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RECCAS, REMOVE, and SIRAKI02: discrepant outcomes and a potential explanation

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We read with interest the RECCAS trial by Hohn et al., investigating intraoperative hemoadsorption (HA) with CytoSorb during cardiopulmonary bypass (CPB) in patients over 65 years undergoing elective on-pump cardiac surgery. In this randomized controlled trial (RCT), patients were assigned to either intraoperative HA or standard care. The primary outcome was the difference in mean interleukin (IL)-6 serum concentrations upon ICU admission, while secondary outcomes included various clinical and biochemical endpoints. The authors reported no significant differences in cytokine levels, organ dysfunction, ICU/hospital lengths of stay, or mortality between groups [1]. As HA is less effective in CPB without significant inflammation [2], we turned to the REMOVE trial, which assessed CytoSorb in patients undergoing cardiac surgery for infective endocarditis (IE). This RCT used the change in SOFA score (Δ SOFA) as the primary outcome, comparing the total postoperative score (up to day 9) with the baseline. REMOVE found no significant reduction in postoperative organ dysfunction with HA [2].

In contrast, the SIRAKI02 trial evaluated extracorporeal blood purification (BP) with oXiris for cardiac

surgery-associated acute kidney injury (CSA-AKI). Among 343 patients (mean age 69 years, 119 female), BP significantly reduced CSA-AKI rates (28.4% vs. 39.7%; $P=0.03$) with an adjusted difference of 10.4% ($P=0.01$). The benefits were particularly notable in patients with chronic kidney disease, diabetes, hypertension, reduced left ventricular ejection fraction ($<40\%$), and lower BMI (<30). However, no significant differences were observed in most secondary or exploratory endpoints [3].

The divergent results between RECCAS, REMOVE, and SIRAKI02 may be explained by differences in adsorption mechanisms. While CytoSorb targets cytokines, oXiris also removes endotoxins, which play a critical role in the inflammatory cascade [4]. One study found elevated endotoxin levels in 73% of patients with CPB >90 min, compared to 36% with CPB <90 min [5]. Both RECCAS and SIRAKI02 included patients with prolonged CPB, but only SIRAKI02 demonstrated efficacy. This suggests that endotoxin removal is crucial in addressing the "endotoxin storm" that precedes the cytokine storm. Without effective endotoxin control, as seen in RECCAS, cytokine levels may continue to rise post-surgery, undermining the potential benefits of CytoSorb. These findings emphasize the need for comprehensive strategies targeting both endotoxins and cytokines to improve outcomes in CPB-associated inflammation.

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Author contributions

PMH & MMW designed the paper. PMH,EP & MMW participated in drafting and reviewing. PMH,EP, & MMW read and approved the final version of the manuscript.



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Consent for publications

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MMW declare to have competing interests. PMH,SB,EP & MMW declare to have no competing interests.

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