Elevated intracranial pressure (ICP) > 20 mm Hg is associated with poor outcome after traumatic brain injury (TBI). Especially in the early posttraumatic period, elevated ICP is associated with a high risk of secondary ischemic brain damage. Interventions that lower the ICP should be started as soon as possible to optimize cerebral perfusion pressure and save brain tissue. Early diagnosis of elevated ICP is therefore essential in preventing this secondary damage. Elevated ICP and disorders noted on emergency CT scanning of the brain have a poor correlation. Invasive ICP measurement with an intraparenchymal probe is considered to be the gold standard. For safe insertion of the probe, optimal blood coagulation, sterile conditions, and a neurosurgeon are required. These are not readily available at the trauma scene. Therefore, a noninvasive, simple bedside method can be beneficial in early detection of increased ICP, especially in the prehospital and emergency care setting.

Transcranial Doppler (TCD) pulsatility index and transocular ultrasonography have been suggested for rapid assessment of elevated ICP. The TCD pulsatility index detects decreases in cerebral perfusion pressure due to an increased ICP. However, TCD is difficult to perform, even when the user is experienced.

Abbreviations ICP = intracranial pressure; ICU = intensive care unit; ONSD = optic nerve sheath diameter; TBI = traumatic brain injury; TCD = transcranial Doppler.


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DISCLOSURE The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.
Transocular ultrasonography has been used to detect elevated ICP and has been shown to be accurate. All previous studies on the relationship between ICP and optic nerve sheath diameter (ONSD) were performed cross-sectionally. ONSD distension was correlated to the ICP measured at the same moment. However, it remains unclear whether these changes in ONSD resulted only from ICP changes or from papilledema as well. A retrospective study by Rajajee and colleagues suggested a delayed reversal of nerve sheath distension after ICP fluctuations, possibly due to papilledema. This might compromise the specificity of ONSD. Therefore, in this study, we performed dynamic measurements in patients with TBI to examine whether changes in ICP and not papilledema causes changes in ONSD. Changes in ONSD are directly caused by ICP changes and are not influenced by papilledema.

**Methods**

**Study Design**

This observational study was based on single-center prospective research. The Erasmus University Medical Center is the largest trauma center in the southwest of the Netherlands. Patients were included between January 2011 and December 2011 after admission to the intensive care unit (ICU) of our hospital. All patients had suffered TBI and had undergone insertion of an intraparenchymal probe to monitor ICP. Eligible subjects were at least 18 years old and at least one eye and its orbit must have been intact. Informed consent was given by the patients’ representatives. The medical ethics committee of the Erasmus Medical Center, Rotterdam, approved our study.

**ONSD and Invasive ICP Measurement Protocol**

The treatment protocol of increased ICP in the ICU consists of deep sedation, mechanical ventilation, and, if necessary, frequent infusion of mannitol. This regimen is aimed to lower ICP, ideally below 20 mm Hg, and keep the mean arterial pressure between 80 and 100 mm Hg to optimize cerebral perfusion pressure.

During routine nursing procedures, ICP may rise transiently due to manipulation. Especially during suctioning of the endotracheal tube to evacuate sputum, ICP rises rapidly due to irritation of the trachea. Ultrasonography of the ONSD was performed, and ICP measurements were recorded simultaneously before, during, and after this routine procedure. The first (baseline) measurement was recorded 30–60 seconds prior to cleaning the tube. The second measurement was obtained during suctioning, and the third measurement was performed 30–60 seconds after the procedure and all stimulation had stopped.

ONSD was measured in both eyes consecutively starting with the left eye, except for patients with unilateral eye lacerations. In those 3 patients only the intact eye was studied. We applied antiseptic ultrasound cream on the closed eyelid and placed a linear probe (7.5 MHz) in the cream just above the eyelid. We froze the images of the optic nerve sheath with the Micromaxx ultrasound machine (SonoSite Inc.). An integrated ruler was used for measuring the ONSD. The cutoff value for ONSD was ≥ 5.0 mm, representing ICP > 20 mm Hg.

The ICP measurement was recorded by an assisting nurse at the same time the optic nerve sheath image was frozen on the ultrasound machine. The examiner performing the ONSD measurement was blinded to the ICP monitor readings (Pressio [monitoring system] and catheter, Sophysa).

**Statistical Analysis**

Data were analyzed using SPSS statistical software (version 20, IBM). First, the correlation coefficient between ICP measurement and ONSD was determined. To evaluate the diagnostic performance of the ONSD measurement compared with the gold standard, intraparenchymal ICP measurement, receiver operating characteristic curve analysis was used.

**Results**

A total of 18 patients were included. Patient characteristics are shown in Tables 1 and 2. Twelve patients were male, and the mean age was 38 years. All patients were being treated for a proven high ICP by deep sedation, mechanical ventilation, and intermittent mannitol bolus infusions.

As shown in Fig. 1, as expected, ICP increased during tracheal stimulation and after the procedure it rapidly decreased to baseline levels. The diameter of the optic nerve sheath increased simultaneously with an increased ICP and decreased back to the baseline diameter in the same rate as the ICP (Fig. 2). We used unique colors for each of the plots to describe each patient.

The correlation between the ICP measurement and the ONSD measurement showed an R² of 0.80 (r = 0.895). The optimal cutoff for ONSD, for detection of ICP > 20 mm Hg was ≥ 5.0 mm with a sensitivity of 94%, a specificity of 98%, and an area under the curve of 0.99 (95% CI 0.97–1.00). With this cutoff value of ≥ 5.0 mm ONSD, only 1 false-negative measurement was detected. In this subject, the ICP was 20 mm Hg while the ONSD measured only 4.7 mm. No false-positive measurements were observed.

**Discussion**

In our study, we demonstrate that ultrasonographic ONSD measurement is highly correlated with direct ICP changes. Furthermore, the ONSD reflects immediate changes in ICP in patients who have suffered a TBI. An ONSD of 5.0 mm or more predicts an elevated ICP (> 20 mm Hg) with an area under the curve of 0.99.

The correlation between ONSD and direct measure-
ONSD versus ICP in neurotrauma

The cutoff point has been discussed for a number of years. Our results show an optimal cutoff value of 5.0 mm for ONSD in mechanically ventilated patients with traumatic brain injury at the ICU. This is consistent with a previous report.9

All previous studies on ONSD measurement as a diagnostic tool for elevated ICP have been cross-sectional in design.4,7,8,10,14,17,19 In these studies, an increased ONSD was associated with an increased ICP at the same time. Whether this was a result of immediate ICP changes or due to papilledema has not been studied so far. The underlying mechanism of papilledema is assumed to be similar to ONSD distention, but edema takes hours or even days to develop in patients with high ICP.7 This was demonstrated in the retrospective study by Rajajee et al. in which a delayed reversal of ONSD after ICP fluctuations was shown.16

However, in our study, changes in ICP were reflected by immediate changes in ONSD. In all cases ONSD reverted to baseline levels simultaneous with a decrease in ICP, directly after tracheal manipulation was stopped. Changes in ICP are accurately reflected by changes in ONSD on the same day or several days after trauma.

ONSD measurement with ultrasonography has a reproducibility with a median intraobserver reliability of 0.2 mm (range 0.1–0.5 mm).9 Examiners with ultrasonography experience have an estimated learning curve of as few as 10 subjects with 3 abnormal scan results. For physicians with no experience, the needed number of scans is close to 25.10 Although the learning curve is steep, this technique should not be used in nonspecialized units by untrained physicians.14,15,19

Conditions that could influence the ONSD measurement and might alter the tests specificity include Graves’ disease, sarcoidosis, inflammation, and tumors. Bilateral ocular trauma can make it impossible to perform ONSD measurement, but this is uncommon in head trauma patients.16

In ICU settings, invasive, continuous ICP measurement with the ICP probe remains superior to this noninvasive,

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex</th>
<th>Age (yrs)</th>
<th>Initial GCS Score</th>
<th>Mechanism of injury</th>
<th>CT Findings</th>
<th>Inclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>30</td>
<td>E3M1V1</td>
<td>Road traffic collision</td>
<td>Subdural hematoma</td>
<td>1 day later</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>24</td>
<td>E1M4V1</td>
<td>Fall from height</td>
<td>Subdural hematoma</td>
<td>3 days later</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>52</td>
<td>E1M4V1</td>
<td>Fall from height</td>
<td>Brain contusions, subarachnoid bleeding</td>
<td>1 day later</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>24</td>
<td>E1M2V1</td>
<td>Road traffic collision</td>
<td>Epidural and subdural hematoma skull fractures</td>
<td>3 days later</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>25</td>
<td>E1M5V1</td>
<td>Direct blunt trauma to head</td>
<td>Epidural hematoma, subarachnoid bleeding, skull fractures</td>
<td>1 day later</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>71</td>
<td>E1M2V1</td>
<td>Fall from stairs</td>
<td>Subdural hematoma, subarachnoid bleeding, skull fractures</td>
<td>1 day later</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>32</td>
<td>E1M5V1</td>
<td>Road traffic collision</td>
<td>Brain contusions, subarachnoid bleeding</td>
<td>Same day</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>26</td>
<td>E1M1V1</td>
<td>Road traffic collision</td>
<td>Subdural hematoma</td>
<td>1 day later</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>33</td>
<td>E1M1V1</td>
<td>Fall from height</td>
<td>Diffuse axonal injury, brain contusion, blood in ventricles</td>
<td>Same day</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>60</td>
<td>E1M3V1</td>
<td>Direct blunt trauma to head</td>
<td>Epidural hematoma, diffuse swelling of the brain, skull fractures</td>
<td>Same day</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>31</td>
<td>E1M1V1</td>
<td>Road traffic collision</td>
<td>Intracerebral &amp; subarachnoid bleeding facial fractures</td>
<td>2 days later</td>
</tr>
<tr>
<td>12</td>
<td>F</td>
<td>62</td>
<td>E1M2V1</td>
<td>Road traffic collision</td>
<td>Subdural hematoma, diffuse axonal injury</td>
<td>Same day</td>
</tr>
<tr>
<td>13</td>
<td>F</td>
<td>20</td>
<td>E1M5V1</td>
<td>Road traffic collision</td>
<td>Subarachnoid bleeding</td>
<td>2 days later</td>
</tr>
<tr>
<td>14</td>
<td>F</td>
<td>64</td>
<td>E4M4V1</td>
<td>Fall from stairs</td>
<td>Epidural subdural hematoma, subarachnoid bleeding facial fractures</td>
<td>2 days later</td>
</tr>
<tr>
<td>15</td>
<td>M</td>
<td>39</td>
<td>E1M5V1</td>
<td>Unknown</td>
<td>Brain contusions, diffuse swelling of the brain</td>
<td>1 day later</td>
</tr>
<tr>
<td>16</td>
<td>F</td>
<td>22</td>
<td>E1M2V1</td>
<td>Road traffic collision</td>
<td>Brain contusions, subarachnoid bleeding</td>
<td>Same day</td>
</tr>
<tr>
<td>17</td>
<td>M</td>
<td>55</td>
<td>E1M1V1</td>
<td>Fall from height</td>
<td>Subdural hematoma</td>
<td>Same day</td>
</tr>
<tr>
<td>18</td>
<td>M</td>
<td>33</td>
<td>E1M1V1</td>
<td>Road traffic collision</td>
<td>Intracerebral hematoma</td>
<td>1 day later</td>
</tr>
</tbody>
</table>

E = eye; M = motor; V = verbal.

Fig. 1. ICP in mm Hg of the left (○) and right (●) eyes before, during, and after intervention. Colors correspond to the ONSD data from the same patient in Fig. 2. Figure is available in color online only.
intermittent ONSD ultrasonography because it delivers continuous values and requires no additional skills from the attending ICU nurse. However, in emergency care and prehospital conditions ONSD measurement may be useful to distinguish between normal or elevated ICP in comatose patients. Also, if insertion of a probe is contraindicated in case of infection, or if correct function of the probe is questioned, ONSD ultrasonography might be an alternative.

At low levels, ICP changes (8–10 mm Hg) do not affect the ONSD. When ICP rises, a linear correlation is seen between ONSD and ICP. The optic nerve sheath can distort more than 50% if ICP rises. The sheath's pressure response depends on its elasticity. The elasticity is not uniform among individuals. For this reason, measurement of the ONSD is a qualitative rather than quantitative assessment of ICP.

The interobserver variation is low and measurements are reproducible. However, many variables and artifacts might alter the ultrasound findings. Because of acoustic shadows cast by the lamina cribrosa, the ONSD might be overestimated. Off-axis measurements result in erroneous values. To minimize these variables and artifacts, a standardized technique should be used.

Because of the small sample size and the single-center design of this study, we might have selected more seriously injured patients. Because of the single-observer strategy, we were not able to examine the suggested interobserver variability that was described by Dubourg et al. We observed a direct correlation between ICP changes and changes in ONSD. We could not reproduce the suggested effect of delayed return to baseline ONSD by Rajanjee et al. We did not perform ophthalmic examinations to determine the presence of papilledema. Whether papilledema was present, it did not influence the correlation between ICP and ONSD changes, not on the day of trauma or several days later. We performed 2 measurements in each patient: one in the left eye and one in the right eye. We did not have any follow-up in our strategy to find changes in correlation in time in the same patient.

Conclusions

We demonstrated that ultrasonography of the ONSD may be considered as an accurate, simple, and rapid measurement to detect not only increased ICP but also immediate changes in ICP in patients who have sustained a TBI. ONSD changes reflect changes in ICP and are not influenced by edema. This technique is easy to learn and is useful in conditions in which invasive ICP monitoring is not available, such as at trauma scenes. Our data support results from previous studies that ONSD ≥ 5.0 mm is the optimal cutoff value for detecting elevated ICP (> 20 mm Hg).

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Author Contributions
Conception and design: Maissan, Dirven. Acquisition of data: Maissan. Analysis and interpretation of data: Maissan, Hoeks. Drafting the article: Maissan. Critically revising the article: Haitsma, Gommers, Stolker. Reviewed submitted version of manuscript: all authors. Statistical analysis: Hoeks. Approved the final version of the manuscript on behalf of all authors: Maissan.

Supplemental Information
Previous Presentation
Portions of this work were presented in a speech and PowerPoint presentation on the Dutch National Congress of Helicopter Mobile Medical Teams, Duiven, The Netherlands, October 4, 2013.

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