ORIGINAL ARTICLE

Cup-to-Disc Ratio in Idiopathic Intracranial Hypertension without Papilloedema

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ABSTRACT

This study seeks to characterise potential differences in the cup-to-disc ratio (CDR) of patients with idiopathic intracranial hypertension (IIH) with papilloedema (IIHWP) compared with IIH without papilloedema (IIHWOP). The medical charts, optical coherence tomography (OCT), and digital optic disc photos of 30 patients (59 eyes) with IIHWP and 4 patients (8 eyes) with IIHWOP were reviewed retrospectively. The CDR values of the two groups were analysed using the Wilcoxon-Mann-Whitney test. Results showed a statistically significant smaller CDR in patients with IIHWP as compared with IIHWOP. These findings suggest that structural factors of the optic disc may play a role in the development of or lack thereof of papilloedema in patients with IIH.

Keywords: Cup-to-disc ratio, idiopathic intracranial hypertension, papilloedema

INTRODUCTION

Idiopathic intracranial hypertension (IIH) is a syndrome of increased intracranial pressure of unknown aetiology. IIH is typically a disorder of young, obese females often with a history of recent weight gain. The modified Dandy criteria for the diagnosis of IIH includes a negative neuroimaging study (typically magnetic resonance imaging [MRI] with and without contrast and magnetic resonance venography [MRV]); normal cerebrospinal fluid (CSF) contents; symptoms and signs related only to increased intracranial pressure (ICP); and an elevated opening pressure (OP) on lumbar puncture.¹ Although the presence of papilloedema is common in IIH, it is not required for the diagnosis. Several prior reports^{2–7} have documented the existence of IIH without papilloedema (IIHWOP) and the reason for its absence in these patients remains controversial. Some proposed

mechanisms for IIHWOP include (1) anatomic variations in the optic nerve sheath or its trabeculations that might prevent the transmission of elevated ICP to the optic disc⁸; (2) a chronic or presymptomatic form of IIH with resolution of prior papilloedema⁹; or (3) fluctuating elevations in ICP below the threshold required to develop papilloedema.⁴

Interestingly, the particular morphology of the optic disc has been shown to play a role in the development of other optic nerve disorders such as non-arteritic anterior ischaemic optic neuropathy (NAION). In NAION, patients may have a structural “disc at risk” of a small cup-to-disc ratio (CDR) that might predispose to disc oedema and secondary ischaemia.¹⁰ Likewise, translaminal pressure with subsequent optic nerve damage in primary open angle glaucoma (POAG) can manifest as a typical glaucomatous cupping with an increased CDR.¹¹

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Although two previous studies of IIH have documented a smaller CDR in patients with IIH with papilloedema (IIHWP) as compared with normal subjects,^{13,14} to our knowledge, no prior study has examined the CDR in patients with IIHWOP. Based upon our initial clinical impressions about CDR in IIH, we hypothesised that, as in NAION, a small CDR might be a structural risk factor for the development of IIHWP and a larger CDR might be associated with IIHWOP. Thus, to the best of our knowledge, this is the first study to document a statistically significant difference in CDR in IIHWP versus IIHWOP.

MATERIALS AND METHODS

We performed a retrospective chart review of all patients with the diagnosis of IIH seen at the Methodist Eye Associates, Houston Methodist Hospital (HMH), Houston, Texas, from April 2009 to April 2012. This study was approved by The HMH Institutional Review Board (IRB). Inclusion criteria¹ for IIH included the modified Dandy criteria: signs and symptoms of elevated ICP; documented elevated ICP greater than 25 cm H₂O; normal CSF composition; and no evidence of structural abnormalities on neuroimaging. Patients were also included for this study only if there was a well-documented CDR on their first visit or optic disc photography to verify optic disc oedema (IIHWP) or lack thereof (IIHWOP). Subjects were excluded from the study if they did not meet modified Dandy criteria for IIH, had a previous diagnosis of glaucoma, or had optic atrophy. Patients with normal ICP were excluded but those with borderline but elevated ICP (i.e., 20 to 25 cm H₂O) were included in a separate analysis. IIHWP was defined as IIH with optic disc oedema documented by ophthalmoscopy, optical coherence tomography (OCT) of the optic nerve, optic disc photography, or a combination of these modalities. IIHWOP in our study was defined as IIH without disc oedema visible by ophthalmoscopy, OCT, optic disc photography, or a combination of these modalities at any point during the disease. Optic disc photography, when available, was evaluated in a masked fashion using the modified Frisén scale and compared for agreement by a majority of the examiners in IIH and IIHWOP. Patients without sufficient chart or photographic documentation of CDR were also excluded. All patients were seen in HMH neuro-ophthalmology clinic and underwent complete neuro-ophthalmic examinations, including visual acuity, Humphrey (24-2) visual field testing, pupillary, motility, slit lamp, and intraocular pressure examinations. The CDRs of those with IIHWP were measured after complete resolution of disc oedema verified either by ophthalmoscopy, optic disc photography, or both. Statistical significance was assessed using the

Wilcoxon-Mann-Whitney test for comparing differences in CDR between those who have IIHWP and those who have IIHWOP. A *p* value less than or equal to 0.10 was considered to be statistically significant in this study. All analyses were conducted using STATA (Stata Statistical Software, release 11; StataCorp, College Station, TX, 2009).

RESULTS

Initially 78 charts were reviewed but only 34 met inclusion criteria. Of these 34 charts were reviewed, 30 patients (59 eyes; 1 patient had asymmetric papilloedema) met our defined inclusion criteria for IIHWP (88%) and 4 patients (8 eyes) met inclusion criteria for IIHWOP (12%). Of the 30 patients with IIHWP, 11 had resolution of their papilloedema over the course of their treatment and were not considered IIHWOP. In contrast, 4 subjects with IIHWOP had no papilloedema at any point during the course of their disease.

Among those with IIHWP, all subjects were female, 50% (15 subjects) were Caucasian, and 27% (8 subjects) were African American. In comparison, in the IIHWOP group, 75% (3 subjects) were female and all subjects were Caucasian. The average age of the study patients was 32.1 ± 8.86 years.

Best-corrected visual acuity (BCVA) at presentation was 20/20 or better in 47 eyes (80%) and 20/70 or better in the remainder of the IIHWP group compared with 20/20 or better in 6 eyes (75%) and 20/30 or better in the remainder of the IIHWOP group. No patients with IIHWOP had glaucoma, optic atrophy, or optic neuropathy.

The average opening pressure was 34.6 ± 7.5 and 34.8 ± 11.1 cm H₂O in the IIHWP and IIHWOP groups, respectively (*t*-test *p* value of 0.98). Brain MRI and MRV with contrast were normal in all included cases except for findings consistent with increased ICP. Amongst subjects with IIHWOP, one had CSF fluid within the optic nerve sheath (Table 4; patient 3).

The average CDR of our patients with IIHWP was 0.20 ± 0.091 OD and 0.20 ± 0.082 OS, with a range of 0.1 to 0.4, and the average peripapillary retinal nerve fibre layer thickness (RNFL) by OCT was 101.1 ± 22.2 μ m OD and 101.7 ± 20.7 μ m OS, consistent with the presence of disc oedema. In contrast, the average CDR of our patients with IIHWOP was 0.33 ± 0.17 OU, with a range of 0.1 to 0.5. Of the 2 patients with IIHWOP who had OCT measurements, the average RNFL was 94 ± 1.41 μ m OD and 96 ± 5.66 μ m OS, consistent with the absence of optic disc oedema. Statistical analysis with the Wilcoxon-Mann-Whitney test showed that patients with IIHWP had a statistically significant smaller CDR (*p* ≤ 0.1) compared with patients with IIHWOP (Table 1).

TABLE 1 Median CDR values in patients with IIHWP versus IIHWOP meeting all modified Dandy criteria.

CDR	IIH with papilloedema (n = 30)	IIH without papilloedema (n = 4)	p Value*
CDR OD, median (IQR†)	0.2 (0.1, 0.25)	0.35 (0.2, 0.45)	0.10
CDR OS, median (IQR)	0.2 (0.1, 0.25)	0.3 (0.2, 0.45)	0.09

OD = right eye; OS = left eye.

*p-value based on Wilcoxon-Mann-Whitney test.

†Interquartile range.

TABLE 2 Median CDR values in patients with an OP ≥ 20 cm H₂O and meeting all other modified Dandy criteria.

CDR	Papilloedema present (n = 34)	Papilloedema absent (n = 6)	p Value*
CDR OD, median (IQR†)	0.2 (0.1, 0.25)	0.4 (0.3, 0.5)	0.004
CDR OS, median (IQR)	0.2 (0.1, 0.25)	0.4 (0.3, 0.5)	0.004

OD = right eye; OS = left eye.

*p-value based on Wilcoxon-Mann-Whitney test.

†Interquartile range.

Although the modified Dandy criteria require an OP of 25 cm H₂O, some authors believe an OP 20 cm H₂O is sufficient for a diagnosis of increased ICP. Additional analysis of 7 subjects with an OP between 20 to 25 cm H₂O but who met all other modified Dandy criteria was performed. Of these 7 subjects, 4 had papilloedema and 3 did not. Statistical analysis with the Wilcoxon-Mann-Whitney test amongst these 41 patients would again show that patients with papilloedema had a statistically significant smaller CDR ($p < 0.004$) compared with patients without papilloedema but with much stronger significance (Table 2). Two of the three patients without papilloedema and an OP between 20 and 25 cm H₂O had an empty sella on MRI.

DISCUSSION

Although the classic presentation of IIH includes the presence of papilloedema, it is not required for the diagnosis by the modified Dandy criteria and it may be absent in some patients for the entirety of their disease. The role of CDR in the development of papilloedema in IIH is currently not understood. To our knowledge, this the first study of CDR in patients with IIHWOP. Our results show that the CDR in our patients with IIHWOP is both similar to previously published values of those with IIHWP (Table 3) and significantly different from the CDR in our patients with IIHWOP (Table 1). Given the rarity of

TABLE 3 CDR values from our patients with IIHWOP and IIHWOP compared with previously published studies.

CDR	IIHWP subjects of Geddie et al. (n = 55) % (n)	Our subjects with IIHWOP (n = 59) % (n)	Our subjects with IIHWOP (n = 8) % (n)
0.0–0.09	21.82 (12)	–	–
0.10–0.19	67.27 (37)	35.59 (21)	25.00 (2)
0.20–0.29	9.09 (5)	42.37 (25)	–
0.30–0.39	1.82 (1)	16.95 (10)	25.00 (2)
0.40–0.49	–	5.08 (3)	25.00 (2)
0.50–0.59	–	–	25.00 (2)
0.60–0.69	–	–	–
0.70–0.79	–	–	–
0.80–0.89	–	–	–
0.90–0.99	–	–	–

the disease, we decided to also include in the analysis patients with an OP that was elevated (between 20 and 25 cm H₂O) but not over 25 cm H₂O. These 7 patients met all other inclusion criteria and showed a difference in cup-to-disc ratio, with a significance value of $p < 0.004$.

Given that the OP values were similar between the two groups, it is unlikely that differences in ICP alone could account for the presence of papilloedema or lack thereof. These data suggest that anatomical disc variations might be responsible, at least in part, for the absence of papilloedema in IIHWOP. Interestingly, radiographic findings of increased ICP, such as fluid in the optic nerve sheath and an empty sella, were seen in some of our IIHWOP patients and support the hypotheses that the ICP might not be transmitted to the disc head and/or that a larger CDR might preclude the development of ophthalmoscopically visible disc oedema.¹⁰

When considering the implications of a small CDR in patients with IIH, it may be useful to compare and contrast the findings with the structural “disc at risk” of a small CDR¹¹ in NAION. The mechanism for the small CDR producing NAION remains speculative but is presumed to be a mechanical and structural risk factor that predisposes to and/or perpetuates a vicious cycle of disc oedema and further ischaemia that leads to the clinical finding of sector or diffuse oedema in NAION. It may be the case that patients with IIHWOP possess a similar structural morphology that predisposes to or worsens oedema of the optic nerve head in elevated ICP.

Hayreh reported in 1964¹⁵ that the changes of papilloedema are limited to the area of the optic nerve just anterior to the lamina cribrosa. Recent studies from Berdahl et al. suggest that optic disc oedema is the result of an abnormal translaminar pressure difference between the intraocular pressure (IOP) and subarachnoid space at the lamina cribrosa.¹² Thus, it might be that a larger CDR provides a larger surface area of distribution for the translaminar pressure

TABLE 4 Clinical data observed in our patients with IIHWOP meeting all modified Dandy criteria.

Patient	Gender	Age	Race	LP OP	OCT OD	OCT OS	BCVA OD	BCVA OS	CDR OD	CDR OS
1	F	29	C	50	93	100	20/30	20/20	0.5	0.5
2	F	22	C	27	Not on file	Not on file	20/20	20/30	0.4	0.4
3	M	15	C	36	95	92	20/20	20/20	0.1	0.1
4	F	18	C	26	Not on file	Not on file	20/20	20/20	0.3	0.3

differential between the IOP and subarachnoid space, lessening the effects of elevated intracranial pressure and protecting against the development of papilloedema in IIHWOP. We excluded patients in our series with glaucoma to avoid the confounder of increased CDR and therefore cannot comment on the potential role of intraocular pressure (IOP) and translaminar pressure differences between IOP and ICP.

Transmission of CSF pressure along the optic nerve sheath may be necessary but not sufficient for the development of optic disc oedema.¹⁵ Anatomical differences within the optic nerve sheath, such as the number or quality of fibrous bands, may result in a different capacity to transmit CSF pressure down the optic nerve sheath or to the optic nerve head and subsequently affect the translaminar pressure gradient at the lamina cribrosa.^{8,16} It might be that our patient with IIHWOP who had CSF fluid in the nerve sheath (Table 4; patient 3) possessed such morphological features to prevent changes at the optic nerve head.

Some authors believe IIHWOP may be a form of chronic IIH in which papilloedema was present at one point in time but subsequently resolved.⁹ In our study, 11 patients with IIHWOP had resolution of papilloedema after medical therapy was initiated and we did not consider these patients to be IIHWOP for our study. In contrast, papilloedema was not observed in the 4 subjects with IIHWOP at any point in time during evaluation and treatment.

We recognise the limitations of this study. First, quantifying CDR by human observers is notoriously unreliable with significant inter-rater and intra-rater reliability. To this end, all final classifications in this study were agreed upon by multiple clinicians with significant experience evaluating the optic nerve head according to the modified Frisén scale. A second limitation results from the retrospective nature of our study and the problems associated with such analysis. An attempt was made to overcome this limitation with combination modalities of disc assessment through multimodal documentation, which included clinical observation, optic disc photography, and OCT measurements. Some may object to our claim that a p value <0.1 represents statistical significance, as a p value <0.05 is conventionally chosen to represent this threshold. Given the rarity of IIHWOP and our small sample size ($n = 4$), we believe

that a p value <0.1 is justifiably meaningful when considering the potential value in understanding this clinical oddity. Future studies would benefit from a larger sample size and a stronger p value. Finally, some may question the validity of incorporating patients with OP values between 20 and 25 cm H₂O. Given that some authors believe the normal range is 10 to 20 cm H₂O, it is appropriate to consider those with an OP greater than 20 cm H₂O even though they remain below the threshold required by the modified Dandy criteria. Despite these limitations, we hypothesise that the CDR is a potential risk factor for IIHWOP. Further work will be necessary, however, to confirm the hypothesis and elucidate the mechanism.

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