ORIGINAL ARTICLE

Do Optic Canal Dimensions Measured on CT Influence the Degree of Papilloedema and Visual Dysfunction in Idiopathic Intracranial Hypertension?

Nicholas T. Skipper^a, Mark S. Igra^a, Revelle Littlewood^b, Paul Armitage^c, Peter J. Laud^d, Susan P. Mollan^e, Basil Sharrack^{f,g}, Irene M. Pepper^b, Ruth Batty^a, Daniel J. A. Connolly^a, and Simon J. Hickman^f

^aDepartment of Radiology, Royal Hallamshire Hospital, Sheffield, UK; ^bDepartment of Ophthalmology, Royal Hallamshire Hospital, Sheffield, UK; ^cAcademic Unit of Radiology, University of Sheffield, Sheffield, UK; ^dStatistical Services Unit, University of Sheffield, Sheffield, UK; ^eDepartment of Ophthalmology, Queen Elizabeth Hospital, Birmingham, UK; ^fDepartment of Neurology, Royal Hallamshire Hospital, Sheffield, UK; ^gNational Institute for Health Research, Sheffield Neuroscience Biomedical Research Centre, Sheffield, UK

ABSTRACT

A recent study found that increased optic canal area on magnetic resonance imaging was associated with worse papilloedema in idiopathic intracranial hypertension (IIH). We repeated this study using more accurate computerized tomography derived measurements. Optic canal dimensions were measured from 42 IIH patients and 24 controls. These were compared with papilloedema grade. There was no correlation between any of the optic canal measurements and papilloedema grade and no significant difference in optic canal measurements between patients and controls. Our results cast doubt on the existing literature regarding the association between optic canal size and the degree of papilloedema in IIH.

CT delineates bony anatomy more accurately than MRI and our CT-derived optic canal measurements cast doubt on the existing literature regarding the association between optic canal size and the degree of Papilloedema in IIH.

ARTICLE HISTORY

Received 28 April 2018
Accepted 29 May 2018

KEYWORDS

Papilloedema; optic canal;
idiopathic intracranial
hypertension;
pseudotumour cerebri

Introduction

Patients with idiopathic intracranial hypertension (IIH) usually have Papilloedema at presentation and are at risk of visual dysfunction. The optic nerve sheath subarachnoid spaces (ONS-SAS) are often distended in patients with IIH¹ and the pathogenesis of papilloedema is related to high cerebrospinal fluid (CSF) pressure in the ONS-SAS.² The ONS-SAS has traditionally been considered to be in free communication with the suprasellar cistern and intracranial subarachnoid spaces (IC-SAS), which would suggest that as intracranial pressure (ICP) rises, papilloedema should develop symmetrically. However, a number of authors have observed that papilloedema may be asymmetrical in a minority of patients with raised ICP and IIH.^{3–8}

Several mechanisms for this asymmetry have been proposed, including compartmentalization between the suprasellar cistern and ONS-SAS such that the ONS-SAS of the two optic nerves may in fact be at different pressures to the IC-SAS and to each other.⁹ Other proposed mechanisms

include congenital anomalies or perforations of the optic nerve sheath, pre-existing optic nerve atrophy, or asymmetrical intra-ocular pressure.^{3,4}

Evidence of compartmentalization has been found by Killer et al. and others in the form of demonstrable trabeculae in the subarachnoid space, the existence of concentration gradients between the spinal CSF and the CSF within the ONS-SAS and reduced contrast loads within the ONS-SAS compared to the IC-SAS on CT cisternography.^{8,10–12} Compartmentalization may therefore affect the degree of papilloedema and optic nerve damage in IIH, through alterations in the transmission of intracranial CSF pressure to the ONS-SAS.

A study of 559 patients with IIH found that 20 (3.6%) had very asymmetrical papilloedema and in the eight cases where the imaging was sufficient to measure the optic canal dimensions (seven from magnetic resonance imaging (MRI) and one from computerized tomography (CT)), the larger canal was on the side of the higher grade papilloedema.³ This led to a study of 69

patients with IIH who had undergone high-resolution MRI which found a statistically significant reduction in visual fields with increasing optic canal cross-sectional area and increased odds of high grade papilloedema amongst patients with larger canals.¹³ However, when the grade of papilloedema was controlled for, the association between reduction in visual fields and increased canal size was reduced suggesting that this may be a significant confounding factor.

The authors suggested that the asymmetry of the optic canals could either be the cause of the asymmetrical papilloedema or the effect of long-standing raised pressure and bone remodelling. Moodley et al. found optic nerve swelling and hyperintensity on T2 MRI in a patient with fulminant IIH and proposed that the occurrence of optic canal bone remodelling may allow persistent dilatation of the optic nerve sheaths in some patients with IIH whilst in others, where bone remodelling does not occur, the optic nerve sheath may collapse due to the Venturi effect once the ICP rises above a certain threshold leading to optic nerve damage.¹⁴

If optic canal dimensions do play a role in the development of papilloedema, they could potentially be used as a prognostic indicator for visual outcome and as an aid to timing any intervention. However, the studies have mainly utilised MRI for the measurement of optic canal dimensions. This is an inferior technique to volumetric CT for the measurement of optic canal dimensions as CT provides better delineation of the bony margins.

Our routine practice involves volumetric CT venography (CTV) in patients with suspected IIH to rule out a cerebral venous sinus thrombosis, thus providing an opportunity to determine whether CT-derived measures of optic canal dimensions show a similar correlation with papilloedema grade and visual function in patients with IIH.

Methods

This retrospective, observational study was performed in a single neuroscience centre and approved by the Institutional Clinical Effectiveness Unit who waived any requirement for informed consent. The study follows the principles of the Declaration of Helsinki.

A search was made of the local radiological database for all female patients who had been investigated with cranial CTV between 1 January 2007 and 31 May 2016. 1 January 2007 was chosen as this is when the joint neuro-ophthalmology clinic was established. From this database, patients with a new diagnosis of IIH, according to the Friedman-Jacobson criteria,¹⁵ were identified. For inclusion in the study, patients had to have undergone CTV, fundus photography, kinetic perimetry, and lumbar puncture with measurement of CSF opening pressure within a 2-week period.

A control group was identified of female patients without IIH who had undergone CTV for the investigation of acute headache and suspected venous sinus thrombosis but had a normal CSF opening pressure at lumbar puncture, no papilloedema on funduscopy, no venous sinus thrombosis, and in whom no secondary cause for their headache was found.

Demographic and clinical data for all subjects were recorded from the clinical notes, including age, height, weight, body mass index, and CSF opening pressure at lumbar puncture.

Clinical evaluation

Two neuro-ophthalmologists (IMP and SJH) independently graded the degree of papilloedema from fundus photographs of the IIH patients using the modified Frisén grade (MFG) with grade 6 assigned for a pale disc due to optic nerve atrophy.^{13,16} Where there was disagreement, the photographs were graded by two further neuro-ophthalmologists (SM and BS) and the consensus view was recorded. A further independent observer (RL) measured the I4e isopter mean radial degrees (MRD) from kinetic perimetry,¹⁷ using a Goldmann perimeter (Haag-Streit, Köniz, Switzerland) or an Octopus perimeter (Haag-Streit, Köniz, Switzerland). The I4e isopter measurement could not be performed on two perimetry plots for technical reasons.

Radiological evaluation

The cranial CTVs were helical acquisitions performed 50 s after commencing a 50 mL IV injection of either Niopam 300 (Bracco UK limited, Buckinghamshire,

UK) or more recently Omnipaque 300 (GE Healthcare, Chicago, IL, USA) at a rate of 2 mL/s. All scans were performed on a Prospeed 32 detector scanner or a high-speed VCT 64 detector scanner (both GE Healthcare, Chicago, IL, USA). Images were reconstructed using a soft tissue algorithm with a raw slice thickness of 0.625 mm.

For the IIH and control groups, two independent neuroradiologists (MSI and NTS) reformatted the 3D data sets using IMPAX volume viewing 3.1 (Agfa Healthcare, Mortsel, Belgium) in order to produce a coronal oblique plane perpendicular to the axis of each optic canal. This was displayed using a window level of 700 HU and a width of 3500 HU, and the cross-sectional area of the canal was measured on each slice where it was visible as a complete ring of bone (Figure 1). The minimum and mean canal cross-sectional areas were recorded for each canal. The length of the canal was calculated by multiplying the number of cross-sectional measurements made by the slice thickness of the coronal oblique reformats, thus allowing canal volume to be calculated. One observer repeated the reformatting and measurements for 10 data sets. Both observers were blinded to the clinical details and whether the patient was in the IIH or control group.

Figure 1. Reformatted CT images of the right optic canal in the axial oblique, sagittal oblique, and coronal oblique planes with example region of interest and measurements.

Statistical analysis

Statistical analysis was performed using Graphpad Prism (GraphPad Software, La Jolla, CA, USA), R: A language and environment for statistical computing (R Core Team (2017), Vienna, Austria), and the extension package ICC.¹⁸

The data from one eye from each patient were used in the analysis. The eye was chosen at random using a random sequence generator (www.random.org) for control subjects and for patients with symmetrical papilloedema. The eye with the higher MFG was chosen in cases of asymmetrical papilledema.

Inter-rater agreement for optic canal measurements was estimated using intraclass correlation coefficients (ICC) for the mean and minimum canal cross-sectional area and for the canal volume measured by each neuroradiologist for all IIH patients and the control group. Intra-rater agreement was estimated using ICC for the repeat measurements made by one neuroradiologist in 10 data sets.

Correlations were assessed using Pearson correlation coefficients. Comparison of means was performed with independent sample *t*-tests.

When comparing optic canal dimensions between eyes in patients with marked asymmetrical papilloedema (defined as ≥ 2 units of MFG difference between the two eyes³), paired sample *t*-tests were used.

Results

There were 42 patients with IIH who had undergone all of the necessary investigations within the appropriate time frame and the control group totalled 24 subjects. The demographic details for the subjects are listed in Table 1.

Reproducibility of canal measurements

The ICCs for intra-rater agreement were excellent for all measurements (Table 2); however, the ICCs for inter-rater agreement were more modest (Table 3). A scatter plot comparing the mean cross-sectional area measurements made by each neuroradiologist is given in Figure 2 and shows a systematic difference in measurement: neuroradiologist 2 consistently measured higher than neuroradiologist 1. Scatter plots for

Table 1. Patient and control group demographics. NB. All patients and controls were female.

	Patients, <i>N</i> = 42 (range)	Controls, <i>N</i> = 24 (range)	<i>p</i> Value
Mean age (years)	29 (17–53)	33 (20–46)	0.07
Mean weight (kg)	97.6, <i>n</i> = 35 (68.0–143.5)	77.2, <i>n</i> = 13 (52.2–121.7)	0.004
Mean height (m)	1.61, <i>n</i> = 37 (1.48–1.78)	1.63, <i>n</i> = 18 (1.57–1.71)	0.3
Mean BMI (kg/m ²)	37.4, <i>n</i> = 34 (22.8–62.1)	28.8, <i>n</i> = 13 (20.9–42.1)	0.002
Mean LP OP (cm.CSF)	38.9, <i>n</i> = 41 ^a (26–65.5)	17.3, <i>n</i> = 24 (7–25)	<0.0001

BMI = body mass index, CSF = cerebrospinal fluid, LP = lumbar puncture, OP = opening pressure

^aThe OP was recorded as >40 cm.CSF for one patient.

Table 2. Intra-rater agreement for one neuroradiologist on the basis of repeat left optic canal measurements on 10 consecutive subjects.

Optic canal measurement	ICC (95% CI)
Mean area	0.96 (0.85–0.99)
Minimum area	0.88 (0.62–0.97)
Volume	0.84 (0.51–0.96)

ICC = intraclass correlation coefficient.

Table 3. Inter-rater agreement between the two neuroradiologists for optic canal cross-sectional area and volume measurements on one side in each patient from the idiopathic intracranial hypertension and control groups.

Optic canal measurement	ICC (95% CI)
Mean area	0.40 (0.18–0.58)
Minimum area	0.36 (0.13–0.55)
Volume	0.65 (0.49–0.77)

ICC = intraclass correlation coefficient.

minimum cross-sectional area and canal volume reveal a similar relationship.

Only measurements made by neuroradiologist 1 were used in the subsequent analysis although similar findings were seen when the second

neuroradiologist's measurements were used. Averaging was not felt to be sensible as the relationship between the two sets of measurements was linear and trends with increasing canal dimensions were under investigation, rather than associations with absolute canal dimensions.

Correlations

There was no evidence of a correlation between any of the canal measurements and MFG, all correlation coefficients (*r*) being 0.06 or less (Figure 3a–c).

Opening pressure and MFG were positively correlated (*r* = 0.30, or 0.43 if the two grade 6 [optic disc atrophy] patients were removed) (Figure 4). A negative correlation (*r* = −0.52) was found between I4e isopter MRD and MFG (Figure 5).

Patients vs. controls

There were no significant differences in canal measurements between the control subjects and all of the IIH patients (Table 4) nor between the control patients and those IIH patients with higher grade papilloedema (MFG grade 3–6) (Table 5).

Six patients had marked asymmetrical papilloedema; however, no significant differences between eyes were found in any of the optic canal dimensions for these patients.

Discussion

We found no significant correlation between any of the optic canal measurements and the grade of papilloedema. This contradicts the findings of previous authors^{3,13} who used MRI-derived measurements of the optic canals but we believe our CT-derived measurements to be more accurate. We also included a control group in our study design and found no significant difference in canal

Figure 2. Scatter plot of mean optic canal cross-sectional area measurements (mm²) made by each Neuroradiologist.

Figure 3. Scatter plots of optic canal measurements [(a) minimum cross-sectional area (mm^2), (b) mean cross-sectional area (mm^2) and (c) volume (mm^3)] against grade of papilloedema (modified Frisén grade) in the idiopathic intracranial hypertension group, showing no significant correlations.

Figure 4. Scatter plot of modified Frisén grade and lumbar puncture opening pressure (cm CSF) in the idiopathic intracranial hypertension patients, showing a positive correlation.

Figure 5. Scatter plot of modified Frisén grade and visual field measurements using I4e isopter mean radial degrees in the idiopathic intracranial hypertension patients showing a negative correlation.

dimensions between IIH patients and controls, suggesting that at least at presentation, IIH is unlikely to have resulted in bone remodelling. To our knowledge, this has not been done before and

casts further doubt on the findings of the earlier studies.

Our study utilised CTV rather than MRI and measurements are therefore likely to be more

Table 4. Differences between canal measurements in the idiopathic intracranial hypertension and control groups with 95% confidence intervals and *p* values.

	Patients (<i>N</i> = 42)	Controls (<i>N</i> = 24)	Difference	95% CI	<i>p</i> Value
Mean area (mm ²)	13.16	12.45	0.71	−0.27, 1.68	0.152
Minimum area (mm ²)	11.52	10.90	0.62	−0.41, 1.65	0.233
Volume (mm ³)	71.35	61.52	9.83	−1.42, 21.10	0.085

Table 5. Differences between canal measurements in the idiopathic intracranial hypertension group with grades 3–6 modified Frisén grade and the control group with 95% confidence intervals and *p* values.

	Patients with grades 3–6 MFG (<i>N</i> = 27)	Controls (<i>N</i> = 24)	Difference	95% CI	<i>p</i> Value
Mean area (mm ²)	13.26	12.45	0.81	−0.32, 1.93	0.159
Minimum area (mm ²)	11.54	10.90	0.64	−0.52, 1.81	0.275
Volume (mm ³)	70.09	61.52	8.57	−3.32, 20.45	0.153

MFG = modified Frisén grade.

accurate due to higher spatial resolution and signal-to-noise ratio. Whilst CT relies on the difference in electron density between tissues to produce image contrast and is therefore well suited to delineating the bony wall of the optic canal from the low-density contents, the differences in magnetic susceptibility between these same tissues will cause susceptibility artefact at the interface and reduce the accuracy of measurements on MRI. Furthermore, acquisition times will have been longer for MRI compared with CT, resulting in an increased likelihood of movement artefact.

In addition to the differences in scan technique, measurement technique also differed between the earlier studies and ours. Rather than selecting a single cross-sectional area at the narrowest width of the canal in the modified axial plane, we measured the canal cross-sectional area on consecutive slices throughout its length, thereby allowing confident identification of the minimum cross-sectional area along with calculation of mean cross-sectional area and canal volume. This technique provided a more accurate and comprehensive appreciation of the canal as a 3D structure and, whilst there was a systematic difference between the measurements made by the two neuroradiologists, the relationship between the two sets of measurements was linear. The earlier study only reported inter-rater agreement for the *inter-ocular difference* in canal dimensions which would have removed the differences in absolute measurements. By measuring the whole canal, we were also able to highlight the considerable variation in optic canal volume that occurs between individuals, but even

that did not account for the variation in degree of papilloedema. It should be noted that no attempt was made to quantify the different tissue components occupying the lumen of the canal.

Although the estimation of MFG was subjective, reflecting the retrospective nature of the study, and not measured objectively by optical coherence tomography, papilloedema grade correlated negatively with visual field size and positively with CSF opening pressure. These relationships have been demonstrated by others and provide evidence that ours was a representative cohort.^{19,20}

Our study has several limitations, including the retrospective design, relatively small sample size, and the use of an unmatched control group. However, the authors believe the use of CT and the measurement technique employed will have improved accuracy of canal measurements over previous studies using MRI.

In conclusion, the factors at play in determining the degree of papilloedema and visual impairment amongst IIH patients have not been fully elucidated, although a number of suggestions have been made. We found that the degree of papilloedema was related to the CSF opening pressure but our data cast doubt on any association between increasing optic canal dimensions and worsening papilloedema. Optic canal dimensions should not be used to prognosticate about visual outcomes in patients with IIH.

This work has been presented at the 40th Meeting of the European Society of Neuroradiology (Malmo, 2017), the 13th Meeting of the European Neuro-Ophthalmological Society (Budapest, 2017), and the UK CSF Disorders Meeting (Birmingham, 2017).

This manuscript has not been published and is not under consideration for publication elsewhere.

Declaration of interest

The authors declare no conflict of interest and no funding was received for this work.

ORCID

Nicholas T. Skipper <http://orcid.org/0000-0002-6400-0814>

References

1. Brodsky MC, Vaphiades M. Magnetic resonance imaging in pseudotumour cerebri. *Ophthalmology*. 1998;105(9):1686–1693. doi:10.1016/S0161-6420(98)99039-X.
2. Hayreh SS. Pathogenesis of optic disc edema in raised intracranial pressure. *Prog Retin Eye Res*. 2016;50:108–144. doi:10.1016/j.preteyeres.2015.10.001.
3. Bidot S, Bruce BB, Saindane AM, Newman NJ, Biousse V. Asymmetric papilloedema in idiopathic intracranial hypertension. *J Neuro-Ophthalmology*. 2015;35:31–36. doi:10.1097/WNO.0000000000000205.
4. Moster ML. Unilateral disk edema in a young woman. *Surv Ophthalmol*. 1995;39(5):409–416. doi:10.1016/S0039-6257(05)80097-9.
5. Lepore FE. Unilateral and highly asymmetric papilloedema in pseudotumor cerebri. *Neurology*. 1992;42:676–678. doi:10.1212/WNL.42.3.676.
6. To KW, Warren FA. Unilateral papilloedema in pseudotumor cerebri. *Arch Ophthalmol*. 1990;108:644–645. doi:10.1001/archophth.1990.01070070030014.
7. Greenfield DS, Wanichwecharungruang B, Liebmman JM, Ritch R. Pseudotumor cerebri appearing with unilateral papilloedema after trabeculectomy. *Arch Ophthalmol*. 1997;115(3):423–426. doi:10.1001/archophth.1997.01100150425022.
8. Killer HE, Jaggi GP, Flammer J, Miller NR, Huber AR. The optic nerve: a new window into cerebrospinal fluid composition? *Brain*. 2006;129:1027–1030. doi:10.1093/brain/awl045.
9. Killer HE, Subramanian PS. Compartmentalized cerebrospinal fluid. *Int Ophthalmol Clin*. 2014;54(1):95–102. doi:10.1097/IIO.0000000000000010.
10. Killer HE, Laeng HR, Flammer J, Groscurth P. Architecture of arachnoid trabeculae, pillars, and septa in the subarachnoid space of the human optic nerve: anatomy and clinical considerations. *Br J Ophthalmol*. 2003;87:777–781. doi:10.1136/bjo.87.6.777.
11. Killer HE, Jaggi GP, Flammer J, Miller NR, Huber AR, Mironov A. Cerebrospinal fluid dynamics between the intracranial and the subarachnoid space of the optic nerve. Is it always bidirectional? *Brain*. 2007;130:514–520. doi:10.1093/brain/awl324.
12. Liugan M, Xu Z, Zhang M. Reduced free communication of the subarachnoid space within the optic canal in the human. *Am J Ophthalmol*. 2017;179:25–31. doi:10.1016/j.ajo.2017.04.012.
13. Bidot S, Clough L, Saindane AM, Newman NJ, Biousse V, Bruce BB. The optic canal size is associated with the severity of papilloedema and poor visual function in idiopathic intracranial hypertension. *J Neuroophthalmol*. 2016;36:120–125. doi:10.1097/WNO.0000000000000318.
14. Moodley AA, Dlwati MS, Durand M. Intracanalicular optic nerve swelling and signal change in fulminant untreated idiopathic intracranial hypertension. *Neuro-Ophthalmology*. 2017;41(2):84–89. doi:10.1080/01658107.2016.1258581.
15. Friedman DI, Jacobson DM. Diagnostic criteria for idiopathic intracranial hypertension. *Neurology*. 2002;59:1492–1495. doi:10.1212/01.WNL.0000029570.69134.1B.
16. Scott CJ, Kardon RH, Lee AG, Frisen L, Wall M. Diagnosis and grading of papilloedema in patients with raised intracranial pressure using optical coherence tomography vs clinical expert assessment using a clinical staging scale. *Arch Ophthalmol*. 2010;128(6):705–711. doi:10.1001/archophth.2010.94.
17. Newman W, Tocher K, Acheson J. Vigabatrin associated visual field loss: a clinical audit to study prevalence, drug history and effects of drug withdrawal. *Eye*. 2002;16:567–571. doi:10.1038/sj.eye.6700168.
18. Wolak M, Fairbairn D, Paulsen Y. Guidelines for estimating repeatability. *Methods Ecol Evol*. 2012;3(1):129–137. doi:10.1111/j.2041-210X.2011.00125.x.
19. OCT Sub-Study Committee; for the NORDIC Idiopathic Intracranial Hypertension Study Group. Baseline OCT measurements in the idiopathic intracranial hypertension treatment trial, part II: correlations and relationship to clinical features. *Investig Ophthalmol Vis Sci*. 2014;55(12):8173–8179. doi:10.1167/iovs.14-14961.
20. Hayreh SS. Pathogenesis of oedema of the optic disc (papilloedema): a preliminary report. *Br J Ophthalmol*. 1964;48:522–543. doi:10.1136/bjo.48.10.522.