The role of biomarkers in ruling out intracranial injuries in mild cranial trauma

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Background

Mild cranial trauma (mCT) = 79-90% of all cranial trauma

The risk of intracranial injury (ICI) ≅ 5%

CT scan = gold standard for diagnosis of ICI but expensive + radiation

Biomarkers could rule out ICI → less CT scans
Objectives

Project aims

Assessing the diagnostic accuracy and economic value of biomarkers when used to rule out ICI
Methodology

Step 1
- Systematic review and meta-analysis of RCTs

Step 2
- Systematic review of the economic literature

Step 3
- Discussions with experts in the field
Biomarkers – Protein S100B

Most evidence related to protein **S100B**:
Protein secreted by astrocytes that can spill from injured cells and enter the bloodstream

**Serum levels of S100B**

< 0.105 µg/L

→ **Low risk of ICI in mCT**  → **No scan**
Protein S100B Testing

Moderate or High risk

Low Risk when CT Scan would be considered under current practice

If ≥ 6 hours after trauma and/or multiple trauma

If < 6 hours after trauma and isolated trauma

S100B Test

If ≥ 0,105 µ/L

If < 0,105 µ/L

CT scan and/or observation

Low Risk when NO CT scan would be considered under current practice

Discharge with oral and written instructions
Results from Meta-analysis

<table>
<thead>
<tr>
<th>Studies</th>
<th>Participants</th>
<th>Se (%)</th>
<th>Sp (%)</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011 PANDOR</td>
<td>9</td>
<td>2442</td>
<td>96.9 (91.4; 98.9)</td>
<td>42.0 (31.9; 52.8)</td>
<td>1.67 (1.40; 2.00)</td>
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<tr>
<td>UPDATE KCE 2015</td>
<td>10</td>
<td>3795</td>
<td>95.9 (88.2; 98.7)</td>
<td>26.1 (18.2; 35.8)</td>
<td>1.30 (1.16; 1.45)</td>
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<tr>
<td>ALL</td>
<td>19</td>
<td>6237</td>
<td>96.6 (92.3; 98.5)</td>
<td>33.0 (25.6; 41.4)</td>
<td>1.44 (1.28; 1.62)</td>
</tr>
</tbody>
</table>

1. High quality evidence
2. Sensitivity analysis inconclusive
Results from Meta-analysis

Children

- Sensitivity 99.1% (95%CI: 68.7; 100)
- LR- 0.02 (95%CI: 0.0; 0.3)
- Evidence from just 5 studies (n=469) with high risk of bias → quality of evidence low

No conclusion could be made on the diagnostic accuracy of any other biomarker
Economic literature – S100B

Two economic evaluations identified

- Apparent contradicting results:
  - If used in all mCT patients, cost additive
  - If used only in those who would otherwise receive a CT scan, cost saving

Models very sensitive to:

- The proportion of the mCT population in which the protein S100B test should be used
Conclusions

- High quality evidence that protein S100B could help to rule out ICI in adults with mCT

- Points for attention:
  - Patient selection
    - Not to be used on patient populations at higher risk of complications (eg on anticoagulants, elderly, with skull fractures, etc)
    - Not to be performed after 6 hours post-trauma
    - Not to be used in patients with multiple trauma

- Sensitivity not 100%:
  - LR - : between 0.04 and 0.23

- Appropriate patient targeting/use of biomarker tests could pose challenges
To the emergency department clinicians:

- **Use S100B test in patients with low risk of ICI on clinical grounds (<10%), in which a CT scan would be considered, under current practice.**
- **If test is negative, do not perform a CT scan**
- **Do NOT use S100B testing in:**
  - Patients with multiple trauma;
  - Patients in which the test cannot be performed within max. 6 hrs after trauma;
  - Patients on anticoagulants or anti-platelet treatment;
  - Patients aged 65+;
  - Children
  - Patients presenting signs of skull fracture;
  - Patients showing any signs or symptoms that would make an active follow-up clinically appropriate, independently of S100B test results.
To the Minister of Public Health and Social Affairs:

- We recommend to reimburse Protein S100B testing in the population/circumstances previously specified
- Monitoring the appropriate use of the test should be encouraged
Recommendations (3)

To the research community:

• Further research on the effectiveness of S100B testing at ruling out ICI in children is required

• Setting up an effectiveness study to assess how the protein is used in real life in Belgium would be of value