Educational Article

Patient Blood Management from the Perspective of Cell Salvage

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Abstract:

Background and Objective: The reliance on allogeneic blood during high-risk surgical procedures, particularly in cardiac surgery, presents significant challenges for healthcare systems. Complications associated with blood transfusions—including increased susceptibility to infections, immune reactions, coagulopathies, and prolonged hospital stays—emphasize the urgent need for effective patient blood management (PBM) programs. Cell salvage (CS) has emerged as a crucial component within the PBM framework, enabling the collection, washing, and reinfusion of autologous blood. This study aims to provide a comprehensive review of the clinical evidence regarding the safety, efficacy, and advantages of using CS in cardiac surgery.

Materials & Methods: This study employs a narrative review approach, utilizing searches across multiple databases, including Google Scholar, PubMed, ScienceDirect, and Cochrane. A comprehensive examination of the published literature related to CS—comprising clinical evaluations, laboratory studies, and systematic reviews—was performed. No temporal restrictions were applied, and inclusion criteria focused on studies relevant to cardiac surgery and the application of CS in minimizing allogeneic blood consumption.

Results: The reviewed studies consistently demonstrate that the implementation of CS significantly reduces the need for allogeneic blood transfusions, thereby mitigating complications associated with transfusions. Notably, the use of CS enables the recovery of packed red blood cells (PRBCs) with reduced levels of inflammatory mediators, including various cytokines, potentially alleviating postoperative inflammatory responses. Importantly, CS has not been associated with an increased risk of infection transmission or the development of infections. Furthermore, assessments of the coagulation profile of blood processed through CS indicate that the resulting PRBCs maintain normal coagulation factors and do not contribute to thrombotic events. However, it is crucial to adhere to established guidelines recommending coagulation profile assessments and the administration of fresh frozen plasma (FFP) in cases of blood loss exceeding 1000 milliliters, typically at an FFP-to-blood ratio of 1:1.

Conclusion: The findings confirm that CS is a highly effective blood management strategy that significantly reduces allogeneic blood consumption and its associated complications. The observed reduction in inflammatory markers, absence of increased infection risk, and preservation of coagulation profiles further underscore the safety and efficacy of this approach. Therefore, incorporating CS into surgical protocols—particularly for procedures involving moderate to severe bleeding—may improve clinical outcomes and decrease reliance on allogeneic blood products. Additionally, economic analyses from countries with established PBM programs demonstrate substantial reductions in hospital and transfusion-related costs.

Keywords: Blood Transfusion, Autologous, Inflammation Mediators, Hematopoietic Stem Cell Transplantation

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Background and Objective

Blood transfusions are among the most critical clinical interventions performed in healthcare facilities worldwide. However, due to the limited availability and high cost of blood, inefficient and irrational use can significantly increase healthcare expenditures. To address this issue, governments have implemented various strategies aimed at optimizing blood utilization and raising public awareness about the true costs of blood production and processing.[1] Central to these efforts is a comprehensive Patient Blood Management (PBM) program designed to reduce dependence on allogeneic blood. Key components of this program include preoperative autologous donation, erythropoietin administration, cell salvage (CS), and the training of healthcare professionals.

PBM is a multidisciplinary approach designed to optimize care for patients requiring blood transfusions. This strategy emphasizes several measures to reduce allogeneic blood consumption, including the management of anemia without transfusions, the use of antifibrinolytic agents to minimize bleeding, and the utilization of CS, among other interventions.[2] Evidence[3] suggests that adopting CS and other alternative methods to decrease allogeneic transfusions during surgical procedures is not only clinically effective but also economically beneficial, leading to lower costs and fewer transfusion-related complications.

According to the World Health Organization, approximately 112.5 million units of blood are transfused globally each year. Alarmingly, it is estimated that over 50% of all medical interventions are prescribed inappropriately. A study conducted in the United States in 2016 revealed that more than half of blood transfusions were administered without proper indications,[4] leading to an economic burden of $860,000 for the healthcare system across 1,092 blood units. The annual costs associated with blood supply and its components continue to escalate. While most countries depend on voluntary blood donations, expenses related to collection, testing, processing, distribution, human resources, and incident reporting have increased considerably. Research conducted in the United States in 2010 indicated that the actual costs incurred for blood in clinical settings are estimated to be 3.2 to 4.8 times higher than earlier projections.[5] This study suggested that, when accounting for all aspects of blood logistics, the estimated cost of transfusing a single unit of red blood cells (RBCs) ranges from $700 to $1,200.

Despite advancements in surgical techniques and pharmacological interventions, the demand for blood transfusions in cardiac surgery remains significant.[6] Multiple factors contribute to this need, including complications related to surgical procedures, dilution of RBCs, platelets, and clotting factors, impaired platelet function, and activation of coagulation and fibrinolytic systems.[7] A study conducted in 2017 analyzed blood usage at Modarres Hospital in a cohort of 96 cardiac surgery patients[8] and found an average consumption of 3.3 units of packed red blood cells (PRBCs) per patient.

The complications associated with blood transfusions in cardiac surgery are significant and include immunosuppression, renal dysfunction, pneumonia, and increased susceptibility to infections. A study by Paone et al.[9] in 2014 demonstrated that transfusions of even one or two units of PRBC substantially increased mortality rates and healthcare costs for cardiac surgery patients. Moreover, another study estimated the risk of mortality per unit of transfused allogeneic blood to be approximately 0.5%.

In this context, the application of CS during cardiac surgery is an integral component of a multidisciplinary PBM program that necessitates collaboration among surgeons, anesthesiologists, and perfusionists. CS systems enable the collection and processing of blood from the surgical field, allowing for the reinfusion of autologous PRBC back into the patient. The Iranian Blood Transfusion Organization

endorses CS in its national blood care guidelines as a validated method to reduce allogeneic blood transfusion during and after surgical procedures.[10]

Research indicates that the implementation of CS can significantly reduce the need for allogeneic blood transfusions in cardiac surgery. The risks and complications associated with CS, such as immune responses, transfusion reactions, and infection rates—are relatively infrequent compared to those linked to allogeneic blood transfusions. However, it is crucial to avoid suctioning blood from contaminated sources during CS procedures. Although postoperative bleeding is a common complication of cardiac surgery, studies indicate that the use of CS does not increase the risk of bleeding. In summary, blood processed through CS is considered safe for patient reinfusion.

Materials and Methods

This study employed a narrative review methodology, utilizing searches conducted across multiple databases, including Google Scholar, PubMed, ScienceDirect, and the Cochrane Library. A comprehensive examination and analysis were performed on a range of published studies relevant to cardiac surgery, encompassing clinical evaluations, laboratory investigations, and systematic reviews. No temporal restrictions were applied to the inclusion criteria; all studies focused on the role of CS in reducing allogeneic blood transfusion. The heterogeneity of research methodologies, study variables, and reported outcomes precluded the possibility of conducting a meta-analysis. Consequently, data integration was performed qualitatively, with findings categorized into key thematic areas: reduction of blood consumption, quality of RBCs, safety considerations, and clinical outcomes.

The results were organized around several prominent themes, including the quality of recovered RBC products, the extent of reduction in RBC consumption, clinical outcomes for surgical patients, safety considerations related to the application of CS, and the practical and technical implications of implementing this technology. Furthermore, an assessment was conducted on the economic impacts of PBM, encompassing reductions in direct costs associated with blood procurement, storage, and transfusion, as well as decreases in indirect costs resulting from transfusion-related complications, shortened hospital stays, and improved resource efficiency. Evidence indicates that the implementation of PBM strategies and the judicious application of CS can significantly enhance cost-effectiveness in surgical interventions, reduce the financial burden on healthcare systems, and promote the economic sustainability of healthcare facilities, particularly in resource-constrained settings. This review thoroughly examines clinical trends, benefits, limitations, and the economic implications of PBM, providing a comprehensive overview of its role in improving the quality of care and the economic efficiency of healthcare services.

The considerable variability in research design, measurement methodologies, evaluation criteria, and types of reported data made a meta-analysis impractical. Consequently, the data were qualitatively synthesized to provide a deeper understanding of the findings. Key outcomes emphasized the impact of CS on reducing allogeneic blood consumption, the factors influencing the quality of recovered RBCs, the safety of CS utilization, and the clinical outcomes for patients undergoing cardiac surgery. Moreover, trends and notable observations regarding the application of CS across various clinical settings were highlighted to enhance our understanding of this technology.

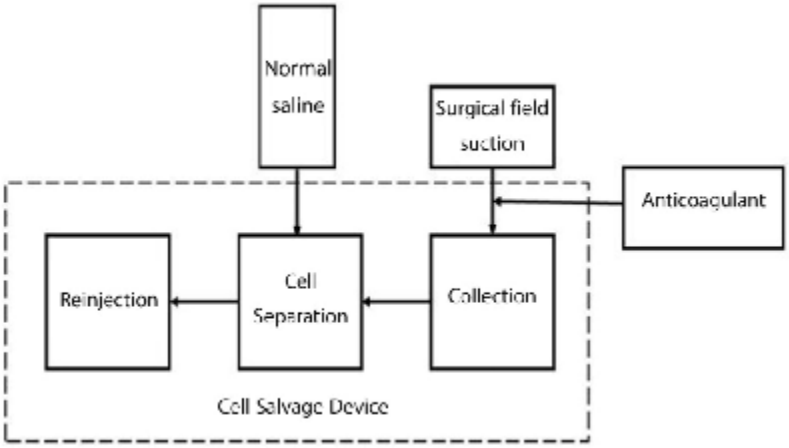

Figure 1- Schematic of the cell salvage process

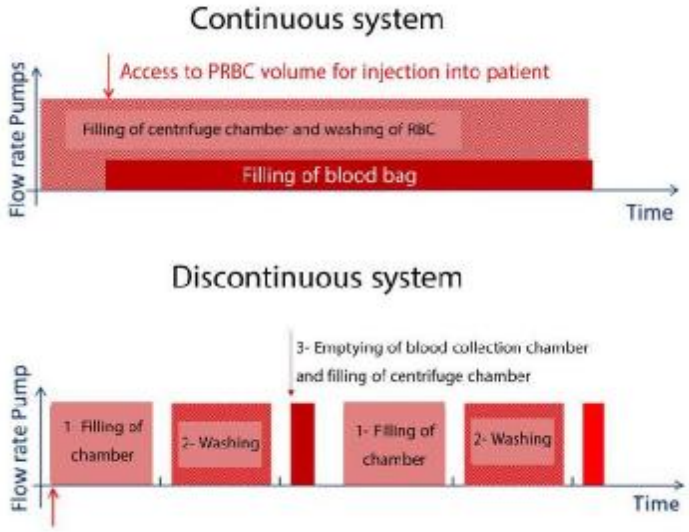

Figure 2- Comparison of RBC separation time in two systems

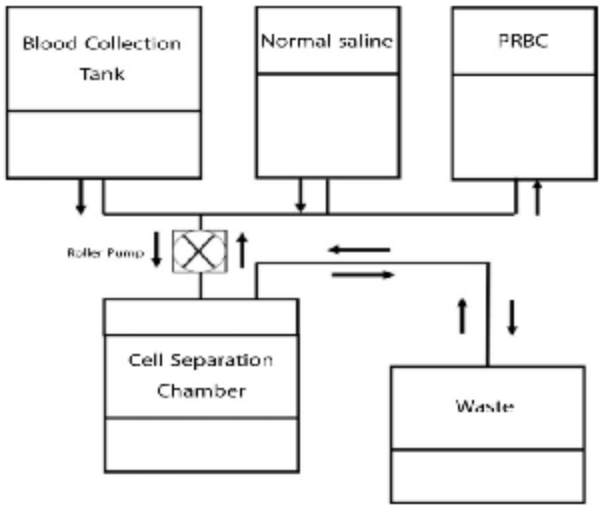

Figure 3- Mechanism of operation of discontinuous systems

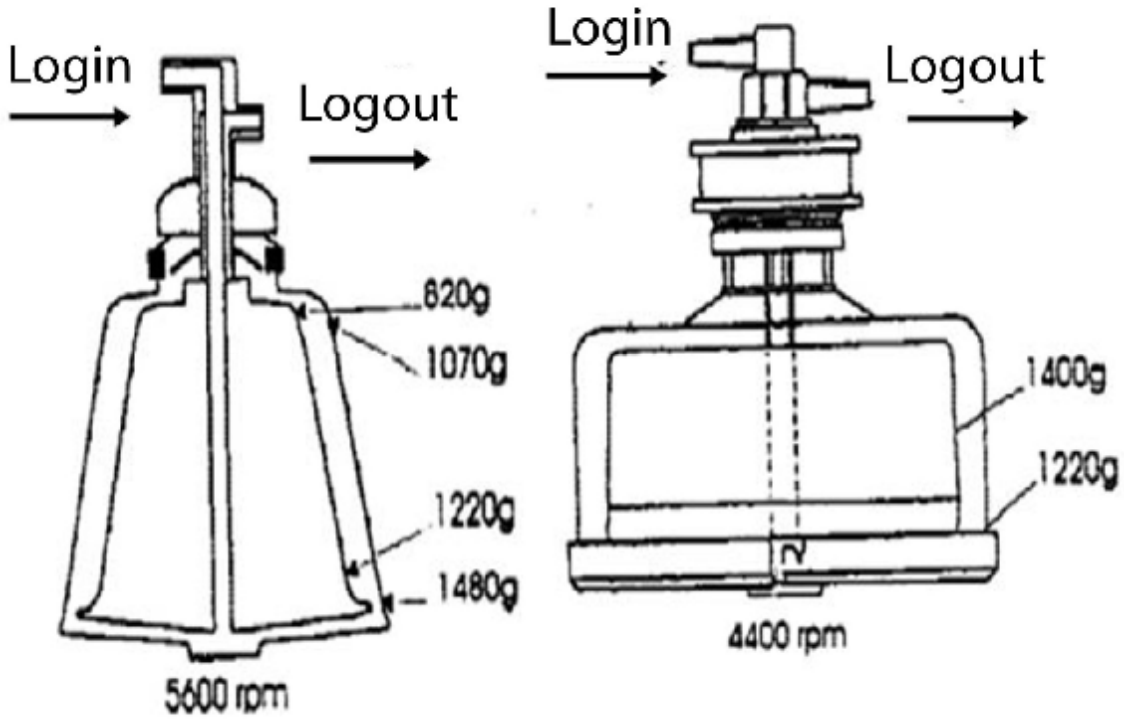

Figure 4- Schematic of the cell separation chamber in the Latham-Bowl intermittent systems

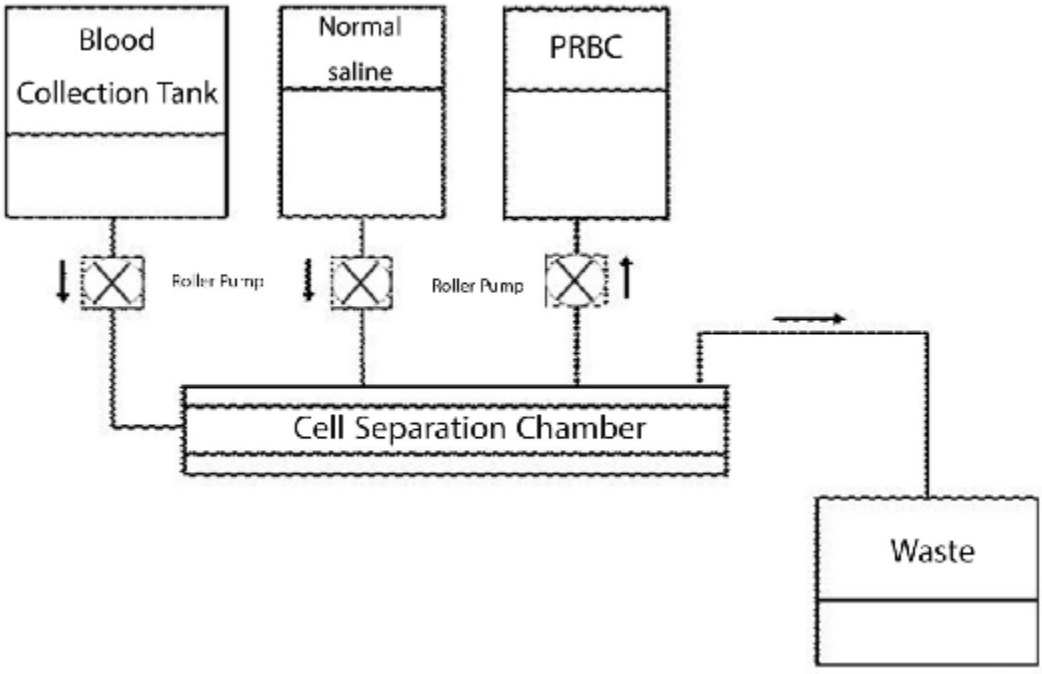

Figure 5- Mechanism of operation of continuous systems

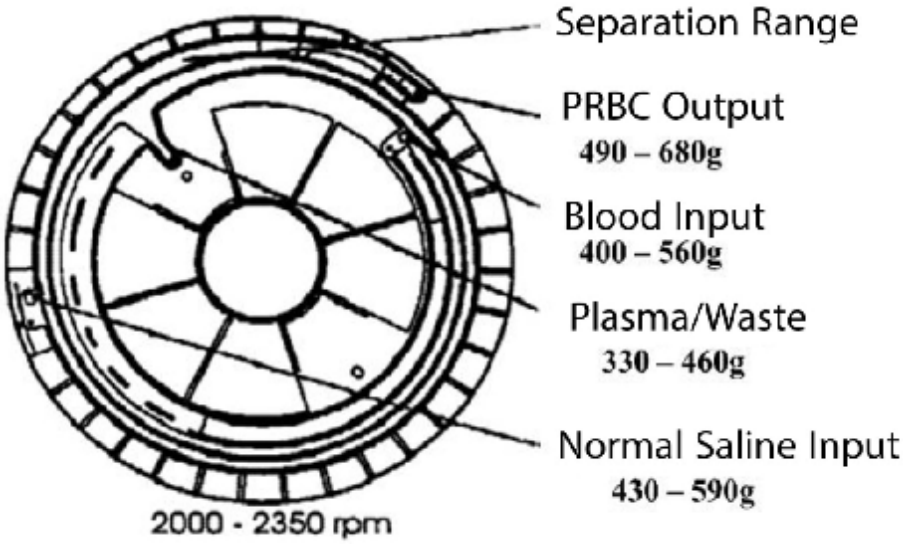

Figure 6- Schematic of cell separation protection in continuous systems

The CS Process

The CS process refers to a procedure in which blood, typically discarded during surgical interventions, is collected, and RBCs are separated from other blood components using a centrifuge-based system. The outcome of this procedure is the production of PRBCs. As shown in Figure 1, this technique has the potential to significantly reduce the need for allogeneic blood transfusions.

CS systems are classified into two categories: continuous and intermittent. The distinction between these systems is primarily based on their blood processing efficiency and speed. Figure 2 summarizes the differences between the two systems regarding the time required to fill the chamber and access the PRBCs. Importantly, there is no variation in the quality of processed blood (as detailed in Table 1); the differentiation primarily relates to the methodologies employed for blood processing.

Intermittent Systems

In intermittent systems, the CS process is executed sequentially, with the cellular separation chamber activated only after it has been partially or fully filled with blood.

Accurate estimation of the anticipated blood loss during surgery is crucial for selecting the appropriate consumable set for this system. Blood is continuously collected from the surgical field until the cellular separation chamber reaches its capacity. A single roller pump transfers blood from the collection reservoir, along with normal saline, into the cellular separation chamber, ultimately resulting in the collection of PRBCs into blood bags. Figure 3 demonstrates the operational mechanism of intermittent systems, while Figure 4 illustrates the cellular separation chamber utilized in these systems, commonly known as the Latham bowl, along with other similar devices, such as apheresis and plasmapheresis machines, which function as cell separators.

Continuous Systems

Continuous systems enable the simultaneous execution of blood collection, washing, and reinfusion. This technology employs three independent roller pumps that aid in transferring blood from the collection chamber, normal saline, and processed PRBCs. This independence permits streamlined operations, enhancing efficiency during critical procedural contexts.

Figure 6 presents a schematic representation of the cellular separation chamber utilized in continuous systems. The centrifugal speeds for isolating pRBCs range

from 2000 to 2350 rpm, classified within the soft spin range. The chamber has a volume capacity of approximately 30 milliliters, enabling continuous cellular separation and allowing the extraction of PRBCs concurrently as blood enters the system. Furthermore, this chamber can process platelet gel and plasma derived from the waste bag. Table 1 details the quality of the blood output produced by the device.[11]

Table 1- Quality of blood processed by cell salvage

Blood components	*Amount*
Hematocrit	*Above 60%*
Heparin	*Above 95%*
Potassium	*Above 95%*
Free hemoglobins	*Above 95%*
Albumin	*Above 95%*
Unsaturated fats	*Above 99%*

Indications for CS

The Association for the Advancement of Blood & Biotherapies (AABB) has outlined specific indications for the use of CS, which include:[12]

- Patients expected to lose more than one liter of blood or over 20% of their total blood volume during or after surgical procedures.
- Patients with low hemoglobin levels who are at an increased risk of significant hemorrhage.
- Patients with rare blood types that may complicate transfusion options.
- Patients with medical conditions that contraindicate the use of allogeneic blood transfusions.

Advantages of CS During Surgery

- Reduction in Allogeneic Transfusions: CS significantly decreases the necessity for allogeneic blood transfusions and the complications associated with them.
- Improved Clinical Outcomes: Patients receiving CS-derived blood products exhibit a lower incidence of non-fatal myocardial infarctions and postoperative infections.[13]
- Preservation of RBC Morphology: The biconcave morphology of RBCs is maintained during the CS process. In contrast, allogeneic blood undergoes morphological changes to echinocytes after 14 days, which impairs their ability to navigate capillary beds. This results in a greater demand for oxygenation capacity in patients receiving allogeneic transfusions.[14]
- Enhanced Erythrocyte Longevity: Comparative studies indicate a greater median survival rate of erythrocytes processed via CS, accompanied by elevated levels of 2,3-diphosphoglycerate (2,3-DPG) and adenosine triphosphate (ATP). The median erythrocyte survival rate for CS has been reported to be approximately 88%.[15]
- Economic Benefits: A meta-analysis conducted in collaboration with Cochrane in 2006 confirmed that the application of CS in elective adult surgeries led to a 39% reduction in allogeneic blood transfusions, resulting in an average savings of 0.67 units per patient.[16]

Risks and Complications Associated with CS

The risks associated with CS are considerably less prevalent compared to those linked with allogeneic blood transfusions, particularly concerning immune responses and transfusion reactions. Research indicates that the use of CS does not correlate with an increased incidence of complications in patients receiving autologous blood transfusions during cardiac procedures.[17] A study conducted by Domen[18] at the Cleveland Clinic in 1998 reported an adverse event rate of merely 0.027% associated with CS. Potential risks related to CS include non-immune hemolysis, air embolism, non-hemolytic febrile reactions, and contamination from cleaning agents or infectious agents, all of which may trigger leukocyte and cytokine activation, as well as the formation of harmful microaggregates. Fortunately, many of these risks have been

mitigated due to significant technological advancements and improved training for staff and technicians.[19]

In contrast to allogeneic blood transfusion, both autologous blood transfusion and CS significantly reduce the risk of allergic reactions, infections, disease transmission, and immune system suppression.[20] Transfusions, irrespective of type, can introduce non-physical cellular contact with external surfaces, such as blood transfer tubes, which may elevate white blood cell (WBC) counts in peripheral blood and enhance the expression of polymorphonuclear (PMN) CD11b. Activation of CD11b stimulates WBCs to produce reactive oxygen species, various proteases, and inflammatory mediators, potentially resulting in damage to vital organs, particularly the lungs.[21]

The modulation of inflammatory factors can positively impact patient outcomes; a decrease in these factors correlates with improved health, whereas an increase is associated with higher mortality rates.[23] A 2004 study demonstrated that leukocyte reconstitution in continuous CS systems was significantly lower than in discontinuous systems.[24] To further reduce inflammatory responses during cardiac surgeries, strategies such as using leukocyte depletion filters (LDF) in heart-lung pumps and CS systems have proven effective in reducing inflammatory levels.[23,25]

A recent study involving 175 patients undergoing cardiac surgery found that routine blood re-filtration in CS did not yield significant differences compared to procedures without it.[26] Additionally, a 2018 study by Lili Xu and colleagues, involving 60 patients,[27] suggested that employing CS in conjunction with LDF resulted in an increased release of dynamic CRS, OI, RI, and SOD, while simultaneously decreasing the release of WBCs, PMNs, NE, SP-A, MDA, IL-6, IL-7, and TNF-α.

The utilization of a heart-lung machine during cardiac surgery has been shown to increase levels of inflammatory factors. A study by Prieto et al. (2013), involving 57 cardiac surgery patients, demonstrated that the application of CS did not result in elevated inflammatory responses after surgery.[21]

Various studies and guidelines on blood management advocate using CS suction rather than cardiotomy suction from the heart-lung pump, as this practice can substantially reduce inflammatory markers, including cytokines. However, some investigations have reported no significant differences in the reduction of inflammatory responses between these two suction techniques.[21]

Microbiology of CS

There is a bidirectional relationship between the volume of allogeneic RBC transfusions and the risk of infection transmission. Specifically, the risk of infection increases by an average of 29% with each additional unit of RBC transfused. While some univariate analyses suggest an elevated risk of infection associated with platelet transfusions, this risk decreases when more than four units of RBCs are administered.[28] Importantly, the use of CS has not been associated with an increased risk of infection.[29] A recent study of blood transfusion strategies in the operating room found that suctioning contaminated blood, including intestinal contents, can increase concentrations of viable bacteria. However, laboratory studies in animal models indicated that the incidence of sepsis associated with CS remained unchanged. Furthermore, a 2007 study involving 38 patients at high risk of infection—predominantly from microorganisms such as Staphylococcus (73%), E. coli (4%), Propionibacterium (4%), and Candida (8%)—detected no pathogens in processed blood up to three days after CS.[30]

The benefits of re-filtration using leukocyte depletion filters (LDF) in minimizing microbial contamination in CS have been substantiated, with findings indicating a significant reduction in contamination risk.[31] However, a 2019 study involving 175 cardiac surgery patients revealed no significant difference in microbial contamination rates between

routinely re-filtered CS blood and non-re-filtered blood.[26]

Ultimately, the most effective strategy for mitigating infection risk in CS involves controlling the source of incoming blood, particularly by avoiding suctioning from contaminated areas.

Postoperative Bleeding

Postoperative bleeding is a common complication following cardiac surgery, influenced by numerous factors, including preoperative medications, the effects of the heart-lung machine—which can induce thrombocytopenia and impair platelet function—use of anticoagulants, hyperfibrinolysis, and residual heparin effects. It is estimated that approximately 2% to 8% of patients undergoing cardiac surgery require reoperation to manage bleeding-related complications.[32]

During blood processing by the cardioplegia system, platelets, coagulation factors, and anticoagulants (such as heparin) are removed, resulting in processed blood bags that predominantly contain RBCs, with hematocrit (HCT) levels ranging from 60% to 80% in saline. Various studies indicate that the removal rate of residual heparin from blood processed by the CS system exceeds 95%. Research conducted in 2004,[33] along with additional investigations from 2019 evaluating the coagulation profiles of CS-processed blood,[34] has demonstrated that PRBCs do not adversely affect coagulation. Furthermore, a study conducted in 2008, involving 213 patients undergoing their initial cardiac surgery,[35] confirmed that the employment of CS was not associated with an increased incidence of re-bleeding complications.

The guidelines published by the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Cardiothoracic Anesthesiology (EACTA) in 2017 advise caution,[29] indicating that processing more than 1,000 milliliters of blood through the CS system may lead to coagulation-related complications. Recent literature on blood transfusion strategies advocates for a 1:1 transfusion ratio of PRBCs to fresh frozen plasma (FFP) to prevent coagulopathy in cases of severe bleeding. Additionally, the 2018 guidelines from the UK Anesthesia Society restrict the use of CS during cardiac surgery to periods when the patient is not receiving heparin,[37] recommending that CS be utilized exclusively before and after the implementation of the heart-lung machine. This precaution is necessary because cardiotomy suction during heart-lung machine use directly conveys all blood components, including platelets and coagulation factors, into the machine's reservoir. Typically, a residual volume of approximately 500 to 1,000 milliliters of blood remains in the heart-lung machine reservoir and tubing following the procedure, which may be processed via CS. A study conducted by Muraki in 2019 found that approximately 583 milliliters of blood could be retrieved from the heart-lung machine reservoir for processing via CS.[38] The results indicated that this approach significantly reduced the need for allogeneic blood and FFP transfusions, with no reported complications related to rebleeding, infections, or inflammation among the 145 participants. The EACTS/EACTA guidelines,[36] in conjunction with findings from various studies, suggest that the utilization of cardiotomy suction may potentially affect thrombin production, neutrophil activation, and platelet functionality, thereby increasing the demand for blood transfusions. Therefore, it is imperative to establish a judicious balance between the beneficial effects of CS and the potential coagulopathy that may result from the loss of plasma and coagulation factors associated with the volume of blood processed by CS.

Economic Evidence Supporting the Implementation of PBM Programs: International Perspectives

The financial foundation of PBM programs primarily stems from the economic benefits generated by their implementation. These programs are strategically designed to achieve considerable cost savings for hospitals by reducing expenses related to the procurement of blood products, disposal of blood product waste, laboratory services,

and management of adverse events.[39] For instance, a PBM initiative launched in Canada, with findings published in 2008, provided robust cost-effectiveness data for elective surgical procedures.[40] This program had a budget of 21 million Canadian dollars distributed across 23 hospitals. Over 12 months, substantial reductions in blood utilization were reported: a 24% decrease in total knee arthroplasties, a 14% reduction in abdominal aortic surgeries, and a 23% decrease in coronary artery bypass grafting. The program's annual expenditure was estimated at 1.8 million dollars, resulting in total savings of approximately 8.64 million dollars. Similarly, a comprehensive PBM program initiated in Western Australia in 2008 lasted four years and yielded an estimated 41% reduction in the utilization of allogenic blood.[41] An investment of 4.5 million dollars in this program translated into savings of nearly 18 million dollars. Collectively, these initiatives generated savings estimated between 80 and 100 million dollars, representing an approximate 10% reduction in national blood transfusion costs. Throughout implementation, notable improvements in patient outcomes were also observed, including a 28% reduction in hospital mortality rates, a 15% decrease in average length of hospital stays, a 21% decline in infection rates, a 31% reduction in stroke occurrences, and a 6% decrease in readmission rates. In Switzerland, a three-year PBM program, initiated in 2015,[42] successfully achieved a 27% reduction allogeneic blood utilization, resulting in savings of $84 per patient and a total savings of $2 million within just one year.

Furthermore, a study conducted by Kotzé and colleagues in 2012 at a public hospital in England evaluated 717 primary hip and knee arthroplasties.[43] Within the framework of this PBM initiative, the blood transfusion rate significantly declined from 23% to 8%. Additionally, patients experienced reductions in hospital stays, with the duration of total hip replacement surgeries decreasing from 6 days to 5 days, and knee arthroplasty stays reducing from 6 days to 4 days. The cumulative savings for this patient cohort were estimated at £160,000.

Conclusion

PBM is a comprehensive, interdisciplinary strategy aimed at conserving patient blood while optimizing the use of both allogeneic and autologous blood transfusion. A critical component of these programs is the application of cardiotomy suction during and after high-risk surgical procedures to effectively manage bleeding. The successful implementation of such methodologies requires the availability of CS devices within healthcare institutions. Research consistently demonstrates that the use of CS during surgery not only significantly reduces reliance on allogeneic blood but also decreases complications associated with allogeneic transfusions. Importantly, blood products processed through this method have been shown to be microbiologically safe and do not trigger immunological responses or transfusion reactions. Additionally, economic evaluations of PBM programs implemented in various countries emphasize the considerable cost savings associated with hospital and transfusion expenditures.

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