

AI Accuracy in Papilledema Diagnosis in Fundus Photographs within 201 Eyes

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ABSTRACT

Objective: To evaluate the AI accuracy in papilledema diagnosis in fundus photographs within 201 eyes.

Methods: This study was designed to evaluate all fundus photographs independently to assign a Frisen score to each eye by human agreement percent with and without CAD method to detect papilledema.

Results: These findings illustrate the clinician's dependency on Frisen scaling to detect papilledema, especially IIHWOP cases, suggested by the low agreement rate (only 24.5%) between three-person and high agreement rate of the CAD method with an ophthalmologist compared to a neurologist.

Conclusion: The diagnosis of papilledema by artificial intelligence (AI) can play a valuable role in the diagnosis of early or mild IIH or in the absence of an expert physician who needs an immediate decision making in telemedicine.

Keywords: Idiopathic Intracranial Hypertension; Papilledema; Fundus Photograph; Frisen; Artificial Intelligence (AI); Telemedicine

Introduction

Preventable or treatable causes of visual loss lead 30 to 40 million blind people. One of the most important reasons is physician unavailability, especially in low-income regions. Telemedicine and artificial intelligence (AI) might reduce these inequalities [1]. Idiopathic Intracranial Hypertension (IIH) and its missed diagnosis is one of the treatable causes of blindness and neurodegeneration. The most important red flag in IIH is Papilledema which is evaluated by indirect ophthalmoscopy by an expert physician. Idiopathic Intracranial Hypertension (IIH) is typically characterized by headaches and papilledema, first identified by Walter Dandy in 1937[2,3]. However, recent studies have indicated that IIH can also have other symptoms and signs [2,4-6]. Papilledema is an important objective finding in IIH and is a critical diagnostic criterion for the condition [2,3,7]. Elevated cerebrospinal fluid (CSF) opening pressure, normal CSF constituents, and brain imaging are used to rule out secondary causes of increased intracranial pressure (ICP) [2,7]. Based on seeing the optic nerve edema (papilledema), diagnostic criteria for idiopathic intracranial hypertension divide to IIH and IIHWOP (IIH without papilledema).

Requirements for the Diagnosis of IIH

- A. Papilledema
- B. Normal neurologic examination except for cranial nerve abnormalities
- C. Neuroimaging: Normal brain parenchyma without evidence of hydrocephalus, mass, or structural lesion and no abnormal meningeal enhancement on magnetic resonance imaging (MRI), with and without gadolinium, for typical patients (obese women), and MRI, with and without contrast, and magnetic resonance venography (MRV) for others; if MRI is unavailable or contraindicated, contrast-enhanced computed tomography (CT) may be used
- D. Normal cerebrospinal fluid (CSF) composition
- E. Elevated lumbar puncture CSF opening pressure [≥ 25 cm CSF in adults and ≥ 28 cm CSF in children (25 cm CSF if the child is not sedated and not obese)] in a properly performed lumbar puncture.

Diagnosis of IIH is definite if the patient fulfills criteria A-E. The diagnosis is considered probable if criteria A-D are met, but the measured CSF pressure is lower than specified for a definite diagnosis.

Diagnosis of IIHWOP

In the absence of papilledema, a diagnosis of IIHWOP can be made if B-E from above is satisfied, and in addition, the patient has unilateral or bilateral abducens nerve palsy. In the absence of papilledema or sixth nerve palsy, a diagnosis of IIHWOP can be suggested but not made if B-E from above are satisfied, and in addition, at least three of the following neuroimaging criteria are satisfied:

- A. Empty Sella
- B. Flattening of the posterior aspect of the globe

- C. Distention of the perioptic periodic subarachnoid space with or without a tortuous optic nerve
- D. Transverse venous sinus stenosis

However, IIHWOP is not widely acknowledged, but it has been classified as a type of headache by the International Headache Society since 2004 [8]. While most patients with IIHWOP have similar characteristics to those with IIH, it is uncertain whether IIHWOP is a distinct classification from IIH [9-11]. The occurrence of IIHWOP among individuals with chronic refractory headaches differs greatly (ranging from 2.5 to 86%), which reflects the uncertainty of diagnosing IIHWOP [9]. The lack of research on IIHWOP has been identified as a priority in a partnership for IIH by healthcare professionals and patients [10]. Currently, there are no recommended treatment options for IIHWOP [9].

A funduscopy examination is the most common method to diagnose papilledema clinically [9-11]. Lars Frisen utilized fundus photography to document his observations of papilledema, Fundi were photographed at different magnifications to distinguish between normal and abnormal conditions [12] then he classified into the Frisen scaling system [12,13] based on major findings as below:

- a) Grade 0 (Normal Optic Disc)

Prominence of the retinal nerve fiber layer at the nasal, superior, and inferior poles in inverse proportion to disc diameter.

Radial nerve fiber layer striation, without tortuosity

- b) Grade 1 (Minimal Degree of Edema)

C-shaped halo that is subtle and grayish with a temporal gap; obscures underlying retinal details.

Disruption of normal radial nerve fiber layer arrangement striations Temporal disc margin normal

- c) Grade 2 (Low Degree of Edema)

- Circumferential halo
- Elevation (nasal border)
- No major vessel obscuration

- d) Grade 3 (Moderate Degree of Edema)

- Obscuration of ≥ 1 segment of a major blood vessels leaving disc
- Circumferential halo
- Elevation (all borders)
- Halo (irregular ocular fringe with finger-like extensions)

- e) Grade 4 (Marked Degree of Edema)

- Total obscuration on the disc of a segment of a major blood vessel on the disc
- Elevation (Whole nerve head, including the cup)

- Border obscuration (complete)
 - Halo (complete)
- f) Grade 5 (Severe Degree of Edema)

Obscuration of all vessels on the disc and leaving the disc.

The fundus photograph, also called the en-face view image of the optic nerve head, has been recognized as useful for utilizing Frisen scaling to diagnose elevated intracranial pressure [14-16]. Medical professionals have noted that fundus photography is widespread in diagnosing this condition [12,13]. However, recent studies suggest that Frisen scaling has a limited correlation with increased intracranial pressure, as low ICP levels are associated with primary Frisen grades [13]. Fundus-based Frisen patterns may not accurately detect slight changes in the nerve head to assess IIH without papilledema [13,16].

Method

The study was conducted after receiving the code of ethics from the Ethics Committee of Medical Education of the National Institute for Medical Research Development: IR.NIMAD.REC.1399.015. This research has been designed to evaluate Frisen scoring for Patients’ data by human decisions and quantitatively measure the result of the agreements and disagreements between three investigators. No control group was required for this study because this investigation is a non-randomized comparative study for Electronic Health Records [17,18]. The patients’ IDs in fundus photographs were covered and replaced by random mixed numerical-alphabetical codes to blind the evaluating investigators [19]. Moreover, to strengthen the accuracy of such comparison studies, it was recommended to approach a dual review method [20].

The inclusion criteria in this comparison study have included the patients with clinical suspicions of IICP who were chosen to undergo this research intervention with their imaging medical records. The criteria under which IIH patients were identified encounter its signs and symptoms, including headaches, tinnitus, and visual impairments that come along with patients who experience either or some of such factors as high Body Mass Index (BMI), nausea, vomiting, and irregular menstruation[2].

The exclusion criteria have included two group;

- a. Before taking a photograph: Somebodies who couldn’t do it testing due to cognitive impairment , being a child under their 4th years and visual loss and

- b. After taking a photograph: other participants who were dropped were patients whose fundus photograph datasets could not meet the qualifying conditions [21] for this purpose, the ophthalmologist reviewed each participant’s disc OCT datasets and fundus photographs to exclude any cases with incomplete visibility of optic disc, OCT quality index lower than 40, high myopia, posterior subcapsular cataracts, exhibiting Pseudopapilledema and disc Drusen that has been a significant factor in implementing such a review [22].

This study was designed to evaluate 201 fundus photographs independently to assign a Frisen score to each eye by human agreement percent to detect papilledema. Three personal ideas quantitatively labeled the data. An experienced neurologist, an expert ophthalmologist, and a medical informatics specialist have independently evaluated all Fundus photographs; the medical informatics specialists usually evaluate Frisen scorings by Frisen’s written criteria in the book of neuro-ophthalmology [23]. These assessments are due to their privilege of using such methods to develop Computer-Aided Diagnosis (CAD) [21]. The modality which has been employed for this study, was a Swept Source DRI Triton OCT (Topcon). The mentioned device can acquire high quality fundus photographs [19]. The fundus snapshots were then extracted from studies and assigned identification numbers to match with a case.

Results

The number of approved patients in this study is less than those who entered; based on mentioned exclusion criteria, 24 patients were exempted from this investigation, which leaves 101 out of 125 (one of our patients has one non blind eye). In this study, the estimation of Friesen’s grading was labeled in 201 Fundus photographs with their Frisen scoring by three entities: one neurologist, an ophthalmologist, and Computer Aided Diagnosis (CAD) tool evaluation by a medical informatics specialist. The results show in detail in Table 1 that only 49 samples (24.5 %) were in total agreement among the three cited entities. In more detail, the ophthalmologist agreed with 37.1% of the neurologist’s evaluation. Otherwise, the agreement rate between the ophthalmologist and CAD methods was 63.4%, significantly higher than the rating between the neurologist and CAD methods met, 38.2%.

Table 1: Rate of Frisen scoring agreements between the three evaluation entities (summary).

State of Frisen Agreement	All the three entities	Ophthalmologist with Neurologist	Neurologist with CAD Methods	Ophthalmologist with CAD Methods
Agreed	24.5 %	37.1 %	38.2 %	63.4 %
Disagreed	75.5 %	62.9 %	61.8 %	36.6 %

Discussion

These findings illustrate the clinician's dependency on Frisen scaling to detect papilledema, especially IIHWOP cases, suggested by the low agreement rate (only 24.5%) between three-person. The agreement rate of the CAD method with an ophthalmologist compared to a neurologist is significantly high. It may be caused that ophthalmologists having more experience in Stereoscopic Color Fundus Photographs [24, 25] than neurologists.

Conclusion

IIH could be more accurately diagnosed because it is a treatable cause of blindness and neurodegeneration. Hence, IIHWOP cases should be re-evaluated by modern optic nerve head imaging if it is suggested in normal-looking clinical ophthalmoscopy. Also, the high degree of agreement in the diagnosis of papilledema between CAD methods and an expert ophthalmologist suggests that artificial intelligence (AI) can play a valuable role in the diagnosis of early or mild IIH or in the absence of an expert physician who needs an immediate decision making in telemedicine.

Compliance with Ethical Standards

There is also no conflict of interest. All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval: All procedures performed in studies involving human participants followed the ethical standards of the Iranian National Institute for Medical Research Development (No.: IR.NIMAD.REC.1399.015) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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