Unexpected negative results for CytoSorb during left ventricular assist device implantation; interpret with caution

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LETTER TO THE EDITOR

Unexpected negative results for CytoSorb during left ventricular assist device implantation: Interpret with caution

To the editor,

We recently read with interest the study by Zhigalov et al. about CytoSorb during left ventricular assist device (LVAD) implantation.[1] The rather unexpected, unfavorable results presented and the concurrent lack of CytoSorb's efficacy in diminishing the inflammation postoperatively temper the previous enthusiasm. In our opinion, several points of this study should be clarified when interpreting its results.

Baseline differences between groups were balanced with propensity score matching (PSM). Nevertheless, information about the PSM is lacking. A plot illustrating the distribution of the propensity scores before and after matching and other balance statistics e.g., the standardized mean differences are deemed necessary for interpreting the results.[2] Interestingly, the conditioning resulted in only 40 matched controls out of 135 patients which were compared to 72 CytoSorb patients. The investigators should have elaborated further on that result since such a limited matching could have imposed bias if a strong balance was not achieved. Furthermore, patient selection criteria for CytoSorb therapy are not provided and could have created rather unbalanced groups in terms of their prognostic factors.

Another concern is that matching factors included all unbalanced variables with a p-value ≤ 0.1. Using unbalanced variables is common practice, but some variables should be matched even if they are in principle not statistically unbalanced. The matching must make both statistical and clinical sense. It has been proposed that all outcome-related variables should be included in PSM.[3] In the current study, more CytoSorb patients were on mechanical ventilation preoperatively (23.6% vs. 17.5%), had more advanced heart failure (INTERMACS profile 1–2: 55.6% vs. 45%), and had more often concomitant procedures (18.1% vs. 10%). A previous study in LVAD patients identified preoperative mechanical ventilation as an independent risk factor for all-cause mortality.[4] Moreover, CytoSorb patients also exhibited higher preoperative interleukin-6 (IL-6) levels (67.7 ± 48.85 vs. 39.6 ± 37.1). Elevated IL-6 levels have been associated with prolonged postoperative mechanical ventilation in cardiac surgery patients.[5] Finally, despite matching for the LVAD model, CytoSorb patients received more often HeartMate III and less often HeartWare compared to controls (22.2% vs. 10% and 77.8% vs. 90%, respectively). From a clinical perspective, these differences are rather important, regardless of the p-value in such a small patient population, and might have influenced outcomes. Consequently, the higher incidence of some major adverse events within the CytoSorb group should be interpreted with caution.

Patient profiles that could benefit from this therapy should be investigated. To that extent, baseline levels of inflammatory mediators should be further evaluated. Moreover, the company's recommendation of a minimum 120-min therapy for cardiopulmonary bypass (CPB) should be taken into consideration. In the current study, the average CPB duration was only 70 min, which might not have been enough for CytoSorb to support proper immunomodulation.

In conclusion, we would like to emphasize that despite the initial enthusiasm about CytoSorb therapy in cardiac surgery, the level of evidence remains low. Therefore, its integration into standard-care protocols cannot be justified. More robust, randomized (placebo-controlled) clinical trials are necessary to expand our knowledge and experience with the device. The ongoing randomized, controlled CYCLONE-LVAD trial will hopefully help to answer these questions better (NCT 04596813).

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