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Review article

How to manage multiple fibroids in reproductive laparoscopic surgery

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ABSTRACT

The incidence of fibroids ranges from 30% to 70% in women of reproductive age, with the peak incidence occurring between 35 and 49 years of age. Risk factors for fibroids include nulliparity, obesity, black ethnicity, family history, polycystic ovarian syndrome, diabetes, and hypertension. Fibroids are present in 5–10% of the patients presenting with infertility. Laparoscopic myomectomy is preferred over abdominal myomectomy because several small incisions are used rather than one larger incision. Related to the small incisions, recuperation is usually associated with minimal discomfort. Women with infertility and fibroids become pregnant after myomectomy in approximately 50% of cases. The pregnancy rate in patients undergoing hysteroscopic and laparoscopic/abdominal myomectomy is 45–49%. Laparoscopic myomectomy is a technically challenging procedure with surgeon-specific limitations. Preoperative treatments with gonadotropin-releasing hormone have been shown to reduce blood loss and shorten operative time. The consensus states that the maximal size must be 8–10 cm and the total number of fibroids should not exceed four. It is important not to perform laparoscopic myomectomies with more than 5–7 large fibroids because in these cases, the procedure is excessively time-consuming and gives the surgeon opportunities to miss the smaller fibroids after the uterus has been incised and repaired in too many places. The role of vasoconstrictors such as vasopressin, epinephrine, and ornipressin help with the control of bleeding from the incised sites. Temporary clipping of the uterine artery is an effective procedure in reducing hemoglobin loss during laparoscopic myomectomy.

Introduction

Uterine fibroids (myomas) are the most common benign tumors in women of reproductive age.[1] The incidence of fibroids ranges from 30% to 70% in women of reproductive age, with the peak incidence occurring between 35 and 49 years of age.[2] Many women are asymptomatic, therefore, a large percentage of fibroids are undiagnosed and the actual incidence is undetermined. Black women are 3–9 times more likely to suffer from uterine fibroids compared with European ethnic groups.[3] Risk factors for fibroids include nulliparity, obesity, black ethnicity, family history, polycystic ovarian syndrome, diabetes, and hypertension.[4] The incidence of fibroids is increased when there is a tendency to delay pregnancy to a later age. However, uterine fibroids are still detected in a small, but significant number of infertile women. If a causal relationship between fibroids and infertility can be established, treatment is indicated for enhancing fertility. However, the impact of fibroids on infertility is still controversial.[5]

Laparoscopic myomectomy was first described in 1979, exclusively for subserous fibroids.[5] The procedure began to be used for intramural fibroids at the beginning of the 1990s.[6,7] Laparoscopic myomectomy is preferred over abdominal myomectomy because several small incisions are used rather than one larger incision.[8] Laparoscopic surgery is usually performed for outpatient surgery under general anesthesia. This procedure can take 1–3 hours, depending on the size, number, and depth of the fibroids within the muscle wall of the myometrium. Patients are able to leave hospital the same day following laparoscopic myomectomy, although a one-night stay may be necessary. Related to the small incisions, recuperation is usually associated with minimal discomfort. Patients are expected to return to normal activity within 10–14 days.[9] Currently, laparoscopic myomectomy is one of the common surgical procedures for infertile patients. Despite the obvious advantages of laparoscopic myomectomy, its role in the treatment of infertility has been an issue of continuous debate.[8]

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Association between fibroids and infertility

The relationship between infertility and uterine fibroids is well known. However, the effect of location and size of fibroids on fertility is not clear. It has been proved that the removal of submucosal fibroids improves fertility, but removal of subserosal fibroids has no impact on fertility.[10,11]

Fibroids are present in 5–10% of the patients presenting with infertility; however, they are found to be the sole identified factor in only 1–2.4% of infertile patients.[12,13] Most studies give an epidemiological estimation of the impact of fibroids on infertility, for example, one published by Buttram and Reiter.[14] They have suggested an association between fibroids and infertility.

Women with infertility and fibroids become pregnant after myomectomy in approximately 50% of cases. Epidemiological studies have not been able to provide definitive evidence of the impact of fibroids on fertility, therefore, a large number of studies have been conducted based on pregnancy rates after myomectomy.[13] A literature review on both prospective and retrospective studies published between 1988 and 2001 has been performed by Donnez and Jadoul.[15] The pregnancy rate in patients undergoing hysteroscopic and laparoscopic/abdominal myomectomy was 45–49%. More recent studies on a large series of women have confirmed these findings.[16,17] During the literature review, only one comparative study was found investigating the chances of pregnancy in women undergoing laparoscopic myomectomy and in a control group of unoperated patients. Patients with causes of infertility other than fibroids were excluded. There were 106 women who underwent myomectomy and 106 who did not receive treatment. The patients were followed for 9 months after allocation. A higher delivery rate was observed in the surgical group (42% vs. 11%).[18]

Several hypotheses explain the mechanisms by which fibroids can lead to infertility. Fibroids can cause distortion and enlargement of the endometrial cavity by submucous and intramural leiofibroids, with an intracavitary component that affects implantation.[19,20] Failure of implantation may also be explained by focal endometrial vascular disturbances, endometrial inflammation, and secretion of vasoactive substances.[21] Leiofibroids may also cause dysfunctional uterine contractility and interfere with sperm and ovum transport. Likewise, intramural leiofibroids may also obstruct the tubal ostia.[22]

The location of the fibroid may play an important role in determining infertility. Both large intramural and subserosal fibroids are considered to interfere with conception and reduce the effectiveness of the assisted reproduction cycles, whereas pedunculated fibroids are not believed to have detrimental effects on fertillity.[23,24] The size of the fibroids may represent another important prognostic factor, with 5 cm in diameter being the size limit that appears to justify myomectomy. In several uncontrolled surgical trials, restoration of fertility after myomectomy has been reported, with pregnancy rates ranging between 44% and 62%. The time to postmyomectomy conception is short, with ~80% of pregnancies occurring during the first year following surgery. Therefore, myomectomy is a valuable approach for treating patients with leiofibroids and otherwise unexplained infertility.[25,26]

Submucosal fibroids are associated with a 70% reduction in delivery rate, whereas intramural fibroids have a lesser effect and reduce the delivery rate by approximately 30%. On the contrary, some studies have demonstrated that subserosal fibroids do not negatively affect fertility.[27]

Laparoscopic myomectomy in multiple fibroids

Myomectomy is the surgery of choice for women who have symptomatic fibroids and who wish to retain their uterus.

Fig. 1. Multiple small fibroids removed by operative laparoscopy (32 myomas). Photo by W.H.

Laparoscopic myomectomy is preferable to the abdominal approach in many ways, offering[28,29]: more rapid recovery, shorter hospitalization, reduced blood loss, formation of fewer adhesions, and increased pregnancy rate. Nevertheless, laparoscopic myomectomy is a technically challenging procedure that requires surgical skill (Fig. 1).

It is known that uterine fibroids are estrogen dependent. During pregnancy these fibroids increase in size, whereas in the puerperium and menopause they shrink. Gonadotropin-releasing hormone (GnRH) agonists were introduced as an efficient new treatment in certain hormone-dependent conditions. GnRH agonists induce hypogonadism. This happens through pituitary desensitization, downregulation of receptors, and inhibition of gonadotropins. They are advantageous in the treatment of various hormone-dependent tumors, endometriosis, and uterine fibroids.[30] GnRH agonists have been used in preoperative treatments to diminish blood loss and shorten operative time. The indication depends on the size, number, and localization of the fibroids. GnRH agonists have two preferred clinical scenarios: a uterus that extends above the umbilicus, and anemia.[31] In the first scenario, the GnRH agonist helps to reduce the uterus to a more manageable size.

The roles of using GnRH agonists, uterine volume, hormonal profile, and hemoglobin concentration have been monitored. In an experiment by Golan,[30] 75 patients aged 34–48 years were scheduled for surgery. The patients in the study group received two injections of depot triptorelin (3.75 mg) at monthly intervals prior to surgery. The author recorded the operative time, the amount of intraoperative blood loss, and the need for blood transfusion, duration of hospitalization, and postoperative complications. A significant drop in uterine volume was observed in the study group after 2 months of preoperative treatment (32%). Compared to the preoperative values of the control group, the hemoglobin concentration increased just prior to surgery in the study group, although the increase did not reach statistical significance. The operative time was significantly shorter in the study group compared with the control group. The intraoperative blood loss was significantly lower in the study group compared to the control group. Therefore, fewer blood transfusions were needed in the study group, although the difference could not be evaluated statistically because of the small numbers. Hospital stay showed no difference between the groups. The shrinkage of uterine fibroids by preoperative GnRH agonists shortened the operative time and reduced blood loss and the need for blood transfusions. Golan[30] also suggest that surgery following triptorelin injection is smoother and has fewer postoperative complications.

Despite its known advantages, laparoscopic myomectomy is still a debatable operation, whose feasibility, indications, and risks are

Fig. 2. Multiple fibroids removed by open laparotomy (18 myomas). Photo by W.H.

still matters of discussion. Universally accepted indications include the presence of submucous or intramural fibroids that distort the uterine cavity, fibroids >3 cm, and multiple fibroids. The feasibility of laparoscopic myomectomy has been demonstrated in numerous clinical studies. The location and size of uterine fibroids are major determinants for making a decision about which type of surgical approach is the most feasible. The consensus states that the maximal size must be 8–10 cm and the total number of fibroids should not exceed four.[32] Some authors' criteria for laparoscopic myomectomy are a single intramural or subserosal fibroid ≤15 cm or ≤3 fibroids of ≤5 cm, whereas, others believe in an individual choice based on pathological findings and surgeon-specific limitations. It is important not to perform laparoscopic myomectomies with more than 5–7 large fibroids, because in these cases, the procedure is excessively time-consuming and the surgeon may miss the smaller fibroids after the uterus has been incised and repaired in too many places.[33] Therefore, in such conditions, surgery should be performed by open laparotomy (Fig. 2).

Dillon had used vasopressin since 1962 for open myomectomy. It has been available in India since 2003.[34] Vasopressin is a synthetic antidiuretic hormone, which induces local vasoconstriction lasting for approximately 30 minutes, and thus helps to reduce blood loss from the incised sites.[34] Vasopressin induced a concentration-dependent increase in vessel tone. The compounds with this slow onset of action reflect the time needed to cross the cell membrane and activate intracellular calcium ions. Likewise, a compound with fast onset (epinephrine) acts preferentially by increasing the calcium influx through receptor-operated channels. The duration of response of vasopressin is longer than that of epinephrine. These vasoconstrictive agents may be useful in conjunction with gynecological endoscopic surgery.[35] Vasopressin must be used with caution for patients suffering from cardiovascular diseases and hypertension because it can lead to a sudden increase in blood pressure and precipitate angina[34] (Fig. 3).

An experiment by Vercellino et al,[36] there were 80 women who underwent laparoscopic myomectomy with uterine artery temporary clipping and 86 women who received laparoscopic myomectomy without clipping. The patients were followed for 3 days after surgery. A lower median hemoglobin decrease was observed in the patients with laparoscopic uterine artery temporary clipping and myomectomy (1.2 g/dL vs. 1.45 g/dL). Temporary clipping of the uterine arteries during laparoscopic myomectomy is a safe procedure for controlling excessive blood loss without jeopardizing the uterine blood supply.[36,37]

Fertility after myomectomy

Recent comprehensive reviews of the literature (23 studies) on leiofibroids and reproduction report an overall conception rate of 57% after myomectomy among prospective studies. The conception rate is 53–70% after myomectomy for submucous fibroids and 58–65% after myomectomy with intramural or subserosal leiofibroids.[38]

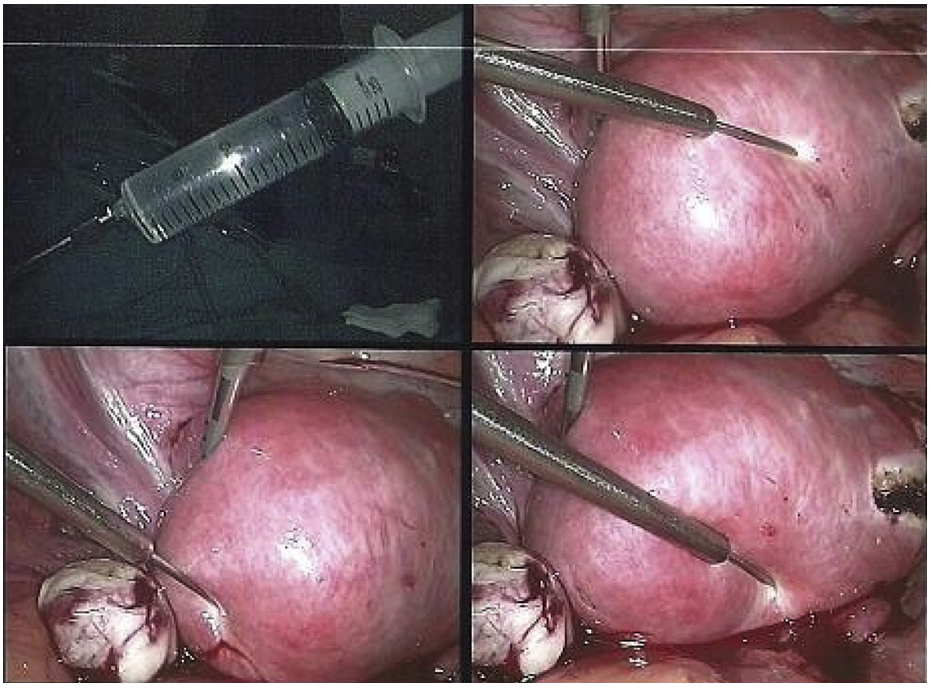

Fig. 3. Injection of vasopressin surrounding the fibroids. Photo by W.H.

Pregnancy after myomectomy

After laparoscopic myomectomy, the pregnancy rate is 54% and comparable to that after abdominal myomectomy.[39] Studies indicate that laparoscopic myomectomy is a feasible choice for infertile women. The best prognosis is found in young women with otherwise unexplained infertility when a fibroid distorts the endometrial cavity. Laparoscopic myomectomy in infertile patients complicated with uterine fibroid is expected to improve the postoperative pregnancy rate as observed with laparotomy. The data are not sufficient to determine whether routine vaginal delivery should be attempted or if cesarean section is advised.[40]

Conclusion

Laparoscopic myomectomy provides an acceptable, and perhaps a preferable, alternative to abdominal myomectomy for women with symptomatic fibroids who desire uterine preservation and who have infertility primarily related to fibroids. Laparoscopic myomectomy clearly provides a faster recovery, diminished blood loss, and decreased adhesions compared to an open approach. The use of GnRH agonists prior to surgery improves the therapy of multiple fibroids. In multiple fibroids, the maximal size must be 8–10 cm and the total number of fibroids should not exceed four because the procedure is excessively time-consuming and the surgeon can miss the smaller fibroids after the uterus has been incised and repaired in too many places. The role of vasoconstrictor such as vasopressin, epinephrine, and ornipressin help in the control of bleeding from the incised sites. Temporary clipping of the uterine artery is an effective procedure in reducing blood loss during laparoscopic myomectomy.

References

1. Tinelli A, Hurst BS, Hudelist G, et al. Laparoscopic myomectomy focusing on the myoma pseudocapsule: technical and outcome reports. *Human Reprod*. 2012;27:427–435.
2. Okolo S. Incidence, aetiology and epidemiology of uterine fibroids. *Best Pract Res Clin Obstet Gynaecol*. 2008;22:571–588.
3. Buttram Jr VC, Reiter RC. Uterine leiomyomata – etiology, symptomatology and management. *Prog Clin Biol Res*. 1986;36:433–445.
4. Vollenhoven B. Introduction: the epidemiology of uterine leiomyomas. *Bailliere's Clin Obstet Gynaecol*. 1998;12:169–176.
5. Semm K, Mettler L. Technical progress in pelvic surgery via operative laparoscopy. *Am J Obstet Gynecol*. 1980;138:121–127.
6. Daniell JF, Gurley LD. Laparoscopic treatment of clinically significant symptomatic uterine fibroids. *J Gynecol Surg*. 1991.
7. Dubuisson JB, Lecuru F, Foulot H, Mandelbrot L, Aubriot FX, Mouly M. Myomectomy by laparoscopy: a preliminary report of 43 cases. *Fertil Steril*. 1992;56:827–830.
8. Hasson HM, Rotman C, Rana N, Sistos F, Dmowski WP. Laparoscopic myomectomy. *Obstet Gynecol*. 1992;80:884–888.
9. Nezhat C, Nezhat F, Silfen SL, Schaffer N, Evans D. Laparoscopic myomectomy. *Int J Fertil*. 1991;36:275–280.
10. Eldar-Geva T, Meager S, Healy DL. Effect of intramural, subserosal and submucosal uterine fibroids on the outcome of assisted reproductive technology treatment. *Fertil Steril*. 1998;70:687–691.
11. Pritts EA, Parker WH, Olive DL. Fibroids and infertility: an update systematic review of the evidence. *Fertil Steril*. 2009;91:1215–1223.
12. Benecke C, Kruger TF, Siebert TI, Van der Merwe JP, Steyn DW. Effect of fibroids on fertility in patients undergoing assisted reproduction: a structured literature review. *Gynecol Obstet Invest*. 2005;59:225–230.
13. Donnez J, Jadoul P. What are the implications of myomas on fertility? A need for a debate? *Hum Reprod*. 2002;17:1424–1430.
14. Buttram Jr VC, Reiter RC. Uterine leiomyomata: etiology, symptomatology, and management. *Fertil Steril*. 1981.
15. Donnez J, Jadoul P. What are the implications of myomas on fertility? A need for a debate? *Hum Reprod*. 2002.
16. Di Gregorio A, Maccario S, Raspollini M. The role of laparoscopic myomectomy in women of reproductive age. *Reprod Biomed Online* 2002;(4 suppl 3): 55–58.
17. Campo S, Campo V, Gambadauro P. Reproductive outcome before and after laparoscopic or abdominal myomectomy for subserous or intramural myomas. *Eur J Obstet Gynecol Reprod Biol*. 2003;110:215–219.
18. Bulletti C, De Ziegler D, Polli V, Flamigni C. The role of leiomyomas in infertility. *J Am Assoc Gynecol Laparosc*. 1999;6:441–445.
19. Fernandez H, Sefrioui O, Virelizier C, Gervaise A, Gomel V, Frydman R. Hysteroscopic resection of submucosal myomas in patients with infertility. *Hum Reprod*. 2001;16:1489–1492.
20. Goldenberg M, Sivan E, Sharabi Z, Bider D, Rabinovici J, Seidman DS. Outcome of hysteroscopic resection of submucous myomas for infertility. *Fertil Steril*. 1995;64:714–716.
21. Deligdish L, Lowenthal M. Endometrial changes associated with myomata of the uterus. *J Clin Pathol*. 1970;23:676–680.
22. Vollen-Hoven BJ, Lawrence AS, Healy DL. Uterine fibroids: a clinical review. *Br J Obstet Gynaecol*. 1990;97:285–298.
23. Stovall DW, Parrish SB, Van Voorhis BJ, Hahn SJ, Sparks AE, Syrop CH. Uterine leiomyomas reduce the efficacy of assisted reproduction cycles: results of a matched follow-up study. *Hum Reprod*. 1998;13:192–197.
24. Dubuisson JB, Chapron C, Chavet X, Gregorakis SS. Fertility after laparoscopic myomectomy of large intramural myomas: preliminary results. *Hum Reprod*. 1996;11:518–522.
25. Rosenfeld DL. Abdominal myomectomy for otherwise unexplained infertility. *Fertil Steril*. 1986;46:328–330.
26. Gatti D, Falsetti L, Viani A, Gastaldi A. Uterine fibromyoma and sterility: role of myomectomy. *Acta Eur Fertil*. 1989;20:11–13.
27. Ezzati M, Norian JM, Segars JH. Management of uterine fibroids in the patient pursuing assisted reproductive technologies. *Womens Health (Lond Engl)*. 2009;5:413–421.
28. 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.
29. Rossetti A, Sizzi O, Soranna L, Cucinelli F, Mancuso S, Lanzone A. Long-term results of laparoscopic myomectomy: recurrence rate in comparison with abdominal myomectomy. *Hum Reprod*. 2001;16:770–774.
30. Golan A. GnRH analogues in the treatment of uterine fibroids. *Hum Reprod* 1996;(11 suppl 3):33–41.
31. Zullo F, Pellicano M, De Stefano R, Zupi E, Mastrantonio P. A prospective randomized study to evaluate leuprolide acetate treatment before laparoscopic myomectomy: efficacy and ultrasonographic predictors. *Am J Obstet Gynecol*. 1998;178(1 Pt 1):108–112.
32. Holub Z. Laparoscopic myomectomy: indications and limits. *Ceska Gynekol*. 2007.
33. Agdi M, Tulandi T. Endoscopic management of uterine fibroids. *Best Pract Res Clin Obstet Gynecol*. 2008;22:707–716.
34. Nikita T. Laparoscopic myomectomy: methods to control bleeding. *J Gynecol Endosc Surg*. 2011;2:33–35.
35. Landstrom G, Wallin A, Lundmark K, Noren H, Lindblom B. The action of vasoconstrictive agents on human tubal arteries. *Hum Reprod*. 1999;14: 151–155.
36. Vercellino G, Erdemoglu E, Joe A, et al. Laparoscopic temporary clipping of uterine artery during laparoscopic myomectomy. *Arch Gynecol Obstet*. 2012;286:1181–1186.
37. Martin V, Christhardt K, Florian E, Susanne K, Achim S. Temporary clipping of the uterine artery during laparoscopic myomectomy – a new technique and the results of first case. *Gynecol Surg*. 2007;4(101–105).
38. Vercellini P, Maddalena S, De Giorgi O, Aimi G, Crosignani PG. Abdominal myomectomy for infertility: a comprehensive review. *Hum Reprod*. 1998;13: 873–879.
39. 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.
40. Kumakiri J, Takeuchi H, Kitade M, et al. Pregnancy and delivery after laparoscopic myomectomy. *J Minim Invasive Gynecol*. 2005;12:241–246.