

Effect of corporal fibroids on outcome following embryo transfer in donor-oocyte recipients

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Summary

Purpose: To evaluate the effect of intramural or subserosal fibroids in the uterine fundus or corpus on pregnancy outcome following transfer of embryos formed from donated oocytes methods.

Methods: Leiomyomata were measured in three dimensions by transvaginal sonography. Scanning was performed in two planes (sagittal and coronal) at the level of maximal width. The location was categorized by depth in the uterus.

Results: There was no difference in pregnancy rates in those with or without fibroids. However, there was a significantly higher miscarriage rate in the former group.

Conclusion: Women with fibroids are generally older. Thus conclusions about the effect on miscarriage rates are complicated by the effect of the aging oocyte on miscarriages. This study eliminated the oocyte factor by using only younger donated oocytes.

Key words: Uterine fibroids; Donated oocytes; Miscarriage rates.

Introduction

There have been several studies published on the effect of uterine fibroids on pregnancy outcome following in vitro fertilization (IVF) in women with smaller fibroids not compressing the uterine cavity. Stovall *et al.* concluded that fibroids < 5 cm decreased implantation rates [1]. No distinction was made as to whether the fibroids were intramural or subserosal in location [1]. Elder-Geva *et al.* found lower implantation rates with submucosal or intramural fibroids if no uterine cavity distortion was present [2].

However, not all studies have found an association of smaller intramural fibroids on outcome following embryo transfer (ET). Farhi *et al.* found that smaller fibroids that do not compress the uterine cavity had no adverse effect on implantation or miscarriage rates [3]. However, they did find an adverse influence when there was encroachment of the uterine cavity [3]. This was supported by a subsequent study by Ramzy *et al.* which concluded that fibroids < 7 cm that do not encroach the uterine cavity do not have an adverse effect on IVF outcome.

The Cooper Center for IVF has also evaluated the effect of intramural fibroids < 5 cm not compressing the uterine cavity on outcome following IVF-ET. A matched control study of 61 pairs found no significant difference between groups in delivered pregnancy rates (37.7% vs 22.9% control vs fibroid group) or implantation rates (20.2% vs 13.6%) but the differences approached significance ($p = .076$ in the former and $p = .08$ for the latter) [5]. Yet another study by the same group found no dif-

ference or even trend in outcome following ET in the controls (32%) vs the fibroid group (33%) [6]. In fact in the study the percent of implanted sacs that delivered was 66.7% for controls and 90% for those with fibroids. These data were based however on a total of 20 women including controls and women with fibroids. The present study attempted to evaluate the effect of fibroids (excluding submucosal or pedunculated types) on outcome following transfer of embryos to a larger series of donor oocyte recipients.

Material and Methods

All patients who were oocyte recipients at the Cooper Center for IVF from 11/1/98 to 6/30/02 were included in this study. Any patients who had uterine abnormalities, previous history of myomectomy, polyps and/or septae of the uterine were excluded. A total of 122 patients were thus enrolled in this study. There were 49 patients with fibroids (40.16%). From the fibroid group, one patient who had a submucosal fibroid, two with pedunculated fibroids, and four with fibroids in the lower uterus segment were excluded. Thus the focus of the fibroid group was on patients with intramural and/or subserosal fibroids in the uterine fundus or corpus. The maximum average diameter of any fibroid was 30.3 mm. Average diameter is based on the average of the length, width, and depth of the fibroid. The analysis is based on the first cycle for each patient in the period of 11/1/98 through 6/30/02. Pelvic ultrasound was carried out routinely on all patients before the treatment cycle. Those with uterine myomata had detailed sonographic evaluation by transvaginal ultrasound. Scanning of the uterus was carried out in two planes (sagittal and coronal) at the level of maximum width. Each leiomyoma was measured in three dimensions (length, width, and height) and the mean diameter of each leiomyoma was calculated. The location of the leiomyoma was categorized by depth in the uterus (intramural, sub-

serosal, or submucosal). Ultrasonography was performed with a multi-frequency transducer on a GE Logic 400 (General Electric Medical Systems, Milwaukee, WI). If more than three months elapsed between the initial sonogram and the start of an IVF cycle, the fibroid was remeasured every three months to determine any increase or decrease in size.

In preparation for ET, all patients were treated with hormone replacement therapy. All embryos were transferred on the fourth day of progesterone (p) supplementation. Hormone replacement therapy was continued until the patient had a negative pregnancy test, or, in the event of pregnancy, through at least the first trimester. A serum B-HCG value > 100 mIU/ml was considered as a chemical pregnancy. Demonstration of a fetus post 12 weeks was considered as viable if appropriate size and fetal activity present. Chi-square analysis was used to compare the pregnancy rates for both groups as indicated. $P \leq 0.05$ was considered significant.

Results

A comparison of the outcome by presence of fibroids is presented in Table 1. Though the fibroid group was significantly older than the controls it does not seem likely that this had an impact on results since both groups received oocytes from younger donors. Probably age merely allowed the fibroids to manifest.

The only outcome parameter that was significantly different was the miscarriage rate (34.5% vs 5.9% fibroid group vs control, $p = .004$).

Table 1. — *Effect of intramural fibroids on pregnancy outcome in donor-oocyte recipients.*

	Oocyte recipients with fibroids	Oocyte recipients without fibroids	p value
No. of patients	49	73	
Average age	43.0 + 5.1	39.5 + 5.7	.001
Number of embryos transferred	3.0 + .8	3.0 + 1.0	.228
Type of transfer			
Fresh transfers	33 (67.3%)	48 (65.8%)	.855
Frozen transfers	16 (32.7%)	25 (34.2%)	
Clinical pregnancy	59.2% (29/49)	46.6% (34/73)	.172
Ongoing/delivered pregnancy	38.8% (19/49)	43.8% (32/73)	.579
Miscarriage rate	34.5% (10/29)	5.9% (2/34)	.004
Implantation rate	29.9% (47/157)	27.4% (60/219)	.591

Discussion

There are data suggesting that the controlled ovarian hyperstimulation (COH) regimen per se may have an adverse effect on outcome following IVF-ET [7-9]. The trend was for lower implantation rates in those having ETs following COH vs no such trend in those receiving estrogen/progesterone replacement therapy for donor oocyte recipients found in our previous two studies [5, 6]. However, the similar implantation rates in controls vs recipients with fibroids could have been related to small sample size [6]. The present study evaluated a 5-fold

larger sample size than the previous study and confirms that in the absence of COH corporal fibroids have no adverse effect on implantation.

The data however do demonstrate an increased miscarriage rate in women with fibroids. Nonetheless, because of a trend for increased clinical pregnancy rate (which may have been fortuitous) the ongoing/delivered pregnancy rates were very similar.

The outcome using donor oocytes in women with fibroids are not so significantly different from controls that the higher miscarriage rate should prompt consideration for myomectomy. However surgery could be contemplated possibly for recurrent miscarriages.

This study should prompt a study of a larger series of ETs in COH and oocyte retrieval cycles to see if fibroids have a greater adverse effect on conception under these circumstances.

References

- [1] Stovall D.W., Parrish S.B., Van Voorhis B.J., Hahn S.J., Sparks A.E., Syrop C.H.: "Uterine leiomyomas reduce the efficacy of assisted reproduction cycles: results of a matched follow-up study". *Hum. Reprod.*, 1998, 13, 192.
- [2] Eldar-Geva T., Meagher S., Healy D.L., 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.
- [3] Farhi 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.
- [4] Ramzy A.M., Sattar M., Amin Y., Mansour R.T., Serour G.I., Aboulghar M.A.: "Uterine leiomyomata on the results of in-vitro fertilization treatment". *Hum. Reprod.*, 1995, 10, 2576.
- [5] Check J.H., Choe J.K., Lee G., Dietterich C.: "The effect on IVF outcome of small intramural fibroids not compressing the uterine cavity as determined by a prospective matched control study". *Hum. Reprod.*, 2002, 17, 1244.
- [6] Dietterich C., Check J.H., Choe J.K., Nazari A., Fox F.: "The presence of small uterine fibroids not distorting the endometrial cavity does not adversely affect conception outcome following embryo transfer in older recipients". *Clin. Exp. Obstet. Gynecol.*, 2000, 27, 168.
- [7] Check J.H., O'Shaughnessy A., Lurie D., Fisher C., Adelson H.G.: "Evaluation of the mechanism for higher pregnancy rates in donor oocyte recipients by comparison of fresh with frozen embryo transfer pregnancy rates in a shared oocyte programme". *Hum. Reprod.*, 1995, 10, 3022.
- [8] Check J.H., Choe J.K., Katsoff D., Summers-Chase D., Wilson C.: "Controlled ovarian hyperstimulation adversely affects implantation following in vitro fertilization-embryo transfer". *J. Assist. Reprod. Genet.*, 1999, 16, 416.
- [9] Check J.H., Choe J.K., Nazari A., Summers-Chase D.: "Ovarian hyperstimulation can reduce uterine receptivity: a case report". *Clin. Exp. Obstet. Gynecol.*, 2000, 27, 89.

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