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Supplemental material

Analysis of intracranial pressure pulse waveform in traumatic brain injury patients: a CENTER-TBI study
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Supplementary Data

Relationship between spectral indices and PSI

The relationships between spectral ICP-derived indices and PSI are presented in Supplementary Fig. 3. AMP and HFC increased with PSI up to PSI level of 3.0 and then reached the breakpoint after which AMP started to decrease while HFC stayed at approximately the same level; see Supplementary Figure 3A and Supplementary Figure 3B, respectively. HHC also increased with rising PSI, but less linearly than AMP and HFC, and it dropped significantly above PSI equal 3.0; see Supplementary Figure 3C.

Correlations between spectral parameters and PSI

HFC was strongly correlated with PSI ($r_s = 0.54; p < 0.001$) but not correlated with AMP. HHC was moderately and reciprocally correlated with AMP ($r_s = -0.23; p = 0.002$) but not related to PSI. AMP was strongly correlated with PSI ($r_s = 0.48; p < 0.001$).

Discussion

Our results demonstrate that AMP and HFC are correlated with rising PSI up to the breakpoint at PSI of 3.0 (corresponding to the likely pathological class of pulse ICP waveform). After these breakpoints, AMP decreases while HFC remains at a similar level with a tendency to decrease. Rising PSI is also associated with increasing HHC, but this relationship was nonlinear and statistically not significant, with a clear drop in HHC at the level of PSI of 3.0. The drops in spectral parameters, particularly AMP and HHC, at elevated values of PSI can be explained by the fact that the pathological rounding of the ICP pulse waveform is not only related to mean ICP\(^1\) but can be influenced by the increased pulse amplitude of cerebral arterial blood volume (C\(_a\)BV)\(^2\). In fact, pathological changes in ICP pulse shape can occur even at normal levels of ICP\(^3\) which is also observed in our data. Results of a previous study also suggested that AMP in TBI patients depends mainly on pulsatile changes in C\(_a\)BV, assessed with the use of transcranial Doppler (TCD) ultrasonography technique, rather than on mean ICP.\(^2\) Similarly, the changes in HHC might be largely influenced by the magnitude of pulsatile changes in C\(_a\)BV. The shape of ICP pulse waves corresponding to classes 3 and 4 is characterized by dominant second peak (P2), which is believed to originate from the C\(_a\)BV pulse, and progressive rounding of the pulse\(^2,4,5\). Thus, the decrease in HHC may reflect the prominence of P2 in the ICP pulse contour (the center of mass of the ICP pulse waveform is...
shifted towards lower number of harmonics) while a decrease in AMP may indicate obstructed cerebral blood flow and/or derangement of cerebrovascular reactivity or simply suggest that the pathological shape of ICP is not always associated with its high amplitude and elevated mean value. HFC, on the other hand, is correlated with PSI but not with either HHC or AMP, suggesting its ability to reflect subtle changes in ICP pulse shape that are not only related to the position of the P2 in the ICP pulse curve.

Assessment of changes in C\textsubscript{a}BV requires high-resolution TCD recordings of cerebral blood flow velocity or the use of imaging techniques such as magnetic resonance. The CENTER-TBI database does not include TCD registrations while imaging techniques do not allow for continuous monitoring of cerebral blood volume changes simultaneously with ICP. Therefore, our observation could not be confirmed at the present stage and should be treated as preliminary.

**References**


ICP pulse waveform-derived parameters versus HR

There was a reciprocal correlation between HR and both AMP and HHC ($r_S = -0.24, p < 0.001$ and $r_S = -0.35, p << 0.001$, respectively). Moreover, PSI was moderately and inversely correlated with HR ($r_S = -0.28, p < 0.001$). There was no significant relationship between HR and HFC, but it was observed that all ICP pulse waveform-derived parameters decreased when HR increased (Supplementary Figure 4).

Discussion

HR may have a significant impact on the ICP pulse waveform. An increase in HR causes a decrease in pulse volume and then, as the result, a decrease in pulse amplitude of ICP. The bias related to HR could be important in the estimation of those metrics where a fixed frequency window is used, such as HFC. However, it has been shown in previous studies that this impact is only significant when HR is greater than 120 bpm. Moreover, in our data it was observed that HFC decreased with HR, which is in line with the previous study. Such decrease in HFC is caused by a reduction in the amplitudes of ICP harmonics in the 4–15 Hz window which exceeded the increase in HFC expected by definition during HR increase. However, the relationship between HR and HFC is complex; therefore, changes in HFC should be interpreted with caution. A significant relationship was observed between HHC and HR. HR has a meaningful impact on the ICP-derived indices and is likely to be acting as a surrogate index for pulse volume. Therefore, since HHC was reciprocally correlated with AMP and HR, it could be interpreted as an early warning sign of reduced pulse volume.

References


**Supplementary Table 1**

MANOVA results for predicting the value of intracranial pressure (ICP) pulse waveform-derived parameters based on the presence of midline shift (MLS) in the first head computed tomography scan after admission and mean ICP > 15 mm Hg.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>AMP</th>
<th>PSI</th>
<th>HFC</th>
<th>HHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICP &gt; 15 mm Hg</td>
<td>F = 18.48</td>
<td>F = 1.37</td>
<td>F = 1.49</td>
<td>F = 0.21</td>
</tr>
<tr>
<td></td>
<td>p &lt; 0.001</td>
<td>p = 0.244</td>
<td>p = 0.225</td>
<td>p = 0.647</td>
</tr>
<tr>
<td>MLS</td>
<td>F = 1.39</td>
<td>F = 15.03</td>
<td>F = 13.33</td>
<td>F = 4.98</td>
</tr>
<tr>
<td></td>
<td>p = 0.240</td>
<td>p &lt; 0.001</td>
<td>p &lt; 0.001</td>
<td>p = 0.027</td>
</tr>
<tr>
<td>ICP &gt; 15 mm Hg and MLS</td>
<td>F = 0.05</td>
<td>F = 0.84</td>
<td>F = 0.16</td>
<td>F = 0.58</td>
</tr>
<tr>
<td></td>
<td>p = 0.831</td>
<td>p = 0.359</td>
<td>p = 0.690</td>
<td>p = 0.449</td>
</tr>
</tbody>
</table>

ICP—intracranial pressure; MLS—midline shift; AMP—spectral amplitude of ICP pulse waveform; PSI—pulse shape index; HFC—high frequency centroid; HHC—higher harmonics centroid; results with p-value < 0.05 are presented in bold.
**Supplementary Figure 1**

Flow chart of study design based on the recordings from the CENTER-TBI high-resolution sub-study database (HR CENTER-TBI). EVD – external ventricular drainage, CPP – cerebral perfusion pressure, ICP – intracranial pressure.

**Supplementary Figure 2**

Illustrative time courses of mean intracranial pressure (ICP) and ICP-derived parameters: pulse amplitude of ICP (AMP), pulse shape index (PSI), high frequency centroid (HFC), and higher harmonics centroid (HHC).

**Supplementary Figure 3**

The relationship between PSI and: A) pulse amplitude of intracranial pressure (AMP), B) high frequency centroid (HFC), and C) higher harmonics centroid (HHC) in the full group of traumatic brain injury patients. Data are presented as median (black square) and interquartile range (whiskers).

**Supplementary Figure 4**

The relationship between mean heart rate (HR) and intracranial pressure (ICP) pulse waveform-derived parameters: A) pulse amplitude of ICP (AMP), B) pulse shape index (PSI), C) high frequency centroid (HFC), and D) higher harmonics centroid (HHC) in the full group of traumatic brain injury patients. Data are presented as median (black square) and interquartile range (whiskers).
HR CENTER-TBI database
HDF5 recordings (n = 282)

Excluded (n = 73):
- patients with EVD (n = 37)
- brain death (CPP < 0 mm Hg) (n = 1)
- ICP > 50 mm Hg (n = 2)
- CPP < 40 mm Hg (n = 2)
- craniectomy before ICP monitoring (n = 29)
- patients age < 16 (n = 2)

Included (n = 209):
recordings until 7th day from TBI

Excluded (n = 25):
- missing follow-up after 6 months (n = 19)
- low signal quality (n = 6)

Finally included (n = 184)