Three-dimensional endometrial volume calculation and pregnancy rate in an in-vitro fertilization programme

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This study was designed to investigate the role of three-dimensional (3D) endometrial ultrasound in predicting the outcome of an in-vitro fertilization (IVF) programme. In 47 IVF cycles measurements of endometrial thickness and volume, as assessed by 3D transvaginal ultrasound on the day of oocyte retrieval, and concentrations of oestradiol and progesterone in the same patient sampled on the day of sonography, were related to the occurrence of a successful implantation. The overall pregnancy rate was 31.9% (15/47). Fifteen pregnant patients had a mean endometrial thickness and volume of 10.8 ± 2.3 mm (mean ± SD) and 4.9 ± 2.2 ml, respectively. Thirty-two non-pregnant patients had corresponding measurements of 11.8 ± 3.4 mm and 5.8 ± 3.4 ml respectively. Endometrial thickness varied widely in both groups, in pregnant patients from 6.9 to 16.0 mm, in non-pregnant patients from 6.5 to 21.1 mm. Oestradiol concentrations were not significantly correlated with either endometrial thickness or volume. The conclusion from the present data is that 3D volume estimation of the endometrium as well as analysis of endometrial thickness on the day of oocyte retrieval had no predictive value for conception in IVF cycles.

Key words: 3D ultrasound/endometrial volume/endometrial thickness/IVF/pregnancy rate

Introduction

Endometrial thickness and pattern have been implicated in the successful outcome of in-vitro fertilization (IVF). Several study groups have reported significant correlations between pregnancy rates and endometrial thickness and/or morphology (Gonen et al., 1989; Check et al., 1991; Dickey et al., 1992; Abdalla et al., 1994; Noyes et al., 1995), while others have failed to show such a relationship (Fleischer et al., 1986b; Welker et al., 1989; Khalifa et al., 1992; Oliveira et al., 1993; Coulam et al., 1994). The common technique to assess the endometrium on transvaginal ultrasound is to measure the maximal thickness in relation to the longitudinal axis of the uterine body. Little attention, however, has been given to the length of the uterine cavity despite its important influence on endometrial volume. As a consequence only few data on endometrial volume estimation exist in the literature, with the majority of these obtained from animal studies with magnetic resonance imaging (MRI) or computerized tomography (CT) (Lee et al., 1997). Both techniques, however, are limited by their costs and will therefore not be widely available. The advent of computerized three-dimensional (3D) ultrasound systems allowing acquisition and storage of volume data has for the first time permitted reliable sonographic volume calculations of pelvic organs. The reproducibility of these measurements was confirmed by Kyei-Mensah et al. (1996) in a study on ovarian and endometrial measurements in assisted reproduction cycles. Lee et al. (1997) performed serial volumetry in 18 patients with spontaneous menstrual cycles to assess uterine and endometrial volumes. Since no data on 3D-volumetry correlated to IVF outcome exist, the following study was undertaken to evaluate the role of 3D-endometrial volume calculation in predicting the pregnancy rate.

Materials and methods

A total of 47 patients was recruited for the study with the predominant diagnosis of male factor infertility (n = 33), tubal occlusion (n = 5) or unexplained infertility (n = 9). All patients underwent transvaginal sonography to assess uterine and ovarian morphology in the follicular phase of the menstrual cycle. Prior to ovulation induction a standard regime of the gonadotrophin-releasing hormone (GnRH) agonist triptorelin (Decapeptyl, Ferring, Kiel, Germany) was administered s.c. at a daily dose of 100 μg started in the mid-luteal phase. After confirmation of pituitary downregulation (no ovarian cyst >2 cm, endometrial thickness <5 mm) ovarian stimulation with recombinant follicle stimulating hormone (FSH) (Puregon, Organon, Aberschleissheim, Germany) in appropriate doses was commenced. All patients underwent serial ultrasound examinations to assess follicular growth until at least three follicles with a mean diameter of ≥17 mm were seen. At this stage 10 000 IU of human chorionic gonadotrophin (HCG; Pregnesin, Serono, Serono, Unterschleissheim, Germany) were used to induce ovulation. On the day of oocyte retrieval, 36 h after HCG administration, oestradiol and progesterone serum concentrations were measured. A transvaginal ultrasound scan was then performed using an electronic 7.5 MHz transducer with 3D facility (Combison 530D; Kretz-Technik, Zipf, Austria). After a true longitudinal view of the uterus was obtained, the endometrial thickness was measured at the point with the maximum thickness between the highly reflective interfaces of the endometrial–myometrial junction. The measurement included both layers of the endometrium. The surrounding low-amplitude echo layer was excluded since it represents the inner layers of the myometrium (Fleischer et al., 1986a). On completion of the B-mode examination, the 3D volume mode was switched on and the region of interest was
Figure 1. Plane A (upper left) shows the transverse view, plane B (upper right) displays the longitudinal view and plane C (lower left) demonstrates the frontal view. The endometrial volume is measured in plane A by delineating the endometrial margin at the myometrial–endometrial interface from the fundus to the internal cervical os in a number of parallel slices which are set ~1–2 mm apart. During the process of measuring the location of the section is indicated in the other planes by the co-ordinated movement of small dot cursors.

defined by a moveable sector on the screen. This sector had the shape of a truncated cone which was manipulated to minimize acquisition time while ensuring that the whole of the endometrial cavity was included in the volume sampling. The slow volume acquisition setting using high resolution was activated and the patient was instructed to remain very still. Movements of the vaginal probe were excluded. Volume sampling took ~4 s, during which time the conventional two-dimensional (2D) plane was rotated through 180° with the rotation axis oriented exactly along the long axis of the vaginal probe. Three orthogonal planes were simultaneously displayed on the screen, with the perpendicular orientation of these planes being maintained throughout any translation or rotation.

The data set was then stored digitally on an internal disk drive for subsequent analysis and the ultrasound probe was removed. While the examinations were done by two physicians (R.L.S. and D.I.), actual volume calculation was performed by one author (R.L.S.), thus reducing interobserver variability to a minimum. For the purpose of volume calculation, the stored 3D-data were retrieved from the hard disk. The volume was then rotated into a pre-defined view with plane A (upper left) showing the transverse view, plane B (upper right) displaying the longitudinal view and plane C (lower left) demonstrating the frontal view (Figure 1). The endometrial volume was measured in plane A by delineating the endometrial margin at the myometrial–endometrial interface from the fundus to the internal cervical os in a number of parallel slices which were ~1–2 mm apart (Figure 1).

During the process of measuring, the location of the section was indicated in the other planes by the co-ordinated movement of small dot cursors. This procedure of area tracing took an average of 5–10 min. The actual volume was calculated by the built-in computer program. Intra-observer variability of measurements was checked in 10 patients and ranged from 0.001 to 0.165 ml (Spearman's correlation coefficient, $r^2 = 0.956$, $P < 0.001$).

After completion of the ultrasound examination, oocytes were collected by transvaginal ultrasound-directed follicular aspiration, and up to three good quality embryos were transferred 48 h after oocyte retrieval. The number of blastomeres and morphological grade of each embryo were recorded. Progesterone vaginal suppositories (400 mg daily) were prescribed for 14 days as luteal support. Serum oestradiol and progesterone concentrations were assayed using a commercially available chemiluminescent immunoassay (Abbott, Abbott Park, USA). Pregnancy was defined as the occurrence of a positive β-HCG (≥10 IU) value on day 12 after transfer and a second, higher value 2 days later. Only pregnancies reaching HCG values >100 IU were considered for evaluation.

All data were analysed using the SAS statistical package on a personal computer. Pearson's correlation coefficient and two-tailed Student's $t$-test were used as appropriate. The correlation coefficient was tested for deviation from zero.

Results

All 47 patients underwent assessment of endometrial thickness and endometrial volume on the day of oocyte retrieval and no measurement due to poor image quality had to be omitted from analysis. The overall pregnancy rate was 31.9% (15/47). The outcome of IVF/embryo transfer was not dependent on patient’s age, cause of infertility, number of previous IVF attempts, duration or total dose of FSH administered, serum oestradiol concentration, number of oocytes harvested or fertilized, sperm concentration and motility, or the mean number of embryos transferred (Table I). Likewise, both endometrial thickness and endometrial volume failed to predict the outcome of IVF (Table I). Thirty-two non-pregnant women had a mean endometrial thickness of 11.8 ± 3.4 mm and 15 pregnant patients had a mean endometrial thickness of 10.8 ± 2.3 mm on the day of oocyte retrieval. Mean values for endometrial volume were 5.8 ± 3.4 ml and 4.9 ± 2.2 ml, respectively. Endometrial thickness varied widely in both groups of patients, in the latter from 6.9 to 16 mm, in the former from 6.5 to 21.1 mm. Pearson’s correlation coefficient between endometrial thickness and volume was 0.83 and 0.66 in the pregnant and non-pregnant group, respectively. In both
Embryos transferred (n) Serum oestradiol (pg/ml) 1068.7
Follicles aspirated (n) Sperm motility (%) 26.9
Days of stimulation (n) 6
Endometrial volume (ml) 4.9
Endometrial thickness (mm) 10.8
Previous IVF attempts (n) 6
et al. Dickey et al. and pregnancy rate (Glissant
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Although the quality of the embryo plays an important
role in initiation of pregnancy, implantation and placentation
will ultimately determine the fate of a pregnancy. What
determines such a favourable endometrial environment, how-
ever, is still controversial. Endometrial thickness as a predictor
of pregnancy outcome has been investigated by numerous
studies with variable results. While some study groups found
a significant correlation between thickness of the endometrium
and pregnancy rate (Glissant et al., 1985; Gonen et al., 1989;
Dickey et al., 1992; Abdalla et al., 1994; Noyes et al., 1995),
others reported no such relationship (Fleischer et al., 1986b;
Welker et al., 1989; Khalifa et al., 1992; Oliveira et al., 1993;
Coulam et al., 1994; Bustillo et al., 1995). The opposing
conclusions drawn by these authors may in part be due to
different techniques used, i.e. vaginal versus abdominal
sonography and different ovarian stimulation protocols (Zaidi et al., 1995). Furthermore, measurement of the maximum
endometrial height is fraught with several problems and
Turnbull et al. (1994) suggest several reasons for this. First,
the uterus may be scanned in an oblique plane thus over-
or underestimating the true endometrial thickness. Second, a
single measurement, usually obtained at the fundus of the
uterus, is used to represent the entire cross-section of the
endometrium. Third, marked ovarian enlargement may distort
the endometrial outline, all of which can lead to incorrect
measurements (Turnbull et al., 1994). Three-dimensional
volumetry may offer a more reliable method to assess the endometrial cavity from the fundal region to the internal
cervical os.

In our study, we found no significant correlation between
both endometrial measurements and the pregnancy rate.
Interestingly, mean values for endometrial thickness and
volume were lower, albeit non-significantly, in the pregnant
group. Even though the number of cases in our study is small,
our data suggest that factors other than biometric parameters
determine IVF outcome. The suggestion that endometrial
thickness is determined by the individual uterine architecture
and therefore not predictive of the likelihood of implantation
(Strohmer et al., 1994) may be related to endometrial volume.
Furthermore, oestradiol concentrations were not significantly
related with endometrial thickness or IVF success which is
in accordance with other reports (Rabinowitz et al., 1986;
Gonen and Casper, 1990; Ueno et al., 1991; Khalifa et al.,
1992; Oliveira et al., 1993). We found the same lack of
correlation between oestrogen concentrations and endo-
metrial volume.

3D-ultrasound is a comparatively new technique with the
potential of accurately tracing the contours of any object of
interest and performing immediate volume calculations. In
contrast to conventional sonography 3D-ultrasound facilitates
the evaluation of the uterine shape in the frontal plane which
can be used for the diagnosis of uterine anomalies (Jurkovic
et al., 1995) or as an additional predictor of extraterine
pregnancy (Rempen, 1998). Effective use of this system,
however, does not preclude scanning experience. Furthermore,
3D ultrasound will be adversely affected by the same conditions
that impair conventional sonography and occasionally several
attempts may be necessary before the examination can be
successfully completed. Previous studies on endometrial
volume estimation by 3D ultrasound demonstrated a high
degree of reproducibility (Kyei-Mensah et al., 1996) which
we could confirm in our series even though we did not test
for interobserver variation. In one study on endometrial volume
changes in normal menstrual cycles, 11 measurements had to
be omitted from analysis due to low contrast (Lee et al., 1997).
We did not encounter similar problems, possibly due to the fact
that we performed our measurements in patients undergoing
ovarian stimulation. We agree with other groups that the
definition of the lower end of the endometrial cavity can

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### Table I. Clinical details of the 15 pregnant and 32 non-pregnant patients

<table>
<thead>
<tr>
<th></th>
<th>Pregnant (mean ± SD)</th>
<th>Non-pregnant (mean ± SD)</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>31.4 ± 4.0</td>
<td>32.2 ± 4.2</td>
</tr>
<tr>
<td>Previous IVF attempts (n)</td>
<td>1.8 ± 1.2</td>
<td>2.0 ± 1.2</td>
</tr>
<tr>
<td>Endometrial thickness (mm)</td>
<td>10.8 ± 2.3</td>
<td>11.8 ± 3.4</td>
</tr>
<tr>
<td>Endometrial volume (ml)</td>
<td>4.9 ± 2.2</td>
<td>5.8 ± 3.4</td>
</tr>
<tr>
<td>Amount of FSH given (IE)</td>
<td>2025 ± 665.5</td>
<td>1953 ± 958</td>
</tr>
<tr>
<td>Days of stimulation (n)</td>
<td>13.2 ± 2.3</td>
<td>12.0 ± 1.5</td>
</tr>
<tr>
<td>Sperm concentration</td>
<td>17.5 ± 20.0</td>
<td>22.9 ± 28.5</td>
</tr>
<tr>
<td>Sperm motility (%)</td>
<td>26.9 ± 27.7</td>
<td>29.5 ± 21.5</td>
</tr>
<tr>
<td>Follicles aspirated (n)</td>
<td>8.8 ± 3.1</td>
<td>7.9 ± 2.9</td>
</tr>
<tr>
<td>Serum oestradiol (pg/ml)</td>
<td>1068.7 ± 276.5</td>
<td>975.5 ± 521</td>
</tr>
<tr>
<td>Embryos transferred (n)</td>
<td>2.7 ± 0.5</td>
<td>2.7 ± 0.9</td>
</tr>
</tbody>
</table>

There was no significant difference between the two groups of patients. SD: standard deviation.

### Table II. Pearson’s correlation coefficient between hormone levels and endometrial measurements in the non-pregnant group. None of the correlation coefficients was significantly different from zero at the 5% level

<table>
<thead>
<tr>
<th></th>
<th>Non-pregnant group (n = 32)</th>
<th>Pregnant group (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oestradiol concentrations (mmol/dl)</td>
<td>-0.21</td>
<td>-0.31</td>
</tr>
<tr>
<td>Progesterone concentrations (mmol/dl)</td>
<td>0.21</td>
<td>-0.59</td>
</tr>
</tbody>
</table>

### Table III. Pearson’s correlation coefficient between hormone levels and endometrial measurements in the pregnant group

<table>
<thead>
<tr>
<th></th>
<th>Pregnant group (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oestradiol concentrations (mmol/dl)</td>
<td>-0.31</td>
</tr>
<tr>
<td>Progesterone concentrations (mmol/dl)</td>
<td>-0.59</td>
</tr>
</tbody>
</table>

*Significant result with P = 0.04. None of the other correlation coefficients was significantly different from zero at the 5% level.

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Discussion

Pregnancy outcome in IVF cycles is dependent on many
groups oestradiol levels were not significantly correlated with
either endometrial thickness or volume (Tables II and III). In
the pregnant group endometrial volume and progesterone
concentrations showed a negative correlation (P = 0.04)
(Table III).

3D-endometrial volume calculation in assisted reproduction

3D-endometrial volume calculation in assisted reproduction

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sometimes be difficult (Kyei-Mensah et al., 1996; Lee et al., 1997). In no case, however, was the image of such a poor quality that the patient had to be excluded from the study.

Our data demonstrate that endometrial volume calculation in hyperstimulated cycles is feasible although the results fail to show any correlation between endometrial 2D/3D measurements and IVF outcome. Our results are therefore in line with the findings of Salle et al. (1998), who concluded that individual ultrasonographic and Doppler parameters were not of sufficient accuracy to predict uterine receptivity. In the aforementioned study, a uterine score including several factors calculated prior to an IVF cycle, rather than individual measurements, appeared to be a useful predictor of implantation (Salle et al., 1998). It remains to be seen whether larger clinical studies can define a threshold value of endometrial volume below which pregnancy seems unlikely and below which any embryos produced should be cryopreserved for transfer in a subsequent cycle.

References


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