

Pregnancies and births in women with previous abdominal myomectomy

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ABSTRACT

Background: Uterine leiomyoma may cause pelvic symptoms and may also interfere with the reproductive desires of many women. Consequently, some women may undergo myomectomy as a fertility sparing method to relieve symptoms or as a method to improve their fertility.

Objective: We aimed to assess pregnancies and deliveries in women with previously myomectomy both in spontaneous pregnancies and with use of assisting reproductive techniques. Also, we aimed to assess if the reproductive prognosis differed between different surgical approaches.

Study design: In this historical cohort study we collected data regarding myomectomies, pregnancies, use of assisting reproductive techniques and births from national health registries. All Danish women were followed from 1996 through 2017.

Results: Of 5.281 women undergoing myomectomy, 97% had one and 3% had two or more myomectomies. Median age at first surgery was 38.5 years (interquartile range 34.1-44.6 years). Of 5.430 myomectomies conducted, 71% were done by laparotomy and 29% by laparoscopy.

Of the 5.281 women treated with myomectomy, 1.586 (30%) became pregnant and 1.145 (22%) gave birth. In the entire cohort of 5.281 women, 1.056 (20%) were treated with assisting reproductive techniques. Of these 1.056 women, 659 (62%) got pregnant and 461 (44%) delivered. Median time from surgery to pregnancy was 1.2 years. Significantly more women became pregnant and gave birth when treated with laparotomy as compared to laparoscopy. However, the effect was only significant for women younger than 30 years or older than 40 years at first surgery.

Conclusion: As the proportion of women attempting pregnancy was unknown, the overall figure of 30% pregnancy rate is a minimum estimate of the real chance of achieving pregnancy after myomectomy.

Keywords: Leiomyomas; Myomectomy; Fertility; Pregnancy

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INTRODUCTION

Uterine leiomyomas are common benign tumors developing from the smooth muscle cells of the uterus. The incidence varies regarding ethnicity and increases with age. Leiomyomas has a cumulated incidence of up to 70% in women of reproductive age [1].

The presence of pelvic symptoms is related to the numbers, size and anatomical location of the leiomyomas.

While a large portion of women with smaller leiomyomas may never experience symptoms, other women experience menometrorrhagia, dysmenorrhea, pelvic pain, infertility, miscarriages, urogynecological problems, or pelvic bulk symptoms. In symptomatic women with leiomyomas, who wish to preserve their fertility, myomectomy is a frequent treatment option. Asymptomatic women with unexplained infertility or repeated miscarriages may be offered myomectomy in order to increase their chance of delivery.

The impact of leiomyomas in infertility has been extensively studied. Suggested pathogenetic mechanisms may include altered vascularization, a chronic non-infectious endometrial inflammation, altered cytokine levels, changes in uterine contractility or combinations of these [2].

While myomectomy may remove the leiomyomas and relieve symptoms, other changes in uterus may follow myomectomy, leaving the long-term effect of myomectomy on fertility uncertain [3-4]. Women with leiomyomas who wish to deliver constitute a heterogeneous group according to age, size and anatomical location of their leiomyomas, medical history, co-morbidities, history of infertility, and use of different assisted reproductive techniques (ART). Therefore, studies regarding the impact of myomectomy on fertility are often very heterogeneous regarding nomenclature, treatment offered, and applied control groups, making comparisons of results between studies challenging [5].

While submucosal leiomyomas negatively impact fertility, subserous leiomyomas rarely have a negative impact on fertility [6,7]. The impact of intramural leiomyomas and myomectomy on fertility has predominantly been examined in cohorts of women treated with ART. While some studies find no or insignificant effect of intramural leiomyomas on outcome of patients treated with ART [8,9],

most studies have demonstrated these to impair results of ART [3,4,10-15]. Also, myomectomy of intramural leiomyomas may improve fertility when compared to nonsurgical management [3,4,10,16,17].

We found only one randomized controlled trial comparing conservative treatment to myomectomy. This 2006 study by Casini et al. [16] demonstrated significantly higher spontaneous pregnancy rates for women undergoing myomectomy for submucous and submucous-intramural leiomyomas, when compared to controls with no surgical intervention. The authors found no difference in fertility for women with intramural, subserous or intramural-subserous leiomyomas.

In a 2017 systematic review, The American Society for Reproductive Medicine concluded that for women with non-cavity disturbing leiomyomas, there were insufficient evidence regarding what size, number and anatomical location of leiomyomas that are associated with reduced fertility or risk of miscarriage. The American Society for Reproductive Medicine recommends that in asymptomatic women with cavity disturbing leiomyomas removal of these could be offered to increase fertility, whereas in asymptomatic women with non-cavity disturbing leiomyomas removal should only be considered after careful evaluation of all circumstances [5].

In the present study, we aimed to evaluate spontaneous and assisted pregnancy- and birth rates in a historical cohort of women after abdominal myomectomy. Data regarding vaginal myomectomies and myomas removed by hysteroscopy are not included in the present study.

MATERIALS AND METHODS

The study was designed as a historical nationwide cohort study, including all women in Denmark undergoing abdominal myomectomy both as laparoscopy and laparotomy during the period 1996 through 2017. All women were followed-up until December 31, 2017.

Data sources

The unique personal social security number assigned to all Danish citizens at birth or immigration allows for merge of data from several health registries and enables long-term follow-up.

The Danish National Health Registry, established in 1976, provided discharge diagnoses and surgical codes from all public and private hospitals. This health registry provided information about women with a surgical code for myomectomy, and any pregnancy and birth after a first myomectomy. We merged the cohort of women with previous myomectomy with data from the Danish Fertility Registry to assess the proportion achieving pregnancy after assisted reproductive treatment.

Statistical analyses

In women having undergone more than one myomectomy, the latest surgical approach was used in the follow-up analyses for time to pregnancy. Women who had myomectomy both as laparoscopy and laparotomy were grouped as the latter for comparison of fertility outcome. Comparison between groups were made with standard chi square tests. A p-value <0.05 was considered significant. SAS Version 9.4 (SAS Institute, NC, USA) was used for data management and statistical calculations

Ethics

Regional approval was achieved from first "Pactius" and later from "Privacy". Ethical approval is not necessary for registry-based studies in Denmark. Data handling was on encrypted data.

RESULTS

Of 5,281 women undergoing myomectomy in the study period, 5,127 (97%) had one myomectomy and 154 (3%) had two or more myomectomies. Median age at first myomectomy was 38.5 years (interquartile range: 34.1 – 44.6). Median time from first surgery to pregnancy was 1.2 years.

Of the total 5,340 myomectomies, 3,848 (71%) were performed by laparotomy and 1,582 (29%) by laparoscopy.

Of the 5,281 women who underwent myomectomy, 1,586 (30%) became pregnant and 1,145 (22%) gave birth. Table 1 demonstrates the rate of pregnancies and births stratified according to age. As illustrated in Tables 1 and Figure 1, significantly more women became pregnant and gave birth when treated with laparotomy as compared to

laparoscopy. The effect was significant, however, only for women younger than 30 or older than 40 years at first surgery.

Table 1: Pregnancies after myomectomy according to surgical technique and age at surgery.

Age years	Myomectomies	Pregnant N (%)	Birth N (%)
<i>Laparotomy</i>			
≤ 29	346	216 (62)	155 (45)
30 – 34	927	492 (53)	373 (40)
35 – 39	1,236	430 (35)	296 (24)
40+	1,241	92 (7)	55 (4)
All	3,750	1,230 (33%)	879 (23)
<i>Laparoscopy</i>			
≤ 29	142	64 (45)***	49 (35)*
30 – 34	279	133 (48)	105 (38)
35 – 39	398	133 (33)	93 (23)
40+	712	26 (4)**	19 (3)*
All	1,531	356 (23)***	266 (17)**

(*) p<0.05, (**) p<0.01, (***) p<0.001 when comparing laparoscopy versus laparotomy

Among all women with myomectomy, 684 (13%) gave birth after spontaneous conception.

In the entire cohort of women, 1,056 (20%) received ART treatment. Of the 1,056 women treated with ART, 659 (62%) became pregnant and 461 (44%) gave birth. Table 2 demonstrates the fertility outcome of women who were referred to ART stratified according to age.

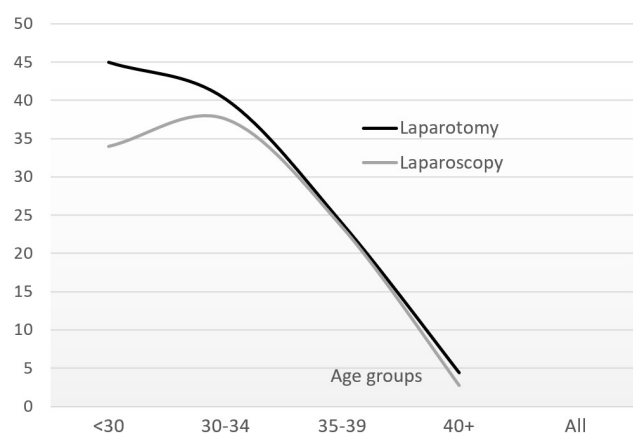


Figure 1: Delivery rate after myomectomy according to surgical technique and age at surgery

Table 2: Assisted reproductive techniques after myomectomy and subsequent pregnancy and delivery rates.

Age group years	ART after myomectomy n (%)	Pregnant after ART n (%)	Birth after ART n (%)
≤ 29	93 (19)	61 (66)	40 (43)
30 – 34	362 (30)	267 (74)	199 (55)
35 – 39	472 (29)	274 (58)	186 (39)
≥40	129 (7)	57 (44)	36 (28)
All	1.056 (20)	659 (62)	461 (44)

ART = assisted reproductive techniques

In the group of women treated with ART, there was no difference in fertility outcome between women treated with laparotomy as compared to laparoscopy, neither in the entire cohort nor when stratified per age group.

Of all women who achieved pregnancy after myomectomy, 93% became pregnant within the first five years of the first myomectomy.

Of the 1.145 women who gave birth after myomectomy, 60% conceived spontaneously and 40% with assisted conception.

DISCUSSION

In this historical cohort study including all Danish women undergoing myomectomy over more than two decades, we demonstrated a better fertility outcome in women undergoing myomectomy by laparotomy as compared to laparoscopy in the entire cohort. For women treated with ART, there was no differences in fertility outcome when grouped according to surgical approach. Also, we demonstrated that approximately one-in-third woman becomes pregnant and one-in-five woman gives birth following abdominal myomectomy.

Our findings correlate well with a study by Kundu et al [20] from 2018, demonstrating higher pregnancy rate of 55% after myomectomy by laparotomy as compared to 21% after myomectomy by laparoscopy. In contrast to our results, Palomba et al [18] demonstrated better outcome regarding pregnancy rate per cycle, cumulative pregnancy rate, live-birth rate per cycle and shorter time to first pregnancy and live-birth after laparoscopic

myomectomy versus minilaparotomy when examining women with symptomatic leiomyomas. For women with unexplained infertility, the authors found no difference in fertility outcome when grouped according to surgical modality.

However, other studies have found no impact on fertility outcome when comparing myomectomy by laparoscopy to laparotomy [19-23].

The reasons for better fertility outcome for women treated with open myomectomy in the entire cohort are not clear from our data. In Denmark, women usually have been examined by transvaginal and/or transabdominal sonography before referred to surgery. Magnetic resonance imaging is rarely used unless malignancy is suspected. When performing myomectomy by minilaparotomy at our institution, we often experience the presence of additional leiomyomas, which were not found by sonography. We speculate that a careful palpation of the uterus during a laparotomy may facilitate the detection of and, consequently, removal of leiomyomas that would not have been found by laparoscopy, where the tactile sensation of the surgeon is reduced. This could also explain why the positive effect of laparotomy was most significant in women undergoing surgery at a young age. The smaller leiomyomas would need time to grow before they become clinically significant to impair fertility.

Myomectomy can be offered as a treatment to increase fertility for women with asymptomatic leiomyomas who wish to become pregnant. Myomectomy may also be offered to women with symptomatic leiomyomas as a fertility preserving treatment. Women with symptomatic leiomyomas who has no wish to preserve fertility would often be recommend hysterectomy to avoid the risk of recurrence of symptoms.

Therefore, it is surprising that only 20% of Danish women with a history of myomectomy were referred to ART treatment since only 13% gave birth after spontaneously conceived pregnancies.

Of the 1.953 women who were 40 years or older at the time of myomectomy, only 129 (7%) conceived by ART while 38 (2%) gave birth after natural conception.

Accordingly, most women in our cohort neither gave birth after spontaneous conception nor were referred to ART. These findings may indicate that

myomectomy is not only used as a method to preserve fertility but is also very frequently used as a method to relieve pelvic symptoms for women who wish to preserve their uterus despite having no desire to conceive.

According to the Danish Hysterectomy and Hysteroscopy Database in one year, from June 2022 to May 2023, 260 women underwent myomectomy in Denmark. Of these, 0.8% had a major complication within 30 days following the operation. In the same period 2.513 women underwent hysterectomy in Denmark on benign indications of which 3.9 % experienced major complications including need for reoperation within 30 days following the operation.

The proportion of women who required an additional myomectomy or a hysterectomy within 5 years of their myomectomy were 3.4% [24].

Consequently, it could be argued that for most women with pelvic symptoms from leiomyomas, myomectomy is a safe and relevant alternative to hysterectomy.

We found no data suggesting myomectomy to be harmful to fertility, which is in accordance with others [5]. Nonetheless, pregnancies after myomectomy carries an increased risk of uterine rupture, preterm delivery, and placental implantation abnormalities site [25] and therefore myomectomy should be not be offered routinely to asymptomatic woman as a method to improve fertility. Our results cannot be used for counseling of specific patients. For asymptomatic and infertile women with non-cavity disturbing leiomyomas it is still not clear if myomectomy increases their fertility. However, our results may help understand and estimate the likelihood of pregnancy and birth in women undergoing myomectomy in different age groups.

The strengths of the study are the inclusion of a whole population, ensuring a high external validity, and a follow-up period of 21 years, ensuring enough time for reproductive outcomes to occur. A major limitation was lack of data on the indication for performing myomectomy and we have no knowledge about the desire to become pregnant except for women undergoing ART treatment. Therefore, the true spontaneous fertility outcome is not available from our data. In addition, apart from age, we had no data on other variables that could influence fertility, and we had no detailed

information about the specific ART procedures. Most important, this is a historical study without a control group, which would be required for a comparison of myomectomy vs a non-surgical approach for asymptomatic women with leiomyomas. We find it uplifting and noteworthy that more than a quarter of women who had a myomectomy at the age of 40 years or older and subsequently were offered ART treatment, ended up with giving birth.

CONCLUSION

We found that in a cohort of women with a history of myomectomy 30% achieved pregnancy and 22% gave birth. For younger women, fertility outcome may be better when undergoing myomectomy by laparotomy when compared to laparoscopy. In addition, only a minority of the Danish women who did not conceive spontaneously after myomectomy were referred to ART, suggesting the wish to conceive was not the most frequent indication for performing myomectomy.

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