Intraoperative immunomodulation during left heart bypass in open thoracoabdominal aortic aneurysm repair

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ABSTRACT

Despite the technical innovations introduced in the previous decades, open thoracoabdominal aortic aneurysm repair still represents an enormous challenge for patients and surgeons. Logically, the systemic inflammatory response resulting from these massive operations appears considerable; however, the response has never been thoroughly investigated. In addition, intraoperative adjuncts to modulate the postoperative activation of the immune system have not yet been introduced into clinical practice. We report a case of intraoperative hemadsorption during open repair of a thoracoabdominal aortic aneurysm through the introduction of a CytoSorb device (CytoSorbents Corp) in the left heart bypass circuit. The technique appeared feasible and safe and probably contributed to the good clinical outcomes. (J Vasc Surg Cases Innov Tech 2023;9:101276.)

Keywords: CytoSorb; Left heart bypass; Thoracoabdominal aortic aneurysm

Open repair of thoracoabdominal aortic aneurysms (TAAAs) still represents one of the greatest surgical challenges. The morbidity and mortality of these massive operations are not negligible even in the most experienced centers, with a mortality rate of 6.2% in the elective setting, which is almost doubled for urgent cases.[1] Spinal cord injuries, acute renal failure, and pulmonary complications are the most feared postoperative complications. However, the long-term potential for aorta-related complications could require high-risk treatments for already fragile patients.[2] The enormous surgical trauma caused by the thoracolaparotomy necessary for aortic exposure, the use of extracorporeal circulation for distal and visceral perfusion, and ischemia–reperfusion injury induce a systemic inflammatory response (SIR) that can cause a physiologic derailment that is potentially lethal for patients.[3,4] In this scenario, the so-called cytokine storm has a central role.[5] Activation of a SIR frequently leads to devastating perioperative complications such as vasoplegia, coagulopathy, and acute respiratory distress syndrome. Therefore, modulation of the SIR, inevitably activated by these massive interventions, could be of the utmost importance in the pursuit of better clinical outcomes. CytoSorb (CytoSorbents Corp) is a new adjunct for extracorporeal circulation systems, which is rapidly increasing in popularity in the treatment of critical patients. The device was designed as an extracorporeal adsorber of cytokines, bilirubin, myoglobin, and drugs (eg, rivaroxaban and ticagrelor). Very recently, Jansen et al[6] demonstrated that the CytoSorb cartridge, integrated into a hemoperfusion circuit, can significantly reduce circulating cytokine concentrations during systemic inflammation in humans in vivo. CytoSorb uses vary from clinical to surgical settings and for a wide spectrum of conditions. In the field of cardiothoracic surgery, CytoSorb is still used in experimental settings; however, the results are encouraging. The device is approved by the U.S. Food and Drug Administration for the treatment of critically ill patients affected by COVID-19 (coronavirus disease 2019) to reduce the incidence and severity of hyperinflammatory syndrome. In Europe, CytoSorb obtained the CE (Conformité Européene) mark for use, not only for patients affected by COVID-19, but also for patients with other extremely severe conditions such as rhabdomyolysis, septic shock, and multiple organ failure. In the cardiovascular field, the device is frequently used in patients requiring extracorporeal membrane oxygenation (ECMO) and for patients with intraoperative use of cardiopulmonary bypass, with a particular indication for patients with endocarditis and patients undergoing long and complex interventions, especially those involving the aorta. The contraindications reported by U.S. Food and Drug Administration regarding the use of CytoSorb include very low platelet counts ($<$20,000/μL), any preexisting contraindication to extracorporeal therapy, allergy to the extracorporeal circuit components, a history of heparin-induced thrombocytopenia, acute sickle cell crisis, morbid obesity with a body mass index of $\geq$40 kg/m^2, a life expectancy of $<$1 month, treatment deemed clinically futile, pregnancy, concomitant use of corticosteroids, and profound immunosuppression. Only

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Fig 1. Intraoperative photograph showing the CytoSorb cartridge integrated into the left heart bypass (LHB) circuit.

a few studies have been reported on its use in aortic surgery, with advantages evident in the blood transfusion rates, hemodynamic stability, lactate levels and metabolic balance, and respiratory complications, resulting in a decreased duration of mechanical ventilation and shorter intensive care unit and hospital stays.[7,8] A single reported study analyzed the use of CytoSorb for open TAAA repair, with the device integrated into a cardiopulmonary bypass circuit with femorofemoral cannulation.[9] To the best of our knowledge, the present case report is the first description of off-label use of CytoSorb with left heart bypass (LHB) during open TAAA repair (Fig 1; Supplementary Video, online only). This work reports the first case of open TAAA repair treated intraoperatively with CytoSorb in our center. However, the device is frequently used with an ECMO circuit and during liver transplantation. For CytoSorb use in aortic surgery, according to the manufacturer's instructions for use, the device is indicated for cases of complex surgery, patients with infection, and estimated long extracorporeal circulation times, characteristics often required during open TAAA surgery. The patient provided written informed consent for the report of his case details and imaging studies.

CASE REPORTS

A 53-year-old man with hypertension, previous aortic valve replacement, and acute type B aortic dissection 10 years before presented to our attention with a

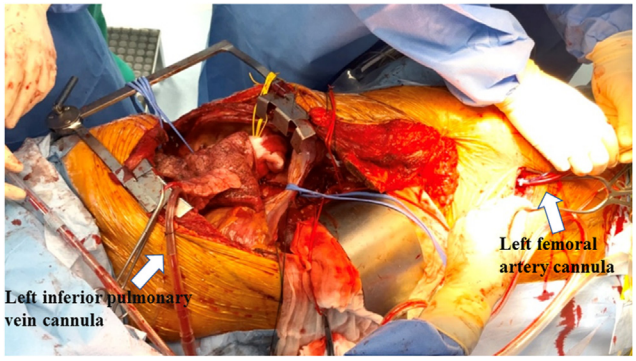

Fig 2. Intraoperative photograph showing the left heart bypass (LHB) circuit.

dissecting type I TAAA, using the Crawford classification, with a maximum diameter of 65 mm. Considering the anatomic and clinical factors, the patient was scheduled for open repair. He underwent standard operative preparation and was monitored in the usual fashion.[10] A spinal drain catheter was placed for cerebrospinal fluid drainage. The patient was placed in the right lateral decubitus position with the upper body at 60° and the hips at 30° using a moldable beanbag. A sigmoid incision was made from the left scapula's tip to the left of the umbilicus. The thoracic cavity was entered through the fifth intercostal space, and the whole descending thoracic aorta was prepared. The abdominal cavity was entered via a transperitoneal approach, and, after medial visceral rotation, the abdominal aorta and its branches were carefully dissected. LHB was instituted by cannulating the left atrium via the left inferior pulmonary vein with a 24F cannula and the left femoral artery with a 16F cannula (Fig 2). The LHB circuit was configured in the standard fashion, except for interposition of the CytoSorb cartridge on the arterial line. A 22-mm straight Dacron graft (Vascutek Ltd; Terumo Aortic) was chosen for repair. After proximal anastomosis, two large intercostal arteries were reimplanted using the island patch technique. During aortic clamping, the celiac trunk and superior mesenteric artery were selectively perfused with isothermic blood from the LHB through 9F Pruitt catheters, and the renal arteries were selectively perfused with 700 mL of Custodiol solution (Dr. Franz Köhler Chemie GmbH) through coronary cannulas (Fig 3).[10] Distally, the dissection membrane was excised at the level of the visceral vessels, creating a single lumen in the native aorta. Finally, a distal beveled anastomosis was performed (Fig 4). The total LHB time was 108 minutes. The total intraoperative blood loss was 3100 mL, of which 750 mL of concentrated red blood cells were reinfused to the patient because of intraoperative blood salvage. Three intraoperative and three postoperative blood samples were taken for measurement of inflammatory markers (interleukin-2 [IL-2], interleukin-

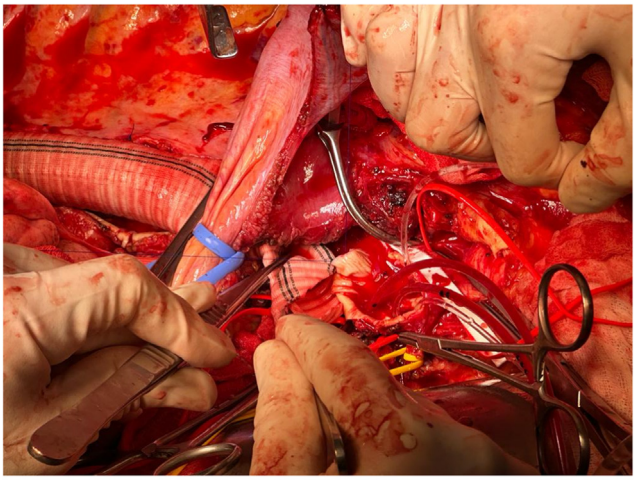

Fig 3. Intraoperative photograph showing selective visceral perfusion with isothermic blood for the celiac trunk and superior mesenteric artery and Custodiol solution for the renal arteries and distal beveled anastomosis.

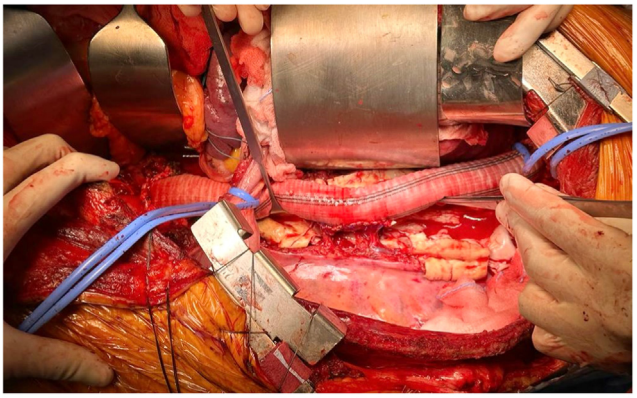

Fig 4. Intraoperative photograph showing final aortic reconstruction with intercostal artery reimplantation through an island patch.

6 [IL-6], C-reactive protein [CRP], and suppression of tumorigenicity 2 [ST-2]; Table). If the first three can be considered general markers of physiologic stress, the ST-2 molecule directly represents an index of cardiovascular damage.[11] Vasopressor support was not necessary during the perioperative course, except for low doses of norepinephrine during surgery (maximum, 0.2 μg/kg/min). The patient was extubated on postoperative day (POD) 1 without respiratory complications. The spinal drain catheter was clamped on POD 2 and removed on POD 3, without any neurologic deficits. The surgical drainage tubes were removed on POD 3, with no relevant postoperative blood loss. During the postoperative course, the patient did not experience acute respiratory distress syndrome, vasoplegia, coagulopathy, or acidosis. The patient was transferred to an ordinary ward on POD 5.

DISCUSSION

The intra- and postoperative inflammatory response to massive operations such as open repair of TAAA is still a poorly understood mechanism; however, the clinical outcomes of a dysregulated SIR can be catastrophic. Despite the worldwide diffusion of intraoperative adjuncts such as cerebrospinal fluid drainage, LHB, and motor and somatosensory evoked potential monitoring, strategies for inflammatory response modulation are not routinely adopted during these operations. CytoSorb could be a useful adjunct to mitigate the dysregulated inflammatory response via adsorption of hyperreleased cytokines, with the aim of preventing the well-known consequences of SIR syndrome. In the present case of open TAAA repair, intraoperative hemadsorption with the CytoSorb device integrated into the LHB circuit was demonstrated to be feasible and safe, with no device-related complications, and probably contributed to the good clinical results. Considering the postoperative course, we believe that our patient's postoperative respiratory independence, hemodynamic stability without the need for vasopressor support, and coagulation normalization were all facilitated by the intraoperative adsorption of proinflammatory molecules. A series of inflammatory markers were measured at different times both intra- and postoperatively. Although CRP, IL-2, and IL-6 are well known as specific markers of immune system activation, ST-2 has recently been discovered as a specific index of cardiovascular stress. Their progressive increase during the postoperative course was easily predictable; however, the potential harmful effects could have been attenuated by the initial intraoperative hemadsorption. We have not yet performed a similar open TAAA repair without the use of CytoSorb and measuring the same inflammatory markers. However, considering the study recently reported by Jansen et al,[6] a reduction in circulating cytokines is very likely. Also, the CytoSorb cartridge, according to the manufacturer's instructions for use, can be easily integrated in every type of extracorporeal circuit, including ECMO, continuous renal replacement therapy, continuous venovenous hemofiltration, and hemoperfusion circuits. These can be considered, if indicated, as potential postoperative uses of CytoSorb. Further studies are needed to analyze and compare the incidence and severity of postoperative SIR syndrome and the evolution of the causative inflammatory markers with these challenging surgeries. We believe that the data on the inflammatory markers reported in our study could be a useful benchmark in the future for a deeper evaluation of the inflammatory response during open TAAA repair and the beginning of new evidence-based immunomodulation during surgery that require extracorporeal circulation.

Table. Intraoperative and postoperative results of inflammatory marker analysis

		LHB		Postoperatively, hours		
Inflammatory marker	Baseline[a]	Start	End	6	12	24
CRP, mg/L	2.84	2.30	1.34	28.6	85.5	191
IL-6, pg/mL	<2.7	8.4	78.5	142	116	154
IL-2, U/mL	477	371	245	621	921	1037
ST-2, ng/mL	15	12	12	216	405	429

CRP, C-reactive protein; *IL,* interleukin; *LHB,* left heart bypass; *ST-2,* suppression of tumorigenicity 2.
[a]Sample taken at anesthesia induction.

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