The shape of the endometrium evaluated with three-dimensional ultrasound: an additional predictor of extrauterine pregnancy

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The objective of this prospective follow-up study was to evaluate the potential utility of three-dimensional (3D) ultrasound to differentiate intrauterine from extrauterine gestations. Fifty-four pregnancies with a gestational age <10 weeks and with an intrauterine gestational sac <5 mm in diameter formed the study group. The configuration of the endometrium in the frontal plane of the uterus was correlated to eventual pregnancy outcome. After exclusion of three patients with a poor 3D-image quality the endometrial shape was asymmetrical with regard to the median longitudinal axis of the uterus in 84% of intrauterine pregnancies, whereas the endometrium showed a symmetry in the frontal plane in 90% of extrauterine pregnancies (P = 0.0000001). Intrauterine fluid accumulation may distort the uterine cavity, thus being responsible for false-positive as well as false-negative results. The evaluation of the endometrial shape in the frontal plane appears to be a useful additional means to distinguish intrauterine from extrauterine pregnancies, especially when a gestational sac is not clearly demonstrated with conventional ultrasound.

**Key words:** endometrium/extrauterine pregnancy/3D ultrasound/transvaginal sonography

**Introduction**

The early and reliable diagnosis of extrauterine pregnancy (EP) still remains a challenge but is essential to avoid life-threatening bleeding or consecutive infertility. Although the introduction of vaginal sonography has improved diagnostic accuracy (Thorsen et al., 1990) the adnexal pathology is not seen with conventional two-dimensional B-mode technique in about one-quarter of EPs whereas an extrauterine choriionic cavity is visible only in about half of EPs (Rempen, 1992). According to a literature review (Brown and Doubilet, 1994) an adnexal mass other than a simple cyst or intraovarian lesion in patients clinically suspected of having an EP was evident in 84% of EP with a likelihood of 96% that this finding represented EP based on an EP prevalence of 26%.

A non-specific sign of EP is the missing gestational sac in the uterine cavity when the human chorionic gonadotrophin (HCG) concentration has passed the discriminatory zone which is usually set at 1000–2000 mIU/ml [1st International Reference Preparation (IRP)] (Barnhart et al., 1994). However, EP cannot be distinguished from miscarriage based on the discriminatory zone when the patient presents with heavy uterine bleeding. In addition nearly 20% of patients with symptomatic early pregnancies in an emergency department have HCG concentrations below a discriminatory zone of 1500 mIU/ml (Barnhart et al., 1994). In this subgroup a small endometrial stripe thickness has been used to predict EP (Spandorfer and Barnhart, 1996). However, 11% of EPs had endometrial diameters above the cut-off value of 8 mm whereas 24% of intrauterine pregnancies [spontaneous abortions (SA) + viable gestations (IP)] had values <8 mm.

With conventional sonography the uterine corpus and its endometrium are examined in sagittal and cross-sectional planes. A uterine view in the frontal plane is usually not possible due to the anteversion or retroversion of most uteri. With the development of 3D-ultrasound machines, frontal sections through the uterus can be calculated after acquisition of a volume box containing the uterine corpus. Thus the echogenous endometrium is displayed with its tubal horns in the fundus and the cervical canal at the opposite site giving the appearance of a triangle. This frontal view of the endometrial cavity has been used formerly to diagnose uterine anomalies (Jurkovic et al., 1995; Raga et al., 1996).

Implantation of the blastocyst in the decidua takes place mostly near the fundus and is accompanied not only by growth of the trophoblast but also by proliferation of the maternal decidua surrounding the tiny blastocyst. Because implantation of the blastocyst in the decidua is usually asymmetrical with regard to the transverse direction of the uterus we observed an ipsilateral enlargement of the decidua. We speculated therefore that this decidual reaction may be present in very early intrauterine pregnancies even when the gestational sac itself is not visible using today's sonographic technology. It should also be apparent in incomplete abortions. According to this concept it was postulated that this asymmetrical decidual reaction is lacking in EP.

The purpose of this study was therefore to prove the hypothesis that the shape of the endometrium viewed in the frontal plane may be used to distinguish intrauterine from extraterine gestations.

**Materials and methods**

Fifty-four early pregnancies at risk for ectopic gestation with a menstrual age of <10 weeks were scanned at the University Department of Obstetrics and Gynecology in Würzburg using a mechanical 7.5 MHz vaginal probe (Combison C530 Voluson™, Kretztechnik, Austria). Intrauterine gestational sacs which already showed an embryo with heart activity or had diameters >5 mm at the initial conventional scan had been excluded because these findings enable an unequivocal diagnosis of intrauterine gestation.

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After the ultrasound evaluation all patients were followed until the definitive diagnosis was made. Intrauterine viable pregnancies were confirmed by visible fetal heart motion in subsequent conventional ultrasound examinations. EPs were confirmed by surgery and pathological examination. Spontaneous abortion was diagnosed through histological examination after curettage or through clinical follow-up. If curettage was not performed, or if the pathologic specimen contained no trophoblast cells, complete abortion was assumed when the patients had experienced heavy bleeding, lacked any symptoms suggestive of EP as well as sonographic signs of an adnexal mass, and had an uneventful follow-up.

χ²-Test, sign-test and Whitney U-test were used where appropriate. Significance was determined at the level of P < 0.05. Means are given with SEM.

Results

Among the 54 gestations there were 21 intrauterine viable pregnancies (IP), 13 spontaneous abortions (SA) and 20 EPs. Mean maternal age, presence of preceding ovulation induction, HCG concentration, and ultrasound diameters of the uterine corpus did not differ significantly between intrauterine and extrauterine pregnancies (Tables I and II). The endometrial thickness was significantly smaller in EP versus IP (P = 0.003) but not versus SA (P = 0.24). This was also true when a cut-off value of 8 mm was used for endometrial thickness (P = 0.0004 and P = 0.73, respectively).

All pregnancies with small endometrial echoes ≤3 mm (class I) were ectopic, whereas irregular contoured endometria (class IV) were only seen in intrauterine gestations. The majority of patients (74%), however, displayed either a class II or class III endometrium both of which were seen in patients with intrauterine as well as extrauterine implantation.

The shape of the endometrium in the frontal view was symmetrical in 90% of EPs (Figure 2, Table III). However, two EPs showed an endometrial asymmetry concerning all three 3D criteria (true false-negatives). The asymmetry in these cases could be attributed to laterally located fluid accumulations which distorted the uterine cavity. In intrauterine pregnancies (IP and SA) criteria of endometrial asymmetry were obvious in 62, 56 and 76% of patients, respectively (Table III). However, in 13 (criterion A), 15 (criterion B) and 8 (criterion C) intrauterine gestations the corresponding parameter of asymmetry was not present (true false-positives). In three of these cases this was due to a poor image quality because of a straight uterus which precluded a sufficient visualization of the uterine fundus. In two other patients intrauterine fluid accumulation in the tubal horns caused asymmetry with regard to all three criteria to be concealed. Concerning criterion A there were, in addition, one twin gestation and one gestational sac not implanted in the fundus uteri but near the cervical canal which were obviously responsible for the symmetry.

Although uterine bleeding was more frequent in EP or SA compared to IP (Table I) this did not affect the test performance. The rate of endometrial asymmetry (criterion C) in case of EP was not statistically different in patients with uterine bleeding when compared with asymptomatic patients [sensitivity: 93% (14/15) versus 80% (4/5); P = 0.45]. Also, the percentages of endometrial asymmetry in cases of IP or SA were similar when
**Table I.** Clinical findings and human chorionic gonadotrophin (HCG) concentrations (mean ± SEM or %) in viable intrauterine pregnancies (IP), spontaneous abortions (SA) and ectopic pregnancies (EP).

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<tbody>
<tr>
<td>Maternal age (years)</td>
<td>29 ± 1</td>
<td>29 ± 2</td>
<td>30 ± 1</td>
<td>0.97</td>
</tr>
<tr>
<td>Ovulation induction (%)</td>
<td>24 (5)</td>
<td>23 (3)</td>
<td>5 (1)</td>
<td>0.13</td>
</tr>
<tr>
<td>Gestational age (days)</td>
<td>40 ± 2 (19)</td>
<td>45 ± 2</td>
<td>49 ± 2</td>
<td>0.008</td>
</tr>
<tr>
<td>Uterine bleeding (%)</td>
<td>5 (1)</td>
<td>77 (10)</td>
<td>75 (15)</td>
<td>0.002</td>
</tr>
<tr>
<td>Abdominal pain (%)</td>
<td>38 (8)</td>
<td>31 (4)</td>
<td>70 (14)</td>
<td>0.01</td>
</tr>
<tr>
<td>HCG (mIU/ml 1st IRP*)</td>
<td>1814 ± 306 (14)</td>
<td>1124 ± 641</td>
<td>4063 ± 2023</td>
<td>0.28</td>
</tr>
</tbody>
</table>

In parentheses: number of patients.

*First International Reference Preparation.

**Table II.** Two-dimensional sonographic findings (mean ± SEM or %) in viable intrauterine pregnancies (IP), spontaneous abortions (SA) and extrauterine pregnancies (EP).

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<tr>
<td>Endometrial structure</td>
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<tr>
<td>Class I (%)</td>
<td>0</td>
<td>0</td>
<td>25 (5)</td>
<td></td>
</tr>
<tr>
<td>Class II (%)</td>
<td>48 (10)</td>
<td>38 (5)</td>
<td>30 (6)</td>
<td></td>
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<tr>
<td>Class III (%)</td>
<td>43 (9)</td>
<td>8 (1)</td>
<td>45 (9)</td>
<td></td>
</tr>
<tr>
<td>Class IV (%)</td>
<td>10 (2)</td>
<td>54 (7)</td>
<td>0</td>
<td>0.0002</td>
</tr>
<tr>
<td>Endometrial thickness (mm)</td>
<td>13 ± 1</td>
<td>10 ± 1</td>
<td>9 ± 2</td>
<td>0.008</td>
</tr>
<tr>
<td>Endometrial thickness ≤8 mm (%)</td>
<td>10 (2)</td>
<td>54 (7)</td>
<td>60 (12)</td>
<td>0.02</td>
</tr>
<tr>
<td>Infracavitary fluid accumulation (%)</td>
<td>14 (3)</td>
<td>- (0)</td>
<td>40 (8)</td>
<td>0.01</td>
</tr>
<tr>
<td>Transverse diameter of the uterus (mm)</td>
<td>57 ± 2</td>
<td>52 ± 3</td>
<td>50 ± 2</td>
<td>0.09</td>
</tr>
<tr>
<td>Antero-posterior diameter of the uterus (mm)</td>
<td>42 ± 2</td>
<td>40 ± 2</td>
<td>39 ± 2 (18)</td>
<td>0.24</td>
</tr>
<tr>
<td>Visible gestational sac (%)</td>
<td>95 (20)</td>
<td>31 (4)</td>
<td>45 (9)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

In parentheses: number of patients.

Figure 2. Frontal section through the uterus acquired by transvaginal three-dimensional ultrasound in a patient with extrauterine pregnancy (6 weeks, human chorionic gonadotrophin: 785 mIU/ml): the endometrium appears as a symmetrical triangle with both tubal horns of equal size and height.

patients with or without bleeding symptoms were opposed [specificity: 9/11 (82%) versus 17/23 (74%); P = 1.0].

After exclusion of the three patients with poor 3D-image quality a sensitivity of 90% was found for all criteria to detect an EP (Table IV). For criterion C which showed the best performance characteristics, the false-positive rate (1 - specificity) was 16%. Based on a prevalence for EP in the study group of 39% the accuracy was 86%, the positive predictive value 78% and the negative predictive value 93%. Assuming an overall prevalence of 2% for EP the following values can be calculated for criterion C via Bayes’ theorem: accuracy 84%, positive predictive value 10%, negative predictive value 99.8%.

The results of criterion C were also calculated for a subgroup of patients with HCG serum concentrations <1500 mIU/ml as well as with regard to the endometrial thickness using a cut-off value of 8 mm (Table IV).

With endometrial asymmetry, more EPs (90%, Table III) were detected than with an endometrium thickness <9 mm (60%, Table II) (P = 0.03). An endometrium thickness ≥8 mm detected as many intrauterine pregnancies (74%) as endometrial asymmetry according to criterion C (76%). When only examinations with good 3D-image quality were considered, the detection rate of IP and SA was 71% (22/31) for an endometrial thickness ≥8 mm versus 84% (26/31) for endometrial asymmetry in the frontal plane (P = 0.34).

After exclusion of the 11 patients with intrauterine fluid accumulation, a sensitivity of 100% and a specificity of 89% were reached with criterion C for 3D ultrasound (Table V).

**Discussion**

Although nearly all intrauterine viable pregnancies showed an gestational sac in the study group it may be difficult to be
Intrauterine deformation in asymmetry is observed also to directional changes of the uterine fundus, which may be impossible to detect with transabdominal scanning in the frontal plane. If three-dimensional (3D) ultrasound therapy is available for examination, the uterine fundus may be displayed clearly with 3D scanning and delineation of the endometrial cavity can often be observed. The orientation of the uterine cavity is shown in the three-dimensional plane, but to the transverse direction of the uterus, an asymmetrical deformation of the triangle shape of the endometrium can mostly be observed when intrauterine first trimester pregnancies are examined in the frontal plane.

In contrast to the current investigation, another study (Harika et al., 1995) aimed to diagnose EP using 3D sonography to image the tube and EP itself. This procedure, however, appears to be more difficult and requires more sophisticated experience of the examiner than the described assessment of the endometrial configuration in a standardized frontal plane.

If a sufficient image quality can be obtained, a symmetrical endometrial shape is demonstrated in almost all ectopic pregnancies. Compared to a small endometrial diameter as a sign of EP (Spandorfer and Barnhart, 1996) the endometrial asymmetry in the frontal plane shows a better sensitivity in our study group. A weakness of the 3D parameter is demonstrated by the fact that fluid accumulation in the uterine cavity, which was observed in ~20% in the study group, may conceal asymmetry in the case of intrauterine gestation or may simulate
asymmetry in case of EP. This is important because it may be difficult even with transvaginal sonography to differentiate this intracavitary distention from a true intrauterine gestational sac.

There may be anatomical abnormalities of the uterus which can impede sonographic findings or even preclude an ultrasound diagnosis. So congenital uterine anomalies with asymmetrical horns such as uteri with one rudimentary horn, but also with less pronounced malformations, may simulate a pregnancy-derived endometriat asymmetry. Furthermore the endometrium may be distorted by submucous myomata which, however, can be reliably detected by the specific echo-texture with low level echogenicity and eventual posterior shadowing (Fedele et al., 1991).

Due to a false-positive rate of nearly one-fifth of the intrauterine pregnancies and the low prevalence of EP in the general population, the positive predictive value of the 3D criterion is too low to be used as a primary screening procedure to detect EP. However, because of the high negative predictive value especially in cases without intrauterine fluid collection, this criterion may serve as a reassuring sign in cases with unequivocal findings or clinically suspected EP. Moreover, the frontal uterine view may be helpful in early abortion situations to decide whether there is residual trophoblastic tissue demanding a curettage although this was not within the scope of the current study.

In conclusion, the assessment of the endometrium in the frontal uterine plane accomplished by three-dimensional sonography seems to be a useful additional diagnostic tool to distinguish intrauterine from extrauterine pregnancy in a population at high risk for EP, when the limitations mentioned above are considered. It is especially helpful in situations where neither an intrauterine nor an extrauterine gestational sac is clearly visible.

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References


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