomectomy at our clinic are interstitial or submucosal leiomyomas, leiomyomas that cause endometrial compression or have a maximum diameter >4

Table 1: Shows the background of all cases with uterine leiomyomas. The pregnancy rate in the surgical and non-surgical group was 63.0% (34 subjects) and 39.3% (35 subjects), respectively, with significant difference.

	Operation Group (n=54)	Non Operation (n=89)	P value
Age (Years)	35.5 ± 3.8	37.0 ± 4.2	0.040
BMI	21.9 ± 2.7	22.4 ± 3.3	0.404
Nullipara	43 (79.6%)	71 (79.8%)	0.983
Number of myoma	4.5 ± 4.6	1.3 ± 0.8	0.001
Maximum diameter of myoma (cm)	4.5 ± 2.3	3.6 ± 1.8	0.015
Day 3 FSH (μIU/ml)	6.15 ± 2.06	7.77 ± 6.15	0.095
ART	31 (57.4%)	24 (27.0%)	<0.001
Time to operation (day)	151 ± 128		
Chemical pregnancy	34 (63.0%)	35 (39.3%)	0.006
Abortion	3 (8.8)%	5 (14.3%)	0.476
Birth weight	2,861 ± 328	2.909±666	0.680
Total amount of bleeding in delivery (g)	673 ± 489	404 ± 304	0.042
Uterine rupture	0	0	
Placenta Accreta	0	0	

Table 2: Shows the univariate analysis of pregnancy-determined factors revealed that age, myomectomy, and the history of ART.

	Pregnancy (n=69)	Non Pregnancy (n=74)	P value
Age (years)	35.0 ± 3.7	37.8 ± 4.1	<0.001
BMI	22.0 ± 2.8	22.4 ± 3.3	0.454
Nullipara	13 (18.8%)	16 (21.6%)	0.679
Number of myoma	2.7 ± 3.3	2.4 ± 3.2	0.526
Maximum diameter of myoma (cm)	3.8 ± 1.8	4.1 ± 2.3	0.479
Day 3 FSH (μIU/ml)	7.08 ± 5.38	7.29 ± 4.19	0.820
Male factor	22 (31.9%)	24 (32.4%)	0.382
Oviductal factor	3 (4.3%)	8 (10.8%)	0.092
Myomectomy	34 (49.3%)	20 (27.0%)	0.006
ART	34 (49.3%)	21 (28.4%)	0.010

cm, and leiomyomas that cause menorrhagia or dysmenorrhea. The factors compared between women who underwent myomectomy (surgical group) and women who did not (non-surgical group) were age at clinic visit, Body Mass Index (BMI), previous pregnancy history, number of leiomyomas, maximum leiomyoma diameter, follicle stimulating hormone level on day 3 of the menstrual cycle (day 3 FSH), presence of male factors, presence of fallopian tube factors, and previous myomectomy or Assisted Reproductive Technology (ART). Male factors were defined as positive if any one item at the sperm test (i.e. semen volume, sperm motility, or progressive motile sperm concentration) was defined as abnormal according to the World Health Organization Guidelines for Evaluation of Human Semen. Fallopian tube factors were defined as positive if fallopian tube obstruction or hydrosalpinx was observed during salpingography. The correlation of the abovementioned factors with chemical pregnancy was investigated by statistical analysis. For subjects who became pregnant, birth weight and intrapartum hemorrhage volume were also compared between the two groups.

JMP ver.12 software (SAS Institute Inc., Cary, NC) was used to perform statistical analysis with the Chi-square test and the Cox's proportional hazards model. Significant differences were set at $p<0.05$. The cumulative pregnancy rate based on the presence of myomectomy was analyzed using the Kaplan–Meier method. This research was approved from the institutional review board of Japan Medical Association (JMA).

Results

From the 143 subjects who had uterine interstitial and submucosal leiomyomas, 54 underwent open uterine myomectomy and the remaining 89 did not. The number of leiomyomas was significantly higher and the maximum leiomyoma diameter was significantly larger in the surgical group in subjects who had undergone ART. Furthermore, pregnancy rate in the surgical and non-surgical group was 63.0% (34 subjects) and 39.3% (35 subjects), respectively, with significant difference in pregnancy rate observed based on history of myomectomy (p=0.006). The corresponding miscarriage rate was 8.8% (3 subjects) and 14.3% (5 subjects), with no significant difference between the groups. The period from first hospital visit to surgery was 151 ± 128 days (mean ± standard deviation) in the surgical group (Table 1).

Univariate analysis of pregnancy-determined factors revealed that age, myomectomy, and the history of ART were related factors (Table 2). Multivariate analysis using Cox's proportional hazards model showed number of leiomyomas and fallopian tube factors were related factors, and no correlation with history of myomectomy was observed (Table 3).

Table 3: Shows the multivariate analysis using Cox's proportional hazards model showed number of leiomyomas and fallopian tube factors were related factors, and no correlation with history of myomectomy.

	Hazard ratio	95% CI	P value
Age (Years)	0.965	0.886 - 1.050	0.415
BMI	0.980	0.875 -1.088	0.719
Nullipara	0.712	0.319 - 1.784	0.447
Number of myoma	1.111	1.002 - 1.215	0.047
Maximum diameter of myoma	0.980	0.830 - 1.133	0.793
day 3 FSH	1.046	0.959 - 1.128	0.280
Male factor	0.796	0.417 - 1.478	0.473
Oviductal factor	0.157	0.016 - 0.755	0.017
Myomectomy	1.668	0.840 - 3.442	0.145
ART	1.490	0.758 - 2.974	0.248

Abbreviations: BMI: Body Mass Index, ART: Assisted Reproductive Technology, FSH: Follicle Stimulating Hormone

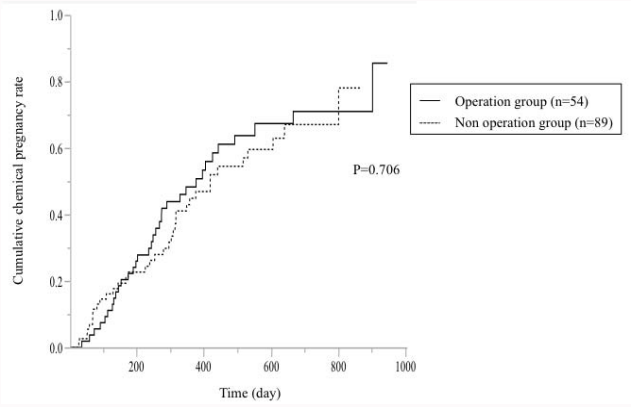

Figure 1: The cumulative pregnancy rate (after myomectomy in operation group) based on the presence of myomectomy using the Kaplan-Meier method.

The median time until chemical pregnancy was not significantly different between the groups, at 377 days in the surgical group and 419 days in the non-surgical group (p=0.706) (Figure 1). In terms of perinatal prognosis, birth weight was 2,861 ± 328 g in the surgical group and 2,909 ± 666 g in the non-surgical group, which was not significantly different (p=0.680). However, a significant different was found in intrapartum hemorrhage volume (673 ± 489 g and 404 ± 304 g, respectively) between the two groups (p=0.042). There were no cases of uterine rupture or placenta accreta in subjects in either group who became pregnant (Table 1).

Discussion

This retrospective observational study at our clinic did not clarify the usefulness of uterine myomectomy in the management of patients with infertility presenting with uterine leiomyoma. According to a report by Casini, myomectomy to treat a single leiomyoma ≤ 4 cm in diameter in infertile women aged ≤ 35 years old with no other identifiable causes resulted in only a significant difference in pregnancy rates after 1 year of timing therapy if those leiomyomas were submucosal, no significant difference was observed in the case of interstitial or subserosal leiomyomas [7]. Nevertheless, the guidelines published by the Practice Committee of the American Society for Reproductive Medicine state that asymptomatic women with deformity of the uterine lumen from interstitial leiomyomas accompanied by submucosal leiomyomas, or by submucosal leiomyomas alone, who undergo open, laparoscopic, or hysteroscopic myomectomy exhibit increased pregnancy rates and a decreased risk of early miscarriage [8]. This shows that leiomyomas vary in terms of symptoms-based on the onset site, leiomyoma diameter, and leiomyoma number-as well as in terms of their effect on pregnancy rate. Compression and vascular insufficiency due to uterine leiomyomas are presumed to cause infertility by impeding sperm transport and embryo implantation [9-11].

The present study was a retrospective observational study performed at a single clinic, so the uterine leiomyomas believed to be causing infertility differed in number, diameter, and site. This made it difficult to perform detailed verification of the usefulness of myomectomy in relation to pregnancy. Although our results could not clarify the utility of myomectomy, we discovered that approximately 50% of women who underwent myomectomy for submucosal or interstitial leiomyomas that were either ≥ 4 cm in size or were ≥ 4 in number were able to become pregnant approximately 1 year postoperatively. Indeed, the pregnancy rate in our clinic was 63.0%, higher than the 57% reported by Vercellini et al. [12].

Regarding safety, we perform myomectomy under direct vision *via* a small lower abdominal incision (approximately 3 cm) at our hospital. The risk of uterine rupture during labor cannot be ignored in patients who become pregnant after myomectomy, and they must deliver by caesarian section. The overall uterine rupture rate in women with previous abdominal myomectomy was 0.2% [13]. Zhang reported that there was no significant difference between the pregnancy rate in the laparoscopic group (49.6%) and the abdominal group (51.3%) [14]. Even for patients who have undergone laparoscopic surgery, the skin incision for subsequent pregnancy would need to be approximately 10 cm. To prevent adhesions, we not only perform myomectomy with concomitant use of intraoperative ultrasound, but also apply two layer hemostatic suturing during surgery under direct vision.

Uterine rupture during pregnancy and delivery after myomectomy is the one of the most dangerous complications. It is caused by the incomplete wound formation due to insufficient suturing [15,16]. The uterine healing process is needed complete at 12 weeks after abdominal myomectomy in the absence of hematoma or edema formation in the myometrium [17]. Although there are no definite standards for timing the resumption of infertility treatment after surgery, we resume it after 1 month at our hospital. We have not observed any fatal complications, such as uterine rupture or placenta accreta, while following this policy.

In terms of the significantly greater intrapartum hemorrhage volume seen in the surgical group, we believe this is attributable to changes in the intrauterine environment. This includes relatively increased blood flow to the normal uterine smooth muscle during leiomyoma enucleation, although none of the subjects required transfusion in the present study.

Conclusion

This retrospective observational study did not clarify the usefulness of uterine myomectomy in the management of patients with infertility presenting with uterine leiomyoma. However, approximately 50% of women who underwent uterine myomectomy for submucosal or interstitial leiomyomas that were either ≥ 4 cm in

size or were ≥ 4 in number might become pregnant approximately 1 year postoperatively.

Acknowledgement

I would like to thank the following individuals who assisted in this study: Dr. Tomoko Shibasaki, Dr. Wakako Iwasaki.

References

1. Ahdad-Yata N, Fernandez H, Nazac A, Lesavre M, Pourcelot AG, Capmas P. Fertility after hysteroscopic resection of submucosal myoma in infertile women. J Gynecol Obstet Biol Reprod. 2016,45(6):563-70.
2. Olive DL. The surgical treatment of fibroids for infertility. Semin Reprod Med. 2011,29(2):113-23.
3. Kroon B, Johnson N, Chapman M, Yazdani A, Hart R, Australasian CREI Consensus Expert Panel on Trial evidence (ACCEPT) group. Fibroids in infertility-consensus statement from ACCEPT (Australasian CREI Consensus Expert Panel on Trial evidence). Aust N Z J Obstet Gyneaecol. 2011,51(4):289-95.
4. Marret H, Fritel X, Ouldamer L, Bendifallah S, Brun JL, De Jesus I, et al. Therapeutic management of uterine fibroid tumors: updated French guidelines. Eur J Obstet Gynecol Reprod Biol. 2012,165(2):156-64.
5. Zepiridis LI, Grimbizis GF, Tarlatzis BC. Infertility and uterine fibroids. Best Pract Res Clin Obstet Gynaecol. 2016,34:66-73.
6. Casini ML, Rossi F, Agostini R, Unfer V. Effects of the position of fibroids on fertility. Gynecol Endocrinol. 2006,22(2):106-9.
7. Practice Committee of the American Society for Reproductive Medicine. Removal of myomas in asymptomatic patients to improve fertility and/or reduce miscarriage rate: a guideline. Fertil Steril. 2017,108(3):416-25.
8. Farhi J, Ashkenazi J, Feldberg D, Dicker D, Orvieto R, Ben Rafael Z. Effect of uterine leiomyomata on the results of *in-vitro* fertilization treatment. Hum Reprod. 1995,10(10):2576-8.
9. Giatras K, Berkeley AS, Noyes N, Licciardi F, Lolis D, Grifo JA. Fertility after hysteroscopic resection of submucous myomas. J Am Assoc Gynecol Laparosc. 1999,6(2):155-8.
10. Lefebvre G, Vilos G, Allaire C, Jeffrey J, Arneja J, Birch C, et al. The management of uterine leiomyomas. J Obstet Gynaecol Can. 2003,25(5):396-418.
11. Khaund A, Lumsden MA. Impact of fibroids on reproductive function. Best Pract Res Clin Obstet Gynaecol. 2008,22(4):749-60.
12. Vercellini P, Maddalena S, De Giorgi O, Aimi G, Crosiqnani PG. Abdominal myomectomy for infertility: A comprehensive review. Hum Reprod. 1998,13(4):873-9.
13. Parker WH, Einarsson J, Istre O, Dubuisson JB. Risk factors for uterine rupture after laparoscopic myomectomy. J Minim Invasive Gynecol. 2010,17(5):551-54.
14. Zhang Y, Hua KQ. Patients' age, myoma size, myoma location, and interval between myomectomy and pregnancy may influence the pregnancy rate and live birth rate after myomectomy. J Laparoendosc Adv Surg Tech A. 2014,24(2):95-9.
15. Desai P, Patel P. Fibroids, infertility and laparoscopic myomectomy. J Gynecol Endosc Surg. 2011,2(1):36-42.
16. Darwish AM, Nasr AM, El-Nashar DA. Evaluation of postmyomectomy uterine scar. J Clin Ultrasound. 2005,33(4):181-6.
17. Tsuji S, Takahashi K, Imaoka I, Sugimura K, Miyazaki K, Noda Y. MRI evaluation of the uterine structure after myomectomy. Gynecol Obstet Invest. 2006,61(2):106-10.