DOI: 10.38103/jcmhch.17.2.11

Original research

UTILIZATION OF UTERINE ARTERY DOPPLER SONOGRAPHY IN HYDATIDIFORM MOLE

Nguyen Van Tuan Anh[1], Nguyen Thi Kim Anh[2], Nguyen Thanh Xuan[1], Dinh Thi Phuong Minh[1], Nguyen Phuoc Thanh Nhan[1]

[1]Center for Obstetrics and Gynaecology, Hue Central Hospital, Viet Nam

[2]Department of Obstetrics and Gynaecology, Hue University of Medicine and Pharmacy, Viet Nam

ABSTRACT

Background: *A hydatidiform mole is characterized by the abnormal proliferation of syncytiotrophoblast and replacement of normal placental trophoblastic tissue by hydropic placental villi. Numerous studies conducted globally have indicated that the uterine artery doppler index can be employed to monitor and predict post-molar gestational trophoblastic neoplasia. This study aims to investigate the characteristics of uterine artery doppler sonography in hydatidiform mole and assess its predictive value for spontaneous remission.*

Methods: *This cross-sectional observational study included 31 molar pregnancy patients treated at Department of Obstetrics and Gynecology - Hue University of Medicine and Pharmacy Hospital and Center for Obstetrics and Gynecology - Hue Central Hospital from March 2020 to June 2022.*

Results: *Post-molar gestational trophoblastic neoplasia developed in 3 out of 31 hydatidiform mole cases. The doppler indices of the low-risk molar pregnancy group (PI 1.77; RI 0.79 and S/D 5.57) were higher than those of the high-risk group (PI 1.48; RI 0.58 and S/D 3.47), $p < 0.05$. The doppler indices of the spontaneous remission group increased significantly from pre-evacuation (PI 1.75; RI 0.75; S/D 5.00) to post-evacuation (PI 2.50; RI 0.86; S/D 6.80). The cutoff values predicting spontaneous remission were pre-evacuation PI ≥ 1.19 (sensitivity 85.7% and specificity 66.7%) and pre-evacuation RI ≥ 0.47 (sensitivity 96.4% and specificity 66.7%).*

Conclusion: *Uterine artery doppler sonography is useful for the diagnosis and monitoring of molar pregnancy patients.*

Keywords: *Hydatidiform mole, Uterine artery Doppler ultrasound, βhCG.*

I. BACKGROUND

Gestational trophoblastic disease (GTD) encompasses a range of conditions characterized by abnormal trophoblast. This includes both benign forms like partial hydatidiform mole (PHM) and complete hydatidiform mole (CHM), as well as the malignant forms known as gestational trophoblastic neoplasms, which include invasive mole, choriocarcinoma, placental site trophoblastic tumor, and epithelioid trophoblastic tumor [1, 2]. Among these, hydatidiform mole is the most prevalent type of GTD, with higher incidence rates observed among American Indian, Eskimo, non-white Hispanic, and Asian populations [3].

The surveillance post-evacuation hydatidiform mole plays a vital role in the detection of gestational trophoblastic neoplasia (GTN). The incidence of GTN after a CHM is between 15-20%, whereas for a PHM, it is between 1 - 3% [4]. According to Zakaria's research conducted in 2020, the prevalence of GTN following CHM and PHM in Egypt was found to be 24.2% and 8% respectively [5]. In contrast, a study by Nguyen Van Thang et al at the National Hospital of Obstetrics and Gynecology in Vietnam reported a GTN incidence rate of 20.2% [6].

Currently, human Chorionic Gonadotropin (hCG) is the primary test used for diagnosing and monitoring gestational trophoblastic diseases.

Received: 07/01/2025. **Revised:** 01/03/2025. **Accepted:** 19/3/2025.

Corresponding author: Nguyen Van Tuan Anh. Email: ngvantuananhdr95@gmail.com. Phone: +84349289808

According to FIGO, after the evacuation, βhCG levels are monitored every 1 - 2 weeks until they become negative [1], with the time to βhCG negativity typically ranging from 8 to 14 weeks [7]. To date, βhCG remains the basis for diagnosing post-molar GTN. Early detection of this condition is crucial, as the complete response rate to chemotherapy is as high as 95.7% [8].

Ultrasound serves as a non-invasive imaging modality that is highly valuable in diagnosing gestational trophoblastic disease and has long been considered the preferred choice for initial diagnosis [9]. In 1987, Taylor K.J. et al. conducted research and discovered that doppler sonography proved beneficial in diagnosing GTD [10]. Doppler ultrasound possesses the capability to assess vascularity and circulatory resistance of blood flow [11]. Gestational trophoblastic tumors are characterized by abundant vascularity, making them exceptionally well-suited for investigation via this method [12]. To date, numerous studies have been conducted in various centers worldwide, demonstrating that uterine artery doppler indices can be used to monitor and predict post-molar gestational trophoblastic neoplasia [13, 14]. A 2017 study by Asmar F.T. et al. found that a pre-evacuation PI ≤ 1.38 and a post-evacuation PI ≤ 1.77 were valuable in predicting the progression of post-molar GTN [13]. At present, there is a limited number of research studies on uterine artery doppler sonography in hydatidiform mole in Vietnam. Therefore, we conducted this study which aimed to investigate the characteristics of uterine artery doppler sonography in hydatidiform mole and evaluate its value in predicting post-molar spontaneous remission.

II. MATERIALS AND METHODS

2.1. Subjects

A study was carried out involving 31 patients with molar pregnancies who received treatment at the Department of Obstetrics and Gynecology at Hue University of Medicine and Pharmacy Hospital, as well as at the Center for Obstetrics and Gynecology at Hue Central Hospital, during the period from March 2020 to June 2022.

Selection criteria included (1) a definitive diagnosis of hydatidiform mole based on ultrasound imaging, βhCG levels, and confirmed histopathological findings; (2) pre - and post-evacuation uterine artery doppler sonography; (3) βhCG follow-up and a routine examination within 6 months after βhCG levels became undetectable and (4) agreement to participate in the study.

Exclusion criteria consisted of (1) patients had pregnant during follow-up period; (2) fail to adhere to their treatment or regularly follow-up and/or (3) initial treatment involving a hysterectomy.

2.2. Methods

The study employed a cross - sectional observational design. Hydatidiform mole (HM) patients were classified into high-risk and low-risk groups based on Berkowitz's scoring system. Post-molar gestational trophoblastic neoplasm (GTN) was diagnosed using the criteria established by the International Federation of Gynaecology and Obstetrics (FIGO) [7].

Doppler indices were calculated as the average of bilateral Doppler parameters. Convenience sampling was applied. Diagnosis was based on elevated βhCG levels and ultrasound findings: complete HM presented a "snowstorm" or "cluster of grapes" appearance [7], while partial HM showed cystic spaces in the placenta with an empty gestational sac, amorphous fetal echoes, or a dead/living fetus [15].

Uterine artery Doppler ultrasonography was performed before and 48 hours post-evacuation using transabdominal and transvaginal techniques [16]

Measurements were taken bilaterally, including pulsatility index (PI), resistive index (RI), and systolic/diastolic ratio (S/D). Evacuation was conducted using suction evacuation and curettage with a Karman syringe or suction machine. βhCG levels were monitored 48 hours post-evacuation, followed by biweekly assessments until negative, with a six-month follow-up to ensure complete resolution [16].

2.3. Data analysis

Statistical analyses were performed using SPSS 20. The Mann - Whitney U and Wilcoxon test were applied. The best DFV parameters and cutoff values for predicting spontaneous remission patients were determined by receiver operating characteristic (ROC) analysis, including calculation of the areas under the curves. Statistical significance was set at $p < 0.05$.

III. RESULTS

3.1. General characteristics of the studied subjects

There were 15 cases of partial hydatidiform mole and 16 cases of complete hydatidiform mole. During follow-up after evacuation, 3 cases progressed to gestational trophoblastic neoplasia. The low-risk group (17 cases) accounted for 54.8%, which was 1.2 times higher than the high-risk group (14 cases) comprising 45.2%

The disease was predominantly found in the age group of 20 - 39, accounting for 87.1%, with a mean age of 29.39 ± 7.47 years. It was more common in cases with a history of ≥ 2 pregnancies, at a rate of 45.2%. The most common clinical symptom was vaginal bleeding, observed in 22.6% of cases. The pre-evacuation serum βhCG levels were primarily between 100,000 and < 1,000,000 mIU/mL, making up 77.4% of cases, with a median βhCG level of 191,706.00 mIU/mL (table 1).

Table 1: Patient characteristics

Characteristics		**Hydatidiform Mole (n = 31)**	
		Quantity	**Percentage (%)**
Age Group	< 20	2	6.5
	20 - 39	27	87.1
	≥ 40	2	6.5
Mean		**29.39 ± 7.47**	
Number of Pregnancies	First Pregnancy	7	22.6
	1 Pregnancy	10	32.3
	≥ 2 Pregnancies	14	45.2
Clinical symptoms	Abdominal Pain	6	19.4
	Vaginal Bleeding	7	22.6
	Ovarian Theca Lutein Cysts	2	6.5
Pre-evacuation βhCG Level (mIU/mL)	< 100,000	6	19.4
	100,000 - < 1,000,000	24	77.4
	> 1,000,000	1	3.2
	Median	191.706,00	

3.2. Characteristics of uterine artery doppler sonography in hydatidiform mole

Pre-evacuation doppler indices in partial HM were higher than those in complete HM, but there were no significant differences between two groups (table 2). Pre-evacuation doppler parameters in low-risk group were significantly higher than those in high-risk group (table 3)

Table 2: Pre-evacuation doppler indices by hydatidiform mole group

Index (Median) / **Group**	**PI**	**RI**	**S/D**
Partial Hydatidiform Mole (n = 15)	1.75 (1.55 - 1.85)	0.74 (0.56 - 0.82)	4.9 (3.48 - 6.55)
Complete Hydatidiform Mole (n = 16)	1.67 (1.17 - 2.01)	0.68 (0.50 - 0.80)	4.62 (3.25 - 6.78)
p*	0.46	0.49	0.84

** Mann - Whitney U test*

Table 3: Pre-evacuation doppler indices by risk

Index (Median) / Group	PI	RI	S/D
Low Risk (n = 17)	1.77 (1.60 - 2.07)	0.79 (0.72 - 0.82)	5.57 (4.50 - 7.07)
High Risk (n = 14)	1.48 (1.14 - 1.77)	0.58 (0.47 - 0.65)	3.47 (3.19 - 5.00)
p*	0.04	< 0.01	< 0.01

** Mann - Whitney U test*

On spontaneous group, post-evacuation doppler parameters were significantly higher than pre-evacuation, meanwhile, the opposite pattern was witnessed in the group developing to GTN (table 4).

Table 4: Comparison between pre and post-evacuation doppler indices

Group / Index (Median)	Spontaneous remission (n = 28)			Progression to GTN (n = 3)		
	Pre-evacuation	Post-evacuation	p**	Pre-evacuation	Post-evacuation	p**
PI	1.75	2.50	< 0.01	1.15	1.05	0.11
RI	0.75	0.86	< 0.01	0.45	0.33	0.11
S/D	5.00	6.80	< 0.01	3.42	3.52	0.59

*** Wilcoxon test*

3.3. Uterine artery doppler indices in predicting spontaneous remission patients

Areas under the ROC curve of pre-evacuation doppler indices in predicting spontaneous remission included PI: AUC = 0.88 (95% CI: 0.73 - 1.00; p = 0.04); RI:

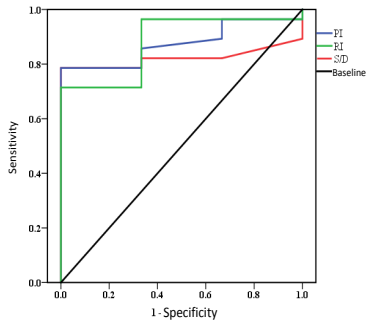

Figure 1: ROC Curve predicting spontaneous remission

AUC = 0.88 (95% CI: 0.00 - 1.00; p = 0.03) and S/D: AUC = 0.82 (95% CI: 0.68 - 0.96; p = 0.07).

The optimal cut-off points for predicting spontaneous remission are: PI ≥ 1.19 (sensitivity of 85.7% and specificity of 66.7%). RI ≥ 0.47 (sensitivity of 96.4% and a specificity of 66.7%) (table 4).

IV. DISCUSSION

Destruction of the uterine vasculature epitomizes a characteristic feature of trophoblastic disease. Beyond the erosion of the myometrium, trophoblasts infiltrate and disrupt the uterine spiral arteries, supplanting their smooth muscle composition [17]. Uterine artery PI and RI values diminish as gestational age advances, an alteration postulated to arise secondary to reduced uterine vascular resistance after trophoblast invasion [18]. In hydatidiform mole, there is trophoblastic invasion into the arteries within the myometrium, with the most prominent feature being the abnormal proliferation of trophoblasts [19].

The PHM group had higher uterine artery Doppler indices compared to the CHM group, but the difference was not statistically significant. A study by Zhou Q. et al. indicated that the mean RI value in the PHM patients was 0.56 ± 0.04, while it was 0.55 ± 0.06 in the CHM ones, demonstrating

that the RI difference between the two groups was minimal [19]. These disparities in uterine artery doppler indices may arise from the varying levels of normal endovascular invasion of decidual vessels at the implantation site. Specifically, it has been observed that the presence of normal endovascular trophoblasts is considerably lower in CHM (25%) than in PHM (80%). Conversely, abnormal endovascular extravillous trophoblasts are witnessed in CHM, while absent in PHM [20]. Nevertheless, in clinical practice, doppler indices does not appear to aid in distinguishing between complete and partial molar pregnancy, except in cases where a CHM coexists with a normal fetus [14].

Table 3 showed that doppler parameters in low-risk group were significantly higher than those in high-risk group. At present, we have not found similar studies classified according to Berkowitz's scoring system. However, doppler ultrasound appears to play a role in predicting the progression of GTN [14] and may also serve as an imaging utility to assess the risk of patients with molar pregnancy, as the rate to post-molar GTN has been reported in some studies to range from 8% to 12% [21, 22].

The uterine artery doppler indices before evacuation in the spontaneous remission group significantly increased after evacuation ($p < 0.01$). However, there was an opposite pattern witnessed in the post-molar GTN and the difference was statistically insignificant ($p > 0.05$). This finding aligned with a 2015 study by Malek M. et al. In the spontaneous remission group, indices such as PI, RI, and S/D increased significantly after evacuation, with PI rising from 1.95 ± 0.9 to 3.12 ± 0.79, RI from 0.76 ± 0.15 to 0.91 ± 0.06, and S/D from 5.55 ± 2.61 to 25.8 ± 2.9, all with statistically significant differences ($p < 0.05$). Conversely, in the post-molar GTN group, these indices decreased post-evacuation, with PI dropping from 2.12 ± 0.85 to 1.91 ± 0.57, RI from 0.79 ± 0.1 to 0.76 ± 0.07, and S/D from 5.62 ± 2.55 to 4.8 ± 1.8, but these changes were not statistically significant ($p > 0.05$) [23]. A 2022 study by Alnemr A. et al. also demonstrated similar findings. Nevertheless, the authors concluded that PI was the most crucial doppler index and had a strong correlation with the increased risk of developing post-molar GTN [24].

Figure 1 displays the ROC curve of pre-evacuation uterine artery doppler indices in predicting the spontaneous remission. However, a research by Asmar F.T. et al. determined that the optimal pre-evacuation PI cutoff for predicting post-molar GTN was ≤ 1.3, with a sensitivity of 77% and specificity of 82% and concluded that the pre-evacuation PI index could be used to predict GTN [13]. Similarly, Alnemr A.A. et al., indicated that pre-evacuation RI ≤ 1 (sensitivity 75% and specificity 56.7%; $p < 0.01$) and S/D ratio ≤ 6.5 (sensitivity 80% and specificity 50%; $p < 0.01$) could predict post-molar GTN. Meanwhile, the pre-evacuation PI index had less predictive value due to $p = 0.076$ [24].

IV. CONCLUSION

Uterine artery doppler sonography can be utilized for the diagnosis and monitoring of patients with hydatidiform mole.

Disclosure

The authors report no other conflicts of interest in this work.

REFERENCES

1. Ngan HYS, Seckl MJ, Berkowitz RS, Xiang Y, Golfier F, Sekharan PK, et al. Diagnosis and management of gestational trophoblastic disease: 2021 update. Int J Gynaecol Obstet. 2021; 155 (Suppl 1): 86-93.
2. Nguyễn Vũ Quốc Huy, Cao Ngọc Thành, Lê Minh Tâm, Trương Quang Vinh, Bệnh nguyên bào nuôi do thai, in Giáo trình Sản Phụ khoa dành cho đào tạo Sau đại học Đoàn Thị Mỹ Hằng, Editor. Nhà xuất bản Đại học Huế: Đại học Y Dược Huế. 2022:132-154.
3. Smith HO. Gestational trophoblastic disease epidemiology and trends. Clin Obstet Gynecol. 2003; 46(3): 541-56.
4. Lurain JR. Gestational trophoblastic disease I: epidemiology, pathology, clinical presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole. Am J Obstet Gynecol. 2010; 203(6): 531-9.
5. Zakaria A, Hemida R, Elrefaie W, Refaie E. Incidence and outcome of gestational trophoblastic disease in lower Egypt. Afr Health Sci. 2020; 20(1): 73-82.
6. Nguyễn Văn Thắng, Hoàng Hải, Vũ Bá Quyết. Tỷ lệ biến chứng u nguyên bào nuôi sau thai trứng khi áp dụng các giải pháp quản lý bệnh nhân ở cộng đồng. Tạp chí Y - Dược Học Quân Sự. 2018; 7(4): 19-24.

7. Callahan TL, Caughey AB, Gestational Trophoblastic Disease, in Blueprints Obstetrics and Gynecology, R. Susan, Editor. Lippincott Williams & Wilkins: Philadelphia. 2013:404-413.
8. Kumar N, Saxena YK, Rathi AK, Chitra R, Kumar P. Host and risk factors for gestational trophoblastic disease: a hospital-based analysis from India. Med Sci Monit. 2003; 9(10): CR442-7.
9. Green CL, Angtuaco TL, Shah HR, Parmley TH. Gestational trophoblastic disease: a spectrum of radiologic diagnosis. Radiographics. 1996; 16(6): 1371-84.
10. Taylor KJ, Schwartz PE, Kohorn EI. Gestational trophoblastic neoplasia: diagnosis with Doppler US. Radiology. 1987; 165(2): 445-8.
11. Chan FY, Pun TC, Chau MT, Lam C, Ngan HY, Wong RL. The role of Doppler sonography in assessment of malignant trophoblastic disease. Eur J Obstet Gynecol Reprod Biol. 1996; 68(1-2): 123-8.
12. Hsieh FJ, Wu CC, Chen CA, Chen TM, Hsieh CY, Chen HY. Correlation of uterine hemodynamics with chemotherapy response in gestational trophoblastic tumors. Obstet Gynecol. 1994; 83(6): 1021-5.
13. Asmar FTC, Braga-Neto AR, de Rezende-Filho J, Villas-Boas JMS, Charry RC, Maesta I. Uterine artery Doppler flow velocimetry parameters for predicting gestational trophoblastic neoplasia after complete hydatidiform mole, a prospective cohort study. Clinics (Sao Paulo). 2017; 72(5): 284-288.
14. Lin LH, Bernardes LS, Hase EA, Fushida K, Francisco RPV. Is Doppler ultrasound useful for evaluating gestational trophoblastic disease? Clinics (Sao Paulo). 2015; 70(12): 810-5.
15. Naumoff P, Szulman AE, Weinstein B, Mazer J, Surti U. Ultrasonography of partial hydatidiform mole. Radiology. 1981; 140(2): 467-70.
16. ISUOG Practice Guidelines: use of Doppler ultrasonography in obstetrics. Ultrasound in Obstetrics & Gynecology. 2013; 41(2): 233-239.
17. Hsieh FJ, Wu CC, Lee CN, Chen TM, Chen CA, Chen FC, et al. Vascular patterns of gestational trophoblastic tumors by color Doppler ultrasound. Cancer. 1994; 74(8): 2361-5.
18. Trương Thị Linh Giang, Siêu âm Doppler trong thăm dò sức khoẻ thai nhi ở thai phụ tiền sản giật, in Bệnh lý tiền sản giật - từ lý thuyết đến thực hành, Đoàn Thị Mỹ Hằng, Editor. Nhà xuất bản Đại học Huế: Huế. 2021:77-98.
19. Zhou Q, Lei X-Y, Xie Q, Cardoza JD. Sonographic and Doppler imaging in the diagnosis and treatment of gestational trophoblastic disease: a 12-year experience. J Ultrasound Med. 2005; 24(1): 15-24.
20. Sebire NJ, Rees H, Paradinas F, Fisher R, Foskett M, Seckl M, et al. Extravillus endovascular implantation site trophoblast invasion is abnormal in complete versus partial molar pregnancies. Placenta. 2001; 22(8-9): 725-8.
21. Joneborg U, Folkvaljon Y, Papadogiannakis N, Lambe M, Marions L. Temporal trends in incidence and outcome of hydatidiform mole: a retrospective cohort study. Acta Oncol. 2018; 57(8): 1094-1099.
22. Schmitt C, Doret M, Massardier J, Hajri T, Schott A-M, Raudrant D, et al. Risk of gestational trophoblastic neoplasia after hCG normalisation according to hydatidiform mole type. Gynecol Oncol. 2013; 130(1): 86-9.
23. Malek M, Moradi B, Mousavi AS, Ahmadinejad N, Kazemi MA, Gity M. Complementary Role of Ultrasound in Management of Gestational Trophoblastic Disease. Iran J Radiol. 2015; 12(2): e13955.
24. Alnemr AA, Alabiad MA, Saraya YS. Uterine Artery Doppler Ultrasound parameters for predicting the occurrence of persistent gestational trophoblastic disease (PGTD) after evacuation of complete hydatidiform mole, a prospective comparative cohort study. Zagazig University Medical Journal. 2022; 28(1): 106-114.