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RESEARCH

Hemodynamic profiles in idiopathic intracranial hypertension: Doppler ultrasonography as a diagnostic tool for pulsatile tinnitus

İdiyopatik intrakraniyal hipertansiyonda hemodinamik profiller: pulsatil tinnitus için tanısal bir araç olarak Doppler ultrasonografi

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Abstract

Purpose: This study aims to evaluate the role of ophthalmic Doppler ultrasonography (USG) in differentiating IIH patients with and without bilateral PT by analyzing hemodynamic changes in the orbital vessels.
Materials and Methods: A prospective, single-center, case-control study was conducted at Harran University from November 2023 to June 2024. The study included 20 IIH patients. Participants underwent clinical assessments, ophthalmic evaluations, brain imaging, lumbar puncture, and transorbital sonography. IIH patients were categorized into PT (n=8) and non-PT (n=12) groups. Doppler USG measured end-diastolic velocity (EDV), peak systolic velocity (PSV), time-averaged velocity (TAV), resistive index (RI), pulsatility index (PI), and systolic to the diastolic ratio (S/D) of the central retinal artery.
Results: Significant differences were observed in left eye EDV and TAV, with lower values in the PT group. Although not statistically significant, right-eye EDV and TAV also trended lower in the PT group. Additionally, both eyes' PSV values showed a trend toward statistical significance, being lower in the PT group. ROC curve analysis identified optimal thresholds for left eye EDV (5.35; sensitivity 75%, specificity 83.33%) and TAV (9; sensitivity 50%, specificity 91.67%).
Conclusion: Orbital Doppler USG reveals distinct hemodynamic profiles in IIH patients with PT, suggesting EDV and TAV as potential biomarkers. Larger cohort studies are needed to validate and clarify IIH-PT mechanisms.

Keywords:. Pseudotumor cerebri, pulsatile tinnitus, central retinal artery, transorbital sonography, flow velocities

Öz

Amaç: Bu çalışmada orbital damarlardaki hemodinamik değişiklikleri analiz ederek bilateral PT olan ve olmayan IIH hastalarını ayırt etmede oftalmik Doppler ultrasonografinin (USG) rolü değerlendirildi.
Gereç ve Yöntem: Kasım 2023 - Haziran 2024 tarihleri arasında Harran Üniversitesi'nde prospektif, tek merkezli, vaka-kontrol çalışması yapıldı. Çalışmaya 20 IIH hastası dahil edildi. Katılımcılara klinik değerlendirmeler, oftalmik değerlendirmeler, beyin görüntüleme, lomber ponksiyon ve transorbital sonografi uygulandı. IIH hastaları PT (n=8) ve PT olmayan (n=12) gruplar olarak kategorize edilmiştir. Doppler USG ile end-diyastolik hız (EDV), pik sistolik hız (PSV), zaman ortalamalı hız (TAV), rezistif indeks (RI), pulsatilite indeksi (PI) ve santral retinal arterin sistolik/diyastolik oranı (S/D) ölçüldü.
Bulgular: Sol göz EDV ve TAV değerlerinde PT grubunda daha düşük olmak üzere anlamlı farklılıklar gözlendi. İstatistiksel olarak anlamlı olmamakla birlikte, sağ göz EDV ve TAV değerleri de PT grubunda daha düşük olma eğilimindeydi. Ayrıca, her iki gözün PSV değerleri PT grubunda daha düşük olmak üzere istatistiksel anlamlılığa doğru bir eğilim göstermiştir. ROC eğrisi analizi sol göz EDV (5,35; duyarlılık %75, özgüllük %83,33) ve TAV (9; duyarlılık %50, özgüllük %91,67) için optimal eşikleri belirlemiştir.
Sonuç: Orbital Doppler USG, PT'li IIH hastalarında farklı hemodinamik profiller ortaya koyarak EDV ve TAV'ın potansiyel biyobelirteçler olduğunu düşündürmektedir. IIH-PT mekanizmalarını doğrulamak ve açıklığa kavuşturmak için daha büyük kohort çalışmalarına ihtiyaç vardır.

Anahtar kelimeler: Psödotümör serebri, pulsatil tinnitus, santral retinal arter, transorbital sonografi, akım hızları

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INTRODUCTION

Idiopathic intracranial hypertension (IIH) is a neurological disorder characterized by an increase in intracranial pressure (ICP) without a discernible reason. It often presents with symptoms such as visual disturbances, headaches, and pulsatile tinnitus. (PT)[1]. The pathophysiology of IIH is still poorly understood, but it is thought to involve impaired cerebrospinal fluid (CSF) absorption or increased cerebral venous pressure. Monitoring IIH can be difficult because optic disc swelling is not an ideal indicator due to its delayed development or regression. Given the progressive nature of IIH, it is crucial to develop diagnostic techniques that enable early detection and effective monitoring of this treatable condition. Doppler ultrasonography (USG) may be a valuable tool in assessing hemodynamic changes in the orbital vessels, potentially providing insights into the cerebrovascular dynamics in IIH[2].

Pulsatile tinnitus, also known as pulse-synchronous tinnitus, is an auditory phenomenon in which individuals perceive a "whooshing" sound that coincides with the rhythm of their heartbeat[3, 4]. A significant proportion of IIH patients (52–60%) experience PT, with a considerable number of PT cases (68–75%) being suspected of having IIH[5]. In the literature, various studies have evaluated the use of Doppler USG to assess the jugular vein, carotid and vertebral arteries in patients with PT[6, 7]. While the association between IIH and PT has been well-documented, the impact of IIH, particularly concerning tinnitus on ophthalmic vascular dynamics, has not been thoroughly investigated.

This study aims to address this gap by evaluating transorbital Doppler USG findings in IIH patients and comparing those with and without PT. By examining the potential hemodynamic differences in orbital vessels, the research seeks to provide new insights into the systemic blood flow velocities associated with IIH and its connection to PT. It was hypothesized that IIH patients with PT would exhibit distinct orbital hemodynamic patterns compared to those without PT. This could potentially enhance the understanding of the systemic blood flow mechanisms underlying PT in IIH and contribute to the development of non-invasive diagnostic and monitoring tools.

MATERIALS AND METHODS

Study design

The study was designed as a pilot study and was carried out at the Harran University, Faculty of Medicine, Department of Neurology and Radiology, between November 2023 and June 2024. All participants, including patients and volunteers, were aged 18-65 and provided informed consent before their involvement. This research involved 20 patients diagnosed with definite IIH based on the revised Friedman diagnostic criteria[8]. The revised Friedman criteria, which include key diagnostic elements such as papilledema, normal neurological exams (except cranial nerve abnormalities), normal neuroimaging findings (including MRI venography), and elevated CSF opening pressure measured (>250 mmH2O) via lumbar puncture, were rigorously applied to confirm the diagnosis of definite IIH in the patient cohort, ensuring that all clinical, imaging, and CSF thresholds were met. The study received ethical approval from the local ethics committee of Harran University on November 21, 2023 (Protocol number: HRU/23.21.19).

Patient assessment

Patients with IIH underwent several procedures at the time of diagnosis, including an initial clinical assessment, an ophthalmic evaluation, brain imaging with cranial magnetic resonance imaging and venography, a lumbar puncture, and transorbital sonography. The study population consisted of patients who were hospitalized for a diagnostic work-up to rule out IIH. If brain imaging revealed a secondary cause of intracranial hypertension, such as brain tumors, metastases, central nervous system infections, subarachnoid hemorrhage, or cerebral venous sinus thrombosis, or if CSF pressure was ≤ 200 mmH2O, the patients were excluded from the study. The patients in the IIH group were categorized based on the presence of PT. Subsequently, they were divided into two groups: those with PT (n=8) and those without PT (n=12). The opening pressure of the CSF was determined by a neurologist using a lumbar puncture conducted in the lateral decubitus position.

Transorbital sonography

The orbital Doppler USG examinations were conducted by a radiologist with substantial experience blinded to the clinical findings. All patients underwent ultrasound examinations utilizing a high-frequency linear array transducer (9L4) (Siemens Acuson S2000, Siemens Medical System Solutions, CA, USA). Patients were positioned in the supine position, and the Doppler probe was placed on the closed eyelid to visualize the ophthalmic artery. Measurements were taken in both eyes, and the mean values were calculated for each parameter.

Orbital color-coded Doppler USG was utilized to measure the end-diastolic velocity (EDV), peak systolic velocity (PSV), time-averaged velocity (TAV), resistive index (RI), pulsatility index (PI), and systolic to the diastolic ratio (S/D) of the central retinal artery (CRA) (Figure 1). The Pulsatility Index (PI) was determined using the conventional Gosling equation: PI = (PSV - EDV) / Vmean. For accuracy, at least three readings of both color and spectral waveforms were obtained approximately 3 mm posterior to the globe, centered on the optic nerve. The average of these measurements was utilized for the ensuing statistical analyses.

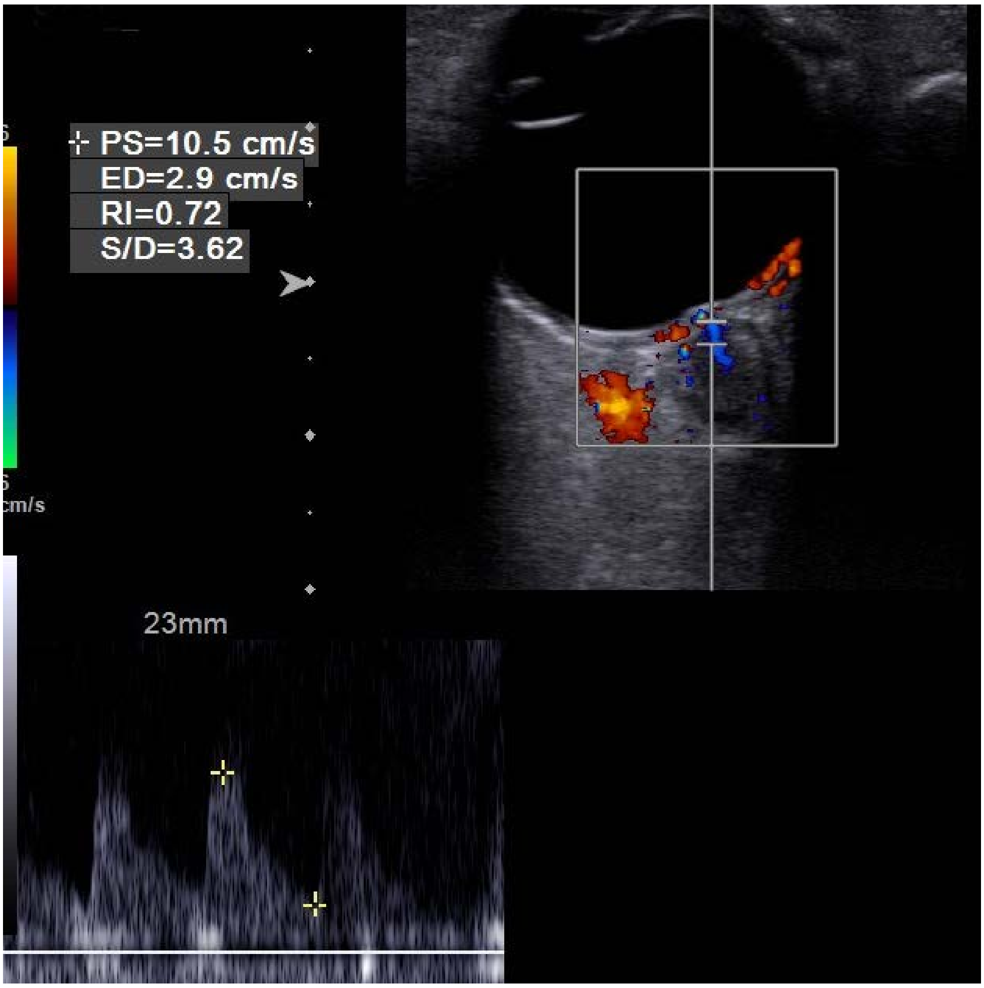

Figure 1. Doppler Ultrasonography of the Central Retinal Artery in a Patient with Idiopathic Intracranial Hypertension

The Doppler ultrasound image shows the central retinal artery with measured parameters including peak systolic velocity (PSV=10.5 cm/s), end-diastolic velocity (EDV=2.9 cm/s), resistive index (RI=0.72), and systolic/diastolic ratio (S/D=3.62). The color-coded flow patterns and spectral waveform are indicative of hemodynamic changes within the orbital vessels.

The Doppler ultrasound image shows the central retinal artery with measured parameters including peak systolic velocity (PSV=10.5 cm/s), end-diastolic velocity (EDV=2.9 cm/s), resistive index (RI=0.72), and systolic/diastolic ratio (S/D=3.62). The color-coded flow patterns and spectral waveform are indicative of hemodynamic changes within the orbital vessels.

Procedure

The patients were hospitalized for a diagnostic work-up due to suspected IIH, during which time they underwent comprehensive neurological and ophthalmic evaluations conducted by neurologists and ophthalmologists who had significant expertise in diagnosing IIH. Radiological assessments were performed on these patients prior to confirming the IIH diagnosis through lumbar puncture. All diagnostic procedures were carried out in the Radiology Department by a single, experienced radiologist to ensure consistency and minimize inter-operator variability. The radiologist, who was extensively trained in transorbital sonography, performed all examinations according to standardized protocols in line with established clinical guidelines. To further ensure accuracy, the radiologist conducted Doppler USG assessments, and the image quality was reviewed periodically as part of the department's quality assurance processes. Following the Doppler USG, a lumbar puncture was performed, and patients with CSF pressure above 250 mmH2O were diagnosed with definite IIH and included in the study.

Statistical analysis

Data was analyzed using IBM SPSS Statistics, Version 24.0 (Armonk, NY: IBM Corp). Qualitative data were summarized as frequencies and percentages, while quantitative data were described using mean±standard deviation (SD). Normality was assessed using the Shapiro-Wilk test. The Student's t-test was used for parametric variables to compare the groups, and the Mann-Whitney U test was applied for non-parametric variables.

Receiver operating characteristics (ROC) curve analyses were performed to verify the best cut-off values of EDV and TAV in distinguishing between patients with and without PT. The optimal cut-off points were selected based on the maximum value of the Youden index (sensitivity+specificity-1). Results were considered significant at p-value<0.05, based on two-sided testing. The area under the curve (AUC), sensitivity, and specificity were derived from the ROC curve, while positive predictive value (PPV), negative predictive value (NPV), and overall accuracy were calculated via cross-tabulation.

RESULTS

A total of 45 patients hospitalized for diagnostic work-up for suspected IIH were approached for the study, of which eight patients declined participation. Following evaluation, five patients were excluded due to the detection of cerebral venous sinus thrombosis. Additionally, six patients were excluded either because their CSF pressure ranged between 200-250 mmH2O, and another six patients declined lumbar puncture, resulting in a diagnosis of possible IIH. In total, 25 patients were excluded based on these criteria, and 20 patients were included in the final analysis. The study ultimately included 20 participants, with eight individuals experiencing bilateral PT and 12 without PT. The mean age of participants with PT was 40.625±10.46 years, while those without PT had a mean age of 36.917±10.335 years (p=0.444). There were 18 females (11 without PT and 7 with PT) and two males (one without PT and one with PT). The gender distribution showed no significant variation between the groups (p=1). The mean BMI for the PT group was 32.925±4.595, compared to 30.965±5.23 in the non-PT group, with no significant difference (p=0.401). The opening CSF pressure was similar between the two groups, with means of 31.125±5.194 and 30.667±4.03, respectively (p=0.969).

The left eye EDV and TAV values were statistically significant and lower in the PT group (p=0.004, p=0.021, respectively). Although the EDV values for the right eye were not statistically significant (p=0.076), they were lower in the PT group. The differences in right eye TAV, as well as both eyes PSV values, between the PT and non-PT groups exhibited trends towards statistical significance, with the PT group demonstrating lower values in each of these parameters (p=0.056, p=0.058, p=0.056, respectively). The sonographic characteristics of the groups are presented in Table 1.

Table 1. Comparative analysis of sonographic characteristics between pulsatile tinnitus (PT) and Non-PT groups

		PT group (n=8)	Non-PT group (n=12)	p
EDV(cm/s), mean±SD	R	3.229±1.613	5.7±2.553	0.076
	L	3.6±1.996	6.95±1.957	**0.004**
PSV(cm/s), mean±SD	R	11.114±7.198	19.84±9.468	0.058
	L	14.5±11.085	23.84±7.567	0.056
TAV (cm/s), mean±SD	R	6.571±3.372	10.89±4.707	0.056
	L	8.1±5.051	13.77±4.002	**0.021**
RI, mean±SD	R	0.667±0.115	0.704±0.059	0.921
	L	0.693±0.112	0.696±0.078	0.946
PI, mean±SD	R	1.079±0.306	1.297±0.351	0.204
	L	1.166±0.38	1.232±0.36	0.720
S/D, mean±SD	R	3.334±1.052	3.506±0.722	0.922
	L	3.719±1.61	3.484±0.932	0.708

EDV=End-Diastolik Velocity, PSV=Peak Systolic Velocity, TAV=Time Averaged Velocity, RI=Resistive Index, PI=Pulsatility Index, S/D=Systolic to Diastolic ratio, R=Right, L=Left, SD=Standart Deviation.

The AUCs of the ROC curve for left EDV and TAV scores are illustrated in Figure 2. An EDV level of 5.35 was identified as the optimal threshold for PT, yielding a sensitivity of 75% and a specificity of 83.33%. Similarly, for TAV, a level of 9 was determined to be the optimal threshold, also achieving a sensitivity of 50% and a specificity of 91.67%. The PPV, NPV, and accuracy of the predictive performance for PT are presented in Figure 3.

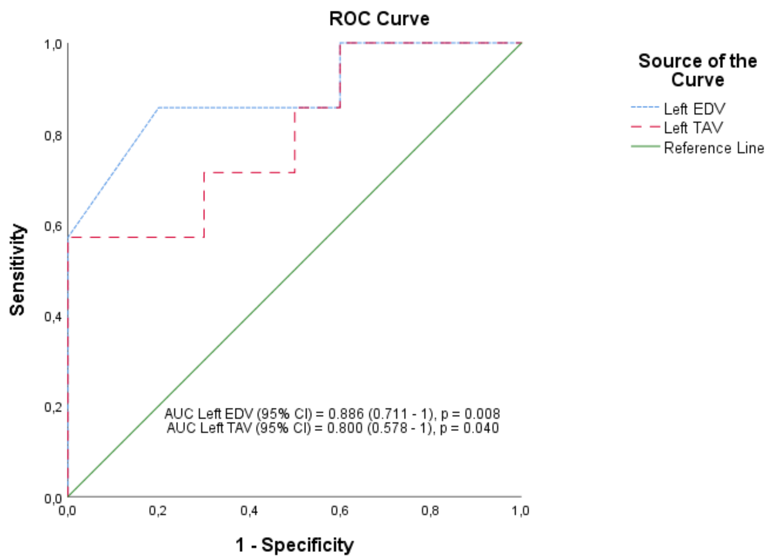

Figure 2. Receiver operating characteristic (ROC) curves of the EDV and TAV for PT

AUC=Area under the curve; EDV=End-Diastolic Velocity; TAV=Time-Averaged Velocity; CI=Confidence Interval; PT=Pulsatile Tinnitus.

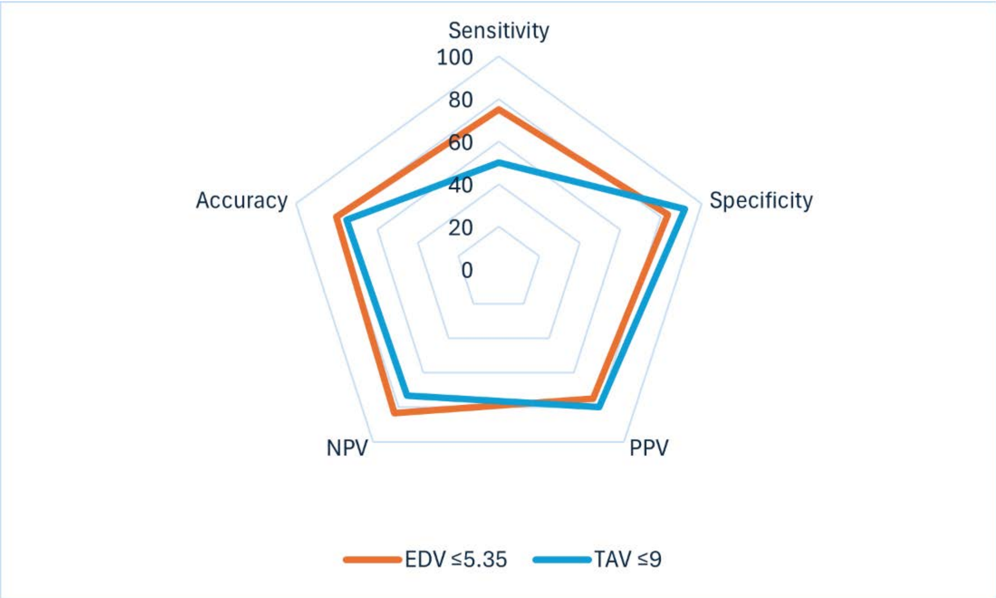

Figure 3. Predictive performance of EDV and TAV for PT.

EDV=End-Diastolic Velocity; TAV=Time-Averaged Velocity; CI=Confidence Interval; NPV=Negative Predictive Value; PPV=Positive predictive value; PT=Pulsatile Tinnitus.

DISCUSSION

Pulsatile tinnitus often suggests abnormal blood flow due to vascular issues like stenosis, arteriovenous fistulas, or increased blood flow from conditions such as anemia[9]. Despite the established prevalence of PT in patients with IIH, the underlying physiological mechanisms that cause PT in some individuals but not in others remain unclear. There was no correlation between the presence of PT and the severity of IIH or cerebrospinal fluid opening pressure[5]. The etiology of PT may be attributed to changes in blood flow resulting from intrinsic, extrinsic, and systemic pathologies, all of which are believed to contribute to patients with intracranial hypertension[10-12]. This study focuses on evaluating and comparing the systemic blood flow velocities in IIH patients, differentiating for the first time between those with PT and those without.

In patients with IIH, the prevalence of PT is higher in those with a higher BMI, elevated pulse pressure, and a greater prevalence of comorbidities such as sleep apnea and migraines. Given that CSF pressure levels do not differ significantly between patients with and without PT, it can be inferred that PT may not be a direct indicator of increased disease severity. Instead, it could be linked to complications associated with obesity, like increased pulse pressure and sleep apnea[12]. In our study, there was no significant difference in BMI and CSF opening pressure between the groups with and without PT.

Blood flow velocities can potentially act as a useful quantitative marker for cerebral perfusion. Doppler USG facilitates non-invasive and continuous monitoring of blood flow velocities in the brain arteries[13, 14]. Indices from Doppler USG waveforms of the ophthalmic and central retinal arteries can serve as an alternative method for evaluating ICP increases. Doppler USG allows for the clear visualization of these arteries within the orbital cavity, particularly at their points of intersection with the optic nerve[15, 16]. Our results reveal significant differences in EDV and TAV between IIH patients with PT and those without, suggesting distinct hemodynamic profiles within these subgroups.

Elevated ICP may exacerbate PT by increasing vascular pressure while also altering blood flow dynamics within the ophthalmic arteries. Some individuals with PT may be more sensitive to internal body sounds, perceiving normal blood flow noises transmitted to the inner ear through bone conduction. This sensitivity may be exacerbated by elevated intracranial pressure[17]. The significant differences in EDV and TAV between IIH patients with and without PT underscore the potential of these parameters as biomarkers for differentiating these subgroups. These changes could be more pronounced in patients with PT due to the increased sensitivity to intracranial hemodynamic alterations.

Our research findings indicate that both EDV and TAV demonstrate low sensitivity but high specificity. Sensitivity is a measure that reflects the proportion of true positives accurately identified, while specificity refers to the proportion of true negatives correctly classified. The high specificity observed for EDV and TAV indicates that lower levels of these parameters are highly indicative of the absence of the condition. Consequently, they can be considered reliable markers for excluding the presence of PT. Although the low sensitivity implies that EDV and TAV are not effective in identifying all true cases of PT, their high specificity underscores their utility in confirming patients without PT.

Our study has several limitations. The small sample size of 20 IIH patients and the single-center design limit generalizability, necessitating larger, multi-center cohort studies for confirmation. The study did not assess other vascular contributors to PT, such as the jugular vein and carotid artery.

In conclusion, this study indicates that orbital Doppler USG may have utility in distinguishing IIH patients with PT from those without. The evidence presented in this study suggests that significant differences in EDV and TAV may serve as potential biomarkers for IIH-associated PT, and this is a novel finding. These findings suggest that incorporating Doppler USG into the diagnostic framework for IIH, particularly in patients presenting with PT, could enhance early detection and monitoring of hemodynamic changes. Future research should aim to expand the sample size, including other vascular contributors (such as the jugular and carotid arteries), and further explore how orbital vascular dynamics contribute to the pathophysiology of PT in IIH. Moreover, longitudinal studies are necessary to assess the potential of Doppler USG parameters as reliable markers for disease progression and treatment outcomes, ultimately improving the management of IIH and PT. Another promising area for future research would be to compare PT patients with and without IIH, examining whether Doppler USG parameters could accurately differentiate IIH-related PT without the need for invasive lumbar puncture. Such studies could pave the way for a non-invasive diagnostic tool, improving patient care by reducing reliance on invasive procedures while providing clear differentiation between PT due to IIH and other causes.

Author Contributions: Concept/Design : DA, MD; Data acquisition: DA, MD; Data analysis and interpretation: DA, MD; Drafting manuscript: DA; Critical revision of manuscript: MD; Final approval and accountability: DA, MD; Technical or material support: DA; Supervision: DA; Securing funding (if available): n/a.
Ethical Approval: The study was approved by the local ethics committee of Harran University Medical Faculty in 2023 (Protocol number: HRU/23.21.19).
Peer-review: Externally peer-reviewed.
Conflict of Interest: Authors declared no conflict of interest.
Financial Disclosure: Authors declared no financial support

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