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Pregnancy outcomes following robot-assisted myomectomy†

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STUDY QUESTION: What are the characteristics of the pregnancy outcomes in women undergoing robot-assisted laparoscopic myomectomy (RALM) for symptomatic leiomyomata uteri?

SUMMARY ANSWER: Despite a high prevalence of women with advanced maternal age, obesity and multiple pregnancy in our cohort, the outcomes are comparable with those reported in the literature for laparoscopic myomectomy.

WHAT IS KNOWN ALREADY: Reproductive outcomes after traditional laparoscopic myomectomy are well documented. However, reproductive outcomes following robotic myomectomy are not well studied. This paper describes the pregnancy outcomes for a large cohort of women after robotic myomectomy.

STUDY DESIGN, SIZE, DURATION: This is a retrospective cohort of women who became pregnant after robot-assisted myomectomy at three centers. Of the 872 women who underwent robotic myomectomy during the period October 2005–November 2010, 107 subsequently conceived resulting in 127 pregnancies and 92 deliveries through 2011.

PARTICIPANTS/MATERIAL, SETTING, METHODS: Women of reproductive age with fibroids who wanted a minimally invasive treatment option and desired uterine preservation were recruited. We conducted a multicentre study with three centers, two in a private practice and one in an academic setting. Pregnancy outcomes and their relationship to myoma characteristics were analyzed.

MAIN RESULTS AND ROLE OF CHANCE: Mean $\pm$ SD age at myomectomy was 34.8 $\pm$ 4.5 years and 57.4% [95% confidence interval (CI) 48.0, 66.3] of women were overweight or obese. The mean number of myomas removed was 3.9 $\pm$ 3.2 with a mean size of 7.5 $\pm$ 3.0 cm and mean weight of 191.7 $\pm$ 144.8 g. Entry of the myoma into the endometrial cavity occurred in 20.6% (95% CI 15.0, 27.7) of patients. The mean time to conception was 12.9 $\pm$ 11.5 months. Assisted reproduction techniques were employed in 39.4% (95% CI 32.6, 46.7) of these women. Seven twin pregnancies and two triplet pregnancies occurred, for a multiple pregnancy birth rate of 9.8% (95% CI 5.0, 17.8). Spontaneous abortions occurred in 18.9% (95% CI 13.0, 26.6). Preterm delivery prior to 35 weeks of gestational age occurred in 17.4% (95% CI 10.9, 26.5). One uterine rupture (1.1%; 95% CI 0.3, 4.7) was documented. Pelvic adhesions were discovered in 11.4% (95% CI 7.0, 18.0) of patients delivered by Cesarean section. Higher preterm delivery rates were significantly associated with a greater number of myomas removed and anterior location of the largest incision (compared with all other sites) in logistic regression analyses ($P = 0.01$). None of the myoma characteristics were related to spontaneous abortion.

BIAS, CONFOUNDING AND OTHER REASONS FOR CAUTION: Given the retrospective nature of the data collection, some pregnancies may not have been captured. In addition, owing to the high prevalence of infertility patients in this cohort, the data cannot be used to counsel women who are undergoing RALM about fertility rates after surgery.

GENERALIZABILITY TO OTHER POPULATIONS: Prospective studies are needed to determine if the results shown in our cohort are generalizable to all women seeking a minimally invasive option for the conservative treatment of symptomatic fibroids with pregnancy as a desired outcome.

STUDY FUNDING/COMPETING INTEREST(S): There was no funding source for this study.

Key words: pregnancy / robotic surgery / laparoscopy / myomectomy

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Introduction

Uterine leiomyomata are common in women of reproductive age (Stewart, 2001). These benign neoplasms may become symptomatic and can result in subfertility among those trying to become pregnant (Pritts *et al*., 2009). While hysterectomy is the most frequent surgical treatment for symptomatic myomas (Becker *et al*., 2005), myomectomy is the choice for women desiring uterine preservation or future pregnancies.

Although several prospective RCTs have shown that laparoscopic myomectomy results in less post-operative morbidity and faster recovery than open procedures (Mais *et al*., 1996; Seracchioli *et al*., 2000), the majority of myomectomies are still performed by laparotomy. Reluctance to adopt conventional laparoscopy has been attributed to surgical difficulty in enucleating and extracting myomas, and in performing multilayer closure using this technique (Liu *et al*., 2010). More recently, robot-assisted laparoscopic myomectomy (RALM) has been performed by surgeons with the expectation that it could improve on the shortcomings of traditional laparoscopy (Advincula *et al*., 2004; Senapati and Advincula, 2007) and thereby offer an approach more easily adoptable by gynecologic surgeons with access to a robot (Payne and Pitter, 2011). Accumulating evidence suggests that robot-assisted compared with open myomectomy results in less blood loss, fewer complications and faster recovery (Advincula *et al*., 2007; Ascher-Walsh and Capes, 2010; Barakat *et al*., 2011). Several studies report that these short-term outcomes are similar for robot-assisted and conventional laparoscopic myomectomy (Bedient *et al*., 2009; Nezhat *et al*., 2009; Barakat *et al*., 2011). Data also indicate that robotic techniques can provide a minimally invasive approach to removal of larger, more difficult myomas that are less often attempted with traditional laparoscopic surgery (Barakat *et al*., 2011).

While these studies provide evidence that RALM has favorable short-term outcomes, long-term outcomes, including pregnancy outcomes, have not yet been reported in large series (Lönnerfors and Persson, 2011). Pregnancy following myomectomy is usually considered at a higher risk of complications, such as uterine rupture and surgical obstetrical complications associated with the presence of peri-uterine adhesions. We designed the present investigation to examine pregnancies and perinatal outcomes as they related to characteristics of the myomas in women who underwent RALM. Given the retrospective nature of the data collection, this study could not be designed to ascertain fertility rates of women who conceived after robotic myomectomy.

Materials and Methods

Literature review

Multiple searches were performed in PubMed as well as Scopus to identify all papers on robotic or robotic-assisted surgery and myomas, leiomyomata, fibroids, myomectomy or pregnancy.

Patients

Patients from the practices of two community-based gynecologists and two gynecologists at an academic center formed the cohort for this study. Three of the four participating physicians were specialized in reproductive endocrinology and infertility. They had been performing RALMs since October 2005 (M.C.P.), June 2006 (L.M.B.) and January 2007 (A.R.G and S.S.S.), and were experienced laparoscopists prior to the introduction of robotic surgery. In this time period, candidates for robotic myomectomy included women with symptomatic leiomyomata that were predominantly intramural with deformation of the endometrial cavity and with submucosal components not amenable to hysteroscopic resection. The symptoms typically included bleeding, pain and pelvic pressure. The women in this study also underwent preoperative magnetic resonance imaging (MRI) which showed <15 myomas, no evidence of adenomyosis and a uterine size $\leq 18-20$ weeks.

During the study period from October 2005 to November 2010, 872 women had RALM at the three centers. These women desired uterine preservation; however, not all of them were immediately considering pregnancy. We searched electronic medical records for all women who subsequently became pregnant. All women for whom medical records were available indicating subsequent pregnancy and all women who contacted our clinics stating that they conceived following robotic myomectomy were included. Given that oocyte donation is offered to women up to the age of 50 years, inclusion criteria for this study were all premenopausal women less than or equal to age 51 years at the time of pregnancy. If a patient conceived more than once during this time, data were abstracted for all pregnancies. All women consented to RALM and approval for the study was obtained from three respective Institutional Review Boards.

Surgical techniques

RALM was performed using the da Vinci Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA, USA) in a similar fashion at all three institutions: Newark Beth Israel Medical Center, Newark, NJ, USA; Brigham and Women's Hospital, Boston, MA, USA; Deaconess Women's Hospital of Southern Indiana, Newburgh, IN, USA. Some myomectomies were also performed at Hackensack University Medical Center, Hackensack, NJ, USA. Dilute concentrations of vasopressin were injected prior to performing the initial hysterotomy, and repeat doses were administered if more than one hysterotomy was performed. The concentration of vasopressin used was typically 20 units in 60 ml of normal saline and this was injected using a 22 gauge, 12.7 cm Quincke needle placed trans-abdominally and directly into the serosa overlying the myomas. Hysterotomies were transverse, vertical or elliptical in nature depending on the location of the myoma. Hysterotomies were performed with the Endowrist Hot Shears™ (Intuitive Surgical, Inc.) (L.M.B. and M.C.P.) or ultrasonic energy (A.R.G. and S.S.S.) utilizing the Harmonic Shears (Ethicon Endo-Surgery, Inc., Cincinnati, OH, USA) to reach the proper avascular plane under the pseudocapsule, mimicking open myomectomy techniques. Once the hysterotomy was performed and a clear cleavage plane identified, limited thermal energy was utilized, as enucleation is typically accomplished with traction and countertraction forces. After enucleation, the closure of the hysterotomy incision at the deep layer was done with either 0—polygalactin 910 interrupted figure of eight sutures, followed by a running suture or with a running closure with barbed polydiaxanone sutures (Quill or V Loc). Serosal closure varied between 2–0 or 3–0 poliglecaprone 25 and barbed polydiaxanone. Closures were multilayered depending on the depth of the incision or tumor defect created.

Data collection and follow-up

A member of the physician team, using a standardized protocol, abstracted data from electronic medical records as well as traditional records and communication with the referring obstetrician where necessary. Information was double-checked against master lists of procedures and confirmed for accuracy. The doctors tracked outcomes of each patient during follow-up at the respective clinics and hospitals from the time of conception through delivery. Data abstracted also included patient characteristics at the time of myomectomy (age, ethnicity, BMI, gravidity, parity and prior myomectomy or prior Cesarean delivery), characteristics of the surgery and myomas (operative time, estimated blood loss, uterine size, greatest myoma size and weight, myoma number, location of the largest incision, entry into the endometrial cavity and conversion to laparotomy) and early pregnancy parameters (mode of conception, time to conception after surgery, spontaneous abortion and ectopic pregnancy). Obesity was defined when the BMI was ≥ 30 kg/m^2 and overweight was defined as a BMI range between 25.0 and 29.9 kg/m^2. The delivery characteristics were obtained from obstetrical records and delivery notes and they included maternal age, gestational age, route of delivery, noted uterine abnormalities including adhesions at Cesarean section, forceps vacuum assistance, premature preterm rupture

Table I Characteristics of each patient at the time of RALM.

Patient characteristics	*N* = 107
Age at myomectomy, years	
Mean (SD)	34.8 (4.5)
95% CI	34.0–35.7
Median	35.0
Range	23–48
Ethnicity, *n* (%; 95% CI)	
Caucasian	57 (53.3; 45.4, 61.0)
African–American	38 (35.5; 28.4, 43.3)
Hispanic	8 (7.5; 4.3, 12.8)
Other	4 (3.7; 1.7, 8.0)
BMI (kg/m^2), *n* (%; 95% CI)	
<25	46 (42.6; 35.0, 50.5)
25–29.9	31 (28.7; 22.1, 36.3)
30+	31 (28.7; 22.1, 36.3)
Mean (SD)	27.4 (5.5)
95% CI	26.3–28.4
Median	26.6
Range	18.4–44.0
Gravidity, *n* (%; 95% CI)	
0	56 (52.8; 44.9, 60.5)
1	29 (27.4; 20.9, 34.9)
2+	21 (19.8; 14.3, 26.8)
Unknown	1
Parity, *n* (%; 95% CI)	
0	92 (88.5; 82.5, 92.6)
1	9 (8.6; 5.1, 14.1)
2+	3 (2.9; 1.2, 6.9)
Unknown	3
Multiple myomectomies, *n* (%; 95% CI)	7 (6.5; 3.6, 11.6)
Prior Cesarean delivery, *n* (%; 95% CI)	4 (3.8; 1.7, 8.1)

95% CI, 95% confidence interval.

Table II Characteristics of surgery and removed myomas.

Characteristics at myomectomy	*N* = 108
Operative time, min	
Mean (SD)	174.6 (77.0)
95% CI	159.4–189.7
Median	172.0
Range	54.0–335.0
Unknown	6
Estimated blood loss, ml	
Mean (SD)	134.5 (115.5)
95% CI	112.1–156.8
Median	100
Range	10–750
Unknown	3
Uterine size (greatest dimension), cm	
Mean (SD)	12.3 (3.1)
95% CI	11.7–13.0
Median	12.0
Range	6–20
Unknown	20
Myoma size (greatest dimension), cm	
Mean (SD)	7.5 (3.0)
95% CI	6.9–8.1
Median	6.9
Range	3–18
Unknown	3
Myoma weight, g	
Mean (SD)	191.7 (144.8)
95% CI	163.1–220.3
Median	149.0
Range	8–665
Unknown	7
Myoma number	
Mean (SD)	3.9 (3.2)
95% CI	3.3–4.5
Median	3.0
Range	1–14
Unknown	1
Location of largest incision, *n* (%; 95% CI)	
Posterior	33 (32.3; 25.4, 40.0)
Anterior	39 (38.2; 30.9, 46.1)
Ant/post	8 (7.8; 4.5, 13.1)
Cervical	3 (3.0; 1.2, 7.1)
Fundal	17 (16.7; 11.6, 23.4)
Cornual	2 (2.0; 0.6, 5.7)
Unknown	6
Entry into endometrial cavity, *n* (%; 95% CI)	22 (20.6; 15.0, 27.7)
Unknown	1

Table III Characteristics of all pregnancies after RALM.

Pregnancy characteristics	N = 127
Mode of conception, n (%; 95% CI)	
Spontaneous	77 (60.6; 53.3, 67.4)
ART	50 (39.4; 32.6, 46.7)
Estimated time from myomectomy to first conception, months	
Mean (SD)	12.9 (11.5)
95% CI	10.5–15.3
Median	9.3
Range	0.71–65.4
Spontaneous abortion <14 weeks, n (%; 95% CI)	21 (16.5; 11.8, 22.6)
Spontaneous abortion 14–20 weeks, n (%; 95% CI)	3 (2.4; 0.9, 5.8)
Ectopic pregnancy, n (%; 95% CI)	2 (1.6; 0.5, 4.7)
Hypertension in pregnancy, n (%; 95% CI)	15 (11.9; 8.0, 17.4)

ART, assisted reproduction techniques.

Table IV Characteristics of deliveries in patients who became pregnant after RALM.

Delivery characteristics	N = 92
Maternal age at delivery, years	
Mean (SD)	35.8 (4.3)
95% CI	34.9–36.8
Median	36.0
Range	23.0–51.0
Age ≥ 35 years, n (%; 95% CI)	59 (64.1; 53.9,73.2)
Estimated gestational age at delivery, weeks	
Mean (SD)	36.6 (2.6)
95% CI	36.1–37.1
Median	37.3
Range	24.4–41.7
Route of delivery, n (%; 95% CI)	
Vaginal	4 (4.3; 1.9, 9.3)
Cesarean	88 (95.7; 90.7, 98.1)
Forceps or vacuum assistance, n (%; 95% CI)	0 (0, 2.8)
Premature preterm rupture of membranes, n (%; 95% CI)	7 (7.6; 4.2, 13.5)
Premature delivery, n (%; 95% CI)	
<28 weeks	2 (2.2; 0.7, 6.4)
28–32 weeks	1 (1.1; 0.3, 4.7)
33–35 weeks	13 (14.1; 9.1, 21.1)
Uterine dehiscence, n (%; 95% CI)	1 (1.1; 0.3, 4.7)
Uterine rupture, n (%; 95% CI)	1 (1.1; 0.3, 4.7)
Placenta accreta, n (%; 95% CI)	1 (1.1; 0.3, 4.7)
Placenta previa, n (%; 95% CI)	1 (1.1; 0.3, 4.7)
Adhesions[a], n (%; 95% CI)	10 (11.4; 7.0, 18.0)
Malpresentation of fetus, n (%; 95% CI)	9 (9.8; 5.8, 16.1)

Continued

Table IV *Continued*

Delivery characteristics	N = 92
Estimated blood loss, ml	
Mean (SD)	758.7 (297.1)
95% CI	692.6–824.6
Median	700.0
Range	200–2500
Unknown	8
Post-partum hemorrhage, n (%; 95% CI)	5 (5.4; 2.0, 12.4)
Birthweight, g	
Mean (SD)	3036.1 (669.4)
95% CI	2895.1–3177.1
Median	3140.0
Range	666.7–4560.0
Unknown	3
Apgar, 1 min	
Mean (SD)	7.9 (1.2)
95% CI	7.7–8.2
Median	8
Range	0–9
Unknown	6
Apgar, 5 min	
Mean (SD)	8.8 (1.1)
95% CI	8.5–9.0
Median	9
Range	0–10
Unknown	6

[a]Percentage based on Cesarean deliveries only, $n = 88$.

Table V Characteristics associated with preterm delivery up to 35 weeks of gestation.

Parameter[a]	Estimated coefficient (SE)	95% CI around the coefficient	P-value
Intercept	5.565 (1.166)	3.286, 7.834	<0.0001
Multiple pregnancy (no, yes)	4.534 (1.197)	2.198, 6.862	0.0002
Anterior location of myoma (all other locations, anterior)	2.235 (0.869)	0.544, 3.916	0.01
Number of myomas	0.258 (0.104)	0.054, 0.446	0.01
BMI (kg/m^2) (<25, 25–25.9, 30+)	0.975 (0.499)	−0.006, 1.914	0.05

Results of forward stepwise logistic regression.
SE, standard error of the coefficient.
[a]Parameters are listed in order of entry into the regression model.

of membranes, premature delivery up to 35 weeks of gestational age, hypertension in pregnancy, uterine rupture or dehiscence, abnormal placentation, hemorrhage, malpresentation of the fetus, estimated blood loss, birthweight and Apgar scores.

Statistical methods

Results were primarily descriptive using the mean, SD, 95% confidence intervals (CI), median and range for continuous variables and percentages and CIs for discrete data. CIs around the percentages were calculated using Agresti–Coull limits for binominal CIs. Myomectomy characteristics (number of myomas, myoma size, myoma weight, location, entry into the endometrial cavity and multiple myomectomies) were examined in relationship to three outcomes: spontaneous abortion up to 20 weeks, preterm delivery (up to 35 weeks of gestational age) and time from myomectomy to first conception. Factors associated with spontaneous abortion or with premature delivery were identified using a *t*-test, χ^2 or Fisher's exact statistics. Statistically significant findings were then examined in a forward stepwise logistic regression model with other variables that could increase risk, including maternal age, multiple pregnancy, obesity and hypertension in pregnancy, in order to identify independent associations with each outcome. Ordinary least squares regression was used to identify individual myomectomy characteristics related to the time from surgery to conception as a continuous variable. Significant findings were examined in a multivariate model including maternal age, obesity and hypertension in pregnancy to identify independent associations with the outcome. There were no missing data for the outcomes of interest and no missing value imputations were used for the independent variables in these analyses. *P*-values <0.05 were considered statistically significant. All data computations were executed using SAS software version 9.2.1 (SAS Institute, Cary, NC, USA).

Results

During the time period of this study, 872 women underwent robotic myomectomy. One hundred seven subsequently conceived resulting in 127 pregnancies and 92 deliveries through 2011. One hundred eight RALM were performed in the 107 women who later conceived. Age at the time of myomectomy was 34.8 ± 4.5 years (Table I). The majority of the cohort was Caucasian and classified as either overweight or obese. Over 50% of patients were nulligravid and 88.5% were nulliparous. About 10% had undergone a previous myomectomy or a prior Cesarean delivery. Thirty-three percent (95% CI 24.3, 41.7) had prior gynecologic procedures (e.g. laparoscopy and dilatation and curettage).

Operative time for the robotic procedure averaged just under 3 h (Table II). Estimated blood loss was generally low, but three women (2.8%; 95% CI 0.6, 8.2) received blood transfusions. The uterine size and the myoma size (greatest dimension) were 12.3 ± 3.1 and 7.5 ± 3.0 cm, respectively. The myoma weight was 191.7 ± 144.8 g. The number of myomas removed was 3.9 ± 3.2 with the largest number being 14. The most common locations of the largest incision were the anterior portion of the uterus, posterior aspect and fundal region. Entry of the myoma into the endometrial cavity occurred in ~20% of myomectomies. None of the robotic surgeries resulted in a conversion to laparotomy.

A total of 127 pregnancies occurred in the 107 women including seven twin and two triplet pregnancies. The majority of conceptions were spontaneous. The remainder originated from assisted reproduction techniques (ART), with IVF being the most common (Table III). The time to conception was 12.9 ± 11.5 months. Spontaneous abortions up to 20 weeks occurred in 19% of pregnancies with very few after 14 weeks of gestation. Patient age was unrelated to this outcome (mean age 35.7 ± 4.6 versus 34.6 ± 4.3 years, spontaneous abortion yes versus no, *t*-test $P = 0.21$). In addition, there were two ectopic pregnancies. Women became hypertensive in 12% of pregnancies.

During the study period, there were 92 deliveries (83 singletons, 7 twins, 2 triplets) while 7 pregnancies were ongoing. About two-thirds of the women delivered at age 35 years or older with only 3 women (3.3%; 95% CI 0.7, 9.6) over the age of 43 (Table IV). The gestational age at delivery was 36.6 ± 2.6 weeks. The majority delivered by Cesarean section; <5% delivered vaginally. None required forceps or vacuum assistance. Premature preterm rupture of membranes occurred in seven women. A large proportion of babies were preterm deliveries (up to 35 weeks of gestational age) with 2 at <28 weeks, 1 at 28–32 weeks and 13 from 33 up to 35 weeks.

One pregnancy resulted in uterine rupture and fetal demise and another in uterine dehiscence (Table IV). Abnormal placentation included one occurrence of placenta accreta and one of placenta previa. The placenta accreta did not occur at the site of the hysterotomy incision for the robotic myomectomy. Peri-uterine adhesions were observed in 11% of women who delivered by Cesarean section. Malpresentation of the fetus occurred in <10% of births. Estimated blood loss during delivery was 758.7 ± 297.1 ml. There were five cases of post-partum hemorrhage, two of them requiring blood transfusions (2.2%; 95% CI 0.7, 6.4). One of the patients requiring transfusion was the patient with a documented uterine rupture, and the remaining patient experienced preterm premature rupture of membranes at 17 weeks of gestation and declined any interventions. She ultimately developed chorioamnionitis, sepsis and disseminated intravascular coagulation. The remaining patients had unremarkable post-partum courses.

Birthweight was 3036.1 ± 669.4 g. Apgar scores at 1 and 5 min were ~8 and 9, respectively.

Analysis of the relationship between myomectomy characteristics (number of myomas, myoma size, myoma weight, location, entry into the endometrial cavity and multiple myomectomies) and preterm delivery risk indicated a significantly higher number of myomas removed among women who later had preterm deliveries (*t*-test $P = 0.004$, comparing the mean number of myomas 5.6 ± 3.8 versus 3.5 ± 3.1). Anterior location (of the largest incision) compared with all other sites also was associated with higher preterm delivery rates (χ^2 $P = 0.006$, 27.3% anterior location versus 8.3% all other sites). Both of these findings were significant ($P = 0.01$) in stepwise logistic regression analysis that included multiple births, maternal age, BMI and hypertension in pregnancy (Table V). Other variables associated with increased preterm delivery risk included multiple births ($P = 0.0002$) and a greater BMI ($P = 0.05$). Maternal age, myoma size, myoma weight, entry into the endometrial cavity and previous multiple myomectomies were unrelated to this outcome. Neither patient age nor the characteristics of the myomas were significantly associated with spontaneous abortion or time to conception following myomectomy.

Table VI summarizes the published medical literature on pregnancy outcomes after laparoscopic myomectomy identified through PubMed and Scopus searches. Only one small study by Lönnerfors and Persson (2011) has been published on outcomes after RALM in women who

Table VI Studies on pregnancy and delivery outcomes after laparoscopic myomectomy.

First author (year)	Pts with myoma data	Mean age at myo, years	Mean no. of myomas (range)	Mean size of largest myoma, cm (range)	Enter endometrial cavity, %	No. of pregnancies	Mean time to pregnancy (months)	SAB < 20 weeks, %	Live preterm births, %	Live term births, %	C-section, %	Uterine rupture, %
Robotic surgery												
Pitter *et al* (present study)	107	34.8	3.9 (1–14)	7.5 (3–18)	20.6	127	13.9	18.9	12.6 (up to 35 weeks)	59.8 (5.5% not yet born)	95.7	1.1
Lönnerfors and Persson (2011)	31	Median 35	Median 1 (1–5)	Median 7 (4–11)	NR	18	Median 10	16.7	0	55.6 (16.7% not yet born)	50	0
Conventional laparoscopy												
Liu *et al.* (2011)	83	32	NR (1–8)	5.9 (3–11)	10.8	18	NR	11.1	44.4	44.4	NR	NR
Malzoni *et al.* (2010)	350	Median 34.3	Median 2.5 (1–5)	Median 6.3 (4–9)	NR	59	NR	13.6	5.1	81.4	55.9	0
Kumakiri *et al.* (2008 abstr)	111	NR	3.5	6.6	11.7	111	NR	NR	NR	NR	46.8	NR
Palomba *et al.* (2007, RCT)	68	Median 28	Median 1 (1–3)	Median 7.6 (3–10)	NR (excluded submucosal myomas)	36	Median 5.0	11.1	2.8	86.1	71.9	0
Sizzi *et al.* (2007, multicenter)	2050	36.1	2.3	6.4	NR (excluded some submucosal myomas)	386	NR	19.9	2.3	77.7	78.0	0.3
Paul *et al.* (2006)	115	Median 30	Median 1 (1–5)	Median 5 (3–16)	7.8	141	8.9	19.9	2.1	73.0	82.1	0
Seracchioli *et al.* (2006)	127	33.7	2.6	5.4	3.9	158	17.9	27.2	1.3	65.8	74.5	0
Kumakiri *et al.* (2005)	40	34.5	3.2	6.8	5.0	47	13.0	23.9	2.2	67.4	40.6	0
Campo *et al.* (2003)	68	34.3	2.9 (1–7)	4.4 (3–8)	NR	14	NR	7.1	0	92.9	30.8	0

Seracchioli *et al*. (2003)	34	34.9	2.8	6.5 (4–15)	100% (by study design)	9	<12	22.2	0	77.8	85.7	0
Soriano *et al*. (2003)	88	36.1	1.7 (1–4)	6.2 (3–11)	0 (by study exclusion)	44	7.5	13.6	0	77.3	23.5	0
Landi *et al*. (2003)	72	32.5	3.1	5.4 (1–13)	8.3	76	NR	15.8	3.9	71.1	45.6	0
Malzoni *et al*. (2003)	144	33.7	NR	7.8 (5–18)	NR	26	<12	15.4	0	80.8	57.1	0
Rossetti *et al*. (2001)	29	Median 36	2.3 (1–7)	5.4 (1–10)	NR (excluded submucosal myomas)	21	7.6	19.0	14.3	52.4	71.4	0
Stringer *et al*. (2001)	7	34.4	4.3 (1–9)	8.0	100% (by study design)	7	NR	0	14.3	57.1	80.0	0
Seracchioli *et al*. (2000)	66	34.0	2.9	7.1	3.0	30	NR	20.0	3.3	66.3	65.0	0
Seinera *et al*. (2000)	54	NR	1.2 (1–3)	3.9 (3–8)	6.2	65	9.0	12.3	3.1	83.1	80.4	0
Dubuisson *et al*. (2000)	98	33.2	1.8	4.8	6.1	145	Median 16.0	26.4	9.7	59.7	42.0	1
Nezhat *et al*. (1999)	31	34.5	3.0	5.9 all	NR	42	NR	20.0	2.50	72.5	78.6	0
Roemisch *et al*. (1996)				6.3 max diameter								
Ribeiro *et al*. (1999)	161	36.4	NR	6.0	NR (all 18 with intramural myomas)	18	NR	22.2	0	77.8	57.1	0
Stringer *et al*. (1997)	49	36.7	NR	NR (largest = 7 cm)	16.3	7	NR	28.6	0	42.9	100.0	0
Dubuisson *et al*. (1996)	21	37.4	2.2 (1–10)	6.2 (5–10)	NR (all intramural myomas)	7	NR	14.3	0	71.4	80.0	0
Miller *et al*. (1996)	40	NR	(1–5)	(4–10)	NR	30	NR	13.3	0	86.7	NR	0

Pts, patients; Myo, myomectomy; NR, not reported; SAB, spontaneous abortion.

had up to five deep intramural myomas measuring 11 cm or less. The other listed papers describe studies of pregnancy outcomes following traditional laparoscopic myomectomy. Many of these also excluded women based on the number or size of myomas. The examined studies reported spontaneous abortions in 7–29%, live preterm births in 0–44% and uterine rupture in 0–1% of all pregnancies followed.

Discussion

This report is the first to describe pregnancy outcomes in a large cohort of women who had undergone a robotic myomectomy. Women in this series had obstetrical outcomes that were comparable with parameters described in the literature following laparoscopic myomectomy (Table VI). This is especially reassuring given that the women in this group were generally of advanced maternal age and overweight, and had a high prevalence of infertility and multiple births, all factors that are associated with pregnancy complications (Spellacy *et al*., 1990; Baetan *et al*., 2001; Jackson *et al*., 2004; Cleary-Goldman *et al*., 2005). Furthermore, findings at the time of Cesarean section revealed a very low rate of pelvic adhesion formation (11.4%), providing additional evidence to support this minimally invasive approach for treatment of uterine fibroids.

Major adverse outcomes were uncommon. However, one case of uterine rupture was reported in this series with a resultant rate of 1.1%. This uterine rupture occurred in a patient who conceived 18 weeks after myomectomy and had no history of prior abdominopelvic surgery. Ten myomas were removed weighing 256 g, with the largest 10 cm in diameter on the anterior surface of the uterus. The endometrial cavity was not entered. Hysterotomies were performed using a monopolar electrosurgical instrument, and a multilayered closure was performed. The uterine rupture occurred on the posterior fundal aspect of the uterus at ~33 weeks of gestation during precipitous labor. In addition, one uterine dehiscence was noted at the time of delivery as an incidental finding and occurred in a patient with no remarkable surgical history or myoma characteristics; however, she was carrying twins and delivered at term. There was no adverse outcome on either mother or infant. In that case a monopolar electrosurgical instrument was used. In our series, 34% of myomectomies were performed using monopolar electrosurgical energy.

The rate of uterine rupture in this study is consistent with data reported for laparoscopic and open myomectomy, and lower than the estimated risk of uterine rupture after a classical Cesarean section (Dubuisson *et al*., 2000; Stotland *et al*., 2002). In a recent review of risk factors for uterine rupture after laparoscopic myomectomy, Parker *et al*. (2010) identified minimizing the use of electrosurgery and performing multilayered closures as techniques that could decrease the risk of rupture. An advantage of RALM is the ability to perform an identical multilayer closure to the abdominal approach that controls hemostasis without the need for significant use of electrosurgical instruments. Owing to the risks of electrosurgery, ultrasonic energy can be utilized with the robot to perform the hysterotomy. The robotic harmonic shears are unable to articulate in a similar manner to all other robotic instruments, thus losing two of the seven degrees of freedom in movement. Despite this limitation, the surgeons in this study who exclusively utilized the robotic harmonic shears have not been limited in their ability to access or enucleate myomas, regardless of the location.

The observed miscarriage rate (~19%) was in the range of rates reported in the conventional laparoscopic myomectomy literature (Table VI) and was lower than the 28% shown by Lönnerfors and Persson (2011) in their prospective study of pregnancy in 31 women following robotic surgery for deep intramural myomas: results in the latter report also indicated that all miscarriages occurred in pregnancies resulting from IVF. In contrast, our data show that miscarriages up to 20 weeks were about evenly divided among those who conceived spontaneously and those who used ART.

We analyzed our data to determine if there was any relationship between myoma characteristics and pregnancy outcomes. Myoma number and anterior location were significantly associated with preterm delivery up to 35 weeks of gestational age, even after adjustment for other risk factors for preterm delivery. The published myomectomy literature has limited comparable data but Roemisch *et al*. (1996) reported that women who delivered at term had significantly fewer myomas (1.9 versus 4.8, $P < 0.01$) than the group of women who delivered preterm, miscarried or had ectopic pregnancies. It should also be noted that the maximum myoma number and size as well as the proportion of hysterotomies with entry into the endometrial cavity were greater in our study than in most studies of women undergoing conventional laparoscopic myomectomy (Table VI). These findings regarding the increased risk of preterm delivery associated with certain myoma characteristics need to be further evaluated in a large-scale prospective investigation.

Although this study was performed to investigate the long-term outcome of pregnancy, we also observed a low rate of adhesion formation (11.4%) at the time of Cesarean delivery in these women. Given that this population often desires fertility and that adhesions are known to cause infertility (Diamond and Freeman, 2001), it is an advantageous finding that the risk of adhesions may be lower than has been reported in both abdominal myomectomy and laparoscopic myomectomy patients (Tinelli *et al*., 2011; Kumakiri *et al*., 2012). Since adhesion formation following myomectomy may reduce fertility, formal second-look laparoscopic studies in non-pregnant women following RALM may be needed for a more definitive measure of post-operative adhesion formation.

A limitation of our study is the inability to generalize these findings to other practices. All surgeons in this study were experienced robotic surgeons and no conversions to laparotomy occurred. The use of MRI images to determine the exact location of the myomas removed and also suturing of the hysterotomy defect in a multilayered fashion help to minimize excessive bleeding, which typically results in conversions. In addition, the women in our study were generally of advanced maternal age, overweight and obese, and had a high prevalence of infertility treatment and multiple births. These risk factors have been associated with higher rates of miscarriage, hypertensive complications, gestational diabetes and preterm delivery (Spellacy *et al*., 1990; Baetan *et al*., 2001; Jackson *et al*., 2004; Cleary-Goldman *et al*., 2005). Furthermore, women who have IVF pregnancies are also at a higher risk for having preterm deliveries and infants of low birthweight (Jackson *et al*., 2004; Tomic and Tomic, 2011). Seventeen percent of our patients ($n = 16$) delivered before 35 weeks gestational age; however, upon further review of these deliveries, a clear causative relationship between their prior myomectomy and an indication for delivery was not identified. For example, five of the deliveries occurred in women carrying twin or triplet pregnancies, three occurred in the setting of severe pre-eclampsia and one in a patient with a prior history of cervical incompetence. Additionally, given the absence of pregnancy outcome data after robotic myomectomy in the literature, obstetricians conservatively managed these pregnancies as if they had prior classical Cesarean sections.

Another limitation of this study is that because of its retrospective nature and the high prevalence of infertility patients in this cohort, the data cannot be used to counsel women who are undergoing RALM about fertility rates after surgery. Although compliance was not universal, our patients were routinely advised to wait 3–4 months prior to attempting conception or initiating infertility treatment but this was not a prospective study and did not include all women who attempted conception after surgery and were perhaps unsuccessful. In addition, some patients who became pregnant may not have been captured by our methods of ascertainment. Thus, we cannot provide data regarding a true average of time to conception. Prospective studies are needed to obtain these pregnancy rates and to allow for a direct comparison of pregnancy outcomes in women undergoing RALM versus open or laparoscopic myomectomy.

This multicenter study allowed us to evaluate pregnancy outcomes in a larger group of women than could have been accomplished by one or two centers alone. Our study observed pregnancy outcomes after RALM that were comparable with those reported in the conventional laparoscopic literature. Robotic surgical techniques can overcome some of the shortcomings of traditional laparoscopy (Barakat *et al*., 2011), thus facilitating the use of minimally invasive surgery over laparotomy for more gynecologic surgeons (Payne and Pitter, 2011). This enabling treatment modality may offer a minimally invasive alternative for uterine preservation for women with uterine fibroids.

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Authors' roles

M.C.P. satisfied the requirements for authorship by making a substantial contribution to the conception and design of the manuscript, drafting parts of the main body, discussion section and abstract, revising it critically for intellectual content and approving the final version for publication. A.R.G. satisfied the requirements for authorship by participating in the acquisition and analysis of data, drafting of the Materials and Methods section of the paper and interpretation of the data, revising it critically for intellectual content and approving the final version for publication. L.M.B. satisfied the requirements of authorship by participating in the acquisition of data, revising the manuscript critically for intellectual content and approving the final version submitted for publication. J.S.L. satisfied the requirements for authorship by assisting Dr Pitter in the acquisition of data, drafting parts of the initial abstract and approving the final version submitted for publication. S.S.S. satisfied the requirements of authorship by helping with the design of the study, analyzing and interpreting the data, drafting the discussion section of the article, revising it critically for intellectual content and approving the final version for publication.

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Conflict of interest

Dr Pitter is on the Speaker's Bureau for Intuitive Surgical. None of the other authors have any relevant disclosures.

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