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Ultrasonographic characteristics of the endometrium among patients with fibroids undergoing ART

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Abstract

Abstract Capsule: Ultrasonographic endometrial thickness is not affected by the presence of fibroids in patients undergoing ART. However fibroids, especially intramural fibroids, appear to increase the frequency of a non-proliferative endometrial pattern and are associated with a reduction in live birth rates.

Narrative Abstract: A retrospective cohort study examining all completed, non-donor, first ART cycles was performed to evaluate the ultrasonographic appearance of the endometrial pattern and thickness at time of HCG administration among pre-cycle screened patients with uterine fibroids as compared to patients without fibroids. There was no difference in the endometrial thickness (10.3 ± 2.0 mm vs. 10.0 ± 2.6 mm; $p=NS$) between those with fibroids and controls; however, the rate of non-proliferative endometrial pattern (3.1 vs. 1.0%; $p=0.02$) and live birth rates (34.4% vs. 43.0%; $p=0.04$) were significantly different, most notably among those patients with intramural fibroids.

Keywords

fibroids; endometrial thickness; ultrasonographic pattern; assisted reproductive technologies; in vitro fertilization

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The impact of uterine leiomyomas on the outcome of assisted reproductive technology (ART) cycles has been the subject of great interest in recent years. Rarely fibroids are the sole cause of infertility, yet their potential reproductive effects are of keen interest given the overall prevalence among infertile women (20–50%) (1). Numerous studies have shown a detrimental effect of fibroids on ART outcome (2–8). Fibroids have been associated with increased venous congestion and impaired uterine blood flow (9). This may result in histological alterations such as a reduction in the proportion of endometrial glands overlying leiomyomas (10) that may have implications for implantation. Sampling a patient's endometrium while undergoing ART remains impractical so investigators have looked for less invasive ways of evaluating the endometrium.

Evidence suggests that a tri-laminar, or proliferative, endometrial pattern is important to the pregnancy outcome with ART. Women without fibroids who demonstrate a tri-laminar endometrial appearance have been shown to have a 44.8% pregnancy rate compared to 0% among those patients demonstrating a homogenous appearance of the endometrium ($p=0.039$) (11). Furthermore, endometrial thickness has been shown to be predictive of fecundity. One study demonstrated that among those patients with an endometrial thickness of less than 6 mm there were no pregnancies seen (12).

If uterine fibroids alter endometrial blood flow or if they exert some undefined effect on endometrial proliferation, this may result in an increased incidence of a non-proliferative endometrial pattern on ultrasound with a subsequent decline in endometrial thickness among these patients. Thus in this study, we set out to investigate whether the presence and location of fibroids were associated with alterations in endometrial pattern or thickness, as assessed by ultrasound, in those undergoing ART at the time of hCG administration.

After obtaining Institutional Review Board approval, we performed a retrospective cohort study examining only completed, fresh, non-donor, first ART cycles from January, 1999 to December 2003 at a university-based ART center. Patients were excluded from consideration if they had undergone previous ART attempts and as no donor cycles are performed at our institution, none were included in this study. The sample size was determined by the study period. All patients were screened prior to the ART cycle with saline sonography for uterine fibroids or other pathology and were surgically treated as appropriate.

When presenting for the baseline evaluation, a transvaginal ultrasound was performed by physicians in our group utilizing similar equipment and a notation of the presence, location and size of any uterine lesions was made. For the purposes of this study, a fibroid was diagnosed when a well-circumscribed heterogeneous appearing nodule with a distinct margin was present in the myometrium (13). All such lesions were considered to be leiomyomas. If more than one fibroid was noted, the fibroid closest to the cavity was utilized to categorize its size and location.

Endometrial thickness was determined on the day of hCG administration by imaging the thickest dimension in the sagittal plane approximately 1 cm from the fundus. Additionally the endometrial pattern was considered proliferative if a hypoechoic area with a central hyperechoic stripe or an isoechoic area with an echogenic stripe was present. A non-proliferative pattern was defined as a homogenous appearance to the endometrium without an intervening hyperechogenic line.

Patient cycle characteristics were evaluated between groups. A comparison of endometrial thickness (mm) and ultrasonographic pattern (proliferative compared to non-proliferative pattern) on the day of HCG administration was performed and was stratified according to the presence, size and location of the largest fibroid and its proximity to the endometrial cavity. To be considered abutting the endometrial cavity, the fibroid was found to be encroaching upon the linear demarcation of the myometrial-endometrial junction. Student's t-test, ANOVA and

chi-square were used as appropriate. Stata 8.2 (College Station, TX) was used for calculation and $p \leq 0.05$ was considered to be significant for all analyses.

During the study interval, 1119 completed, fresh, non-donor, first ART cycles were performed. One hundred and sixty-three (14.6%) patients in our study population were noted to have uterine fibroids of any size in any location and 90% were solitary lesions. The size, location and proximity to the endometrial cavity could be determined in 133, 133 and 147 patients respectively. All fibroids that abutted the endometrial cavity were determined not to be submucosal as a recent saline sonography was performed that showed no intra-cavitary distortion.

An analysis of the demographic variables among controls and those with fibroids revealed that age (33.0 vs. 35.6; $p < 0.001$) and African-American race (14.8 vs. 42.0%; $p < 0.001$) were statistically different between groups. When evaluating the endometrial thickness and pattern among groups, it was noted that there were no statistically significant differences in endometrial thickness among any group analyzed. (Table 1) However, when evaluating the percentage of patients with a non-proliferative endometrial pattern, we found that those with fibroids of any size or in any location had an increase in non-proliferative pattern compared to controls (3.1% vs. 1.0%; $p = 0.02$) and this was associated with a reduction in live birth rates (34.4% vs. 43.0%; $p = 0.04$). Moreover, when evaluated by subgroup analysis, those with intramural fibroids had a 4% non-proliferative rate ($p = 0.01$) and a 31.4% live birth rate ($p = 0.02$). Intramural fibroids that abutted the endometrial cavity exhibited an even stronger tendency towards a non-proliferative endometrial pattern (5.3%; $p = 0.07$) and a significantly reduced live birth rate (19.1%; $p = 0.02$). Subserosal fibroids appeared to have no effect endometrial pattern or thickness, as might be predicted. As our sample size was determined by the study period, we performed a post-hoc power analysis and found that our study had 99% power to detect a 1 mm difference in endometrial thickness.

As patients in this study were undergoing ART, there was no in-cycle surgical confirmation of the suspected fibroids. Patients in this study were deemed not to require surgery based on pre-cycle saline sonography. Studies have shown that transvaginal sonography alone can accurately detect fibroids in 95% of cases (13). While this study did not set out to examine differences between those who had prior surgical treatment for fibroids, there is evidence that prior myomectomy would be unlikely to interfere with ART performance (14) and patients undergoing myomectomy prior to ART have been shown to have outcomes similar to those who had never had fibroids (15).

In this study we hypothesized that fibroids would alter the endometrial pattern and/or thickness during ART stimulation. Our study did not demonstrate a difference in endometrial thickness among those with fibroids regardless of location or proximity to the endometrial cavity. However there was a statistically significant increase in non-proliferative pattern among those with fibroids, especially when intramural in location, and this was associated with a reduction in the live birth rate. While there remains debate regarding the role endometrial thickness has on the outcome of ART (16–19) there is evidence to suggest that endometrial ultrasonographic pattern is an important prognostic indicator of endometrial receptivity and cycle outcome (11,20). Histological evaluation of the endometrium in these women may yield further information regarding the local micro-environment that may account for these findings. However access to these samples during an ART cycle is limited. Therefore further prospective investigation may be warranted to determine whether ultrasonographic markers may predict success with ART among patients with fibroids

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Table 1

Impact of fibroids on endometrial thickness and pattern

Parameter	Endometrial Thickness		Non-Proliferative pattern		Live birth rate	
	mm	p-value	%	p-value	%	p-value
Controls (n=956)	10.3 ± 2.0	--	1.0	--	43.0	--
Any fibroid (n=163)	10.0 ± 2.5	NS	3.1	0.02	34.4	0.04
Size ≥ 3 cm (n=58)	10.1 ± 2.6	NS	1.8	NS	32.8	NS
Intramural (n=102)	10.0 ± 2.7	NS	4.0	0.01	31.4	0.02
Subserosal (n=31)	9.8 ± 1.8	NS	0	NS	45.2	NS
Abutting cavity (n=21)	10.7 ± 3.3	NS	5.3	0.07	19.1	0.02

Note: Values are means ± SD. NS = not significant