

Occurrence and Outcome of Residual Trophoblastic Tissue

A Prospective Study

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Objective. The purpose of this study was to evaluate the occurrence of residual trophoblastic tissue after miscarriage or delivery, to assess the diagnostic value of sonography with color Doppler examination in the detection of retained tissue, and to define in what cases expectant management may be an option. **Methods.** We conducted a prospective observational study using sonography with color Doppler imaging in consecutive patients at routine follow-up after miscarriage or delivery. Expectant management was proposed in all patients with suspected retained tissue providing they were hemodynamically stable and in the absence of signs of infection. In case of surgical removal of retained tissue, the histologic examination was compared with the sonographic findings. **Results.** In total, 1070 patients were assessed. In 67 patients (6.3%), sonographic and color Doppler examination showed retained tissue, and in 41 (61%) of them, curettage was performed. In all but 1 case, retained tissue was confirmed on histologic examination. Cases of retained tissue were more often seen after first-trimester (17%) or second trimester (40%) miscarriage, in the presence of abnormal uterine bleeding (57%), and with areas of enhanced myometrial vascularity (77.3%). **Conclusions.** Sonography with color Doppler examination is clinically useful to confirm or exclude residual trophoblastic tissue. **Key words:** enhanced myometrial vascularity; residual trophoblastic tissue; sonography.

Abbreviations

AUC, area under the receiver operating characteristic curve; D&C, dilation and curettage; EMV, enhanced myometrial vascularity; LS-SVM, least squares support vector machine; PSV, peak systolic velocity; TOP, termination of pregnancy

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After pregnancy, be it a term delivery or a miscarriage, retained tissue may cause hemorrhage or infection. Both complications are associated with substantial maternal morbidity. If retained tissue is suspected in a patient with heavy postpartum bleeding or endometritis, surgical evacuation is indicated. However, in about two thirds of cases with secondary postpartum hemorrhage (defined as abnormal uterine bleeding occurring at least 24 hours after delivery), no placental tissue can be obtained at surgical evacuation.¹

Subinvolution of the placental bed, with vessels underlying the placental site remaining patent, may be another cause of secondary postpartum hemorrhage.^{2,3} These sometimes highly perfused subendometrial vessels can be damaged during curettage, and this may exacerbate bleeding.⁴ In addition to serious hemorrhage, postpartum curettage can be complicated by uterine perforation, infection, or Asherman syndrome.

Retained products of conception may be suspected on sonography in an asymptomatic or mildly bleeding patient. It is uncertain whether the sonographic diagnosis of residual trophoblastic tissue is correct in all of these cases and whether surgical removal is always necessary. There might be a place for expectant management, awaiting spontaneous expulsion of retained tissue.

The objective of this study was first to evaluate the prevalence of residual trophoblastic tissue after miscarriage or delivery, second, to assess the diagnostic value of sonography with color Doppler examination in the detection of retained tissue, and third, to define in what cases expectant management may be an option.

Materials and Methods

In this prospective observational study, sonographic and color Doppler examinations were performed in 1070 patients at the 6-week routine follow-up visit after delivery or miscarriage. All scans were done by 1 examiner (T.V.d.B) using an SSD-1700 (Aloka Co, Ltd, Tokyo, Japan) or a Sonoline Versa Pro (Siemens Aktiengesellschaft, Erlangen, Germany) ultrasound machine with a 5- to 7.5-MHz endovaginal probe or a 3.5- to 5-MHz semiconvex transabdominal probe in women seen earlier after delivery who had had an episiotomy repair. The study was approved by the local Ethics Committee, and informed consent was obtained in all patients.

On sonography, retained tissue was recorded as “absent,” “highly suspicious,” or “possible.” Highly suspicious for retained products was an echogenic well-defined mass inside the uterine cavity with or without a distinct vascular pedicle reaching the center of the suspected intracavitary lesion. Enhanced myometrial vascularity (EMV) was defined as the presence on color Doppler imaging of an area of marked flow over the full thickness of the myometrium and reaching the uterine cavity.^{5,6} In these women, maternal blood analysis was performed to exclude infection (blood sedimentation, white blood cell count, and C-reactive protein) or anemia (hemoglobin) and for β -human chorionic gonadotropin levels. Expectant management was proposed in all patients with suspected retained tissue providing they were hemody-

namically stable and in the absence of signs of infection. These patients were followed clinically and by regular sonographic and color Doppler examinations until spontaneous resolution had occurred. Surgical evacuation of the uterine cavity was performed when the patient became symptomatic (severe bleeding or signs of intrauterine infection), at the patient's request, or in the absence of spontaneous resolution over 6 weeks. If the patient declined expectant management, surgical removal was performed within 1 week. Curettage was performed under sonographic or hysteroscopic guidance. Histologic examination was performed in all surgically treated cases.

In the descriptive statistics, the prevalence of residual trophoblastic tissue diagnosed on sonography and the incidence of surgical interventions for evacuation of retained tissue were reported for the total group as well as for different subgroups. In those who subsequently underwent curettage, the accuracy of sonography was evaluated against the histologic findings. In women with successful expectant management, we evaluated whether some variables were associated with spontaneous resolution.

The prediction of residual trophoblastic tissue and surgical evacuation of residual trophoblastic tissue was first evaluated by univariate analysis using the Wilcoxon rank sum test, logistic regression, the Fisher exact test, and the Wald χ^2 test as appropriate. Further analysis included multivariate logistic regression analysis with an ordinal response using stepwise selection in the Logistic procedure from SAS software package release 9.1 (SAS Institute Inc, Cary, NC). Least squares support vector machine (LS-SVM) models with a linear kernel⁷ were used to predict retained tissue and surgical removal of retained tissue based on patient characteristics and sonographic and color Doppler features.

Results

The study included 1070 consecutive pregnancies: 873 third-trimester deliveries (81.6%), 15 second-trimester demises (1.4%), 25 terminations of pregnancy (TOPs) (2.3%), and 157 first-trimester miscarriages (14.6%). The mean (SD) gestational ages were 38.3 (1.8), 16.3 (3), 8.6 (3.2),

and 8.1 (2) weeks, respectively. The average patient age was 29.3 (4.5) years with a mean parity and gravidity of 1.5 (0.9) and 2 (1.3).

In the third-trimester deliveries, the placenta was delivered spontaneously in 76.8%, by cesarean delivery in 19.9%, and by surgical removal in 3.2%. Curettage was performed to deliver the placenta in 5 of the 15 cases of second-trimester demises. In 63.7% of the first-trimester miscarriages, curettage was performed. Eight percent (2) of the 25 TOPs were medically induced, whereas 92% were performed by suction curettage.

The median interval between the delivery/miscarriage and the sonographic examination was 6 weeks (mean, 6.3; SD, 3.2; 54 patients [5%] did undergo examination within the first week). In 67 patients (6.3%) residual trophoblastic tissue was reported at sonographic examination, whereas in another 61 women (5.7%), the presence of retained tissue was recorded as possible. Residual trophoblastic tissue was seen in 2.7% after third-trimester delivery, in 40% after second-trimester demise, in 17.8% after first-trimester miscarriage, and in 36% after TOP (Table 1). At the time of sonographic examination, 161 women (15%) had abnormal uterine bleeding; in 37 of them (23%), remnants were seen on sonography, and in 27 (16.8%), possible retained tissue was recorded. Fifty-seven percent of women with retained tissue on sonography had abnormal uterine bleeding, versus 45% in the group with possible remnants and 10% in women without sonographic evidence of retained products. Focal EMV^{6,7} was described in 77.3% of the cases of residual trophoblastic tissue, in 34.3% of those with possible remnants, and in 1.5% of the women

without suspicion of retained tissue. The average peak systolic velocity (PSV) in cases of EMV was 46.1 (range, 14–141.8; SD, 23.4) cm/s.

Thirteen patients (1.2%) were not candidates for expectant management and underwent curettage on the same day of the sonographic evaluation. In total, 50 women eventually underwent curettage for alleged retained products: 24 (2.8% of the subgroup) in the subgroup of third-trimester deliveries, 7 (46.7%) after second-trimester demise, 12 (7.6%) after first-trimester miscarriage, and 7 (28%) after TOP. Of the 67 patients with retained tissue on sonography, 41 (61%) eventually underwent surgical evacuation. In all but 1 (97.6%), retained tissue was confirmed on histologic examination; EMV was present in 77.5% of them. Of the 26 patients with retained tissue on sonography who did not undergo surgical removal, 14 had follow-up sonography confirming the absence of residual tissue; 5 became pregnant during follow-up; 2 had normal clinical gynecologic examination findings; 1 had an endometrial biopsy showing normal endometrial tissue 3 months later; and 4 did not appear again. Of those women with possible retained products on sonography, 8 (13.1%) went for curettage; at histologic examination, retained products were reported in half of them, and all of them had areas of EMV. In 1 patient, an area of high-velocity EMV (PSV, 90.6 cm/s) was visualized, but initially no remnants were seen. Because subsequent sonographic examination was suggestive of a polypoid lesion with a prominent vascular pedicle (PSV, 76.3 cm/s), a surgical hysteroscopy was performed, confirming a placental polyp.

Table 1. Last Pregnancy Versus Residual Trophoblastic Tissue Seen on Sonography

Last Pregnancy	n	Sonographic Findings on Residual Tissue					
		Highly Suspicious		Absent		Possible	
		n	%	n	%	n	%
3rd trim	873	24	2.7	815	93.4	34	3.9
2nd trim	15	6	40	5	33.3	4	36.7
1st trim	157	28	17.8	112	71.3	17	10.8
TOP	25	9	36	10	40	6	24
Total	1070	67	6.3	942	88	61	5.7

1st trim indicates first-trimester miscarriages; 2nd trim, second-trimester demises; and 3rd trim, third-trimester deliveries. There is a significant difference between 3rd trim and 2nd trim ($P = 4.17 \times 10^{-9}$), 1st trim ($P = 3.9 \times 10^{-14}$) and TOP ($P = 10.06 \times 10^{-11}$), 2nd trim and 1st trim ($P = .0082$), and 1st trim and TOP ($P = .0065$) (Fisher exact test).

Table 2. Comparison of Those Patients Who Ultimately Underwent Surgical Removal for Residual Trophoblastic Tissue on Scans Versus Those Who Did Not as to Patient Characteristics and Sonographic and Color Doppler Findings (Based on the Training Set; n = 720)

Variable	P	OR	95% CI
Last pregnancy*	7.39 × 10 ⁻⁰⁶	1.44	1.25–1.66
GA†	.0005	0.96	0.93–0.98
Transfusion*	.004	6.04	2.33–15.67
Bleeding symptoms*	2.3 × 10 ⁻¹⁴	11.33	6.14–20.91
Residual trophoblastic tissue on sonography*	9.83 × 10 ⁻³⁶	>999.9	199.96–>999.99
EMV on color Doppler imaging*	1.85 × 10 ⁻²⁷	78.91	37.13–167.7
2nd trim‡§	<.0001	28.49	8.65–93.86
1st trim‡§	.01	2.99	1.30–6.9

CI indicates confidence interval; 1st trim, first-trimester miscarriages; GA, gestational age; OR, odds ratio; and 2nd trim, second-trimester demises. Last pregnancy was recorded as term pregnancy, second-trimester demise, or first-trimester miscarriage or TOP; GA at delivery/miscarriage was recorded as the number of fulfilled weeks; transfusion, bleeding symptoms, and EMV were recorded as yes or no; and residual tissue on sonography was recorded as yes (possible) or no.

‡P values and ORs were obtained with the Fisher exact test () or Wald χ^2 test (‡). †P value was obtained with the Wilcoxon rank sum test, and OR was obtained with logistic regression.

§Versus third-trimester delivery.

Surgical evacuation of retained tissue was performed more often after first- and second-trimester demise, in cases of uterine bleeding, in patients who had a postpartum blood transfusion, and especially in women with retained tissue on sonography or EMV on color Doppler examination (Table 2).

The prediction LS-SVM models for surgical evacuation of residual trophoblastic tissue based on patient characteristics selected the following variables: second-trimester miscarriage, gestational age, postpartum transfusion, and bleeding symptoms (area under the receiver operating characteristic curve [AUC], 0.90), whereas the

model based on both patient characteristics and sonographic findings selected the following variables: first-trimester miscarriage, retained tissue according to sonography, and EMV on color Doppler examination (AUC, 0.99; Table 3).

Discussion

This study shows that residual trophoblastic tissue is commonly seen on sonography, especially after TOP or after first- or second-trimester miscarriage.

Because of the study design, not all patients underwent dilation and curettage (D&C) to confirm or refute the presence of retained tissue. Therefore, our results do not allow a definitive conclusion as to the accuracy of sonography in the diagnosis of retained tissue. However, in almost all women in whom sonographic findings were highly suspicious for residual trophoblastic tissue and who underwent D&C, retained tissue was confirmed at histologic examination. Sonography can reliably show retained tissue, at least in those cases in which the sonographer is confident about the diagnosis. A previous series reported the difficulty in making a definitive sonographic diagnosis in all cases.⁸ In about 6% of the cases in our study, the sonographer reported possible remnants. Dilation and curettage was performed in 13% of these patients, and remnants were confirmed in only half of them. All of them had areas of EMV. However, because of the study design, we cannot conclude that most cases in the subgroup with possible remnants did not have retained tissue because at least part of them could have had genuine remnants that may have been expelled spontaneously. The clinical relevance of our results is that expectant management is justified when the sonographer is uncertain about the presence of remnants, especially if no EMV is visualized.

Table 3. Multivariate Analysis With Model Building Using LS-SVM Models With a Linear Kernel Predicting Surgical Removal of Retained Tissue Based on Patient Characteristics With and Without Sonographic and Color Doppler Features

Basis of Model	AUC (95% CI)	AUC (95% CI)
	Training Set (n = 720)	Prospective Validation (n = 350)
Patient characteristics without sonographic features	0.9 (0.87–0.97)	0.78 (0.71–0.84)
Patient characteristics with sonographic features	0.99 (0.990–0.995)	0.98 (0.98–0.99)

CI indicates confidence interval. The nonoverlapping 95% CIs show a statistically significant difference between the models based on patient characteristics with and without sonographic with color Doppler features in both the training and validation sets.

To evaluate the natural history in cases of alleged retained tissue, patients and clinicians should ideally have been blinded to the sonographic results, and all patients should have opted for expected management for at least 6 weeks. In this study, expectant management was proposed to all hemodynamically stable patients. Forty-six percent of patients with retained tissue of conception opted for D&C within 1 week because they found it psychologically difficult to wait or because they feared abdominal cramps or vaginal bleeding. From those initially opting for expectant management, some became impatient during follow-up and asked for D&C before completion of the 6-week interval. Taking those study weaknesses into account, this study still showed that about 40% of women in whom retained tissue was seen on sonography did not need D&C. For those with possible retained tissue, almost 9 of 10 resolved spontaneously. These results indicate that expectant management is justified in many patients with sonographic evidence of retained tissue.

The models based on both patient characteristics and the sonographic and color Doppler findings provide an excellent prediction of the need for curettage for retained tissue. The presence of remnants on sonography, especially if EMV is visualized on color Doppler examination, is associated with a dramatic increase in the risk for surgical intervention (Table 3). However, because the clinician and the patient were not blinded to the results of sonography, this could have induced a bias. Notwithstanding the fact that the presented results must be interpreted with caution, they indicate that the use of color Doppler imaging may play an essential role in the diagnosis of retained tissue: if an echogenic well-vascularized intracavitary lesion is seen after miscarriage or delivery, retained tissue is most likely.⁹⁻¹²

We conclude that, unlike in previous reports,⁸ sonography with color Doppler examination is reliable for confirming or excluding residual trophoblastic tissue. When the presence of retained products of conception is uncertain on a scan, expectant management may be proposed. The question of whether cases with retained tissue on scans are better managed conservatively or whether they need immediate surgical evacuation needs further investigation.

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