Journal of
Gynecology and Women's Health
ISSN 2474-7602

Juniper Publishers
key to the Researchers

Review Article
Volume 26 Issue 1 - September 2023
DOI: 10.19080/JGWH.2023.26.556177

J Gynecol Women's Health

Myomectomy for Infertility: Does it Do More Damage Than Good?

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Submission: September 12, 2023; **Published:** September 25, 2023

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Abstract

Gynecological surgery-related adhesion development is still difficult to control. De novo adhesion formation can be prevented, but not completely, by using minimally invasive surgical techniques like conventional or robotic-assisted laparoscopy along with meticulous microsurgical techniques and the administration of adhesion-reducing agents. The kind of surgery that is most likely to cause adhesions is myomectomy, and postoperative adhesions can significantly affect a woman's ability to conceive. Therefore, care should be taken to consider whether the advantages exceed the hazards when surgery is used as a reproductive treatment. The quest for efficient methods to prevent adhesion formation in this situation is of utmost importance since, among a number of other factors, the size and location of fibroids are the most responsible for adhesion development and postsurgical infertility. This review's objective is to assess the likelihood that adhesions may form, their contributing variables, and the most effective preventative strategies currently available.

Keywords: Fertility; Minimal Invasive; Myomectomy; Adhesion

Introduction

The most prevalent benign gynecologic condition affecting women of a reproductive age is uterine fibroids. Fibroids can cause infertility and other obstetrical difficulties, as well as result in irregular uterine bleeding, discomfort, and pelvic heaviness [1]. Numerous theories, including augmented uterine contractility, an aberrant cytokine profile, altered vascularization, and chronic inflammation, have been put up to explain how fibroids could result in infertility. However, it is still unclear if there is a direct causative link between the existence of fibroids, infertility, and the true benefit of myomectomy [2]. Furthermore, there is no question that myomectomy itself, being a highly intrusive treatment, has a risk of damaging the uterine myometrium and endometrium in addition to the risk causing scar tissue in the cavity within the pelvis [3]. Myomectomy-related postoperatively adhesions are an accepted consequence [4]. It is unclear if these adhesions actually reduce the likelihood of becoming pregnant, although a posterior wall myomectomy may be particularly relevant given the possibility of adnexa involvement. Therefore, the surgeon must weigh the benefits of this type of surgery in regards to fertility enhancement on the other hand, and the implications caused by adhesion development on the other, in order to avoid unneeded myomectomies along with involuntary iatrogenic damages in women with otherwise unknown infertility or needing therapy for symptomatic fibroids [5]. This review's goal is to aid the surgeon in this challenging task by concentrating on three key areas: a) the frequency and seriousness of adhesions after myomectomy; b) the efficiency of myomectomy in enhancing fertility; and c) the preventive measures that are available to reduce the risk and the effects of adhesion development.

Methods

The phrases "myomectomy" alone and in conjunction with "adhesion", "infertility outcome", and "medical treatment/management therapy" were used to conduct a literature search on PubMed, Web of Science, Scopus, and the Cochrane Library. Preferably, cohort studies and systematic reviews with cohort studies and/or randomized controlled trials were considered. The most recent search was conducted on July 20, 2023.

Postoperative Adhesions

According to reports, post-operative pelvic adhesions can range from 28% to 90% [6], and myomectomy is thought to be the

surgical treatment that causes the greatest adhesions in the pelvis [7]. All patients having abdominal surgery should be informed about the dangers and effects of postoperative adhesions, according to a group of European specialists (Anti-Adhesion in Gynaecology Expert Group-"ANGEL" and the European Society of Gynaecological Endoscopy-"ESGE") [8].

Laparoscopic v/s Abdominal Myomectomy

The incidence of adhesions during abdominal and laparoscopic myomectomy has been the subject of several research. According to estimates, the reported abdominal myomectomy adhesion rate ranges from 31.1% [9] to 79% [10]. Following laparoscopic myomectomy, comparable incidences that range from 24.7% [9] to 78% [11] have been documented. Tinelli et al.'s randomized controlled study (RCT) [9] offers a useful comparison of adhesion formation after both. In a large patient population (n = 546) with similar baseline characteristics, these authors retrospectively studied the impact of an anti-adhesion agent (Interceed®) and found no difference in fibroid size. At a second-look laparoscopy, they discovered an incidence of adhesion development that was only marginally lower after laparoscopy compared to abdominal (29.2% vs. 23.8%) [9]. Thus, there is a considerable chance of adhesion development, despite expectations suggesting laparoscopic myomectomy would reduce this risk. Animal findings showing that pneumoperitoneum itself might be an adhesiogenic factor [12] may provide an explanation for this unsatisfactory conclusion. Insufflators, which supply preheated and humidified gas, have recently been developed, and it is hoped that this would reduce the formation of post-surgical adhesions [13,14]. It must be understood that the size of the fibroid, especially if in excess of 10cm, is a limiting factor for a minimally invasive approach; in such instances, the challenge and the time required for the specimen removal, should not be underestimated [15]. Currently, laparoscopy myomectomy is favored over open myomectomy because of its benefits in terms of less postoperative pain, decreased likelihood of postoperative infection, and less hospital stay [14]. Another significant limiting factor for a laparoscopic operation might be the amount and location of fibroids. Robotic surgery is a newly developed technique that allows for quick and efficient sutures while also utilizing various perspectives.

Size And Site of Fibroids Acting as Cofactor for Adhesions

In reality, the decline in fertility after fundal as well as anterior incisions is minor in comparison to posterior incisions, wherein involvement of the adnexa inside the scar frequently occurs. Adhesion incidence varies depending on fibroid location. In one research, those who had posterior wall incisions had postoperative adhesions in 97% of cases, but only in 51% of cases with anterior uterine wall incisions [16,17]. In the 1990s, Keckstein et al. [7] and Dubuisson et al. [18] proposed an early second-look laparoscopy routinely following posterior laparoscopic myomectomy in order to help with adhesion lysis after myomectomy and to evaluate the quality of myomectomy scars. In accordance with the recommendations they provided, second look laparoscopy was used in several trials, and the findings were intriguing: in addition to the site, fibroid size and incision length were identified as cofactors that led to a greater likelihood and severity of adhesion development. Only 28% of patients had at least one adnexa that was completely free of adhesions, according to Diamond et al.'s prospective multicenter analysis, which comprised 129 women who had undergone uterine myomectomy having at minimum 1 posterior uterine incision that was longer than 1cm [19]. In research involving 22 patients who underwent an abdominal myomectomy followed by a second look laparoscopy, Coddington et al. found that the total adhesion area over the uterine serosal rose by 0.62 cm^2 for every extra centimeter of incision length [20]. In their analysis of the effects of several surgical parameters (blood loss, time, number of incisions, and knots), Trew et al. [21] discovered a strong correlation between the formation of adhesions and incision lengths more than 5cm. There is a link with incision length and adhesions. In a study, patients with adhesions had an average total incision length of 10cm (range, 4.6cm-17.5cm), while those with a median incision length of 8cm (range, 2cm-23.9cm) did not experience adhesions [22]. In a different investigation, Takeuchi et al. [23] sought to identify the variables affecting the formation of surgical adhesions and discovered that fibroid diameter affected the frequency of new adhesions. Because of redundant serosa, the enucleation of a big fibroid do not result in the development of a smooth wound, and the ensuing wound bulge is a crucial element determining adhesion. In order to avoid the development of adhesions, these experts advise a precise restoration of the uterine wall, cutting or burying the excess tissue after the excision of fibroids. According to the findings of the aforementioned research, myomectomy is a highly adhesiogenic surgery and, more significantly, posterior myomectomy is impacted by a high rate of adhesion. The possibility of the adnexa being involved in these situations might lead to post-surgical reproductive impairment. Therefore, it is prudent to balance the potential benefits of surgical intervention versus the risk of unintended post-surgical infertility when selecting how to treat this clinical situation. Unfortunately, research addressing the issue of the possible advantages associated with myomectomy are quite far from offering firm results, as recently highlighted by Freytag et al. [24].

Does Myomectomy Result in Improved Fertility?

Recent research that looked at the relationship among reproductive outcomes and fibroids' locations addressed the topic of whether myomectomy increases fertility [25]. Although subserosal fibroids appear not to impair fertility, it is generally agreed that they can disrupt implantation [26], and as a result, they must be treated. On the other hand, it is less apparent how intramural fibroid [type 3 to 5 according to the most current International Federation of Gynecology and Obstetrics (FIGO) classification] contributes to the development of infertility and how myomectomy affects reproductive results [27].

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What We Can Learn from IVF?

In vitro fertilization (IVF) is a type of procedure that can explain the connection between fibroids and infertility in women who have them. Studies that contrast the results of IVF cycles in women with intramural fibroids and those without tend to show a considerable detrimental influence of intramural fibroids on reproductive potential and advise surgical excision of fibroids prior to IVF. In an updated comprehensive analysis of 31 trials comprising 10,213 patients, Wang et al. [28] found that embryo implantation as well as live birth rates were significantly lower in individuals with intramural fibroids. Compared to women without fibroids, those who had non-cavity-distorting intramural fibroids had 41% lower chances of having a live birth and 34% lower odds of becoming pregnant clinically, according to a study of 17 studies by Rikhraj et al. [29]. The size and location of the fibroids evaluated by Donnez et al. and Dolmans et al. as cofactors potentially accounting for the adverse effects of fibroids on fertility [30] are not clearly outlined in these reviews, which is unfortunate.

Regarding the Link Between a Fibroid's Location and Size

The above-mentioned authors draw the conclusion that the concomitant size and closeness of a fibroid to the uterine cavity are crucial for revealing the detrimental effect of intramural fibroids on fertility. This is based on the study of several published research. Therefore, a type 3 fibroid that is just 2cm in diameter and close to the endometrial lining will negatively impact fertility outcomes; in contrast, a type 4 or 5 intramural fibroid that is 3cm in diameter yet not in close proximity with the underlying endometrium is considered to have a fertility impairment [31]. This assertion is justified by the fact that intramural fibroids can have a deleterious impact on the endometrium's homeostasis and receptivity through the production of signaling molecules that can enter the endometrial cavity [32]. An agreement on the dimension of a fibroid that qualifies as a sign of a reproductive impairment is still a long way off, though. When women who had IVF with intramural fibroid with a diameter >3 cm, regardless of location, were compared with a matched control group, Yan et al. [33] found a substantial detrimental influence on the delivery rate. The same authors' extensive retrospective analysis with 153 cases and 464 matched controls [34], as well as Christopoulos et al. [35] who reported no difference in pregnancy outcome for women having IVF with one fibroid less than 3cm compared to controls, corroborated these findings. On the other hand, Behbehani et al. studied a total of 929 fresh single-blastocyst transfer cycles and found that even a single and relatively small intramural fibroid (>2cm) proved able to affect clinical pregnancy and live conception rates [36]; alternatively, Somigliana et al. in prospective research did not succeed to find a detrimental effect on IVF outcome in the presence of fibroids smaller than 5cm and not distorting the endometrial contour [37]. As summarized, these researches do not offer firm findings about the link between intramural fibroids and decreased fertility. It becomes clear that the surgical choice must be carefully considered, taking all necessary precautions to reduce adhesion development. This uncertainty is compounded by the concerns of reduced fertility owing to postoperative adhesion development, particularly in cases with posterior fibroid.

Preventing Adhesions

Effective adhesion prevention following myomectomy is crucial for women who want to become pregnant and necessitates using the right surgical methods [38]. The enlarged perspective offered by laparoscopy makes it simple to dissect anatomical structures precisely and with more care, when required [39]. It is crucial to obtain total hemostasis; nevertheless, it is important to pay attention to limit cautery duration and aspirate aerosolized tissues after this treatment. Adhesions can happen more frequently the higher the leftover volume of blood, thus it is important to accomplish complete hemostasis. Following surgery, the abdominal cavity should be frequently irrigated with a significant volume of Ringer's lactate [40] (Table 1). Regarding the kind of suture and the method that should be used to stop adhesion development, there isn't much consensus in the literature. However, it appears that more knots are linked to a greater adhesion rate [21]. A flowing suture is therefore preferable to single stitches in order to prevent the formation of adhesions. It is important to keep in mind that monofilament appears to be less responsive and trigger less inflammatory reactions than multifilament sutures, although the surgeon may not always choose it because of its higher memory and a smaller coefficient of friction. Finally, the barbed suture that does not require the tying of knots and has been proven to facilitate laparoscopic myomectomy by reducing the total operative time, seems to have the same effect impact on reproductive outcomes as conventional threads [41]. Disappointingly, these measures have not proven to be sufficient, and even the results of antiadhesion agents are considered only partially satisfactory [42,43]: the most frequently utilized products used to prevent adhesion formation (e.g., INTERCEED, Ethicon; SEPRAFILM,Baxter.) Physical barriers prevent the process of adhesion formation but and act as a spacer separating the surfaces of the wound surfaces during tissue regeneration. There will be new options to address this problem as a result of novel medicines that can alter the pathophysiology underpinning adhesion development [44]. Although there isn't enough data to justify their routine adoption in every myomectomy, these recommendations should nevertheless be made in the event of posterior myomectomy because to the high incidence of adnexal post-surgical adhesions.

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Table 1: describes the adhesion-reduction strategy used during myomectomy.

Steps Used During A Myomectomy to Reduce Adhesion
Ensure careful cautery usage while doing careful hemostasis
lessen the chance of infection
Limit your suture usage and only use tiny, nonreactive sutures.
Slash the time of the operation
Stay away from foreign objects, such as textiles with loose fibers.
Reduce the amount of heat and light used to dry tissues
During open surgery
hardly use sponges or dry cloths
In laparoscopic surgery, use gloves devoid of starch and latex
Use aspiration and regular irrigation
Shorten the duration and pressure of the pneumoperitoneum

Shrinking the Fibroid

The length of the uterine surface incision is a crucial indicator of adhesion development following myomectomy. It seems like reasonable surgical judgment to use preoperative fibroid size reduction techniques to shorten incision length. Currently, the pharmacological treatments with the strongest evidence of fibroid volume reduction are selective progesterone receptor modulators (SPRMs) and GnRH agonists (GnRH-a). Through a considerable reduction in fibroid size, short-term pre-operative GnRH-a therapy may reduce the chance of post-operative adhesion [45]. The therapeutic advantages of GnRH-a prior to myomectomy were validated by a comprehensive evaluation of 29 randomized controlled trials [46]. In a recent trial, goserelin 3.75mg subcutaneously given twice before surgery at intervals of 4 weeks led to a decrease in fibroids size up to 58.6% [47]. The effectiveness of shrinking in the prevention or decrease of adhesion formation is a critical subject that has not yet received satisfactory answers. Unfortunately, Coddington et al. [20] prospective randomized research is the only one that is currently available, and it raises some concerns about the efficacy of this treatment. In this trial, 20 patients were randomly assigned to receive either GnRH -a or a placebo three months prior to their initial surgery. Postoperative adhesions were then assessed using a second-look laparoscopy three to twelve weeks later. The authors discovered that presurgical GnRH-a treatment had no greater anti-adhesion effects than placebo. The absence of specific information on the size of the fibroids before and after therapy, in addition to the study's small sample size, prevents drawing firm conclusions on the effectiveness of GnRH-a as a preventive measure for adhesion development. Due to the alteration in the clotting and fibrinolytic system brought on by the induced hypoestrogenism, GnRH-a also has a favorable influence on adhesion formation [48]. Accordingly, experimental studies on the rodent model of uterine serosal injury have confirmed this beneficial effect induced by GnRHa in adhesion prevention [49]. Since the introduction of GnRH antagonists and selective progesterone receptor modulators (SPRMs), other pharmacological By rapidly inhibiting pituitary GnRH receptors, GnRH antagonists decrease the release of FSH and LH, and are therefore much more efficient than placebo at reducing uterine fibroid growth [50,51]. Ganirelix was effective to reduce fibroids and overall uterine volumes from as early as 21 days following therapy commencement, according to an open-label research including 19 patients [52]. Clinical research on the use of SPRMs for the preemptive treatment of uterine fibroids has been encouraged by mounting evidence of progesterone's critical involvement in the pathogenesis of uterine fibroids [53]. treatments for fibroid pre-surgery have been examined. A SPRM lacking hypoestrogenic side effects, ulipristal acetate (UPA) was initially authorized for the pre-operative treatment of symptomatic fibroids [54], but is currently being temporarily pulled off the market due to safety concerns associated with a few reports of liver harm [55]. It is yet unclear how UPA and GnRH-antagonist vary from one another in terms of effectiveness. On one hand, a double-blind randomized controlled trial showed that GnRH-a pretreatment was linked to a greater reduction in volume than UPA (47% with GnRH antagonist compared to 20% with 5mg UPA for up to 13 weeks treatment) [53], but on the opposite hand, a randomized trial by Donnez et al. - comparing UPA with GnRH-a - failed to show significant differences in fibroid volume.

Re- look Laparoscopy

Even if it is burdened by the danger of adhesions reformation limiting to some extent the efficacy of these procedures, re- look surgery is a possible treatment conducted within a specific period of time following the original surgery to diagnose and cure any newly-formed pelvic adhesions [56]. There is a dearth of published information on patients' chances of getting pregnant following relook surgery. Following adhesiolysis, a recent in-depth review based on 7 randomized controlled trials was unable to demonstrate any meaningful improvements in reproductive outcomes; however, as the authors stated, this finding was based on studies that were either of low quality or underpowered [57]. Kubinova et al. [58] compared patients who received re- look procedure (which includes adhesiolysis) with a group of patients who did not get intervention in order to explicitly examine the reproductive result following laparoscopic/laparotomic myomectomy. The results of a recent clinical trial by Li et al. on a sizable (n = 216) number of women who originally had endoscopic salpingostomy for ectopic pregnancy and were then randomly assigned to adhesiolysis or no intervention at 3 months later [59] provide intriguing information. In light of these findings, Frishman G. N. [60] in an Editorial on "The Journal of Minimally Invasive Gynecology" recommends the sole inclusion of women with severe adhesion as study methodology for determining the effect of re- look laparoscopy on reproduction outcome-if any-considering these individuals as ideal candidates to benefit from

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this procedure. The best timing to execute re- look surgery, which is still up for discussion, is saved for further consideration. Most experts agree that the first three to five days after surgery are when adhesion development takes place. In fact, some authors advise very early re- look surgery (within 8 days) [61]; however, other authors advise re- look surgery within the start of serosal healing (eight days) and the point at which fibrotic adhesions can be deemed permanent (21 days) [62]. These authors contend that the very early fine fibrinous adhesions are typical complications of tissue repair caused by the local release of breakdown mediators during the remodeling process and will eventually fade away with time. This approach may be encouraged (in some circumstances) by the introduction of mini-laparoscopy and the use of regional anesthetic for laparoscopic surgery, with quick recovery after day surgery [63].

Ovariopexy

When it is desired to avoid the ovary from being hidden in the fibrous adhesive bands involving the Douglas pouch, which would adversely impair the reproductive capacity, transitory ovariopexy is performed in order to maintain the ovary away from the wounded peritoneum. For many years, this treatment has been touted as a secure, easy, and effective strategy for preventing postoperative ovarian adhesion in women having endometriosis surgery [64]. The procedure entails securing the ovary loosely and temporarily to the anterolateral wall of the abdomen or, less commonly, to the circular ipsilateral ligament using a synthetic absorbable/nonabsorbable monofilament suture [65]. The amount of time that the attached ovaries should remain detached from the wall of the abdomen is controversial and ranges from 5 days [66] and 7-9 days, as proposed by Trehan et al. [67], in order to permit complete blood absorption in the cavity, which poses a significant danger for adhesion development. Ovariopexy may also be helpful for patients who experience significant adhesion following posterior myomectomy since it may make it easier for them to undergo IVF or ICSI later on, which needs the ovary to be properly positioned in the pelvis for effective egg retrieval.

Conclusion

The effectiveness of myomectomy in regaining fertility must be carefully evaluated versus the risks of adhesion formation if the workup for fertility problems shows a fibroid, with the right patient selection. Due to the significant potential of adnexal adhesion development that may negatively impact reproductive function, this meticulous approach is particularly pertinent in cases with posteriorly situated big fibroids. When a myomectomy is performed initially to improve fertility, it is crucial to ascertain when this is the case and, if so, to take all appropriate precautions to prevent postoperative sterility. The use of surgical myomectomies will certainly decline even more as more alternative treatments become available, particularly if preserving fertility is the main objective.

Author Contributions

SS, VM performed the searches. SS contributed to data extraction. SS drafted the manuscript, participated in data analysis and interpretation, and preparation of the manuscript. VM critically revised the paper. VM conceived the idea of the manuscript. All authors contributed to the article and approved the submitted version.

Conflict of Interest

The study was carried out without any financial or commercial ties that may be viewed as a possible conflict of interest, according to the authors.

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How to cite this article: Vineet Mishra, Smit Bharat Solanki . Myomectomy for Infertility: Does it Do More Damage Than Good?. J Gynecol Women's Health 2023: 26(1): 556177. DOI: 10.19080/JGWH.2023.25.556177

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DOI: 10.19080/JGWH.2023.25.556177

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