ISSN: 2754-6667

Journal of Critical Care & Emergency Medicine

SCIENTIFIC Research and Community

Review Article

Open Access

An In-Depth Analysis of the Multi-Faceted Benefits of Cytosorb Filter Utilization during Cardiopulmonary Bypass

Salman Pervaiz Butt[1]*, Gaurav Pandey[1], Rashid Aziz[2], Simon Phillips[3], Yasir Saleem[4], Arun Kumar[1], Fazil Ashiq[1], Umer Darr[1] and Gopal Bhatnagar[1]

[1]Cleveland Clinic Abu Dhabi

[2]Mater Misericordiae University Hospital Dublin, Ireland

[3]St Georges University Hospitals, UK

[4]All India institute of Medical Sciences-Rishikesh, India

ABSTRACT

Introduction: Cardiopulmonary bypass (CPB) is a vital component of many cardiac surgeries, but it can trigger systemic inflammatory responses, leading to post-operative complications. The CytoSorb filter, a cytokine adsorber, has emerged as a potential adjunctive therapy in CPB to mitigate inflammation.

Method: A literature review was conducted to assess the impact of CytoSorb on inflammation and clinical outcomes during cardiac surgery with CPB. Various databases were searched including PubMed, MEDLINE, and Google Scholar using relevant keywords.

Results: Studies have shown mixed results regarding CytoSorb's efficacy in reducing pro-inflammatory cytokines and improving clinical outcomes. Some studies reported reduced cytokine levels, improved hemodynamics, and decreased need for vasopressors. However, others found no significant cytokine reduction or clinical improvement. CytoSorb was generally well-tolerated with no device-related serious adverse events reported. Additionally, CytoSorb demonstrated potential benefits in reducing bleeding complications when used in patients taking antiplatelet or anticoagulant medications during cardiac surgery.

Discussion: The use of CytoSorb in cardiac surgery with CPB holds promise but requires further research. Future directions include evaluating long-term benefits and safety, refining patient selection criteria, conducting comparative studies, standardizing guidelines for CytoSorb integration, and exploring its utility in other cardiac surgery scenarios.

Conclusion: CytoSorb offers potential benefits in attenuating systemic inflammation during cardiac surgery with CPB. While evidence suggests positive outcomes in specific contexts, more research is needed to establish its regular use and optimize patient care. Collaborative decision-making and individualized patient management are essential when considering CytoSorb therapy. Continued investigation will provide valuable insights into its precise role in managing inflammation during CPB, enhancing patient outcomes, and refining clinical protocols.

***Corresponding author**

Salman Pervaiz Butt, Perfusionist and ECMO Specialist, Heart Vascular and Thoracic Institute, Cleveland Clinic Abu Dhabi, UAE.

Received: September 17, 2023; **Accepted:** September 20, 2023; **Published:** September 23, 2023

Keywords: Cytosorb, Inflammatory Response, Cardiopulmonary Bypass, Cytokines, Adsorption

Abbreviations
CPB: Cardiopulmonary Bypass
SOFA: Sequential Organ Failure Assessment
SIRS: Systemic Inflammatory Response Syndrome
IE: Infective Endocarditis
HA: Hemoadsorption
RCT: Randomised Control Trial

Introduction

During CPB, the patient's blood is diverted from the heart and lungs to a heart-lung machine, which takes over the function of oxygenating and circulating the blood. While this procedure is crucial in many cardiac surgeries, it can also activate systemic inflammatory responses, which can contribute to post-operative complications.

Recognizing the detrimental effects of the systemic inflammatory response associated with CPB, researchers and clinicians have been exploring strategies to attenuate its impact and improve patient outcomes. In recent years, the CytoSorb filter has emerged

as a promising adjunctive therapy in cardiac surgery with CPB. The CytoSorb system consists of a highly porous polymer cartridge that acts as a cytokine adsorber, effectively removing circulating inflammatory mediators from the patient's bloodstream.The mechanism of action of CytoSorb relies on the principles of adsorption. The cartridge contains biocompatible polymer beads with a large surface area, allowing for the efficient binding and removal of cytokines, myoglobin, bilirubin, and others.

Harmful molecules. By eliminating these inflammatory mediators, CytoSorb aims to modulate the exaggerated immune response triggered by CPB and mitigate the associated complications.

Clinical studies investigating the use of CytoSorb in cardiac surgery have shown mixed results. Researchers have observed a significant reduction in the levels of pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) following CytoSorb treatment. Moreover, the use of CytoSorb has been associated with improved hemodynamic stability, reduced organ dysfunction, and decreased need for vasopressors and inotropic support.

The safety profile of CytoSorb in cardiac surgery appears favorable, with no reported serious adverse events directly attributed to the device. The filter is generally well tolerated, and its use does not interfere with the standard CPB circuit. However, as with any medical intervention, careful patient selection and monitoring are essential to ensure optimal outcomes.

The incorporation of CytoSorb into the management of patients undergoing cardiac surgery with CPB holds significant potential. By attenuating the systemic inflammatory response, CytoSorb may contribute to improved post-operative recovery, shorter hospital stays, and reduced morbidity and mortality rates. Additionally, its use may allow for the exploration of less invasive surgical techniques, as the attenuated inflammatory response could potentially minimize tissue damage and enhance tissue healing.

Further research and larger-scale studies are necessary to establish its long-term efficacy, cost-effectiveness, and impact on patient outcomes. However, the current evidence suggests that CytoSorb may play a valuable role in optimizing patient care and improving the success rates of cardiac surgeries involving CPB.

Integration into CPB Circuit

Filter is designed to be compatible with standard CPB systems and can be easily incorporated into the circuit. The exact placement and configuration of the CytoSorb filter within the CPB circuit may vary depending on the specific CPB setup and Perfusion preference but It is very important to follow the manufacturer's instructions.

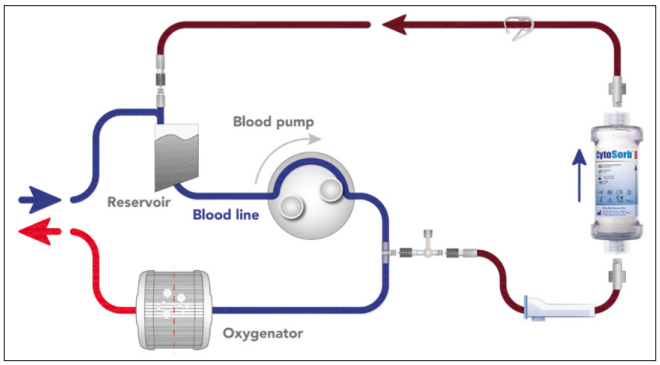

Figure 1: Illustration of Cytosorb Filter Integration into CPB Circuit[13]

Method

To conduct a comprehensive literature review on the utilization of CytoSorb in cardiac surgery with CPB, a systematic approach was adopted. The primary objective of this review was to assess the impact of CytoSorb on the systemic inflammatory response and clinical outcomes in CPB patients undergoing cardiac surgery, while also exploring additional applications of CytoSorb during CPB.

The literature search involved an extensive exploration of various reputable databases, including PubMed, MEDLINE, and Google Scholar. To identify pertinent publications, relevant keywords such as "cardiac surgery," "cardiopulmonary bypass," and "cardiopulmonary bypass and CytoSorb" were employed.

The selected studies underwent a rigorous critical appraisal process to extract valuable information regarding the benefits, safety and efficacy of utilizing CytoSorb during CPB for diverse applications and reasons. Overall, this method employed a systematic and comprehensive approach to ensure the inclusion of relevant literature and the extraction of meaningful insights regarding the use of CytoSorb in cardiac surgery with CPB.

Discussion

A Porcine model study by Craig R. Vocelka aimed to investigate the effect of cardiopulmonary bypass (CPB) on cardiac function and assess whether hemoadsorption of cytokines using Cytosorb during bypass could attenuate acute organ dysfunction. Twelve Yorkshire pigs were used, with baseline measurements of cardiac mechanics and cytokine expression (TNF, IL-6, IL-10) obtained before and hourly after 1 hour of normothermic CPB. The animals underwent bypass with or without the Cytosorb device, and a control group underwent observation without bypass. After 5 hours from separation from bypass or observation, the animals were euthanized, and myocardial water content was determined. The study found that neither TNF nor IL-6 showed significant elevation in either experimental group compared to controls at any time point. Preload recruitable stroke work and dP/dtmax were significantly decreased immediately after separation from bypass in both the CPB+HA and CPB groups, and this depression in cardiac function persisted throughout the experiment. Although Tau remained unchanged, dP/dTmin was significantly reduced in both bypass groups at all time points after separation from bypass. Cytokine hemoadsorption using Cytosorb did not have any effect on the measured indices of cardiac function. There were no evident differences in postmortem data between the groups. Based on the findings, it was concluded that one hour of normothermic CPB led to a significant and sustained decline in left ventricular function, which did not appear to be related to changes in cytokine expression. Since there was no significant change in cytokine concentrations post-bypass, the potential of cytokine hemoadsorption in attenuating CPB-induced ventricular dysfunction could not be assessed in this study [1].

The clinical data and outcomes from a case series by Karl Träger et al. of 39 patients with infective endocarditis undergoing cardiac surgery with a CytoSorb adsorption device showed promising results. The treatment was found to be safe and well-tolerated with no device-related adverse events. However, due to the study's limitations, including its retrospective and observational design, it is challenging to draw definitive conclusions about the primary therapeutic effect of CytoSorb [2].

On the other hand, in a single-center pilot randomized controlled

trial by E C Poli et al, the potential of CytoSorb in decreasing peri-operative cytokine levels in cardiac surgery was evaluated. Thirty patients undergoing elective cardiac surgery and at risk of complications were randomly assigned to either the standard of care group (n = 15) or the CytoSorb haemoadsorption (HA) group (n = 15) during cardiopulmonary bypass (CPB). The primary outcome measured the difference in cytokine levels (IL-1a, IL-1b, IL-2, IL-4, IL-5, IL-6, IL-10, TNF-α, IFN-γ, MCP-1) between the two groups at different time points.Baseline and peri-operative characteristics were similar between the two groups, and the use of CytoSorb HA during CPB did not lead to an increased incidence of adverse events. However, the intervention did not result in a significant decrease in pro- or anti-inflammatory cytokine levels, nor did it show any improvement in relevant clinical outcomes. The procedure was considered feasible and safe, with no significant coagulation factors' adsorption observed, although there were signs of coagulation activation. Based on these findings, the use of CytoSorb HA during CPB did not demonstrate a reduction in cytokine levels or improvement in clinical outcomes [3].

A study by Kambiz Hassan et al aimed to analyze the results of CytoSorb adsorption during emergency open heart operations in patients at high risk of bleeding due to treatment with coagulation-active substances. The research included 55 consecutive patients who underwent emergency cardiac surgery between June 2016 and June 2018. Of these patients, 43 were receiving ticagrelor therapy, and 12 were receiving rivaroxaban therapy. CytoSorb adsorption was routinely implemented in 39 out of the 55 cases, while 16 patients did not receive adsorption.

In the group with CytoSorb adsorption, no re-explorations were required, and the drainage volumes in 24 hours were minimal (350 mL after ticagrelor therapy and 390 mL after rivaroxaban therapy). Most patients did not require transfusions of blood products. In contrast, the group without adsorption experienced multiple bleeding complications. This group had longer total operation times, higher drainage volumes, and increased transfusions of red blood cells and platelets. The re-exploration rate was significantly higher, along with prolonged stays in the intensive care unit and the hospital. Based on these findings, the study concludes that intraoperative CytoSorb adsorption of ticagrelor and rivaroxaban in emergency open heart operations is a safe and effective method for reducing bleeding complications. The authors recommend the use of CytoSorb for patients undergoing emergency cardiac surgery while receiving ticagrelor or rivaroxaban to enhance safety and mitigate bleeding risks. This study provides valuable evidence supporting the efficacy of CytoSorb in this specific clinical scenario [4].

A pilot study by M Diab et al. called REMOVE-pilot compared cytokine levels and outcomes between Infective Endocarditis (IE) patients and those with non-infectious valvular heart disease. The study found that IE patients had higher cytokine levels during and after CPB, as well as higher Sequential Organ Failure Assessment (SOFA) scores and in-hospital mortality. This led to the design of the REMOVE trial, which aimed to demonstrate the efficacy of CytoSorb (a cytokine-adsorbing column) in preventing multiorgan dysfunction in IE patients undergoing cardiac surgery [5].

REMOVE trial enrolled a total of 282 patients, with 138 patients receiving CytoSorb during CPB and 144 patients in the control group. The results showed that the use of CytoSorb led to a reduction in certain inflammatory cytokines in the postoperative period compared to the control group, indicating its potential anti-inflammatory effect.

However, despite the favorable cytokine modulation observed, there were no significant differences in clinical outcomes or the occurrence of organ dysfunction between the CytoSorb group and the control group. The trial did not demonstrate a reduction in postoperative organ dysfunction, 30-day mortality, or any clinically relevant secondary outcome measures.

These findings suggest that although CytoSorb effectively modulated inflammatory cytokines, it did not translate into tangible clinical benefits in terms of preventing organ dysfunction or improving patient outcomes in the specific context of cardiac surgery for infective endocarditis.

It is important to note that the trial's findings are specific to the REMOVE study and may not necessarily apply to other clinical scenarios or conditions. Further research and analysis are needed to fully understand the potential benefits and limitations of CytoSorb in different patient populations and surgical contexts [6].

Several other studies have investigated the efficacy of the CytoSorb filter during CPB. A systematic review and meta-analysis by Vinci Naruka et al aimed to compare the outcomes of cardiac surgery involving cardiopulmonary bypass (CPB) with and without haemoadsorption therapy. The analysis included fifteen studies, comprising eight randomized controlled trials and seven observational studies. The results revealed that in non-elective surgeries, such as emergency cases and infective endocarditis, the use of cytokine filters during CPB significantly reduced the 30-day mortality rate and resulted in shorter ICU stays. Additionally, on day-1 post-surgery, the group receiving CPB with haemoadsorption therapy showed a significant decrease in c-reactive protein (CRP) levels. However, there were no significant differences in white blood count (WBC), procalcitonin (PCT), tumour necrosis factor-alpha (TNF-α), IL-6, IL-8, and lactate between the two groups. Overall, the findings suggest that haemoadsorption therapy during non-elective cardiac surgeries, particularly in emergency cases and patients with a higher inflammatory burden like infective endocarditis, may lead to a notable reduction in 30-day mortality and ICU stay. However, no significant differences were observed in operative mortality, ventilation duration, hospital stay, and ICU length of stay when comparing cytokine filters and control across all studies [7].

From safety perspective Marianne Alarie et al. suggested that CytoSorb use during cardiopulmonary bypass was safe and feasible and may have contributed to improved postoperative outcomes in our patient. In his case report, a 61-year-old male with congestive heart failure and multiple comorbidities underwent mitral valve surgery. Preoperative assessments revealed severe mitral regurgitation and moderate mitral stenosis, as well as moderate aortic cusp calcification with stenosis. The patient also had significant coronary artery disease. Due to the complexity of the surgery and the patient's kidney dysfunction, a CytoSorb cartridge was integrated into the cardiopulmonary bypass circuit to mitigate inflammation. The patient's vasoactive support requirements were lower than expected, and there were no device-related complications. Although studies on CytoSorb in cardiac surgery patients have shown mixed results, its use in this case appeared safe and may have contributed to improved postoperative outcomes. Further research is needed to determine the potential benefits of CytoSorb in similar patients at high risk of vasoplegia and multiorgan injury [8].

According to C Ng Yin Ling et al. Cytosorb has shown great potential in urgent or emergent CABG surgery to remove anti-

platelet medications and anti-coagulants, resulting in improved clinical outcomes such as reduced blood transfusions, shorter ICU stays, and lower rates of bleeding complications. However, the evidence is inconclusive for the use of Cytosorb in elective CABG surgery to remove pro-inflammatory cytokines. Larger, high-quality clinical trials are needed to determine if there are clinically significant benefits in this cases [9].

Several studies have also explored the application of the CytoSorb filter in COVID-19 patients. For instance, a systematic review and meta-analysis by Sören Becker et al. aimed to assess the efficacy of the CytoSorb adsorber in reducing mortality across various clinical settings. After analyzing 34 studies involving 1297 CytoSorb-treated patients and 1314 controls, the researchers found that CytoSorb intervention did not significantly lower mortality rates in any of the examined situations, including sepsis, cardiopulmonary bypass surgery, severe illness, and SARS-CoV-2 infection. Notably, untreated controls in the cardiac arrest subgroup had a significant survival advantage. The analysis also revealed no significant differences in ICU length of stay, lactate levels, or IL-6 levels after treatment. Based on these findings, the authors do not recommend the routine use of CytoSorb unless further evidence is generated through well-designed randomized controlled trials targeting specific medical conditions and patient populations [10].

An interesting study by Harky et al. highlights the role of CytoSorb in purifying extracorporeal blood and its potential benefits in reducing bleeding complications during on-pump cardiac surgery. The use of CytoSorb is particularly relevant in patients who are taking pre-operative antiplatelet or anticoagulation medications, as these individuals have a higher risk of bleeding. Current guidelines recommend stopping such medications prior to surgery, but in urgent and emergency cases, this may not always be possible. CytoSorb utilizes haemoadsorption to selectively remove molecules, including inflammatory mediators and antithrombotics, from the blood. It has shown promise in eliminating key contributors to the cytokine storm and reducing the risk of bleeding in high-risk patients [11].

In an intriguing case report by Andreas Koster et al. the use of the CytoSorb filter for eliminating residual therapeutic argatroban concentrations during heparinized CPB for heart transplantation was examined. The report featured a 34-year-old patient who underwent urgent heart transplantation and had received prior anticoagulation with argatroban. Despite discontinuing the argatroban infusion before surgery, the concentration only showed minimal decline. During the procedure, microvascular bleeding occurred. However, integrating a CytoSorb absorption column into the cardiopulmonary bypass circuit successfully reduced the argatroban concentration and achieved satisfactory hemostasis. These findings suggest that the CytoSorb filter is an effective method for eliminating therapeutic argatroban concentrations during cardiopulmonary bypass, presenting a potential extracorporeal removal strategy [12].

A pilot randomized controlled trial by Doukas P et al, the researchers investigated the feasibility and impact of perioperative hemoadsorption during open thoracoabdominal aortic repair. The study included 27 patients scheduled for open TAAA repair with the use of CPB. Ten patients were assigned to the intervention group receiving intraoperative hemoadsorption during CPB, while the control group consisted of 17 patients who received standard of care. The baseline and perioperative characteristics were generally similar between the two groups, and no device-related adverse events were reported. The intervention group showed a trend towards shorter ventilation times compared to the control group (median 88 hours vs. 510 hours, $p = 0.08$, $\Delta 422$). Additionally, the incidence of severe acute respiratory distress syndrome was significantly lower in the intervention group ($p = 0.02$).

Based on these findings, this pilot study suggests that the intraoperative use of hemoadsorption in open thoracoabdominal aortic repair patients may be feasible and safe. The observed trend towards shorter ventilation times and the significant reduction in severe acute respiratory distress syndrome indicate potential clinical benefits associated with hemoadsorption. However, the study emphasizes the need for larger trials to further evaluate the efficacy of intraoperative hemoadsorption and its impact on clinical outcomes in this patient population. The findings highlight the importance of investigating cytokine adsorption for controlling the early inflammation cascade and its potential role in improving patient outcomes in aortic surgery with cardiopulmonary bypass [13].

Another case report by Erich Moresco et al. examined the integration of CytoSorb into the CPB in patients with acute coronary syndrome (ACS) who underwent emergent coronary artery bypass graft surgery (CABG) after failed percutaneous coronary intervention (PCI). The goal was to assess whether using CytoSorb could reduce the risk of perioperative bleeding associated with the antiplatelet drug prasugrel.The patient experienced minimal intraoperative and postoperative bleeding, despite ongoing platelet inhibition indicated by the Multiplate results. The need for transfusions was lower than expected. While the precise impact of CytoSorb on prasugrel adsorption could not be directly measured, it was hypothesized that the adsorber may have contributed to reducing the drug's effects. This case report acknowledged limitations, such as the absence of plasma level measurements and the absence of a control group. Further clinical trials are needed to better understand the role of CytoSorb in reducing bleeding risk in prasugrel-loaded patients undergoing emergent cardiac surgery [14].

A recent study by Nilufar Jabayeva investigated the early use of extracorporeal cytokine adsorbers during open-heart surgery with prolonged cardiopulmonary bypass (CPB). The study included patients undergoing planned open cardiac surgery with CPB durations over 120 minutes. The patients were divided into three groups: CytoSorb-300, HA 330, and control. The results showed that intraoperative hemadsorption using cytokine adsorbers had a positive impact on the postoperative period after cardiac surgery. It was associated with a reduced incidence of acute kidney injury (AKI) and a potential decrease in the need for renal replacement therapy.Baseline parameters and surgical characteristics did not differ significantly among the groups. However, the HA 330 group had a higher rate of bleeding complications, while the control group had a higher incidence of liver injury. In conclusion, early hemadsorption with cytokine adsorbers during open-heart surgery with prolonged CPB may be beneficial. It has the potential to reduce the occurrence of AKI and decrease the need for renal replacement therapy. Further research is needed to validate these findings and assess long-term outcomes [15].

In summary, several studies have reported positive outcomes with CytoSorb in emergency cardiac surgery, including shorter operative times, lower blood transfusions, and shorter intensive care unit stays. The use of CytoSorb has also been associated with cost savings in patients treated with ticagrelor or rivaroxaban before surgery. However, the current evidence is limited to case series and observational studies, few RCTs and larger randomized

trials are needed to establish the regular use of CytoSorb in on-pump cardiac surgery.

Future Directions

Long-term Benefits and Safety

Further research and large-scale clinical trials are needed to establish the long-term benefits and safety profile of the CytoSorb filter during CPB. These studies should include a diverse range of patients and evaluate outcomes over an extended period to assess the sustained impact of CytoSorb therapy on inflammation, organ function, and overall patient outcomes.

Patient Selection and Individualized Management

It should focus on identifying patient characteristics and disease severity factors that can help guide the appropriate use of CytoSorb therapy. Developing risk scores or predictive models could assist in identifying high-risk patients who are most likely to benefit from CytoSorb treatment. Additionally, exploring the optimal timing, duration, and dosage of CytoSorb therapy tailored to individual patient needs could enhance the effectiveness of treatment.

Comparative Studies

Conducting comparative studies between CytoSorb therapy and other interventions used during cardiopulmonary bypass procedures would provide valuable insights into its relative efficacy and safety. Comparisons with alternative cytokine filters or immunomodulatory therapies could help determine the most effective approach for attenuating the inflammatory response and improving patient outcomes.

Standardization and Guidelines

Developing standardized protocols and guidelines for incorporating the CytoSorb filter into cardiopulmonary bypass procedures would enhance its consistent and optimal use. These guidelines should consider various factors, including filter placement, configuration within the circuit, and monitoring parameters. Collaborative efforts among healthcare professionals, including perfusionists, cardiac surgeons, and intensivists, would be essential in formulating comprehensive guidelines.

Other Cardiac Surgery Applications

Exploring the potential benefits of the CytoSorb filter in other cardiac surgery scenarios, such as left ventricular assist device implantation, heart transplantation, or complex congenital heart surgeries, would expand its clinical utility. Investigating its impact on outcomes specific to these procedures and patient populations would help identify additional areas where CytoSorb therapy can be beneficial.

Conclusion

The CytoSorb filter has emerged as a promising tool in addressing inflammatory responses during cardiac surgery procedures. Multiple studies have demonstrated its potential in reducing pro-inflammatory cytokines, improving hemodynamic stability, and potentially reducing complications in various applications involving cardiopulmonary bypass. It is crucial for healthcare professionals to remain updated with the evolving literature and guidelines to effectively incorporate CytoSorb therapy into clinical practice.

To optimize outcomes, collaborative decision-making, individualized patient management, and close monitoring are essential when utilizing the CytoSorb filter. While the available evidence showcases the potential benefits, further research is necessary to fully comprehend its efficacy, safety, and optimal utilization in different patient populations and surgical contexts. Continued investigation and exploration will provide valuable insights into the precise role and impact of CytoSorb in managing systemic inflammation during CPB ultimately enhancing patient outcomes and refining clinical protocols.

References

1. Vocelka CR, Jones KM, Mikhova KM, Ebisu RM, Shar A, et al. (2013) Role of cytokine hemoadsorption in cardiopulmonary bypass-induced ventricular dysfunction in a porcine model. The journal of extra-corporeal technology 45: 220-227.
2. Träger K, Skrabal C, Fischer G, Datzmann T, Schroeder J, et al. (2017) Hemoadsorption Treatment of Patients with Acute Infective Endocarditis during Surgery with Cardiopulmonary Bypass - A Case Series. The International Journal of Artificial Organs 40: 240-249.
3. Poli EC, Alberio L, Bauer-Doerries A, Marcucci C, Roumy A, et al. (2019) Cytokine clearance with CytoSorb® during cardiac surgery: a pilot randomized controlled trial. Critical Care 23: 108.
4. Hassan K, Kannmacher J, Wohlmuth P, Budde U, Schmoeckel M, et al. (2019) Cytosorb Adsorption During Emergency Cardiac Operations in Patients at High Risk of Bleeding. The Annals of Thoracic Surgery 108: 45-51.
5. Diab M, Platzer S, Guenther A, Sponholz C, Scherag A, et al. (2020) Assessing efficacy of CytoSorb haemoadsorber for prevention of organ dysfunction in cardiac surgery patients with infective endocarditis: REMOVE-protocol for randomised controlled trial. BMJ Open 10: e031912.
6. Diab M, Lehmann T, Bothe W, Payam Akhyari, Platzer S, et al. (2022) Cytokine Hemoadsorption During Cardiac Surgery Versus Standard Surgical Care for Infective Endocarditis (REMOVE): Results From a Multicenter Randomized Controlled Trial 145: 959-968.
7. Naruka V, Salmasi MY, Arjomandi Rad A, Marczin N, Lazopoulos G, et al. (2022) Use of Cytokine Filters During Cardiopulmonary Bypass: Systematic Review and Meta-Analysis. Heart, Lung and Circulation 31: 1493-1503.
8. Alarie M, Savelberg M, Vautour D, Ribeiro IB (2022) Use of CytoSorb® hemoadsorption column during prolonged cardiopulmonary bypass in complex cardiac surgery patient. Journal of Cardiothoracic Surgery 17: 172.
9. Ng Yin Ling C, Umakumar K, Moss L, Stock UA, Raja SG, et al. (2022) Cytosorb® haemoadsorption: a potential game changer for patients needing myocardial surgical revascularisation. Vessel Plus 6: 6.
10. Sören Becker, Hannah Lang, Clara Vollmer Barbosa, Zhejia Tian, Anette Melk (2023) Efficacy of CytoSorb®: a systematic review and meta-analysis 27: 215.
11. Amer Harky, Abdul Badran (2021) Reducing antithrombotic-related bleeding risk in urgent and emergency cardiac surgery. British Journal of Cardiology 28: 26.
12. Koster A, Warkentin H, von Dossow V, Morshuis M (2022) Use of the CytoSorb® filter for elimination of residual therapeutic argatroban concentrations during heparinized cardiopulmonary bypass for heart transplantation. Perfusion 38: 1088-1091.
13. Doukas P, Hellfritsch G, Wendt D, Magliani M, Barbati ME, et al. (2023) Intraoperative Hemoadsorption (CytosorbTM) during Open Thoracoabdominal Aortic Repair: A Pilot Randomized Controlled Trial. Journal of Clinical Medicine 12: 546.
14. Moresco E, Hannes Dejaco, Humbert V, Thoma M (2023) The use of CytoSorb® in a prasugrel-loaded patient undergoing emergent coronary artery bypass graft surgery 11: e6990.

15. Lesbekov T, Nurmykhametova Z, Kaliyev R, Kuanyshbek A, Faizov L, et al. (2023) Hemadsorption in patients requiring V-A ECMO support: Comparison of Cytosorb versus Jafron HA330. Artif Organs 47: 721-730.