Human Reproduction Vol.20, No.4 pp. 1107–1111, 2005 doi:10.1093/humrep/deh689
Advance Access publication January 13, 2005

Sonographic versus clinical evaluation as predictors of residual trophoblastic tissue

Ido Ben-Ami[1], David Schneider, Ron Maymon, Zvika Vaknin, Arie Herman and Reuvit Halperin

Department of Obstetrics and Gynecology, Assaf Harofeh Medical Center, Zerifin (affiliated with Sackler School of Medicine, Tel-Aviv University, Tel-Aviv), Israel

[1]To whom correspondence should be addressed at: Department of Obstetrics and Gynecology, Assaf Harofeh Medical Center, Zerifin, 70300, Israel. E-mail: idorit@netvision.net.il

BACKGROUND: The study aims to compare the diagnostic accuracy of sonographic evaluation versus clinical estimation in women suspected to have retained trophoblastic fragments. METHODS: The study group consisted of 68 consecutive patients admitted to our department due to suspected residual trophoblastic tissue. Each woman underwent ultrasound and physical examination by expert clinicians. The clinicians performing the physical examination were not informed of the sonographic findings, and vice versa. RESULTS: Patients were divided into three subgroups: clinical suspicion only of residual trophoblastic tissue ($n = 8$), sonographic suspicion only ($n = 44$) and combined sonographic and clinical suspicion of residual trophoblastic tissue ($n = 16$). In the latter group, in 14 out of 16 women (87.5%) retained trophoblastic tissue was confirmed by histological examination, a significantly higher rate compared to ultrasonographic (45.5%, $P < 0.002$) or clinical suspicion only (62.5%, $P = 0.07$). The specificity and positive predictive value of the clinical examination were significantly higher compared to ultrasonographic evaluation ($P < 0.05$), while the sensitivity of the ultrasonographic evaluation was higher than the clinical estimation ($P < 0.05$). There was no statistically significant difference in the negative predictive value or in diagnostic accuracy between the two methods. CONCLUSIONS: Based on our current experience, it seems that the combination of both clinical and ultrasonographic evaluation is recommended before uterine curettage is performed, thus lowering the rate of unnecessary invasive procedures.

Key words: clinical estimation/diagnostic accuracy/residual trophoblastic tissue/sensitivity and specificity/transvaginal sonography

Introduction

Residual trophoblastic tissue complicates nearly 1% of all pregnancies. It occurs most commonly after termination of pregnancy, but may also occur following spontaneous vaginal delivery and Caesarean section (Achiron *et al.*, 1993; Zalel *et al.*, 2001). Common symptoms include fever, vaginal bleeding and abdominal or pelvic pain. Residual trophoblastic tissue is considered to be a cause of uterine adhesions and Asherman's syndrome (Romero *et al.*, 1990). Because the possible sequel may be serious, early diagnosis of residual trophoblastic tissue is crucial.

The introduction of ultrasonographic examination into the gynaecological practice contributed greatly to the identification of remnants of a recent pregnancy. Yet, sonographically detected intrauterine findings following termination of pregnancy or delivery could be either residual trophoblastic tissue or blood clots (Shen *et al.*, 2003). Normal sonographic findings might obviate the need for exploration of the uterine cavity, while a questionable sonographic finding might lead to unnecessary curettage.

The aim of the current study was to compare the diagnostic accuracy of clinical evaluation versus sonographic examination in women suspected to have retained products of conception. The study also compares between women in whom retained trophoblastic tissue was found by histological examination and a group of women suspected to have such residua, which was not confirmed by histological examination. The comparison refers to their gynaecological history and to the clinical presentation following antecedent delivery or termination of pregnancy.

Materials and methods

The study group consisted of 68 consecutive women admitted to our department between April 1, 2000 and March 31, 2004 due to suspected residual trophoblastic tissue. The presenting symptoms included vaginal bleeding, and/or lower abdominal pain and/or fever.

Every woman in the study group was evaluated by ultrasound and by physical examination. The clinicians performing the physical examination were not informed of the sonographic findings,

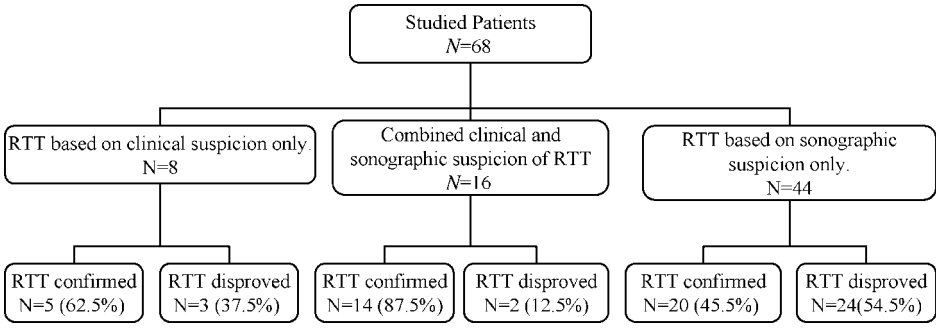

Figure 1. Patient enrolment and distribution by cause of retained trophoblastic tissue (RTT) suspicion.

and the sonographers were not informed of the clinical findings or presenting symptoms. Both the ultrasonic evaluation and the physical examination were performed by experienced clinicians. The patient's flow chart is presented in Figure 1.

The inclusion criteria in the study group was, therefore, either clinical or ultrasonographic suspicion of residual trophoblastic tissue or both. All the women underwent curettage and the extracted material was sent for pathological evaluation. One woman, in whom there was neither clinical nor ultrasonographic suspicion of retained trophoblastic tissue, was excluded.

The ultrasound examination consisted of a two-dimensional transvaginal sonography scan performed by an experienced sonographer within 24 h of admission, as well as a colour Doppler evaluation of any suspected mass. Sonographic predictors for the presence of retained trophoblastic tissue were hyperechogenic, hypoechogenic and mixed echogenic patterns measuring >5 mm, as well as blood flow signals within an intracavitary finding. After completion of the ultrasonographic examination, an evaluation of the degree of suspicion of retained trophoblastic tissue was made. Similarly, all women in the study group underwent bimanual gynaecological examination by an experienced clinician. The amount of bleeding, cervical dilatation, uterine consistency and tenderness were examined. Clinical predictors for the presence of retained trophoblastic tissue were enlarged, soft and tender uterus, cervical dilatation and active bleeding, as observed by speculum. After completion of the clinical examination, an evaluation of the degree of suspicion of retained trophoblastic tissue was made.

Following both examinations, all women in the study group underwent curettage, either because of the sonographic or clinical suspicion of retained trophoblastic tissue, or both. The extracted material obtained from the curettage was sent for histological examination, reporting also the volume of the material. The final diagnosis of the retained trophoblastic tissue was made on the basis of the presence of retained products of conception, as confirmed by histological examination.

Gynaecological history and the description of clinical presentation were obtained from the patients' medical records.

Statistical analysis

The sensitivity, specificity, positive and negative predictive values, and diagnostic accuracy of the ultrasonic and clinical evaluations were calculated and compared. For each evaluation, patients were classified into four categories: true-positive (a), true-negative (b), false-positive (c), and false-negative (d). The parameters were calculated using the following equations: sensitivity $= [a/(a + d)] \times 100$, specificity $= [b/(b + c)] \times 100$, positive predictive value $= [a/(a + c)] \times 100$, negative predictive value $= [b/(b + d)] \times 100$, diagnostic accuracy $= [(a + b)/(a + b + c + d)] \times 100$.

Descriptive parameters are expressed as mean ± SD. Frequencies are given as percentages. Student's *t*-test was used to analyse demographic variables. The StatsDirect comparison of two independent proportions test was used to compare sensitivity, specificity, positive and negative predictive values, and diagnostic accuracy. $P < 0.05$ was considered to be significant. Calculations were performed using SPSS for Windows version 11.0.

Results

A total of 68 women were recruited. They were divided into three subgroups: those with only clinical suspicion of residual trophoblastic tissue ($n = 8$), those with only sonographic suspicion ($n = 44$) and those with combined sonographic and clinical suspicion of residual trophoblastic tissue ($n = 16$). In the latter group, there were 14 out of 16 (87.5%) women in whom retained trophoblastic tissue was confirmed by histological examination, a significantly higher rate compared with the rate based on ultrasonographic (45.5%, $P < 0.002$) or clinical suspicion only (62.5%, $P = 0.07$).

The mean age of the 68 patients in the study group was 29.8 (range 19–42), gravidity 3.2 (range 1–15), and parity 1.6 (range 0–9). The mean elapsed time after delivery or abortion was 28.4 days (range 1–131). Forty-five of the 68 patients (66.2%) were admitted after early abortion, 20 patients (29.4%) after spontaneous term vaginal delivery, two (2.9%) after late abortion, and one woman (1.5%) was admitted after a Caesarean section. Of the 68 patients, 39 (57.4%) had retained trophoblastic tissue, as confirmed by histological examination. Of these 39 women, 23 (59%) were admitted after early abortion, and 16 (41%) after spontaneous term vaginal delivery.

Sixteen out of 20 women (80%) who were admitted after spontaneous term vaginal delivery had retained trophoblastic tissue as confirmed by histological examination, a rate which was significantly higher than that of the 23 out of 45 women (51.1%) who were admitted after early abortion and had retained trophoblastic tissue ($P < 0.05$).

The clinical data of the 39 women in whom trophoblastic tissue was retained was compared to the clinical data of the 29 women in whom no such tissue was found (Table I). There was no statistically significant difference between the two groups in the age, gravidity, parity, gynaecological history and the elapsed time from delivery or abortion to admission.

Table I. Gynaecological and obstetric history of patients with and without retained trophoblastic tissue

	Retained products of conception ($n = 39$)	No retained products of conception ($n = 29$)	P
Age (years)	30.1 ± 5.3	29.7 ± 7.2	NS
Gravidity	3.2 ± 2.7	3.4 ± 3.7	NS
Parity	1.5 ± 1.7	1.8 ± 2.4	NS
Caesarean section	0.3 ± 0.6	0.06 ± 0.23	NS
Early missed abortion	0.3 ± 0.4	0.5 ± 1.2	NS
Early induced abortion	1.1 ± 1.2	0.8 ± 0.9	NS
Previous abdominal surgery	0.7 ± 2.4	0.4 ± 0.9	NS
Time elapsed after delivery/abortion (days)	36.1 ± 30.2	21.9 ± 29.7	NS

Values are means ± SD.
NS = non-significant.

Table II. Clinical symptoms of patients with and without retained trophoblastic tissue

	Retained products of conception ($n = 39$)	No retained products of conception ($n = 29$)	P
Presenting symptom[a]			
Vaginal bleeding	31 (79.5)	20 (69)	NS
Fever	3 (7.7)	9 (31)	<0.05
Abdominal pain	7 (17.9)	4 (13.8)	NS
Amount of material obtained from curettage			
Low (<4 ml)	5 (12.8)	6 (20.7)	NS
Medium (4–6 ml)	19 (48.7)	16 (55.2)	NS
Large (>6 ml)	15 (38.5)	7 (24.1)	NS

Values in parentheses are percentages.
[a]There were cases with more than one presenting symptom.
NS = non-significant.

The presenting symptoms on admission were further compared between the two groups. Although the presence of fever ($>38\,^{\circ}C$) was more prevalent in women with no retained trophoblastic tissue (31%) as compared to the women with trophoblastic residua (8.3%) (Table II), there was no significant difference regarding the other presenting symptoms, such as vaginal bleeding and abdominal pain. There was also no statistically significant difference in the amount of material obtained from curettage comparing the two groups of patients (Table II).

While comparing the eight women with only clinical suspicion of retained trophoblastic tissue to the 44 patients with only ultrasonographic suspicion of residual trophoblastic tissue, no statistically significant difference was found regarding the age, gravidity, parity, gynaecological history and the elapsed time from delivery or abortion to the date of admission. There was also no significant difference in the presenting symptoms (Table III). Nevertheless, a decreased amount of material (<4 ml), obtained from curettage, was more prevalent in women with only ultrasonographic suspicion of retained trophoblastic tissue compared to those with only clinical suspicion (Table III).

Finally, we compared the sensitivity, specificity, positive and negative predictive values and diagnostic accuracy between ultrasonographic evaluation and clinical estimation as predictors for retained trophoblastic tissue (Table IV). The specificity and positive predictive value based on clinical examination were significantly higher compared to those based on ultrasonographic evaluation, while the sensitivity of the ultrasonographic evaluation was higher than the clinical estimation. There was no statistically significant difference in the negative predictive value or in the diagnostic accuracy comparing the two methods of evaluation (Table IV).

Table III. Clinical symptoms of women with clinical-only suspicion of residua, compared to women with sonographic-only suspicion of residua

	Clinical-only suspicion of residua ($n = 8$)	Sonographic-only suspicion of residua ($n = 44$)	P
Presenting symptom[a]			
Vaginal bleeding	6 (75)	33 (75)	NS
Fever	1 (12.5)	8 (18.2)	NS
Abdominal pain	2 (25)	8 (18.2)	NS
Amount of material obtained from curettage (ml)			
Small (<4 ml)	1 (12.5)	16 (36.3)	<0.05
Medium (4–6 ml)	4 (50)	16 (36.3)	NS
Large (>6 ml)	3 (37.5)	12 (27.3)	NS

Values in parentheses are percentages.
[a]There were cases with more than one presenting symptom.
NS = non-significant.

Table IV. Comparison between sonographic and clinical evaluation, regarding the retained trophoblastic tissue as confirmed by histological examination

	Sonographic evaluation	Clinical estimation	P
Sensitivity	34/39 (87.2)	19/39 (48.7)	<0.05
Specifity	3/29 (10.3)	24/29 (82.8)	<0.01
Positive predictive value	34/60 (56.7)	19/24 (79.2)	<0.05
Negative predictive value	3/8 (37.5)	24/44 (54.5)	NS
Diagnostic accuracy	37/68 (54.4)	43/68 (63.2)	NS

Values in parentheses are percentages.
NS = non-significant.

Discussion

The diagnosis of residual trophoblastic tissue presents a major clinical challenge, especially due to the possible consequences of unnecessary curettage. Since the first report by Robinson (1972), ultrasonography has been used as a diagnostic tool to help the clinician treating patients with suspected retained trophoblastic tissue. However, the reliability of sonographical diagnosis considering the retained trophoblastic tissue has been quite variable (Carlan *et al.*, 1997; de Vries *et al.*, 2000; Shalev *et al.*, 2002; Wong *et al.*, 2002; Zalel *et al.*, 2002).

The main aim of the present study was to compare the diagnostic accuracy of ultrasonographic evaluation versus clinical estimation in women suspected to have retained trophoblastic tissue. To the best of our knowledge, this is the first study addressing this issue.

The division of the study group into three subgroups (Figure 1) revealed that in women presenting with combined

clinical and sonographic suspicion of retained trophoblastic tissue, there was the highest rate of detection of residual tissue as confirmed by histologic examination, compared with the other two subgroups. This rate of close to 90% was significantly higher compared with the rate based on sonographic evidence only ($P < 0.05$), and showed a trend when compared to those with clinical suspicion only. Yet, we assume that if the sonographic-only suspicion subgroup had been larger, then there would have been a statistically significant difference.

We found that the sensitivity of ultrasonographic evaluation was higher compared to that of the clinical estimation. This high rate of sensitivity of the ultrasonographic evaluation is also supported by previous reports (Carlan *et al.*, 1997; de Vries *et al.*, 2000; Shalev *et al.*, 2002; Wong *et al.*, 2002; Zalel *et al.*, 2002). Furthermore, we found that a decreased amount of material (<4 ml) obtained from curettage was more prevalent in women with ultrasonographic as compared with clinical suspicion of retained trophoblastic tissue. These findings support the hypothesis that once there is a relatively low volume of retained trophoblastic tissue in the uterine cavity, the cervical status and thus the clinical estimation are not as sensitive as ultrasonographic evaluation.

On the other hand, we observed that both the specificity and the positive predictive value of the clinical estimation were superior to that of ultrasonographic evaluation. In other words, whenever the bimanual gynaecological examination, performed by an expert clinician, suggested the diagnosis of retained trophoblastic tissue, a relatively high rate of residual trophoblastic tissue was indeed found, as confirmed by histological examination.

Thirty-nine of the 68 patients (57.4%) had retained trophoblastic tissue, confirmed by histological examination, constituting a relatively low rate as compared with the previous reports (Carlan *et al.*, 1997; de Vries *et al.*, 2000; Shalev *et al.*, 2002; Wong *et al.*, 2002; Zalel *et al.*, 2002). A possible explanation for this relatively low rate of true residual tissue might be due to the false-positive cases diagnosed ultrasonographically, as well as by clinical estimation, while the other reports included the false-positive cases evaluated only ultrasonographically.

None of the women in the study group, admitted after late abortion or Caesarean section, was found to have residual trophoblastic tissue as confirmed by histological examination. Even though our department is a referral centre for late abortions (13–24 weeks of gestation), performed by the method of dilatation and evacuation (~500 per year), only two women in the study group were admitted after late abortion (2.9%), and actually none of them had retained trophoblastic tissue, as confirmed by histological examination. A reasonable explanation for such uneventful outcome might be due to the use of a large number of laminarias, causing the uterine cervix to become ripened and dilated satisfactorily and possibly because late abortions are performed only by expert clinicians whereas early abortions are done mainly by residents, and not always using laminaria.

A higher rate of residual trophoblastic tissue confirmed by histological examination was found in women admitted after spontaneous term vaginal delivery compared to women admitted after early abortion ($P < 0.05$). This finding is supported by a recent publication, according to which most re-evacuation samples taken during a re-evacuation procedure for suspected residua after early abortions are negative for gestational tissue (Maslovitz *et al.*, 2004).

We compared the gynaecological and obstetric history of women in whom retained products of conception were confirmed by histological examination to women in whom no such retained tissue was found. There was no statistically significant difference in any of the characteristics, thus demonstrating no anamnestic parameter that could preliminarily be effective in distinguishing between women with and without histologically confirmed retained trophoblastic tissue.

Comparison of the presenting symptoms on admission between women with and without retained trophoblastic tissue revealed a higher prevalence of fever (>38 °C) in women without residual tissue (Table II). Moreover, most of the patients presenting with fever >38 °C were falsely diagnosed by ultrasonography as having suspected remnant trophoblastic tissue, a fact which contributed to the relatively high false-positive rate of the ultrasonographic examination. It may be that in cases with fever, appearing as part of a clinical presentation of endomyometritis, the hyperaemic uterus produces such Doppler imaging, falsely suggesting the existence of residual trophoblastic tissue.

Since the completion of the current study, our approach to women in whom there is suspicion of retained trophoblastic tissue has been modified. According to this new protocol, only women in whom there is a combined clinical and sonographic suspicion of retained trophoblastic tissue undergo curettage. Conversely, women in whom there is only either clinical or sonographic suspicion of retained trophoblastic tissue are managed at first expectantly, using uterotonics and in case of fever also antibiotics. These women undergo a clinical and sonographic re-evaluation 24 h later. We thus hope to lower the rate of unnecessary curettage.

In conclusion, our data suggest that transvaginal Doppler ultrasonography as compared with clinical estimation is more sensitive in identifying women suspected to have residual trophoblastic tissue. On the other hand, the clinical estimation demonstrates higher specificity and positive predictive value. Furthermore, women in whom there is combined sonographic and clinical suspicion of retained trophoblatic tissue have more chance of having such tissue as compared to those who have only clinical or sonographic suspicion. Therefore, the combination of both clinical and sonographic evaluation is recommended before a decision to proceed with uterine curettage, thus lowering the rate of unnecessary invasive procedures.

Further studies are needed to validate these preliminary results and to suggest additional diagnostic protocol.

References

Achiron R, Goldenberg M, Lipitz S and Mashiach S (1993) Transvaginal duplex Doppler ultrasonography in bleeding patients suspected of having residual trophoblastic tissue. Obstet Gynecol 81,507–511.

Carlan SJ, Scott WT, Pollack R and Harris K (1997) Appearance of the uterus by ultrasound immediately after placental delivery with pathologic correlation. J Clin Ultrasound 25,301–308.

de Vries JI, van der Linden RM and van der Linden HC (2000) Predictive value of sonographic examination to visualize retained placenta directly after birth at 16 to 28 weeks. J Ultrasound Med 19,7–12.

Maslovitz S, Almog B, Mimouni GS, Jaffa A, Lessing JB and Many A (2004) Accuracy of diagnosis of retained products of conception after dilation and evacuation. J Ultrasound Med 23,749–756.

Robinson HP (1972) Sonar in the puerperium. A means of diagnosing retained products of conception. Scot Med J 17,364–366.

Romero R, Hsu YC, Athanassiadis AP, Hagay Z, Avila C, Nores J, Roberts A, Mazor M and Hobbins JC (1990) Preterm delivery: a risk factor of retained placenta. Am J Obstet Gynecol 163,823–826.

Shalev J, Royburt M, Fite G, Mashiach R, Schoenfeld A, Bar J, Ben-Rafael Z and Meizner I (2002) Sonographic evaluation of the puerperal uterus: correlation with manual examination. Gynecol Obstet Invest 53,38–41.

Shen O, Rabinowitz R, Eisenberg VH and Samueloff A (2003) Transabdominal sonography before uterine exploration as a predictor of retained placental fragments. J Ultrasound Med 22,561–564.

Wong SF, Lam MH and Ho LC (2002) Transvaginal sonography in the detection of retained products of conception after first-trimester spontaneous abortion. J Clin Ultrasound 30,428–432.

Zalel Y, Cohen SB, Oren M, Seidman DS, Zolti M, Achiron R and Goldenberg M (2001) Sonohysterography for the diagnosis of residual trophoblastic tissue. J Ultrasound Med 20,877–881.

Zalel Y, Gamzu R, Lidor A, Goldenberg M and Achiron R (2002) Color Doppler imaging in the sonohysterographic diagnosis of residual trophoblastic tissue. J Clin Ultrasound 30,222–225.

Submitted on June 7, 2004; resubmitted on September 13, 2004; accepted on November 25, 2004