Cytokine hemoadsorption during cardiac surgery vs standard surgical care for infective endocarditis: results from a multicentre, randomised, controlled trial
Background / Study Objective

• Cardiac surgery often represents the only treatment option in patients with infective endocarditis (IE)

• IE surgery may lead to a sudden release of inflammatory mediators, which correlates with the severity of post-operative organ dysfunction

• We tested the hypothesis that intraoperative use of hemoadsorption to blunt mediators release during IE surgery reduces the severity of post-operative organ dysfunction, as measured by sequential organ failure assessment (SOFA) score
Patients

• We performed a multi-centre, randomised, controlled trial in 14 German hospitals
• IE patients with indications for surgery were randomly assigned in a 1:1 ratio to hemoadsorption during cardiopulmonary bypass (CPB) using CytoSorb® or control (no hemoadsorption)
• Post-operative sequential organ failure assessment (SOFA) score was assessed within 24 hours before surgery and from the first post-operative day until discharge from the intensive care unit (ICU) or intermediate care (up to the 9th post-operative day)
• In a run-in phase (the first 25 in each study arm), cytokine measurements were performed to assess the efficacy of the hemoadsorption in reducing cytokines.
Methods

• Primary endpoint was defined as difference between mean total post-operative SOFA scores and baseline pre-operative SOFA score (ΔSOFA)

• Secondary outcomes included 30-day mortality, durations of mechanical ventilation, vasopressor and renal replacement therapy

• Analyses were by intention-to-treat.

• This trial (NCT03266302) is registered with ClinicalTrials.gov.
Results 1

Figure 1: Trial flowchart

740 were assessed for eligibility

288 randomised

142 assigned to hemoadsorption

146 assigned to control

4 did not undergo surgery

2 did not undergo surgery

138 were included in intention-to-treat analysis

144 were included in intention-to-treat analysis

Figure 2: plasma levels of IL-1β (A), IL-6(B); t0: skin incision; t1: 30 minutes after starting CPB; t2: 60 minutes after starting CPB; t3: end of CPB; t4: 24h after surgery; IL: interleukin; CT-proET-1: C-terminal proendothelin-1.
Results 2

Primary Endpoint

![Box plot comparing hemoadsorption and control groups](image)

p = 0.666

Figure 2: The primary endpoint between the 2 study arms (mean difference: 0.23 points lower in hemoadsorption group, 95% CI: -1.30 to 0.83)

Secondary Endpoints

<table>
<thead>
<tr>
<th></th>
<th>Cytosorb</th>
<th>Control</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-d mortality</td>
<td>29 (21.0)</td>
<td>32 (22.4)</td>
<td>0.782</td>
</tr>
<tr>
<td>hemodialysis (days)</td>
<td>0 (0-1)</td>
<td>0 (0-2)</td>
<td>0.791</td>
</tr>
<tr>
<td>ventilation (days)</td>
<td>1 (0-7)</td>
<td>1 (0-3)</td>
<td>0.165</td>
</tr>
<tr>
<td>Vasopressors (days)</td>
<td>3 (1-8)</td>
<td>3 (1-7)</td>
<td>0.896</td>
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<tr>
<td>ICU stay</td>
<td>7 (3-12)</td>
<td>6 (3-10)</td>
<td>0.241</td>
</tr>
<tr>
<td>Hospital stay</td>
<td>20 (13-30)</td>
<td>19 (12-29)</td>
<td>0.392</td>
</tr>
</tbody>
</table>
Conclusion

• Although intraoperative hemoadsorption reduced plasma cytokines at the end of CPB, it did not reduce the severity of post-operative organ dysfunction or any of the secondary endpoints including 30-day mortality and durations of post-operative hemodialysis, ventilation, and vasopressor therapy.