

Uterine Artery Doppler Flow Velocimetry Parameters for Predicting the Occurrence of Persistent Gestational Trophoblastic Neoplasia After Evacuation of Complete Hydatidiform Mole (A Prospective Cohort Study)

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ABSTRACT

Background & Objective: Persistent gestational trophoblastic disease (PGTD) develops in approximately 15% to 20% of cases following the evacuation of a complete hydatidiform mole. Early risk stratification is imperative to prevent delayed intervention or unnecessary systemic chemotherapy. Serial serum human chorionic gonadotropin (β -hCG) monitoring remains the gold standard but presents limitations in early prediction. This prospective cohort study aimed to evaluate the predictive efficacy of uterine artery transvaginal Doppler flow velocimetry—specifically Pulsatility Index (PI), Resistance Index (RI), and Systolic/Diastolic (S/D) ratio—measured prior to and 4–6 weeks after suction evacuation for the early development of PGTD.

Methods: A prospective cohort investigation was carried out on 175 patients diagnosed with complete hydatidiform mole at Minia University Maternity Hospital. Transvaginal Doppler ultrasound parameters of both right and left uterine arteries were captured baseline (pre-evacuation) and during routine follow-up (4–6 weeks post-evacuation). Clinical, demographic, and biochemical (serum β -hCG) parameters were recorded. Logistic regression models and Receiver Operating Characteristic (ROC) curves were executed to delineate independent predictors and diagnostic cut-off thresholds.

Results: Of 175 initially enrolled participants, 167 completed the full clinical protocol (32 developed PGTD [19.16%], and 135 achieved spontaneous remission [80.84%]). Demographic characteristics were comparable between groups. Pre-evacuation serum β -hCG failed to maintain independent predictive significance in multivariate regression. Conversely, multivariate logistic regression confirmed pre-evacuation PI (OR = 7.18, 95% CI: 1.12–45.94, P = 0.037) and post-evacuation PI (OR = 0.018, 95% CI: 0.002–0.173, P = 0.0005) as the sole independent predictors of malignant transformation. ROC curve analysis demonstrated superior diagnostic performance for post-evacuation PI, achieving an AUC of 0.942.

Conclusion: Transvaginal uterine artery Pulsatility Index seems to be a safe, effective non-invasive alternative biophysical marker for early prediction of post-molar PGTD alongside traditional serum β -hCG tracking.

Keywords: Complete Hydatidiform Mole; Persistent Gestational Trophoblastic Disease (PGTD); Uterine Artery Doppler; Pulsatility Index; Gestational Trophoblastic Neoplasia; Transvaginal Ultrasonography; Predictive Hemodynamics.

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INTRODUCTION

Gestational Trophoblastic Disease (GTD) encompasses a heterogeneous spectrum of inter-related pregnancy-related disorders stemming from abnormal trophoblastic proliferation within the placenta. This spectrum ranges from benign pre-

malignant entities, such as complete hydatidiform mole and partial hydatidiform mole, to frank malignant manifestations collectively referred to as Gestational Trophoblastic Neoplasia (GTN) or Persistent Gestational Trophoblastic Disease (PGTD). PGTD includes invasive mole,

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choriocarcinoma, placental site trophoblastic tumor (PSTT), and epithelioid trophoblastic tumor (ETT). Among molar gestations, complete hydatidiform mole represents the most prevalent clinical presentation, carrying a substantial risk of malignant transformation.

Epidemiological studies indicate that following standard therapeutic suction evacuation, approximately 15% to 20% of women diagnosed with complete hydatidiform mole will subsequently develop persistent gestational trophoblastic disease. Conversely, partial hydatidiform moles exhibit a markedly lower rate of malignant progression, estimated at 0.5% to 5%. In low- and middle-income clinical settings, gestational trophoblastic disease presents additional diagnostic and therapeutic challenges due to variable patient compliance during long-term follow-up, limited health resources, and late patient presentation with advanced uterine enlargement or severe clinical complications.

The primary cornerstone of post-evacuation surveillance relies universally on serial monitoring of quantitative serum human chorionic gonadotropin (β -hCG) levels. The International Federation of Gynecology and Obstetrics (FIGO) has established standardized biochemical criteria for diagnosing PGTD based on serum β -hCG plateauing or secondary re-elevation. Although serial serum β -hCG surveillance demonstrates exceptional diagnostic sensitivity, sole reliance on biochemical markers possesses inherent clinical limitations. Serum β -hCG plateauing requires multiple weekly assessments, during which invasive trophoblastic tissue may continue to proliferate, potentially leading to delayed initiation of single-agent or multi-agent systemic chemotherapy. Furthermore, biochemical monitoring alone provides no spatial or anatomical detail regarding deep myometrial invasion, extra-uterine extensions, or localized pelvic vascular malformations.

Physiologically, normal early pregnancy is characterized by profound maternal vascular remodeling. Trophoblastic cells invade the maternal decidua and uterine spiral arteries, replacing the muscular and elastic components of the arterial wall. This process converts high-resistance, low-flow spiral vessels into low-resistance, high-capacity channels that ensure adequate uteroplacental perfusion. In molar gestations, hyperplastic trophoblastic invasion induces exaggerated vascular remodeling. Crucially, when trophoblastic tissue invades deeper myometrial layers or undergoes malignant transformation into invasive mole or choriocarcinoma, it induces extensive neo-angiogenesis, extensive vessel destruction, and direct arteriovenous shunting within the myometrium.

Transvaginal Color Doppler Ultrasonography (TV-CDS) enables non-invasive, real-time visual and quantitative assessment of pelvic hemodynamic changes. By evaluating uterine artery flow velocimetry parameters—including Pulsatility Index (PI), Resistance Index (RI), and Systolic to Diastolic (S/D) velocity ratio—clinicians can non-invasively quantify downstream vascular impedance. Invasive trophoblastic proliferation lowers downstream vascular resistance, producing characteristic low-resistance, high-velocity arterial blood flow waveforms. However, historical literature presents conflicting data regarding whether pre-evacuation or post-evacuation uterine artery Doppler indices possess superior diagnostic accuracy, and whether Doppler parameters act as independent risk predictors when adjusted for baseline serum β -hCG levels and clinical risk factors.

Therefore, the objective of this prospective cohort study was to comprehensively evaluate the predictive efficacy of uterine artery transvaginal Doppler velocimetry—measured both prior to evacuation and at 4–6 weeks post-evacuation—in predicting the development of persistent gestational trophoblastic disease among patients treated for complete hydatidiform mole at Minia University Maternity Hospital. By establishing precise biophysical parameters, this study aims to refine post-molar risk stratification, facilitating early therapeutic interventions for high-risk cohorts while alleviating patient anxiety and over-monitoring in low-risk populations.

MATERIALS AND METHODS

This prospective observational cohort study was conducted at the Department of Obstetrics and Gynecology, Minia University Maternity Hospital, Minia, Egypt, over a 20-month period spanning from December 2023 to July 2025. The study protocol was reviewed, approved, and granted institutional clearance by the Institutional Review Board (IRB) and Ethics Committee of the Faculty of Medicine, Minia University. This study was registered in clinicaltrials.gov (Identifier: NCT07333326). All clinical procedures were performed in strict compliance with the ethical principles for medical research involving human subjects set forth in the Declaration of Helsinki. Prior to enrolment, written informed consent was obtained from all eligible participants after providing a comprehensive explanation of the study objectives, ultrasound examinations, serial blood sampling, follow-up schedules, and potential risks.

Inclusion criteria of the study were female patients presenting with suspected molar pregnancy who had confirmed histological diagnosis of complete hydatidiform mole following suction evacuation,

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were hemodynamically stable undergoing standardized surgical suction evacuation, and expressed full commitment to complete the rigorous 6-month biochemical and clinical follow-up protocol. While cases with histological confirmation of partial hydatidiform mole, non-molar hydropic degeneration, ectopic pregnancy, co-existing severe maternal medical conditions (such as chronic hypertension, pre-existing renal disease, systemic lupus erythematosus, or underlying vascular disorders that alter pelvic hemodynamics), prior receipt of systemic chemotherapy or surgical hysterectomy as primary management, or incomplete follow-up data and withdrawal of consent were excluded from the study.

Following initial clinical, biochemical, and Doppler evaluations, all enrolled patients underwent standardized surgical management. Suction evacuation was performed under general anesthesia in the operating room. Intravenous oxytocin infusion (20 IU in 500 mL Normal Saline at 125 mL/hr) was initiated intraoperatively following initial uterine decompression to promote uterine contraction and minimize perforation risks. Evacuated tissue specimens were immediately fixed in 10% neutral buffered formalin and submitted to the Department of Pathology for histopathological evaluation. Diagnosis of complete hydatidiform mole was confirmed by board-certified pathologists based on diffuse trophoblastic hyperplasia, circumferential villous edema, total absence of embryonic/fetal tissue, and absence of fetal erythrocytes.

Ultrasound examinations were executed using a high-resolution GE Voluson E8 ultrasound system equipped with a 6-12 MHz transvaginal probe. All Doppler evaluations were performed by experienced senior sonographers who were blinded to the patients' baseline quantitative serum β -hCG levels to eliminate investigator bias. Doppler flow velocimetry assessments were carried out pre-evacuation (within 24 hours prior to suction evacuation upon initial hospital admission) and post-evacuation (during routine follow-up between 4 to 6 weeks following surgical evacuation). Patients emptied their bladder immediately before transvaginal scanning. The probe was inserted gently into the anterior vaginal fornix. The main uterine artery was identified in the sagittal plane at the level of the internal os, using color Doppler flow mapping to locate the vessel as it turns superiorly along the lateral margin of the cervix and lower uterine segment. The Doppler sample volume gate was set at 2 mm and positioned in the center of the vessel. The angle of insonation was manually adjusted to be as close to 0 degrees as possible, strictly maintained below 30 degrees. Spectral Doppler waveforms were recorded across at least

three to five consecutive, uniform cardiac cycles during periods of absent maternal breathing motion. Pulsatility Index (PI), Resistance Index (RI), and Systolic/Diastolic Ratio (S/D) were automatically calculated. For each patient, Doppler measurements were obtained independently from both right and left uterine arteries, and the mean value of the two sides was utilized for statistical computations.

Following discharge, patients entered a strict post-molar surveillance program. Quantitative serum β -hCG levels were measured weekly using enzyme-linked immunosorbent assay (ELISA) until three consecutive weekly samples yielded undetectable levels (<5 mIU/mL). Thereafter, monthly serum β -hCG levels were obtained for 6 consecutive months. Primary study outcome was the development of Persistent Gestational Trophoblastic Disease (PGTD), defined strictly according to FIGO 2000 diagnostic criteria: plateau of serum β -hCG levels (less than 10% decrease) across four consecutive measurements taken over a period of at least three weeks; progressive rise in serum β -hCG levels of 10% or greater across three consecutive measurements over a period of at least two weeks; or histopathological identification of invasive mole or choriocarcinoma on tissue re-evaluation or metastatic biopsy. Patients meeting FIGO criteria for PGTD were promptly transferred to the Gynecologic Oncology Unit for staging and initiation of appropriate single-agent or multi-agent chemotherapy. Patients who maintained steady decay of serum β -hCG reaching normal thresholds (<5 mIU/mL) were classified into the 'Spontaneous Remission' group.

Sample size estimation was conducted prior to study initiation using G*Power software (v3.1.9). Based on historical PGTD incidence rates of 18% post-CHM, a minimum sample size of 150 patients was required to achieve 80% statistical power ($\beta = 0.20$) with a two-sided alpha level of 0.05 ($\alpha = 0.05$) to detect a significant difference in mean Pulsatility Index between Remission and PGTD cohorts. To account for an anticipated 15% loss to follow-up, enrollment was targeted at 175 patients. Statistical analyses were executed using SPSS Version 21.0 (IBM Corp., Armonk, NY, USA). Continuous variables were tested for normality using the Kolmogorov-Smirnov test and compared using Independent Student's t-test or ANOVA. Categorical variables were compared using Pearson's Chi-square test or Fisher's exact test. Factors demonstrating $P < 0.10$ in univariate models were entered into multivariate binary logistic regression to derive adjusted Odds Ratios (OR) and 95% Confidence Intervals (CI). Receiver Operating Characteristic (ROC) curve analysis was conducted to establish optimal predictive cut-off values, Area

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Under Curve (AUC), sensitivity, and specificity. P-values < 0.05 were considered statistically significant.

RESULTS

The study included 175 female patients presenting with complete hydatidiform mole between December 2023 and July 2025. Among these, 8 patients were lost to follow-up, leaving 167 patients who completed the full surveillance protocol (32 developed PGTD, representing 19.16%, while 135 achieved complete spontaneous remission, representing 80.84%). The demographic characteristics are seen in Table 1.

Ultrasound findings prior to evacuation showed higher frequencies of enlarged uterine size and theca lutein cysts in the PGTD group, though these differences did not reach statistical significance, as detailed in Table 2.

Regarding main hemodynamic outcomes, pre-evacuation serum β -hCG levels were not significantly

different between groups, whereas pre-evacuation uterine artery Doppler indices (PI, RI, and S/D ratio) showed statistically significant differences, as seen in Table 3.

Furthermore, post-evacuation uterine artery Doppler parameters demonstrated that patients developing PGTD had significantly lower mean PI and S/D ratio compared to the remission group, as detailed in Table 4.

In univariate logistic regression analysis, pre-evacuation β -hCG and all Doppler indices were significantly associated with PGTD development, as shown in Table 5. However, in multivariate logistic regression, only pre-evacuation PI (OR = 7.18, P = 0.037) and post-evacuation PI (OR = 0.018, P = 0.0005) remained significant independent predictors of PGTD, as shown in Table 6. Other findings and predictive modeling metrics are seen in the corresponding tables.

Table 1. Comparison of Baseline Demographic and Obstetric Characteristics Among Missed Follow-up, PGTD, and Remission Groups

Parameter	Missed follow up (N=8)	PGTD (N=32)	Remission (N=135)	Test	P Value
Age (Mean $\pm$ SD)	31.9 $\pm$ 6.6	32.4 $\pm$ 7.1	31.3 $\pm$ 6.3	F = 0.38	0.67
Parity (Mean $\pm$ SD)	2.8 $\pm$ 1.7	3.4 $\pm$ 2.3	2.7 $\pm$ 1.9	F = 1.63	0.19
Gravidity (Mean $\pm$ SD)	6.3 $\pm$ 3.1	7.5 $\pm$ 3.9	6.99 $\pm$ 3.99	F = 0.36	0.69
Gestational age (Mean $\pm$ SD)	9.8 $\pm$ 2.2	10.8 $\pm$ 3.7	10.4 $\pm$ 3.4	F = 0.32	0.72

Table 2. Comparison of Ultrasound Findings Among Missed Follow-up, PGTD, and Remission Groups

Parameter	Missed follow up (N=8)	PGTD (N=32)	Remission (N=135)	Test	P Value
Large Uterus: Yes	1 (12.5%)	11 (34.4%)	33 (24.4%)	X ² = 2.1	0.34
Large Uterus: No	7 (87.5%)	21 (65.6%)	102 (75.6%)	-	-
Theca Cyst: Yes	0 (0%)	8 (25%)	16 (11.9%)	X ² = 5.1	0.07

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Theca Cyst: No	8 (100%)	24 (75%)	119 (88.1%)	-	-
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Table 3. Comparison of Pre-evacuation Serum β -hCG and Uterine Artery Doppler Parameters

Parameter	Missed follow up (N=8)	PGTD (N=32)	Remission (N=135)	Test	P Value
Pre hCG (Mean $\pm$ SD)	310275.2 $\pm$ 844452.1	372828.3 $\pm$ 745320.1	156302.2 $\pm$ 444775	F = 2.3	0.102
Pre PI (Mean $\pm$ SD)	1.31 $\pm$ 0.41	1.70 $\pm$ 0.53	1.27 $\pm$ 0.38	F = 14.11	<0.001*
Pre RI (Mean $\pm$ SD)	1.14 $\pm$ 0.37	0.84 $\pm$ 0.16	1.12 $\pm$ 0.33	F = 10.8	<0.001*
Pre SD (Mean $\pm$ SD)	6.78 $\pm$ 3.78	4.05 $\pm$ 1.34	6.01 $\pm$ 2.89	F = 7.3	<0.001*

Table 4. Comparison of Post-evacuation Uterine Artery Doppler Parameters

Parameter	PGTD (N=32)	Remission (N=135)	Test	P Value
Post PI (Mean $\pm$ SD)	1.32 $\pm$ 0.31	3.01 $\pm$ 0.95	t = 10.3	<0.001*
Post RI (Mean $\pm$ SD)	0.87 $\pm$ 0.19	1.09 $\pm$ 0.33	t = 3.77	<0.001*
Post SD (Mean $\pm$ SD)	3.90 $\pm$ 1.52	6.99 $\pm$ 3.99	t = 4.48	<0.001*

Table 5. Univariate Logistic Regression Analysis of Predictors of PGTD

Variable	B	S.E.	Wald	Sig.	Exp(B)	95% C.I. Lower	95% C.I. Upper
Age	0.027	0.031	0.756	0.3847	1.027	0.967	1.091
Gestational age	0.042	0.056	0.557	0.4554	1.043	0.934	1.163
Gravidity	0.033	0.049	0.439	0.5078	1.033	0.938	1.138
Parity	0.172	0.093	3.443	0.0635	1.188	0.990	1.425
Uterus large	0.482	0.423	1.300	0.2543	1.619	0.707	3.707

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Theca cyst	0.908	0.487	3.470	0.0625	2.479	0.954	6.445
Pre hCG	0.000	0.000	3.950	0.0469	1.000	1.000	1.000
Pre PI	2.374	0.547	18.856	0.0000	10.745	3.679	31.382
Post PI	-4.530	0.966	22.008	0.0000	0.011	0.002	0.072
Pre RI	-3.905	0.933	17.531	0.0000	0.020	0.003	0.125
Post RI	-2.788	0.816	11.683	0.0006	0.062	0.012	0.304
Pre SD	-0.312	0.091	11.821	0.0006	0.732	0.613	0.874
Post SD	-0.538	0.113	22.869	0.0000	0.584	0.468	0.728

Table 6. Multivariate Logistic Regression Analysis of Independent Predictors of PGTD

Variable	B	S.E.	Wald	Sig.	Exp(B)	95% C.I. Lower	95% C.I. Upper
Pre hCG	-0.000	0.000	0.042	0.8376	1.000	1.000	1.000
Pre PI	1.971	0.947	4.333	0.0374	7.180	1.122	45.942
Post PI	-4.030	1.161	12.056	0.0005	0.018	0.002	0.173
Pre RI	-1.881	1.956	0.924	0.3363	0.152	0.003	7.051
Post RI	0.588	1.710	0.118	0.7309	1.801	0.063	51.454
Pre SD	-0.209	0.219	0.919	0.3378	0.811	0.528	1.245
Post SD	-0.436	0.258	2.858	0.0909	0.646	0.390	1.072

DISCUSSION

This prospective cohort investigation was carried out over a 20-month period (December 2023 to July 2025) at Minia University Maternity Hospital to evaluate the predictive efficacy of uterine artery transvaginal Doppler flow velocimetry in women undergoing suction evacuation for complete hydatidiform mole. Early detection of persistent gestational trophoblastic disease (PGTD) remains crucial to prevent malignant morbidity and avoid unnecessary systemic chemotherapy.

The main outcome of this study demonstrates that post-evacuation Pulsatility Index (PI) is a highly significant independent predictor of malignant transformation, showing a significant decrease in

impedance among patients who developed PGTD versus those who achieved spontaneous remission ($P = 0.0005$). Pre-evacuation PI also maintained independent predictive value ($P = 0.037$), whereas initial serum β -hCG lost independent significance in multivariate analysis. Our findings align with previous work by Seckin et al. (2015) and Epstein et al. (2011), who similarly noted that post-evacuation low vascular resistance strongly correlates with persistent trophoblastic activity. In contrast, earlier studies by Lurie et al. (2004) and Hsieh et al. (1994) evaluated smaller patient cohorts and observed variable predictive performance of pre-evacuation parameters, likely attributable to differences in sample size, timing of sonographic assessment, and

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varying degrees of initial myometrial vascularization. Furthermore, Ayas et al. (2013) demonstrated that persistent low impedance at 4 weeks post-evacuation had superior diagnostic accuracy over static serum β -hCG values, which reinforces our findings regarding the clinical utility of post-evacuation Doppler surveillance.

Points of strength of this study include its rigorous prospective cohort design, single-center consistency in surgical management, double-blinded sonographic evaluation, and high protocol completion rate over a standard 6-month FIGO follow-up period. On the other hand, limitations were the single-center setting at a tertiary hospital, potential operator dependency inherent to Doppler ultrasonography, inability of main uterine artery Doppler to detect very small focal myometrial invasive lesions, and loss to follow-up in 8 patients.

CONCLUSION

Transvaginal uterine artery Pulsatility Index (PI) appears to be a safe, non-invasive alternative biophysical marker for early prediction of PGTD following evacuation of complete hydatidiform mole, offering comparable diagnostic effectiveness alongside standard β -hCG monitoring. Its low complication rate and strong safety profile can be weighed favorably against potential diagnostic delays. Further large multi-centric randomized controlled trials and prospective studies are needed to confirm the findings of this study.

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