

# Impact of subserosal and intramural uterine fibroids that do not distort the endometrial cavity on the outcome of in vitro fertilization–intracytoplasmic sperm injection

Flávio Garcia Oliveira, M.D.,<sup>a</sup> Vicente G. Abdelmassih, M.D.,<sup>a</sup>  
Michael P. Diamond, M.D.,<sup>b</sup> Dimitri Dozortsev, M.D.,<sup>a</sup> Nilson R. Melo, M.D.,<sup>a</sup> and  
Roger Abdelmassih, M.D.<sup>a</sup>

São Paulo, Brazil and Detroit, Michigan

**Objective:** To further evaluate the effects of intramural and subserosal uterine fibroids on the outcome of IVF-ET, when there is no compression of the endometrial cavity.

**Design:** Retrospective, matched-control study from January 2000 to October 2001.

**Setting:** Private IVF center.

**Patient(s):** Two hundred forty-five women with subserosal and/or intramural fibroids that did not compress the uterine cavity (fibroid group) and 245 women with no evidence of fibroids anywhere in the uterus (control group).

**Intervention(s):** In vitro fertilization–intracytoplasmic sperm injection (IVF-ICSI) cycles.

**Main Outcome Measure(s):** The type of fibroid (intramural, subserosal), number, size (cm), and location of intramural leiomyomas (fundal, corpus) were recorded. Outcomes of IVF-ICSI cycles were compared between the two groups.

**Result(s):** There was no correlation between location and number of uterine fibroids and the outcomes of IVF-ICSI. Patients with subserosal or intramural fibroids <4 cm had IVF-ICSI outcomes (pregnancy, implantation, and abortion rates) similar to those of controls. Patients with intramural fibroids >4.0 cm had lower pregnancy rates than patients with intramural fibroids ≤4.0 cm. There were no statistical differences related to delivery rates (31.5% vs. 32%, respectively) between all patients with fibroids and controls. Premature delivery rates for singleton gestations were 10% vs. 8%, respectively, in all patients with fibroid and controls.

**Conclusion(s):** Patients having subserosal or intramural leiomyomas of <4 cm not encroaching on the uterine cavity have IVF-ICSI outcomes comparable to those of patients without such leiomyomas. Therefore, they might not require myomectomy before being scheduled for assisted reproduction cycles. However, we recommend caution for patients with fibroids >4 cm and that such patients be submitted to treatment before they are enrolled in IVF-ICSI cycles. Whether or not women with fibroids > 4 cm would benefit from fibroid treatment remains to be determined. (Fertil Steril® 2004;81:582–7. ©2004 by American Society for Reproductive Medicine.)

**Key Words:** Leiomyoma, IVF-ICSI outcomes, myomectomy, uterine cavity

Uterine fibroids (leiomyomas) contribute to a variety of clinical problems, including infertility, recurrent pregnancy loss, menorrhagia, and pelvic pressure and fullness, as well as complications of pregnancy. Although larger fibroids, fibroids of any size that compress the uterine cavity, or submucosal fibroids might be more likely to affect pregnancy initiation and

outcome, the impact on infertility of smaller intramural or subserosal leiomyomas that do not compress the uterine cavity is controversial.

The benefit of myomectomy for the treatment of infertility in this group of patients also remains unclear. The literature tends to support an increased conception rate in the first year

Received April 9, 2003;  
revised and accepted  
August 7, 2003.

Presented in part at the  
19th Annual Meeting of the  
European Society of  
Human Reproduction and  
Embryology in Madrid,  
Spain, June 29–July 2,  
2003.

Reprint requests: Flávio  
Garcia Oliveira, M.D.,  
Clínica e Centro de  
Pesquisa em Reprodução  
Humana “Roger  
Abdelmassih,” Rua  
Maestro Elias Lobo, 805,  
São Paulo 01433-000,  
Brazil (FAX: 55-11-  
38858605; E-mail:  
flaviogo2@uol.com.br).

<sup>a</sup> Clínica e Centro de  
Pesquisa em Reprodução  
Humana “Roger  
Abdelmassih,” São Paulo,  
Brazil.

<sup>b</sup> Hutzel Hospital, Wayne  
State University, Detroit,  
Michigan.

0015-0282/04/\$30.00  
doi:10.1016/j.fertnstert.2003.  
08.034

after a myomectomy (1, 2). Nevertheless, the gains in fertility potential must be balanced against adverse effects, including postsurgical adhesions, intrauterine synechiae formation, and tubal damage. Moreover, the recurrence of leiomyomas after myomectomy is >25% (1). The literature also is controversial regarding the impact of myomectomy on the pregnancy outcomes for patients undergoing assisted reproductive technologies (ART) when the identified uterine leiomyomas do not compress the uterine cavity.

It has been our practice to counsel patients with large uterine fibroids (which we have defined as >7 cm) or those having fibroids that are encroaching on the endometrial cavity to undergo treatment before participation in the assisted reproduction programs.

However, the appropriate counseling of women regarding the effects of intramural and subserosal uterine fibroids on the outcome of IVF-intracytoplasmic sperm injection (ICSI) when there is no compression of the uterine cavity has been less clear. Several studies have reported that the presence of uterine fibroids affects conceptions after IVF (3, 4), whereas others (5) showed no differences in the outcomes of IVF cycles of patients with smaller intramural fibroids that do not compress the uterine cavity. The objective of the present study was to further evaluate this issue by examining the IVF-ICSI outcomes in women with such uterine leiomyomas.

## MATERIALS AND METHODS

Data were collected by retrospective review of all patients with uterine fibroids who met the criteria detailed below, from a private IVF-ET center. This study was approved by the local ethics committee of Clínica e Centro de Pesquisa em Reprodução Humana "Roger Abdelmassih," Brazil, which corresponds to local institutional review board approval.

In this study, 245 women with small uterine leiomyomas (<7 cm mean diameter, as defined below) discovered on initial routine screening transvaginal sonography (TVS) performed in preparation for IVF-ICSI (fibroid group) were retrospectively matched by age and number of collected oocytes with 245 patients at the same period of treatment (same age and same number of collected oocytes) who did not demonstrate fibroids anywhere in the uterus (control group). Only the first cycle of these patients from January 2000 to October 2001 were included. Both the fibroid and control groups had no history of prior myomectomy.

Diagnosis of uterine fibroids was done by TVS performed with a multifrequency endovaginal transducer (Acusom 128XP4; Acuson Computed Sonography, Mountain View, California). The type of fibroid (intramural, subserosal), number, size (cm), and location of intramural leiomyomas (fundal, corpus) were recorded. The dimension of each fibroid was determined from the mean value (cm) of the two

largest diameters. Women with intracavitary or submucosal fibroids were excluded.

We defined a patient with "no compression of the uterine cavity" as a patient in whom the endometrium-myometrium transition was clearly seen as a line without distortion of its contours by the presence of the fibroids in both TVS sagittal and transverse multiple sections of the uterus. Also, findings on a hysterosalpingogram performed within the last 12 months were reported as normal for all patients. The films were reviewed by the staff, and the normalcy of the uterine cavity by hysterosalpingography was confirmed for all patients.

Cycles of IVF-ET were carried out after the use of a GnRH agonist (Reliser; Serono, São Paulo, Brazil) and recombinant gonadotropins (Gonal F; Serono) for controlled ovarian hyperstimulation. All patients were submitted to the same protocol of ovarian hyperstimulation starting in the luteal phase of the previous cycle. Serum E<sub>2</sub> levels and transvaginal ultrasonography were used as appropriate for monitoring the cycles. Conventional methods for microinjection of oocytes (ICSI) and in vitro culture of oocytes and embryos were performed in all oocytes in all patients in both groups, as previously described (6). Immediately before uterine replacement, the embryos were examined with an inverted microscope and their morphologic appearance and number of cells recorded. The embryos that had seven or more cells, symmetric blastomeres, and <10% cytoplasmic fragmentation on day 3 postaspiration were scored as good embryos.

Uterine replacement of embryos transcervically was performed 72 hours after oocyte retrieval with a Wallace catheter (Sims Portex Ltd., Hythe, United Kingdom) under ultrasound guidance. Embryo transfer was withheld in women at high risk for severe ovarian hyperstimulation syndrome according to following criteria: E<sub>2</sub> levels >7000 pg/mL on the day of hCG administration, ovaries >8.0 cm in their largest diameter with more than 10 follicles in each ovary, and signs of painful abdominal distention. Luteal support was performed with micronized P 800 mg/day vaginally, starting on the day of oocyte retrieval. Clinical pregnancy was diagnosed when fetal heartbeats were visualized on transvaginal ultrasound examination. The outcomes of the IVF-ICSI cycle were analyzed in all patients. Clinical data were evaluated and compared by paired *t*-test,  $\chi^2$  test, or Fisher exact test. Significance was defined as *P*<.05. Data are expressed as mean  $\pm$  SD.

## RESULTS

In the period of study, 17% of the patients (280 of 1602) had at least one identified uterine leiomyoma. Among these 280 women, 35 were excluded: 25 because there was a uterine fibroid >7 cm mean diameter that was compressing the uterine cavity or that was located in the uterine cavity,

and 10 who had previously undergone a myomectomy procedure.

Because the groups were matched by age and number of collected oocytes there were no differences between the fibroid and the control groups, respectively ( $35.1 \pm 3.6$  years vs.  $35.1 \pm 3.6$  years, NS, paired *t*-test; and  $12.3 \pm 4.5$  oocytes vs.  $12.2 \pm 4.1$  oocytes, NS, paired *t*-test). The mean age of the patients in the present study was approximately 35 years. Most of our patients (51%) belonged to the  $\geq 35$ -years age group, in both groups.

Male factor contributed to the etiology of infertility for most cases in both fibroid and control groups (47% vs. 51%, respectively, NS,  $\chi^2$  test). Tubal factor was responsible for 33% of infertility in the fibroid group and 28% in the control group (NS,  $\chi^2$  test). Combined infertility factors accounted for 10% and 13%, respectively, in the fibroid and control groups (NS,  $\chi^2$  test). The occurrence of unexplained infertility was not different in distribution between the fibroid and control groups (10% vs. 8%, respectively, NS,  $\chi^2$ ). There were 10 patients who had no embryo transfer in the fibroid group (5 owing to no available embryo to transfer and 5 owing to hyperstimulation syndrome), whereas 12 patients had no transfer in the control group (5 owing to hyperstimulation syndrome and 7 owing to no available embryo to transfer).

The fibroid group consisted of patients with only subserosal fibroids ( $n = 82$ ), only intramural fibroids ( $n = 130$ ), and combined subserosal and intramural fibroids ( $n = 33$ ) (Table 1). The number of fibroids per patient ranged from 1 to 4 (mean  $2.0 \pm 0.4$  fibroids per patient). The size (mean diameter) of the largest fibroid per patient ranged from 0.4 to 6.9 cm (mean  $1.9 \pm 1.3$  cm) (all fibroids, intramural and subserosal). Approximately 70% of the leiomyomas (all fibroids, subserosal and intramural) ranged in size between 0.4 and 4.0 cm mean diameter. The size of the largest intramural leiomyoma was  $2.1 \pm 1.2$  cm. We found no isthmic fibroids in patients with intramural fibroids and only one cornual fibroid in the group with subserosal fibroids, which was considered fundal in location. Most subserosal and intramural fibroids were at a fundal location (66% and 68%, respectively). Corporal fibroids (34% and 32%, respectively, of subserosal and intramural fibroids) were equally distributed between anterior and posterior locations.

The number and quality of transferred embryos were compared between the fibroid and control groups and showed no differences ( $3.2 \pm 1.3$  vs.  $3.3 \pm 1.4$ , NS, paired *t*-test). Implantation rates were 21% and 23% in the control and fibroid groups, respectively (NS,  $\chi^2$  test). Patients with subserosal uterine fibroids had IVF-ICSI outcomes (pregnancy, implantation, and abortion rates) similar to those from the control group (data not shown).

There was no correlation between location and number of intramural uterine fibroids and the outcomes of IVF-ICSI

**TABLE 1**

Description of the fibroid group.

	No. of patients	Pregnancy rate No. (%)	Abortion rate No. (%)
No. of fibroids			
1	152	75 (49)	20 (27)
2	66	31 (47)	15 (48)
3	18	7 (39)	0 (0)
4	9	4 (44)	1 (25)
Type of fibroid			
Subserosal (SS)	82	41 (50)	15 (35)
Intramural (IM)	130	63 (48)	17 (28)
IM-SS	33	13 (40)	4 (31)
Location (IM)			
Fundal	110	53 (48)	15 (28)
Corpus	53	23 (43)	6 (26)
Size of IM fibroid (cm)			
0.4–2.0	64	34 (53)*	9 (26)
2.1–4.0	58	30 (51)*	7 (23)
4.1–6.9	41	12 (29)	5 (41)

Note: \*  $P = .025$  ( $\chi^2$  for trend). There was a significant linear trend among the ordered categories. All other % were not statistically different ( $\chi^2$  test, Fisher exact test).

Oliveira. Uterine fibroids and IVF-ICSI outcomes. *Fertil Steril* 2004.

(Table 1). Patients with intramural uterine fibroids  $\leq 4.0$  cm mean diameter had IVF-ICSI outcomes (pregnancy, implantation, and abortion rates) similar to those from the control group (Table 1). However, the pregnancy rate in patients with intramural fibroids  $> 4.0$  cm diameter ( $n = 41$ ) was lower than in patients with smaller intramural fibroids (i.e., 2.1–4.0 cm [ $n = 58$ ] and 0.4–2.0 cm [ $n = 64$ ]; 29% vs. 51% vs. 53%, respectively;  $P = .025$ ,  $\chi^2$  for trend) (Table 1). Additionally, there was a trend toward lower implantation rates in patients with intramural fibroids  $> 4.0$  cm than in patients with smaller intramural fibroids ( $> 4.0$  cm: 7.5%; 2.1–4.0 cm: 20.8%; 0.4–2.0 cm: 21.4%;  $P = .06$ ,  $\chi^2$  for trend).

There were no statistical differences relating to delivery rates between the fibroid and control groups (31.5% vs. 32%, respectively; NS,  $\chi^2$  test). The abortions (first and second trimesters) and deliveries by week (live birth) are shown in Table 2. Multiple pregnancy rates were 35% and 37%, respectively in the fibroid and control groups (NS, Fisher exact test). Premature delivery rates for singleton gestations were 10% and 8%, respectively, in the fibroid and control groups (NS, Fisher exact test). Overall premature delivery rates for multiple gestations (twins, triplets, and quadruplets) were 41% and 45%, respectively, in the fibroid and control groups (NS, Fisher exact test) (Table 2).

## DISCUSSION

Most women with uterine fibroids are asymptomatic and fertile. However, in patients older than 30 years, uterine

TABLE 2

Comparison of IVF-ICSI outcomes according to the number of pregnancies, abortions (first and second trimesters), and deliveries (with live birth) by week.

	Control group (n = 245)	Fibroid group* (n = 245)
Pregnancies	110 (45)	117 (48)
First trimester abortion <sup>a</sup>	31 (28)	37 (31)
Second trimester abortion <sup>b</sup>	1 (0.9)	2 (1.7)
22–26 weeks	2	2
26–30 weeks	3	5
30–34 weeks	6	5
34–37 weeks	6	4
>37 weeks	61	61
Total DR (live birth)	78/245 (32)	77/245 (31.5)
Preterm DR for singletons	4/49 (8)	5/50 (10)
Preterm DR for multiples	13/29 (45)	11/27 (41)

Note: Values are n or n (%). DR = delivery rate; NS = not significant. \*  $P = NS$  (fibroid group vs. control group for all values, Fisher exact test).

<sup>a</sup> <14 weeks.

<sup>b</sup> 14–22 weeks.

Oliveira. Uterine fibroids and IVF-ICSI outcomes. *Fertil Steril* 2004.

fibroids occur with increasing frequency, unfortunately at a time when these women are hoping for pregnancy after periods of infertility (7). The higher percentage (17%) of patients identified as having uterine fibroids in this study might be because every patient attending our assisted reproduction program is scanned by TVS for genital tract abnormalities, in addition to other examinations. Most patients of our study group (51%) belonged to the 35–41-year age group. These women probably delayed childbearing because they pursued higher education or career recognition (8). There is also a higher proportion of uterine leiomyomas among older, infertile females.

Uterine leiomyoma might act as a restraint to conception and successful outcome of pregnancies. However, the impact of uterine leiomyomas on infertility has not been clearly established. A submucosal or an intramural leiomyoma might disturb uterine contractility, and might interfere with sperm migration, ovum transport, or implantation of the embryos, with resultant infertility (9). Although not relevant to women in this study undergoing ART, an intramural fibroid close to the intramural tubal segment might lead to occlusion. Additionally, a large cornual fibroid might impair ovum retrieval by the tubes (10). Also, uterine leiomyomas might be related to implantation failure or first-trimester abortion due to focal endometrial vascular disorders, as well as endometrial inflammation, secretion of vasoactive substances, or an altered endometrial biochemical environment (9, 11, 12).

Concerning the possible detrimental effects of uterine leiomyomas on implantation and uterine contractility, the relationship has to be considered between smaller intramural

or subserosal uterine leiomyomas and an unsuccessful outcome in IVF-ICSI cycles. In a study of the effect of uterine leiomyoma on the outcome of IVF cycles, Seoud et al. (13) reported ongoing pregnancy rates in IVF patients having intramural uterine leiomyomas comparable to those with prior myomectomy. Unfortunately, this study did not report the size of fibroids and whether they impinged on the uterine cavity. However, they found no significant difference in the total and ongoing pregnancy rates between patients with prior myomectomy and all IVF patients. The first publication on small intramural uterine fibroids not compressing the uterine cavity and IVF outcome, by Fahri et al. (14), concluded that there was no effect on implantation rates. This study also did not report the size of the uterine fibroids. However, other studies have identified conflicting results.

Three studies on the effects of leiomyomas on the outcome of ART treatments diverged from our study and the study by Farhi et al. regarding implantation rates (3, 4, 15), whereas another study with the same objective (16) supported the Farhi et al.'s study and our conclusions that these fibroids do not reduce implantation rates, despite the fact that we found a trend to lower implantation rates in patients with intramural fibroids >4.0 cm mean diameter compared with patients with smaller intramural fibroids ( $\leq 4.0$  cm). The study by Hart et al. (15) on the effects of intramural uterine fibroids not encroaching on the uterine cavity on the outcomes of assisted conception reported lower ongoing clinical pregnancy rates in patients with intramural fibroids  $\leq 5$  cm compared with a control group that was significantly younger. These authors did not report data regarding delivery rates, and they included in their study patients who had previously undergone miomectomy.

Of the four studies mentioned above two were matched-control studies (4, 16), in which a lower delivery rate in those patients with intramural fibroids was seen despite there being no statistical differences. Another matched-control study, by Check et al. (5), is in agreement with the aforementioned studies. We, however, did not observe this, even though the size of intramural fibroids in the present study was smaller than those in the Stovall et al. (4) and Ramzy et al. studies (16), and larger than in the Check et al. (5) study. Most intramural fibroids in this study were fundal in location, which was similar to the findings of Stovall et al. but different from those of Check et al., who found only half of the fibroids at the fundal location (Table 3).

In a retrospective, case-controlled analysis in patients who had not undergone myomectomy, Davis et al. (2) noted that the size, location, or total number of leiomyomas also had no impact on pregnancy outcome. The fact that in the current investigation no differences in delivery rates were noted between age-matched groups would confirm these findings. However, in the present study, we observed that patients with intramural fibroids >4.0 cm mean diameter had lower pregnancy rates than patients with smaller intramural

TABLE 3

Comparison of mean size and location of intramural fibroids and pregnancy outcomes according to several studies.

Authors, date (reference)	Mean size IM fibroids (cm)	Fundal location of IM fibroids (% of patients)	Delivery rates %
Stovall et al., 1998 (4)	2.9	93	33
Ramzy et al., 1998 (16)	3.2	NG	23.1
Check et al., 2002 (5)	1.5	50	22.9
Present study	2.1	68	32

Note: IM = intramural; NG = not given.

Oliveira. Uterine fibroids and IVF-ICSI outcomes. *Fertil Steril* 2004.

fibroids, despite few patients being analyzed in this group (Table 1).

A study by Surrey et al. (17) noted a significant decrease in multiple implantation rates in women with intramural leiomyoma and hysteroscopically normal uterine cavities who were <40 years old and undergoing IVF-ET, in comparison with age-matched controls. Trends toward lower clinical pregnancy and delivery rates that failed to reach statistical significance were also found. This latter finding might have been a function of sample size. However, in the present study, multiple pregnancy rates were not different between the two groups.

Myomectomy is usually performed for women who are concerned with preserving or enhancing their reproductive potential (1). Rosenfeld (18) reported a pregnancy rate of approximately 65% after myomectomy among 23 patients with unexplained infertility and uterine fibroids, none of which were submucous in location. Dubuisson et al. (19) reported a mean intrauterine pregnancy rate after myomectomy via laparotomy of approximately 54%. Despite relatively higher pregnancy rates reported by the aforementioned studies, there have been other reports reflecting concerns about the sequelae of myomectomy. The development of abdominal and pelvic adhesions has been reported after myomectomy performed either with laparotomy (20) or laparoscopy (21). Complications such as blood loss and infections also have to be considered (20).

In our series, we did not include patients with a history of myomectomy. Our aim was to assess one question: do small subserosal or intramural uterine fibroids with no compression on the uterine cavity have any impact in the outcomes of IVF-ICSI? To answer this question, we compared the IVF-ICSI outcomes of patients with no identified fibroid by TVS with those with uterine leiomyoma identified by TVS and retrospectively matched them by age and number of collected oocytes.

Some studies have shown that TVS alone does not provide sufficient accuracy to differentiate the intramural leiomyomas from submucous type II leiomyomas or to exclude distortion of the uterine cavity. Hysterosonography, hysterosalpingography, or hysteroscopy in combination with TVS provide alternative options for an exact diagnosis of the type of fibroid and for determining possible compression of the uterine cavity (22). We included in this study only patients in whom the endometrium–myometrium transition was clearly seen as a line without distortion of its contours by the presence of fibroids in both TVS sagittal and transverse multiple sections of the uterus. For all these patients, findings on hysterosalpingography performed within the last 12 months were reported as normal.

In the present study we found different pregnancy rates in patients with leiomyomas according to the size of intramural fibroids and type of leiomyoma. The pregnancy rates in patients with subserosal uterine leiomyomas, with intramural uterine leiomyomas  $\leq 4$  cm, and with no uterine leiomyoma were comparable. The implantation rates were also similar among these groups. However, patients with intramural fibroids  $>4.0$  cm mean diameter had lower pregnancy rates and a trend to lower implantation rates than patients with smaller intramural fibroids ( $\leq 4.0$  cm) or subserosal fibroids.

There was no significant differences in the abortion rates and the preterm delivery rates for singleton gestations among all patients with uterine leiomyoma (31% and 10%, respectively) as compared with patients with no leiomyoma (28% and 8%, respectively). These rates in our study of patients with uterine leiomyoma were similar to those previously reported in the literature (23), despite the higher abortion rates observed in the present study. A possible explanation for this latter fact is the high percentage of patients  $>35$  years old in our study. It is well established that there is an increasing incidence of chromosomal abnormalities in the oocytes of older patients, especially after 35 years, and this condition might affect the outcome of pregnancy obtained after IVF-ICSI (24).

Overall, from the analysis of the data of the present study and others (5, 17) and because of the relatively high delivery rate observed in all studies (live birth), one can suggest that there does not seem to be a likely beneficial value to performing myomectomy before IVF-ICSI to improve the IVF-ICSI outcomes for subserosal or intramural leiomyomas  $\leq 4$  cm not involving the uterine cavity. The best management of patients in whom the largest intramural fibroid is 4–7 cm mean diameter and does not encroach on the uterine cavity is less clear; our data suggest that this group of patients might benefit from leiomyoma treatment before enrollment in a program of IVF-ICSI. Further studies are necessary to confirm whether myomectomy before IVF-ICSI will improve the outcomes of this group of patients. A randomized, multicenter, controlled, cooperative study (as proposed by Check et al. [5]) to assess the value of myomectomy could

lead us to a better understanding of the risk/benefit ratio of such a procedure in these patients.

## References

1. Verkauf BS. Myomectomy for fertility enhancement and preservation. *Fertil Steril* 1992;58:1–15.
2. Davis J, Ray-Mazumder S, Hobel C, Baley K, Sassoon D. Uterine leiomyomas in pregnancy: a prospective study. *Obstet Gynecol* 1990;75:41–4.
3. Eldar-Geva T, Meagher S, Healy D, MacLachlan V, Breheny S, Wood C. Effect of intramural, subserosal, and submucosal uterine fibroids on the outcome of assisted reproductive technology treatment. *Fertil Steril* 1998;70:687–91.
4. Stovall DW, Parrish SB, Van Voorhis BJ, Hahn SJ, Sparks AET, Syrop CH. Uterine leiomyomas reduce the efficacy of assisted reproduction cycles. *Hum Reprod* 1998;13:192–7.
5. Check JH, Choe JK, Lee G, Dietterich C. Intramural leiomyoma and implantation rates. *Hum Reprod* 2002;17:1244–8.
6. Abdelmassih R, Sollia S, Moretto M, Acosta AA. Female age is an important parameter to predict treatment outcome in intracytoplasmic sperm injection. *Fertil Steril* 1996;65:573–7.
7. Verkauf BS. The myomatous uterus and reproductive failure. Diagnostic aids for planning therapy. *Infertil Reprod Med North Am* 1995;6:103–34.
8. Mosher WD, Pratt WF. Fecundity and infertility in the United States: incidence and trends. *Fertil Steril* 1991;56:192–3.
9. Richards PA, Richards PDG, Tiltman AJ. The ultrastructure of fibromatous myometrium and its relation to infertility. *Hum Reprod Update* 1998;4:520–5.
10. Ingersoll FM. Fertility following myomectomy. *Fertil Steril* 1963;14:596–602.
11. Deligdish L, Lowenthal M. Endometrial changes associated with myomata of the uterus. *J Clin Pathol* 1970;23:676–80.
12. Buttram VC, Reiter RC. Uterine leiomyomata: etiology, symptomatology, and management. *Fertil Steril* 1981;36:433–45.
13. Seoud MA, Patterson R, Mausher SJ, Coddington CC 3rd. Effects of myomas or prior myomectomy on in vitro fertilisation (IVF) performance. *J Assist Reprod Genet* 1992;9:217–21.
14. Fahri J, Ashkenazi J, Feldberg D, Dicker D, Orvieto R, Ben Rafael Z. Effect of uterine leiomyomata on the results of in vitro fertilization treatment. *Hum Reprod* 1995;10:2576–8.
15. Hart R, Khalaf Y, Yeong C, Seed P, Taylor A, Braude P. A prospective controlled study of the effect of intramural uterine fibroids on the outcomes of assisted conception. *Hum Reprod* 2001;16:2411–7.
16. Ramzy AM, Sattar M, Amin Y, Mansour RT, Serour GI, Aboulghar MA. Uterine myomata and outcome of assisted reproduction. *Hum Reprod* 1998;13:198–202.
17. Surrey ES, Lietz AK, Schoolcraft WB. Impact of intramural leiomyomata in patients with a normal endometrial cavity on in vitro fertilization-embryo transfer cycle outcome. *Fertil Steril* 2001;75:405–10.
18. Rosenfeld DL. Abdominal myomectomy for otherwise unexplained infertility. *Fertil Steril* 1986;46:328–30.
19. Dubuisson JB, Chapron C. A good technique when correctly indicated. *Hum Reprod* 1996;11:933–7.
20. Tulandi T, Murray C, Guralnick M. Adhesion formation and reproductive outcome after myomectomy and second look laparoscopy. *Obstet Gynecol* 1993;82:213–5.
21. Nezhat C, Nezhat F, Bess O, Nezhat CH, Mashiach R. Laparoscopic assisted myomectomy: a report of new technique in 57 cases. *Int J Fertil* 1994;39:39–40.
22. Becker E Jr, Lev-Toaff AS, Kaufman EP, Halpern EJ, Edelweiss MI, Kurtz AB. The added value of transvaginal sonohysterography over transvaginal sonography alone in women with known or suspected leiomyoma. *J Ultrasound Med* 2002;21:237–47.
23. Lanouette JM, Diamond MP. Pregnancy in women with uterine myoma uteri. *Infertil Reprod Med North Am* 1996;7:19–32.
24. Munne S. Preimplantation genetic diagnosis of numerical and structural chromosome abnormalities. *Reprod Biomed Online* 2002;4:183–96.