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# The Contribution of Neuroimaging to Diagnosis in Idiopathic Intracranial Hypertension

## *İdiyopatik İntrakraniyal Hipertansiyonda Nöro-Görüntülemenin Tanıya Katkısı*

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## Abstract

**Objective:** Due to difficulties in diagnosis, the presence of patients with idiopathic intracranial hypertension (IIH) without papilledema has led to the addition of neuro-radiologic features, which are indicative of increased intracranial pressure, to new diagnostic criteria. In this study, it was aimed to investigate the inter-rater agreement regarding the evaluation of neuroimaging findings of patients diagnosed as having definite IIH and to detect their possible contribution to diagnosis.

**Materials and Methods:** Forty-one consecutive patients with definite IIH who had both brain magnetic resonance imaging (MRI) and MR-venography (MRV) examinations were included in the study. Images were evaluated by two experienced neurologists, who were blinded to the clinical presentation of the cases, in terms of empty sella, flattened posterior globe/sclera, tortuosity of optic nerve, transverse sinus stenosis/hypoplasia, and additionally non-specific white matter lesions using a standardized form. The results were evaluated using kappa (κ) analysis in terms of inter-rater agreement.

**Results:** The mean body mass index and cerebral spinal fluid opening pressure of the patients (38 female, 3 male) were 29.2±5.48 kg and 371±149.4 mm$H_2O$, respectively. Six patients did not have papilledema. When MRI and MRV examinations were evaluated in terms of the presence of additional evidence supporting diagnosis, there was fair agreement for MRI (κ=0.333, p=0.021), and substantial agreement for MRV (κ=0.735, p<0.0001). Regarding subheadings, there was moderate agreement for empty sella, tortuosity of the optic nerve, and non-specific white matter lesions (κ=0.417, p=0.001; κ=0.523, p=0.001; κ=0.443, p=0.002, respectively), fair agreement for flattened posterior globe/sclera and transvers venous sinus stenosis (κ=0.291, p=0.06; κ=0.389, p=0.006, respectively), and substantial agreement for transverse venous sinus hypoplasia (κ=0.801, p<0.001).

**Conclusion:** In our study, it was found that additional neuroradiologic findings, especially those described in the new Friedman diagnostic criteria for patients without papilledema, showed fair-to-moderate agreement, even between two experienced neurologists. We believe that it is appropriate to examine the neuroradiologic images carefully for new criteria without evaluating only mass lesions, and to take clinical findings into account while evaluating patients with IIH.

**Keywords:** Idiopathic intracranial hypertension, MRI, MRV, neuroimaging, neuroradiology

## Öz

**Amaç:** Tanısında zorluklar yaşanabilen papilödemsiz idiyopatik intrakraniyal hipertansiyon (İİH) olgularının varlığı, yeni tanı ölçütlerinde kafa içi basınç artışına işaret eden nöro-radyolojik özelliklerin eklenmesine neden olmuştur. Bu çalışmada kesin İİH tanısı konmuş hastaların nöro-görüntüleme bulgularının araştırmacılar arasındaki tutarlılığının ve tanıya olan olası katkısının incelenmesi hedeflenmiştir.

**Gereç ve Yöntem:** Kesin İİH tanısıyla takipli, kraniyal manyetik rezonans görüntüleme (MRG) ve MR-venografi (MRV) incelemelerinin her ikisine ulaşılabilen ardışık 41 hasta çalışmaya dahil edildi. Görüntülemeler boş sella, glob posteriorunda düzleşme, optik sinir kıvrımlanması, transvers sinüs stenozu/hipoplazisi ve ek olarak non-spesifik ak madde lezyonları yönünden, olguların klinik verilerine kör, alanında tecrübeli iki ayrı nörolog tarafından standart bir formla incelendi. Sonuçlar araştırmacılar arası uyum bakımından kappa (κ) analizi kullanılarak değerlendirildi.

**Bulgular:** Hastaların (38 kadın, 3 erkek) ortalama vücut kitle indeksi 29,2±5,48; beyin omurilik sıvısı açılış basıncı 371±149,4 mm$H_2O$ idi. Altı hastada papilödem saptanmadı. MRG ve MRV incelemeleri tanıyı destekleyen ek bir bulgu olup olmamasına göre değerlendirildiğinde, araştırmacılar arasında MRG açısından zayıf (κ=0,333, p=0,021), MRV açısından iyi düzeyde (κ=0,735, p<0,0001) uyum olduğu görüldü. Alt başlıklar değerlendirildiğinde boş sella, optik

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**Abstract**

sinir kıvrımlanması ve non-spesifik ak madde lezyonları yönünden orta (sırasıyla κ=0,417, p=0,001; κ=0,523, p=0,001; κ=0,443, p=0,002), glob posteriorunda düzleşme ve transvers sinüs stenozu yönünden zayıf (sırasıyla κ=0,291, p=0,06; κ=0,389 p=0,006), transvers sinüs hipoplazisi yönünden ise iyi düzeyde (κ=0,801, p<0,001) uyum mevcuttu.

**Sonuç:** Çalışmamızda, yeni Friedman tanı kriterlerinde özellikle papilödemsiz hastalar için tanımlanmış olan ek nöro-radyolojik bulguların, iki deneyimli nörolog arasında bile zaman zaman zayıf-orta uyum gösterdiği görülmüştür. İİH hastasını değerlendirirken sadece kitle lezyonlarını dışlamakla yetinmeyip nöro-radyolojik görüntülemelerin yeni ölçütler yönünden dikkatle incelenmesinin ve klinik bulguların mutlaka göz önünde bulundurulmasının uygun olacağı düşünülmektedir.

**Anahtar Kelimeler:** İdiyopatik intrakraniyal hipertansiyon, MRG, MRV, nöro-görüntüleme, nöro-radyoloji

## Introduction

Idiopathic intracranial hypertension (IIH) is a syndrome characterized by increased intracranial pressure (ICP) of unknown etiology with normal neurologic examination and normal cerebrospinal fluid (CSF) findings, except for symptoms and signs such as headache, papilledema, tinnitus, sixth nerve palsy, and loss of vision (1). The diagnostic criteria were first proposed by Dandy (2) in 1937. An atypical variant of the classic clinical presentation described is patients with IIH without papilledema. These cases were included in the classification of the International Headache Society (3) and were published in many case reports and case series (4,5,6,7,8,9,10). Although its exact prevalence is not known, IIH without papilledema is less frequent. Therefore, the absence of papilledema in a patient does not exclude the possibility of IIH in the presence of other IIH symptoms and signs. In addition to the above-defined criteria, neuroimaging findings were reviewed and it has been recently finalized (11).

Magnetic resonance imaging (MRI) and MR-venography (MRV) are important in the exclusion of other clinical causes that may increase ICP. In addition, the presence of at least 3 neuroimaging findings consistent with the diagnosis of IIH (empty sella, flattened posterior globe/sclera, transverse cerebral venous sinus stenosis and distention of the perioptic subarachnoid space with or without tortuosity of the optic nerve) supports the diagnosis of IIH in patients without papilledema. However, it is thought that these neuroimaging findings are sometimes interpreted differently by physicians and therefore may not be sufficiently objective.

In this study, it was aimed to investigate the inter-rater agreement and the possible contribution of the neuroimaging findings of patients diagnosed as having definite IIH.

## Materials and Methods

### Patient Selection

The sample was selected from patients who were already being followed up by the headache and general neurology outpatient clinics or were newly admitted during the study and were diagnosed as having definite IIH according to the revised Friedman criteria. A total of 41 consecutive patients with both cranial MRI and MRV were included in the study.

### Evaluation of Neuroimages

Neuroimages were evaluated by two neurologists, who were blinded to the clinical presentation of the cases, in terms of (a) empty sella, (b) flattened posterior globe/sclera, (c) tortuosity of the optic nerve, (d) transverse sinus stenosis/hypoplasia, and (e) non-specific white matter lesions, using a standardized form. Small, cortico-subcortical, hyperintense white matter lesions on T2-weighted images were defined as 'non-specific white matter lesions' in our study. Given that one of the study objectives was to examine the familiarity of the neurologists with the relevant imaging findings regardless of the opinion of a radiologist in clinical practice, two neurologists experienced (Researcher 1: 32 years and Researcher 2: 13 years) in the field of neuro-imaging in a reference neurology center who were thought to be more familiar with these findings were included in the study. The standard form in this study consisted of 5 items and included structured questions with two options (present or absent) related to the aforementioned findings.

### Statistical Analysis

The SPSS v22.0 program was used for the statistical analysis of the data. The results were evaluated by using kappa (κ) analysis in terms of interrater agreement.

## Results

Thirty-eight patients were female and 3 were male. The mean body mass index was 29.2±5.48 and CSF opening pressure was 371±149.4 $mmH_2O$.

When MRI and MRV examinations were evaluated according to whether there was any additional finding supporting the diagnosis, there was fair agreement for MRI (κ=0.333, p=0.021) and substantial agreement for MRV (κ=0.735, p<0.0001). Regarding subheadings, there was moderate agreement for empty sella (Figure 1), tortuosity of the optic nerve (Figure 1) and non-specific white matter lesions (κ=0.417, p=0.001; κ=0.523, p=0.001; κ=0.443, p=0.002, respectively), fair agreement for flattened posterior globe/sclera and transverse venous sinus stenosis (Figure 2) (κ=0.291, p=0.06; κ=0.389, p=0.006, respectively), and substantial agreement for transverse venous sinus hypoplasia (κ=0.801, p<0.001) (Table 1).

Empty sella, tortuosity of the optic nerve, and transverse sinus stenosis were evaluated as 'present' by both raters with perfect agreement in six patients without papilledema, (κ=1.00, p<0.0001).

## Discussion

Regarding possible individual variability in the evaluation of neuroimaging findings that are related to the increase in ICP and are defined to assist in the diagnosis of IIH without papilledema,

MRI and MRV findings of patients with IIH were evaluated by two blinded raters in this study and there was fair agreement for MRI and substantial agreement for MRV. Regarding subheadings, there was moderate agreement for empty sella, tortuosity of the optic nerve, and non-specific white matter lesions, fair agreement for flattened posterior globe/sclera and transverse venous sinus stenosis, and substantial agreement for transverse venous sinus hypoplasia.

IIH leads to an increase in CSF opening pressure without an intracranial mass or ventriculomegaly and its pathophysiology is not yet understood (12). Although the main role of neuro-imaging in IIH is to exclude other pathologies that cause increased CSF pressure, MRI findings that can be detected by modern neuro-imaging methods such as empty sella, tortuosity of optic nerve, flattened posterior globe/sclera, contrast enhancement of vessels in the optic disc, meningocele formation, diffusion restriction at the

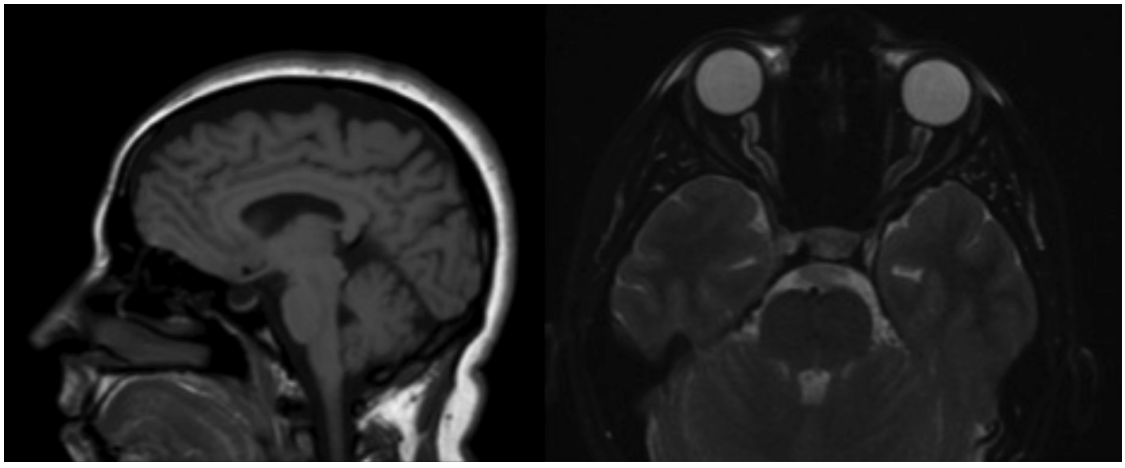

**Figure 1.** Empty sella (left) and tortuosity of the optic nerve (right) in two different patients with idiopathic intracranial hypertension

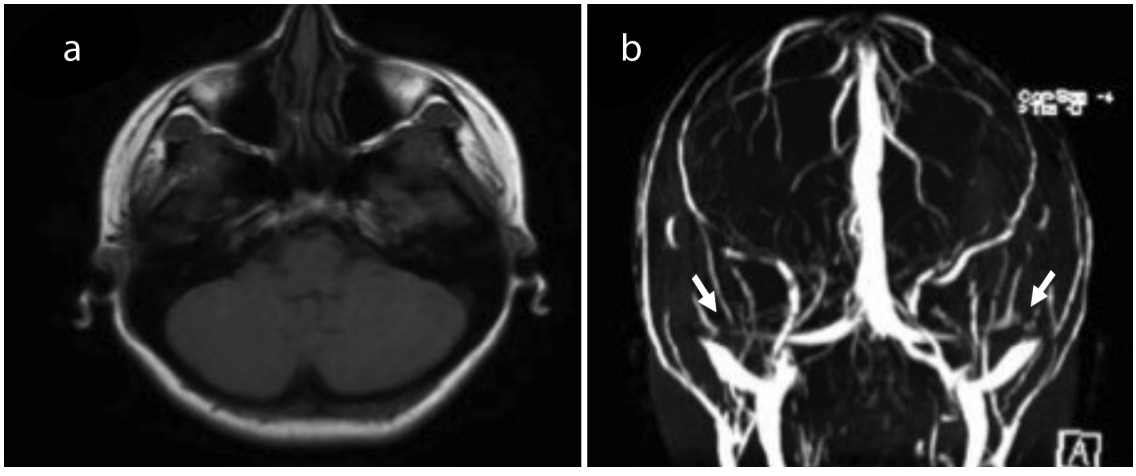


**Figure 2.** Magnetic resonance imaging (MRI) and MR-venography (MRV) samples of a patient with bilateral transverse sinus stenosis (BTSS). (a) Venous flow is intact and there is no finding compatible with thrombosis in T1-weighted MRI, (b) MRV compatible with BTSS (white arrows)

| Table 1. Comparison of neuroimaging findings of two researchers and interrater reliability | | | |
|---|---|---|---|
| | **Researcher 1 (n)** | **Researcher 2 (n)** | **Inter-rater reliability** |
| Empty sella | 18 | 7 | κ=0.417, p=0.001** |
| Flattened posterior globe/sclera | 10 | 8 | κ=0.291, p=0.06* |
| Tortuosity of the optic nerve | 13 | 16 | κ=0.523, p=0.001** |
| Transverse sinus stenosis | 23 | 14 | κ=0.389, p=0.006* |
| Transverse sinus hypoplasia | 19 | 15 | κ=0.801, p<0.001*** |
| Non-specific white matter lesions | 10 | 5 | κ=0.443, p=0.002** |
| *Fair agreement, **Moderate agreement, ***Substantial agreement | | | |

optic nerve head, and transverse sinus stenosis were found to be related to diagnosis (13). Although the sensitivity and prevalence of these findings vary between 6% and 66% in the literature, it is debateable as to whether they are really helpful to physicians in diagnosing IIH in patients without the classic presentation, as in IIH cases without papilledema presenting with a chronic daily headache profile with migrainous features (6,9,14,15).

Although empty sella is the oldest and most commonly reported neuroimaging finding in patients with IHH, it is also common in the general population (16). Although the sensitivity of empty sella in IIH ranges from 65% to 80% and its specificity ranges from 70% to 100%, this finding is not specific to IIH and may be observed in various causes of chronic intracranial hypertension such as cerebral venous sinus thrombosis and intracranial mass lesions (15,17,18,19,20,21). In our study, there was a moderate agreement for empty sella ($\kappa$=0.417) among the raters, who were trained in the same clinic and are colleagues.

Ophthalmic neuroimaging findings in IIH reflect the mechanical deformations of the optic nerve sheath, lamina cribrosa, and posterior sclera due to increased CSF pressure transferred through the intraorbital optic nerve, and these findings are generally reported based on subjective radiologic interpretations in studies (18,22,23). The sensitivity of flattened posterior globe/sclera varies between 43% and 85%, whereas its specificity is 98% (15,17,18,23). Flattened posterior globe/sclera is not specific for IIH because it can also be seen in cases such as ocular hypotonia (24). Tortuosity of the optic nerve has a sensitivity of 43% and specificity of 90% in IIH based on only subjective impressions (15,18,23). Our study also supported this subjectivity and there were fair ($\kappa$=0.291) and moderate ($\kappa$=0.523) inter-rater agreement for flattened posterior globe/sclera and tortuosity of the optic nerve, respectively.

The main role of intracranial vascular imaging in patients with suspected IIH is cerebral venous sinus thrombosis (25) and, more rarely, the exclusion of dural fistulae. Advances in neuroimaging studies have enabled reliable visualization of transverse venous sinuses in patients with IIH, in whom focal stenosis was previously missed (26,27,28). Farb et al. (26) demonstrated the presence of bilateral transverse sinus stenosis with a sensitivity and specificity of 93% in patients with IIH using MRV. In one study, according to the definition of transverse venous sinus stenosis, it was reported that 100% of the patients with IIH had bilateral stenosis on MRV (29). However, such bilateral transverse venous sinus stenosis is also common in patients with intracranial hypertension not associated with IIH (21,30) and it may also be seen in normal individuals (31). Although it is difficult to evaluate the sensitivity of bilateral transverse venous sinus stenosis due to inconsistent definitions in studies, the presence of artifact and the use of various venous imaging techniques, the pooled sensitivity of contrast-enhanced MRV is estimated to be 97% (26,29,32). Fair agreement ($\kappa$=0.389) between the raters in terms of transverse sinus stenosis in our study indicates that this finding can be interpreted differently between the evaluators and its value is not very reliable.

As mentioned in a previous study in our clinic (33), non-specific white matter lesions, which are sometimes confused with demyelinating diseases by physicians in patients with IIH, were evaluated in our study although they are not included in the Friedman diagnostic criteria, and moderate agreement was found ($\kappa$=0.443).

Although the two evaluators were experienced in their fields, the fair-to-moderate agreement for neuro-imaging findings defined in IIH in our study was interpreted in relation to the recent recognition of these imaging findings in the diagnosis of IIH, as well as the fact that these evaluations remained highly subjective in line with the literature.

## Conclusion

When evaluating a patient with IIH, it was thought that it would be appropriate to exclude mass lesions and examine the neuro-radiologic images carefully in terms of new criteria, and to consider the clinical findings. The findings becoming measurable with the help of new studies will provide more standardized results when interpreting them.

### Ethics

**Ethics Committee Approval:** Retrospective study.
**Informed Consent:** Retrospective study.
**Peer-review:** Internally peer-reviewed.

### Authorship Contributions

Concept: B.S., E.Ş., E.E., N.Y., O.Ç., B.B., Design: B.S., E.Ş., E.E., N.Y., O.Ç., B.B., Data Collection or Processing: B.S., E.Ş., Y.S., E.E., N.Y., O.Ç., B.B., Analysis or Interpretation: B.S., E.Ş., E.E., N.Y., O.Ç., B.B., Literature Search: B.S., E.Ş., Y.S., E.E., N.Y., O.Ç., B.B., Writing: B.S., E.Ş., Y.S., E.E., N.Y., O.Ç., B.B.

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