Supplemental Material

Description of Methods Commonly Used in Transorbital Sonography

Transorbital B-scan sonography is a suitable method for measuring the optic nerve. TOS is performed with a high-frequency linear-array transducer with an emitted minimum frequency of 7.5 MHz and a lateral axial spatial resolution < 0.4 mm [4]. Every other parameter such as time-gain compensation, grayscale, brightness, and contrast settings are modified as needed.

TOS should be performed carefully since high mechanical and thermal indexes can damage sensitive structures such as the lens, retina, and vitreous body as a result of the formation of gas bubbles due to high negative pressure and heating of tissue [5]. Therefore, the mechanical index must be decreased to 0.23, according to the ALARA (as low as reasonably achievable) principle. The procedure time must be as short as possible in order to avoid damage to the lens, choroid, and retina [3].

ONSD examinations were performed according to a previously described protocol ([1], Suppl. Fig. 1). In order to measure the ONSD, the distance between the external borders of the hyper-echogenic area surrounding the optic nerve is quantified (Suppl. Fig. 1). The OND is measured marking the internal borders of this formation (Suppl. Fig. 1). Furthermore, it is important that the examination technique follows methodological standards [2] since the time of image acquisition, interpretation of the anatomy of the optic nerve and sheaths, and resolution of the probes can influence the results. Finally, an average of three measurements should be obtained to reduce intra-observer variability [1].

The presence of papilledema is assessed as the elevation of the optic disc (ODE) above the level of the retina. In order to quantify the ODE, the examiner freezes the image and utilizes the zoom function. The first caliper is placed on the uppermost part of the swollen disc and the second caliper on the strongly reflecting line, which represents the lamina cribrosa (Suppl. Fig. 1). The presence of ODE values above 0.6 mm predicts the presence of fundoscopic optic disc edema with a sensitivity of 82% and a specificity of 76%, whereas a threshold value of 1.0 mm has a sensitivity of 73% and a specificity of 100% [6] (Suppl. Fig. 1).

References:

▶ Suppl. Fig. 1A, B Transorbital sonography in B-mode of the eyeball and the optic nerve in a patient with IIH in a “zoomed” and normal representation. Optic nerve sheath diameter (ONSD) and optic nerve diameter (OND) were measured 3 mm behind the papilla (2) in an axial plane showing the optic nerve in its longitudinal course. The dotted lines denote the OND (inside the pia mater (3)) and the ONSD (inside the dura mater (4)). Optic disc elevation (ODE) is gauged between the fundus and the dome of the papilla (1). C Overview of OND and ONSD.
Suppl. Fig. 2 Flowchart of study identification, inclusion, and exclusion for meta-analysis.

1917 articles were identified through different sources:
- PUBMED (n=993)
- EMBASE (n= 894)
- COCHRANE (n= 36)
- Other sources (n=2)

Excluded duplicates (n=548)

Articles without duplicates screened for title (n=1372)

1191 Excluded
- Articles with irrelevant topics (n=1144)
- Comments/Letters/Summaries (n=31)
- Case reports (n=16)

Articles screened for abstract (n=139)

125 Excluded
- Articles excluded by abstract for not fulfilling the following criteria: Type of article or study design

Number of screened full text articles (n=14)

9 Excluded
- Full text articles excluded for specific reasons

5 articles were included in the review and the meta-analysis
### Suppl. Table 1  List of excluded studies and reasons for exclusion.

<table>
<thead>
<tr>
<th>excluded articles with title and first author</th>
<th>reference</th>
<th>reasons for exclusion</th>
</tr>
</thead>
</table>
| 1. Ultrasonography (US) Findings in Idiopathic Intracranial Hypertension Gaye Saavedra A. | Journal of the Neurological Sciences, Volume 357, e220; 2015 | - case study with three patients  
- only OND and no ONSD was measured |
- only OND and no ONSD was measured |
| 3. Measurement of optic nerve sheath diameter in Egyptian females with idiopathic intracranial hypertension Kishk N. | Cerebrovascular Diseases. 35: 53, MAY 2013 | - only abstract available |
| 4. Low energy diet and intracranial pressure in women with idiopathic intracranial hypertension Sinclair AJ | BMJ. 2010; 341: c2701 | - other modality used to quantify the ONSD |
- ONSD not included |
| 6. Ultrasound study of optic nerves in intracranial hypertension Eliseeva NM | Vestn Oftalmol. 2008; 124(6): 29 – 33 | - study in conditions other than IIH |
- participants younger than 18 years  
- study in conditions other than IIH |
| 8. Comparison of the measurement of optic nerve sheath diameter (ONSD) with B scan and MRI as a surrogate for patients with idiopathic intracranial hypertension (IIH) Kilji M | Neurology, 2016, 86. Jg., Nr. 16 Supplement, S. P6. 316 | - no healthy control group  
- only abstract available |
| 9. Ultrasound study of optic nerves in intracranial hypertension Eliseeva N.M. | Vestnik oftalmologii 124.6 (2008): 29 – 33 | - Other criteria to measure ONSD  
- Study in conditions other than IIH |

### Suppl. Table 2 Methodological quality assessment of included studies by Newcastle-Ottawa scales of case control and cohort study.

<table>
<thead>
<tr>
<th>study</th>
<th>selection</th>
<th>comparability</th>
<th>exposure</th>
<th>total</th>
</tr>
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<tbody>
<tr>
<td>Rehman et al., 2016 [8]</td>
<td>****</td>
<td>*</td>
<td>**</td>
<td>7</td>
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<tr>
<td>Saucedo et al., 2016 [6]</td>
<td>****</td>
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<td>***</td>
<td>8</td>
</tr>
</tbody>
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A single asterisk indicates 1 score, two asterisks indicates 2 scores, three asterisks 3 scores, and four asterisks 4 scores.
Suppl. Fig. 3 Proportion meta-analysis plot (fixed effects) of papilledema.