DOI: 10.7860/IJARS/2025/79228.3055

Original Article

Oncology Section

Gestational Trophoblastic Neoplasia: A Retrospective Study from a Tertiary Cancer Care Centre in Eastern India

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ABSTRACT

Introduction: Gestational Trophoblastic Disease (GTD) represents a rare group of pregnancy-related tumours arising from the abnormal proliferation of trophoblastic tissue within the uterus. This condition is associated with elevated levels of the beta subunit of Human Chorionic Gonadotropin (β-hCG). Early diagnosis and appropriate treatment are essential due to the tumour's high sensitivity to chemotherapy and excellent prognosis, even in metastatic cases.

Aim: To evaluate the clinical presentation, treatment response, and follow-up outcomes of patients with Gestational Trophoblastic Neoplasia (GTN) treated at a tertiary cancer care centre in Eastern India.

Materials and Methods: A retrospective observational study was conducted at the College of Medicine and Sagore Dutta Hospital, Kolkata, West Bengal, India, between January 2021 and December 2023. Twenty eight consecutive patients with histologically confirmed GTN were included. Patients were stratified into low risk (score <7, n=21) and high risk (score ≥7, n=7) categories based on the World Health Organisation (WHO) prognostic scoring system. Treatment decisions were made according to International Federation of Gynaecology and Obstetrics (FIGO) guidelines. Low risk patients received intramuscular Methotrexate (1 mg/kg on days 1, 3, 5, and 7) with leucovorin rescue, whereas high risk patients were treated with multi-agent EMACO (Etoposide, Methotrexate, Actinomycin-D, Cyclophosphamide, and Vincristine) chemotherapy. Treatment response was evaluated through weekly serum β-hCG monitoring until normalisation, followed by monthly surveillance for 12 months. Descriptive statistical analysis was performed using IBM Statistical Package for Social Sciences (SPSS) version 26.

Results: Among the 28 patients analysed, the most common presenting symptom was abnormal vaginal bleeding, noted in 24 patients (85.7%), while 4 patients (14.3%) were asymptomatic. The majority were aged below 40 years (67.9%) and nulliparous (57.1%). Serum β-hCG levels at presentation varied widely, with 35.7% showing levels ≥100,000 mIU/ml. Based on WHO scoring, 21 patients were classified as low-risk and 7 as high-risk. All low-risk patients received Methotrexate, of whom 4 required a switch to Actinomycin D due to suboptimal response. High-risk patients were treated with EMACO; 2 required escalation to EMA/EP, with one patient undergoing hysterectomy for persistent uterine disease. All patients achieved remission with no recurrence during a 12-month follow-up.

Conclusion: GTN is a highly chemo-sensitive tumour with an excellent prognosis when treated promptly according to established risk stratification guidelines. Early initiation of appropriate chemotherapy regimens results in high cure rates, even in the presence of metastases, highlighting the importance of timely diagnosis and treatment.

Keywords: Beta-human chorionic gonadotropin, Chemotherapy, Methotrexate, Pregnancy-related tumour, Methotrexate

INTRODUCTION

The GTD encompasses a spectrum of pregnancy-related tumours originating from abnormal trophoblastic proliferation within the uterus. Although GTD predominantly affects women of reproductive age, it can rarely present in postmenopausal women as well [1]. The disease spectrum includes complete and partial hydatidiform mole, invasive mole, choriocarcinoma, of Placental Site Trophoblastic Tumour (PSTT) and Epithelioid Trophoblastic Tumour (ETT) [2,3].

The global incidence of GTD varies significantly, ranging from 23 to 1299 cases per 100,000 pregnancies depending on geographical and ethnic factors [4]. Clinical manifestations of GTD typically include abnormal vaginal bleeding in early pregnancy, uterine enlargement disproportionate to gestational age, pelvic discomfort, hyperemesis gravidarum, and symptoms related to metastasis involving organs such as the lungs, liver, vagina, or brain. Biochemically, serum levels of beta subunit of hCG are consistently elevated and serve as a sensitive marker for diagnosis, monitoring treatment response, and long-term surveillance [5].

Following evacuation of molar tissue, persistent or rising serum β-hCG levels necessitate the diagnosis of GTN according to FIGO criteria. Chemotherapy is indicated for plateaued or rising β-hCG titres or evidence of metastatic disease. Risk stratification is based on the WHO prognostic scoring system, where patients with scores less than seven are categorised as low risk and are treated with single-agent chemotherapy, typically Methotrexate, whereas patients with scores of seven or higher are classified as high-risk and require multi-agent chemotherapy [6-8].

The most commonly employed multi-agent regimen for high-risk GTN is EMACO, comprising Etoposide, Methotrexate, Actinomycin-D, Cyclophosphamide, and Vincristine [8]. However, a Cochrane systematic review highlighted that the optimal combination regimen for high-risk GTN remains to be definitively established [9]. Despite this, outcomes with modern chemotherapy protocols are excellent, with remission rates approaching nearly 100% in low risk cases and around 90% in high-risk cases, even when metastases are present.

Given the curable nature of GTN with appropriate therapy and the importance of risk-adapted management, continuous evaluation and updating of institutional experience are critical for optimising patient outcomes. This study was undertaken to retrospectively analyse the clinical characteristics, treatment modalities, and outcomes of patients with GTN treated at a tertiary cancer care centre in Eastern India.

MATERIALS AND METHODS

A retrospective observational study was conducted at the Radiotherapy Department of College of Medicine and Sagore Dutta Hospital, Kolkata, West Bengal, India, between January 2021 and December 2023. The study included 28 consecutive patients with histologically confirmed GTN attending the radiotherapy outpatient department. Ethical clearance for the study was obtained from the Institutional Ethics Committee, and a scanned copy of the application was submitted.

Inclusion criteria: Inclusion criteria encompassed all patients diagnosed with GTN based on histopathological examination and elevated serum β-hCG levels following molar evacuation or diagnosis of choriocarcinoma.

Exclusion criteria: Patients with incomplete medical records were excluded.

Study Procedure

Data regarding clinical presentation, treatment protocols, and follow-up outcomes were collected retrospectively from patient records. No intervention or alteration of treatment protocols was made for the purposes of this study. Each patient was designated with a unique identification number to maintain confidentiality, and at no point was patient identity disclosed.

Patients were staged according to the International Federation of Gynaecology and Obstetrics (FIGO) system, and risk categorisation was performed using the WHO prognostic scoring system. Patients with a score less than 7 were classified as low risk and those with a score of 7 or more as high-risk. Baseline investigations for all patients included complete blood count, fasting blood glucose, liver and renal function tests, thyroid function tests, and imaging studies. Contrast-enhanced Computed Tomography (CT) scans of the thorax, abdomen, and pelvis were performed for staging, while contrast-enhanced Magnetic Resonance Imaging (MRI) of the brain was reserved for symptomatic patients.

Low risk patients were treated with single-agent Methotrexate administered intramuscularly at a dose of 1 mg/kg on days 1, 3, 5, and 7, alternating with intramuscular leucovorin rescue (15 mg) on days 2, 4, 6, and 8. Chemotherapy cycles were repeated every two weeks. Patients showing inadequate response to Methotrexate, based on plateauing or rising β-hCG levels, were switched to Actinomycin D at a dose of 1.25 mg/m² intravenously every two weeks.

High-risk patients received multi-agent EMACO chemotherapy comprising Etoposide (100 mg/m² intravenous infusion over 30 minutes on days 1 and 2), Actinomycin D (0.5 mg intravenous push on days 1 and 2), Methotrexate (100 mg/m² intravenous push followed by 200 mg/m² continuous infusion over 12 hours on day 1), Cyclophosphamide (600 mg/m² intravenous infusion over 30 minutes on day 8), and Vincristine (1.0 mg intravenous push on day 8). Folinic acid rescue at a dose of 15 mg intramuscularly was administered every 12 hours for four doses, starting 24 hours after the initiation of Methotrexate.

Patients who failed to respond to the EMACO regimen were switched to the EMA/EP regimen, which included Etoposide (100 mg/m² intravenous infusion over 30 minutes on days 1, 2, and 8), Actinomycin D (0.5 mg intravenous push on days 1 and 2), Methotrexate (100 mg/m² intravenous push followed by 200 mg/m² continuous infusion over 12 hours on day 1), and Cisplatin (60 mg/m² intravenous infusion on day 8). Folinic acid rescue was continued as per the EMACO protocol.

Serum β-hCG levels were monitored weekly during treatment. If after two cycles of chemotherapy there was no fall in β-hCG levels by one logarithmic value, ie. less than a 10% decrease, or an increase in β-hCG levels, or the appearance of new metastatic lesions, the chemotherapy regimen was changed. After normalisation of serum β-hCG levels, two to three additional consolidation cycles were administered. Following completion of therapy, patients were followed monthly with serum β-hCG measurements for at least 12 months to monitor for recurrence. Treatment-related toxicities such as anaemia and febrile neutropenia were managed according to institutional protocols.

STATISTICAL ANALYSIS

Data were analysed using descriptive statistical methods with IBM SPSS Statistics for Windows, Version 26.

RESULTS

A total of 28 patients with histologically confirmed GTN were included in the study. The pretreatment demographic and clinical characteristics are summarised in [Table/Fig-1].

Patient profile		Number
Age (years)	<40	19
	≥40	9
Previous pregnancy	Nulliparous	16
	Abortion	9
	Term pregnancy	3
Symptoms	Vaginal bleeding absent	4
	Vaginal bleeding present	24
Pretreatment serum β-hCG levels (mIU/mL)	<1000	4
	1000 to <10000	4
	10000 to <100000	10
	≥100000	10
FIGO stage	I	24
	II	2
	III	2
	IV	0
WHO prognostic score	<7	21
	≥7	7

[Table/Fig-1]: Pretreatment demographic and clinical profile of patients diagnosed with Gestational Trophoblastic Neoplasia (GTN).

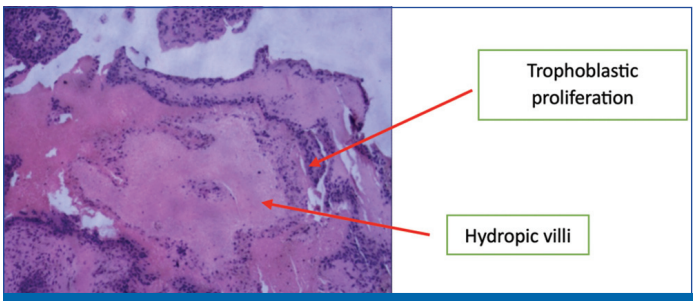
While the WHO prognostic scoring system primarily guided treatment selection, FIGO staging provided essential insights into the anatomical extent of disease, particularly in identifying metastatic involvement. In our study, 24 patients presented with stage I disease, indicating uterine-confined lesions, and were appropriately managed with single-agent or multi-agent chemotherapy based on their risk score. The remaining four patients with stage II or III disease had extrauterine but limited metastases (vaginal and pulmonary, respectively), necessitating closer monitoring. However, FIGO stage alone did not alter the choice of chemotherapy regimen; instead, it served to complement the WHO scoring system in guiding follow-up intensity and imaging protocols. Patients with higher FIGO stages were assessed more rigorously for metastatic burden and response, especially in high-risk cases.

Sixteen patients had a histopathological diagnosis of complete hydatidiform mole, nine had partial hydatidiform mole, and three were diagnosed with choriocarcinoma. Among the patients, 21 (75%) were classified as low risk with a WHO prognostic score of less than seven, while 7 (25%) were classified as high-risk with a score of seven or more. One high-risk patient had evidence of lung metastasis at presentation; however, it did not affect her overall risk scoring. All 21 low risk patients were treated initially with single-agent Methotrexate chemotherapy. Among them, four patients demonstrated inadequate response to Methotrexate and were subsequently treated with Actinomycin D, to which all responded favourably. The remaining 17 low risk patients achieved remission with Methotrexate alone. After achieving normalisation of serum β-hCG levels, all low risk patients received three additional cycles of consolidation chemotherapy.

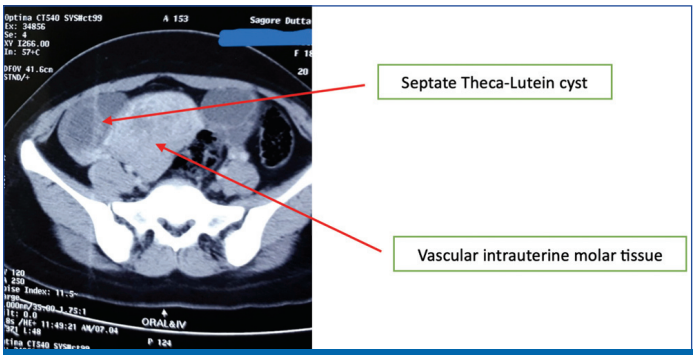
The seven high-risk patients received multi-agent EMACO chemotherapy. Five patients responded completely to the EMACO regimen after three consolidation cycles post normalisation of β-hCG levels. Two patients exhibited resistance to EMACO, necessitating a switch to EMA/EP regimen. Of these, one patient achieved biochemical remission after two cycles of EMA/EP followed by three consolidation cycles. The other patient continued to experience persistent vaginal bleeding and elevated β-hCG levels after two cycles of EMA/EP. Imaging with contrast-enhanced CT of the thorax and abdomen and MRI of the brain revealed a heterogeneously enhancing uterine lesion without distant metastasis. She subsequently underwent hysterectomy, after which serum β-hCG levels normalised. She then completed three further cycles of EMA/EP chemotherapy.

Throughout treatment, all patients were monitored weekly with serum β-hCG levels. Adverse events included anaemia, observed in eight patients from the low risk group and six patients from the high-risk group, which were managed with packed red blood cell transfusions. Febrile neutropenia occurred in five high-risk patients during EMACO therapy, leading to chemotherapy delays of approximately two to three weeks. All patients received prophylactic granulocyte colony-stimulating factor (Inj. Filgrastim) after each chemotherapy cycle.

After a minimum follow-up period of 12 months with monthly serum β-hCG monitoring, none of the patients demonstrated disease recurrence. Imaging findings supporting diagnosis included hydropic villi on histopathology [Table/Fig-2] and vascular intrauterine mass with theca lutein cysts on CT scan [Table/Fig-3]. Risk scoring details for individual patients are shown in [Table/Fig-4].



[Table/Fig-2]: Histopathological examination of the product of conception following suction and evacuation, showing hydropic (distended) chorionic villi along with trophoblastic proliferation at 4x magnification.



[Table/Fig-3]: Contrast-enhanced CT scan of the whole abdomen obtained prior to initiation of chemotherapy, demonstrating vascular trophoblastic tissue within the uterus along with bilateral thin-walled septate theca-lutein cysts, secondary to elevated levels of chorionic gonadotropin.

Serial No.	Score due to Age (Yrs)	Score due to Antecedent pregnancy	Score due to Interval (Months)	Score due to pre-treatment serum β hCG (Miu/ml)	Score due to Largest tumour	Score due to Metastasis	Total Score
1	0	0	0	1	2	0	3
2	1	1	0	0	2	0	4
3	1	0	1	4	2	0	8
4	0	1	1	0	2	0	4
5	0	0	0	2	2	0	4
6	0	0	1	1	2	0	4
7	1	2	1	2	1	0	7
8	0	0	0	2	1	0	3
9	0	0	0	4	2	0	6
10	0	0	0	2	2	0	4
11	0	0	0	4	1	0	5
12	0	1	1	4	2	0	8
13	1	0	0	1	1	0	3
14	0	1	0	0	2	0	3
15	0	2	1	4	1	0	8
16	1	0	0	4	1	0	6
17	0	1	1	0	2	0	4
18	1	0	0	2	2	0	5
19	0	0	0	2	2	0	4
20	0	1	0	4	2	0	7
21	0	0	1	2	2	0	5
22	1	2	1	2	1	0	7
23	0	0	0	4	2	0	6
24	0	1	0	1	2	0	4
25	1	0	0	2	2	0	5
26	0	1	0	4	1	0	6
27	0	1	1	2	2	0	6
28	1	0	1	4	2	0	8

[Table/Fig-4]: Risk Scoring.

DISCUSSION

The GTD represents a unique spectrum of disorders arising from abnormal trophoblastic proliferation, ranging from benign hydatidiform mole to highly malignant forms such as choriocarcinoma, PSTT, and ETT [10-12]. Although hydatidiform mole is often considered benign, it is premalignant and can progress to invasive and metastatic disease if not diagnosed and managed appropriately [10].

The regulatory mechanisms governing trophoblastic growth, normally well-controlled in benign conditions, may become dysfunctional, leading to vascular invasion and metastasis in malignant forms of GTD [13]. Hydatidiform mole is subdivided into complete and partial forms based on cytogenetic and histopathological features. Surgical uterine evacuation remains the cornerstone of management for both complete and partial moles, regardless of uterine size [14]. Ultrasound-guided evacuation is recommended for cases with large uterine size to minimise the risk of complications and ensure complete removal [15].

Hysterectomy is a viable option in selected patients, particularly those who have completed childbearing or in cases of life-threatening haemorrhage or chemotherapy-resistant uterine disease. In the present study, one patient with persistent vaginal bleeding, vascular uterine mass, and elevated serum β-hCG levels following chemotherapy underwent hysterectomy successfully. Hysterectomy may also decrease tumour burden and enhance chemotherapy responsiveness in such settings [15].

Prophylactic chemotherapy after evacuation of a high-risk complete mole has been proposed to decrease the incidence of post-molar GTN [15]. However, current evidence from systematic reviews, including a recent Cochrane review, does not support routine prophylactic chemotherapy due to potential overtreatment and drug toxicity concerns [16]. Therefore, vigilant β-hCG monitoring remains the standard strategy after molar evacuation.

The diagnosis of GTN post-molar evacuation is established using the International Federation of Gynecology and Obstetrics (FIGO)

criteria, which include plateauing or rising β-hCG levels over specified durations, persistence of detectable β-hCG beyond six months, histological evidence of choriocarcinoma, or the presence of metastases [17]. Serum β-hCG monitoring thus plays a critical role not only in early detection but also in guiding ongoing treatment and assessing remission.

Chemotherapy remains the mainstay of treatment for GTN, given the tumour's remarkable chemosensitivity. In low risk disease, single-agent Methotrexate or Actinomycin D achieves complete remission rates approaching nearly 100% [18]. Our study's findings corroborate this, with all low risk patients ultimately achieving remission, though a few required a switch to Actinomycin D upon Methotrexate resistance. High-risk disease requires combination chemotherapy, with the EMACO regimen being the most widely accepted protocol [8].

In our cohort, five out of seven high-risk patients responded well to EMACO. Two patients required escalation to the EMA/EP regimen following EMACO failure, a recognised salvage strategy in resistant GTN cases. Notably, even among metastatic GTN patients, chemotherapy achieves high cure rates, although meticulous risk-adapted management and close monitoring are essential [18]. Radiotherapy, although available, is largely reserved for palliative management of central nervous system or pulmonary metastases causing life-threatening symptoms.

Our study reaffirms that timely risk stratification, adherence to standard chemotherapy protocols, and diligent follow-up using serum β-hCG levels lead to excellent survival outcomes in GTN. The absence of recurrence during a minimum follow-up of one year across our cohort underscores the effectiveness of protocol-driven management in this otherwise aggressive disease entity.

Limitation(s)

The present study has several limitations. Being retrospective in nature, it depended entirely on the accuracy and completeness of existing medical records, which may introduce documentation bias. The small sample size and single-centre experience may limit the generalisability of the results to broader populations. Molecular and cytogenetic analyses, which could provide additional prognostic information, were not performed. Furthermore, no formal statistical analysis was carried out, as the study was purely descriptive in nature with a small cohort size, and the objective was to report clinical outcomes rather than to perform comparative statistical testing. Longer follow-up beyond one year would also be necessary to assess the risk of late recurrences or long-term treatment-related complications.

CONCLUSION(S)

The GTN is a rare but highly curable pregnancy-related malignancy when diagnosed promptly and treated according to established risk-adapted protocols. The tumour exhibits remarkable chemosensitivity, with excellent remission rates even in the presence of metastatic disease. Risk stratification using the WHO prognostic scoring system and staging by FIGO criteria remain critical for guiding treatment decisions. Early initiation of appropriate chemotherapy regimens and diligent β-hCG monitoring during and after treatment are essential to ensure optimal outcomes. The findings from our study reaffirm that standardised management protocols, vigilant follow-up and timely intervention contribute to achieving high cure rates with minimal morbidity in patients with GTN.

REFERENCES

[1] Chittenden B, Ahamed E, Maheswari A. Choriocarcinoma in a post-menopausal woman. Obstetrics and Gynaecology. 2009;114(2.2):462-65.
[2] Soper JT. Gestational trophoblastic disease: Current evaluation and management. Obstet Gynecol. 2021;137(2):355-70.
[3] Joyce CM, Fitzgerald B, McCarthy TV, Coulter J, O'Donoghue K. Advances in the diagnosis and early management of gestational trophoblastic disease. BMJ Med. 2022;1(1):e000321.
[4] Savage P, Williams J, Wong SL, Short D, Casalboni S, Catalano K, et al. The demographics of molar pregnancies in England and Wales from 2000-2009. J Reprod Med. 2010;55(7-8):341-45.
[5] Ostreni I, Colatosti A, Basile EJ, Rafa O. Elevated beta-human chorionic gonadotropin in a non-pregnant female with altered kidney function. Cureus. 2022;14(4):e23747.
[6] Chalouhi GE, Golfier F, Soignon P, Massardier J, Guastalla JP, Trillet-Lenoir V, et al. Methotrexate for 2000 FIGO low-risk gestational trophoblastic neoplasia patients: efficacy and toxicity. Am J Obstet Gynecol. 2009;200:643.e1-643.e6.
[7] Abrão RA, de Andrade JM, Tiezzi DG, Marana HR, Candido dos Reis FJ, Clagnan WS. Treatment for low-risk gestational trophoblastic disease: comparison of single-agent methotrexate, dactinomycin and combination regimens. GynecolOncol. 2008;108(1):149-53.
[8] Lurain JR. Gestational trophoblastic disease II: classification and management of gestational trophoblastic neoplasia. Am J Obstet Gynecol. 2011;204(1):11-18.
[9] Alazzam M, Tidy J, Osborne R, Coleman R, Hancock BW, Lawrie TA. Chemotherapy for resistant or recurrent gestational trophoblastic neoplasia. Cochrane Database Syst Rev. 2012;12:CD008891.
[10] Mittal S, Menon S. Interstitial pregnancy mimicking an invasive hydatidiform mole. Am J Obstet Gynecol. 2019;220(5):501.
[11] Sarmadi S, Izadi-Mood N, Sanii S, Motevalli D. Inter-observer variability in the histologic criteria of diagnosis of hydatidiform moles. Malays J Pathol. 2019;41(1):15-24.
[12] Ning F, Hou H, Morse AN, Lash GE. Understanding and management of gestational trophoblastic disease. F1000Res. 2019;8:F1000 Faculty Rev-428.
[13] Seckl MJ, Sebire NJ, Berkowitz RS. Gestational trophoblastic disease. Lancet. 2010;376(9742):717-29.
[14] Tidy JA, Gillespie AM, Bright N, Radstone CR, Coleman RE, Hancock BW. Gestational trophoblastic disease: A study of mode of evacuation and subsequent need for treatment with chemotherapy. GynecolOncol. 2000;78(3 Pt 1):309-12.
[15] Elias KM, Berkowitz RS, Horowitz NS. State-of-the-art workup and initial management of newly diagnosed molar pregnancy and postmolar gestational trophoblastic neoplasia. J Natl Compr Canc Netw. 2019;17(11):1396-401.
[16] Wang Q, Fu J, Hu L, Fang F, Xie L, Chen H, et al. Prophylactic chemotherapy for hydatidiform mole to prevent gestational trophoblastic neoplasia. Cochrane Database Syst Rev. 2017;9(9):CD007289.
[17] Kohorn EI. The new FIGO 2000 staging and risk factor scoring system for gestational trophoblastic disease: Description and critical assessment. Int J Gynecol Cancer. 2001;11(1):73-77.
[18] 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):531-39.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Mar 13, 2025
- Manual Googling: Apr 28, 2025
- iThenticate Software: May 30, 2025 (12%)

ETYMOLOGY: Author Origin

EMENDATIONS: 4

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval Obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Mar 10, 2025**
Date of Peer Review: **Apr 10, 2025**
Date of Acceptance: **May 31, 2025**
Date of Publishing: **Jul 01, 2025**