Laser scanning tomography measurement of the extent of papilledema in the follow-up examination of patients with idiopathic intracranial hypertension

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Object. The authors evaluated the characteristics of patients with idiopathic intracranial hypertension (IIH), and compared laser scanning tomography (LST) measurements of papilledema with the clinical parameters and cerebrospinal fluid (CSF) opening pressures obtained.

Methods. Twenty-four patients were included in this study; these individuals included 21 women and three men with a mean age of 35.5 ± 9.7 years and a mean body mass index (BMI) of 35.4 ± 8.3 kg/m². The authors conducted a prospective follow-up study over a period of 12 months through a series of four consultations with each patient. These patients had a mean time to treatment of 6.2 ± 7.9 months and, at the time of diagnosis, suffered a mean of 2.8 ± 1.3 symptoms each. Laser scanning tomography of the optic disc revealed a mean global rim volume of 1.693 ± 1.662 mm³ and a mean height of 0.604 ± 0.306 mm. The mean CSF opening pressure was 31.3 ± 6.3 cm H₂O.

Results. During the follow-up period, all patients improved significantly with regard to clinical parameters (p < 0.001), BMI reduction (p < 0.001), and reduction of visual field deficits (p = 0.007); visual acuity remained unchanged. In all patients at each successive consultation, the CSF opening pressure was lower than it had been at the previous consultation (p = 0.001). Laser scanning tomography measurements demonstrated a statistically significant reduction in both optic disc parameters over the follow-up period (global rim volume, p = 0.044; mean height, p = 0.019). The CSF opening pressure and the LST measurements correlated significantly with the number of symptoms (CSF opening pressure, p < 0.001; global rim volume, p = 0.001; mean height, p < 0.001). The mean area under the receiver operating characteristic curve in detecting the presence of clinical symptoms was 0.87 for CSF opening pressure, 0.7 for rim volume, and 0.81 for mean optic disc height.

Conclusions. Laser scanning tomography measurements are useful for evaluating the degree of papilledema in patients with IIH and correspond well with clinical data and measurements of CSF opening pressure. If a diagnosis of IIH is established, LST measurements may replace repeated CSF opening pressure measurements in follow-up monitoring. (DOI: 10.3171/JNS-07/09/0543)

KEY WORDS • idiopathic intracranial hypertension • laser scanning tomography • papilledema • pseudotumor cerebri

IDIOPATHIC intracranial hypertension, also known as pseudotumor cerebri, is characterized by a raised intracranial pressure associated with papilledema, absent focal neurological signs, and normal CSF composition. The most common signs and symptoms in patients with IIH are headache and visual disturbances; in rare cases cranial nerve palsy, tinnitus, or other symptoms such as the Hermitte sign may arise.¹,³,⁷,¹⁸,¹⁹,²³,²⁵ Obesity and female sex are known as risk factors, but the exact pathogenesis of IIH is unknown. Repeated lumbar punctures and pharmacotherapy with acetazolamide, corticosteroids, or indomethacin (as recently reported¹³) are used to normalize intracranial pressure and relieve signs and symptoms despite the lack of randomized controlled trials in the literature to support this treatment.²⁸,³⁹,⁴¹,⁴⁵ If conservative treatment fails, surgical procedures such as optic nerve sheath fenestration or CSF shunt placements are necessary for effective reversal of IIH symptoms.¹⁸,³⁰,₃⁹,₄₅ The course of the disease is often long-term, and therapy must be guided by clinical signs, extent of papilledema, and level of CSF opening pressure.¹₈,¹⁹

Currently, clinical judgments concerning papilledema are made using direct ophthalmoscopy. This method, however, is not very precise and depends on the experience of the examiner. For this reason, we used LST in the present study to provide rapid, reproducible measurements of optic disc topography. This recently developed imaging tech-
nique uses confocal laser scanning microscopy for a 3D assessment of the optic disc and its volume. Recently, we demonstrated that LST measurements (optic disc volume and height) correlate linearly with CSF opening pressure.20 The objective of this prospective study was to compare LST measurements of papilledema with clinical parameters determined at the bedside and CSF opening pressures in the follow-up of patients with IIH.

Clinical Material and Methods

Twenty-four consecutive patients older than 18 years of age with IIH according to the updated diagnostic criteria64 were recruited for this prospective study. These were not the same patients with IIH included in our previous study.20 All patients underwent complete neurological and ophthalmological examinations including visual acuity tests, visual field testing, and funduscopic in mydriasis; 23 patients had bilateral papilledema and one patient had unilateral papilledema. All patients underwent magnetic resonance imaging with venography to exclude the diagnosis of venous sinus thrombosis or stenosis.12,14,33,36 After the diagnosis of papilledema was established, all patients attended three follow-up examinations under inpatient conditions conducted at 4-month intervals. Five patients were lost to follow-up and did not complete all examinations. Patient characteristics are given in Table 1.

All patients underwent confocal LST of the optic disc using the Heidelberg Retina Tomograph (HRT 2; Heidelberg Engineering). In LST, the light from the illuminated area on the fundus is reflected onto a detector, which measures its intensity. A diaphragm with a small aperture is placed in front of the detector to ensure that only reflected light originating from the focal plane of the laser is registered. By varying the focal plane of the laser, cross-sectional images of the structure under examination can be obtained.

The LST parameters of interest were the global rim volume (mm³) and the mean height of the optic disc (mm). All parameters were corrected for refractive error and actual radius of the corneal curvature. All but one patient had bilateral papilledema. In these 23 patients, the mean value of the bilateral LST measurement was taken for analysis.

The LST measurements were obtained just before lumbar puncture, which was performed for the purpose of diagnosis and therapeutic removal of 20 to 30 ml of CSF. The removal of this amount of CSF is routine in our clinical practice and probably works by allowing internal drainage of CSF into the soft tissue surrounding the spinal canal. Written informed consent was obtained from all patients prior to each lumbar puncture. The lumbar puncture and CSF opening pressure measurements were performed with the patient in the supine position lying on the right side (lateral decubitus position),14 and using nontraumatic needles.10 The treatment regimen in these patients was primarily conservative, including pharmacotherapy with acetazolamide, dietary recommendations for reducing BMI, and therapeutic lumbar punctures in patients with CSF opening pressures higher than 25 cm H₂O.

Statistical Analysis

To compare repeated measurements of the variables

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Patient characteristics at the time of diagnosis and at the 12-month follow-up examination*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristics</td>
<td>At Time of Diagnosis (24 patients)</td>
</tr>
<tr>
<td>general</td>
<td></td>
</tr>
<tr>
<td>male sex</td>
<td>3 (12.5%)</td>
</tr>
<tr>
<td>female sex</td>
<td>21 (87.5%)</td>
</tr>
<tr>
<td>age at diagnosis (yrs), mean ± SD</td>
<td>35.5 ± 9.7</td>
</tr>
<tr>
<td>BMI (kg/m²), mean ± SD w/ hypertension</td>
<td>35.4 ± 8.3</td>
</tr>
<tr>
<td>time to diagnosis (mos), mean ± SD</td>
<td>6.2 ± 7.9</td>
</tr>
<tr>
<td>reported symptoms (%)</td>
<td></td>
</tr>
<tr>
<td>headache</td>
<td>24 (100)</td>
</tr>
<tr>
<td>dizziness</td>
<td>18 (75)</td>
</tr>
<tr>
<td>nausea</td>
<td>6 (25)</td>
</tr>
<tr>
<td>tinnitus</td>
<td>4 (17)</td>
</tr>
<tr>
<td>cranial nerve palsy</td>
<td>6 (25)</td>
</tr>
<tr>
<td>relative afferent pupillary dysfunction</td>
<td>2 (8)</td>
</tr>
<tr>
<td>visual obscuration</td>
<td>22 (92)</td>
</tr>
<tr>
<td>other</td>
<td>8 (33)</td>
</tr>
<tr>
<td>ophthalmological findings</td>
<td></td>
</tr>
<tr>
<td>visual acuity (median, range)</td>
<td>1.0, 0.6–1.25</td>
</tr>
<tr>
<td>any visual field deficit</td>
<td>11 (46%)</td>
</tr>
<tr>
<td>optic atrophy</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>no symptoms</td>
<td>0</td>
</tr>
</tbody>
</table>

* FU = follow-up; NA = not applicable; SD = standard deviation.
† Five patients were lost to follow-up.

“number of symptoms” and “presence of visual field defects,” the Friedman and Cochran tests were used. For comparison of repeated measurements in variables with normal distributions (CSF opening pressure, BMI, and LST measurement variables) the MANOVA was used. Correlations were assessed using parametric Pearson and nonparametric Spearman correlation analysis. The accuracy of CSF opening pressure and LST measurements in the identification of clinical symptoms of IIH was assessed on the basis of the area under the ROC curve. These results were expressed as the area under the ROC curve with a 95% confidence interval. All statistical tests were two-tailed with the significance level set at 0.05. Commercially available statistical software (SPSS 12.0, SPSS, Inc.) was used for all analyses. Mean values are expressed with standard deviations.

Results

The 24 patients included 21 women and three men with a mean age of 35.5 ± 9.7 years, a mean BMI of 35.4 ± 8.3 kg/m², and a mean time to treatment of 6.2 ± 7.9 months. At the time of diagnosis, these patients suffered from a mean of 2.8 ± 1.3 symptoms, including visual obscuration, headache, dizziness, nausea, tinnitus, sixth cranial nerve palsy, and relative afferent pupil dysfunction. At the time of diagnosis, 18 patients suffered from headaches, 11 reported visual field deficits, one had visual acuity impairment, 23 had bilateral papilledema, and one patient had unilateral papilledema (the other eye showed optic atrophy). Laser

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scanning tomography measurements revealed a mean global rim volume of $1.693 \pm 1.662$ mm$^3$ and a mean optic disc height of $0.604 \pm 0.306$ mm. The mean CSF opening pressure in our patients was $31.3 \pm 6.3$ cm H$_2$O.

During the follow-up period, all patients improved significantly in clinical parameters ($Friedman \chi^2 = 32.56, p < 0.001$), BMI reduction (MANOVA, $p < 0.001$), and reduction of visual field defects ($Cochran Q = 12.0, p = 0.007$); visual acuity levels remained stable. The CSF opening pressure could be significantly lowered in all patients over all consultations (MANOVA, $p = 0.001$), and LST measurements showed a reduction in all parameters over the follow-up period (MANOVA; $p = 0.044$, mean global rim volume; $p = 0.019$, mean height) (Fig. 1).

We also found that CSF opening pressure and LST measurements correlated significantly with the number of symptoms (Spearman $\rho = 0.717$, $p < 0.001$ for analysis of CSF opening pressure; Spearman $\rho = 0.425$, $p = 0.001$ for the mean global rim volume of the optic disc; Spearman $\rho = 0.529$, $p < 0.001$ for the mean height) (Fig. 2). The ROC curve analysis in which the CSF opening pressure and LST measurements were used to identify the presence of clinical symptoms showed an area under the ROC curve of 0.87 (range 0.74–0.99) for CSF opening pressure ($p < 0.001$), 0.81 (range 0.66–0.87) for mean height ($p = 0.02$), and 0.7 (range 0.52–0.88) for rim volume ($p < 0.05$) (Fig. 3).

**Discussion**

Idiopathic intracranial hypertension is an unusual disorder with an average annual incidence of about one to two cases per 100,000 people in a general population.$^5$ Elevated intracranial venous pressure is thought to be the common pathophysiological mechanism of pseudotumor cerebri. Currently, the disease is classified as an idiopathic form, without any underlying disease, and as symptomatic if associated with cerebral venous thrombosis, prothrombotic abnormalities,$^27,43$ sinus stenosis,$^22,33,36$ or intake of certain drugs.$^14,19$ Obesity is the most frequently encountered risk factor, leading to the hypothesis that central obesity raises intraabdominal pressure, which in turn increases pleural pressure and cardiac filling pressure, impeding venous return pressure and increasing intracranial pressure.$^5,15,32$ Isolated obesity, however, does not lead to abnormal CSF pressure, which suggests that there are other pathophysiological factors at work such as venous abnormalities or venous collapse in the early phase of disease.$^3,4$

Although our understanding of the pathogenesis of IIH remains vague, diagnostic and therapeutic procedures for the management of IIH have been substantially improved in the last decade.$^5$ Papilledema as a prominent clinical sign, hitherto only subjectively monitored by ophthalmoscopy, can now be monitored using LST. Laser scanning tomography was developed in the late 1980s and allows an exact 3D biomorphometric measurement of the optic nerve head with high accuracy and reproducibility.$^42$ In a few published case series, which included one to eight patients each, LST was successfully used to detect changes in optic disc volume during the course of the IIH disease process.$^{17,24,40}$ Reduction in papilledema could be demonstrated to coincide with improvement in visual field defects.$^{40}$
findings in the present study strongly support these observations. Moreover, we extend the knowledge on the relationship between clinical neurological signs and symptoms, CSF opening pressure, and LST measurements. For the first time, we demonstrated that over an observation period of 12 months, the improvement in clinical findings (number of symptoms, visual field defects) and the changes in LST and CSF opening pressure measurements correlate significantly with each other. Also, the ROC curves demonstrate a good accuracy in the LST measurements (especially the variable mean optic disc height) to discriminate between patients with and without symptoms. Thus, we propose to replace invasive repeated CSF opening pressure measurements with LST measurements after the diagnosis of IIH has been established, provided that the patient’s clinical course remains stable. This may contribute to a decreased need for lumbar punctures and consequently to a reduction in the risks associated with these procedures.\textsuperscript{2,21}

Conclusions

Laser scanning tomography measurements of the optic disc in patients with IIH are useful in evaluating the degree of papilledema. These measurements correspond well with clinical data and with CSF opening pressures. If a diagnosis of IIH is established, LST measurements may replace repeated CSF opening pressure measurements in the follow-up.

Acknowledgment

Dr. Faschingbauer and Dr. Heckmann contributed equally to this work.

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