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Kardiyopulmoner Bypass'ta Kullanılan Prime Solüsyonların Organ Fonksiyonları Üzerindeki Etkileri

Effects of Prime Solutions Used in Cardiopulmonary Bypass on Organ Functions

Gülşah Çelik Korhan[1*]

[*1]Harran University, Perfusion Technology, Şanlıurfa, Türkiye, gulsahcelik4861@gmail.com, ORCID: 0009-0001-2949-6287

ÖZET

Kardiyopulmoner bypass (KPB), özellikle kalp cerrahisinde yaygın olarak kullanılan bir yöntemdir ve bu süreçte kullanılan prime solüsyonları, devrenin doldurulması, hemodinamik dengenin sağlanması, elektrolit ve sıvı dengesinin korunması ile organ perfüzyonunun optimize edilmesinde kritik bir rol oynamaktadır. Prime solüsyonlarının içeriği, kullanılan kristalloid veya kolloid türleri, kan bazlı çözeltiler ve eklenen mannitol, albumin gibi katkı maddeleri, hemodinamik yanıtları, inflamatuar süreçleri ve organ fonksiyonlarını doğrudan etkileyebilmektedir. Mevcut bulgular, prime stratejisinin böbrek, nörolojik, pulmoner ve kardiyak fonksiyonlar üzerinde anlamlı etkiler oluşturabileceğini ortaya koymaktadır. Özellikle böbrek fonksiyonları ile ilgili çalışmalar, prime solüsyonlarının akut böbrek hasarı (AKI) riskini etkileyebileceğini göstermektedir. Nörolojik fonksiyonlar açısından, hemodilüsyon derecesi ve prime bileşimi, postoperatif bilişsel değişiklikler üzerinde rol oynayabilmektedir. Pulmoner ve kardiyak parametrelerde de prime içeriğine bağlı farklılıklar gözlemlenmiş, albumin eklenmesi gibi bazı stratejilerin sıvı dengesini düzenleyip postoperatif komplikasyonları azaltabileceği bildirilmiştir. Öte yandan, mannitol gibi katkı maddelerinin renal koruyucu etkileri sınırlı ve çelişkili sonuçlar vermekte, kanlı prime uygulamaları ise inflamatuar yanıtı artırabilmektedir. Prime solüsyonlarının uzun dönem organ fonksiyonları üzerindeki etkilerini değerlendiren çalışmalar oldukça azdır. Çoğu araştırma kısa veya orta dönem sonuçlara odaklanmış olup, randomize kontrollü uzun dönem veriler sınırlıdır. Bu durum, KPB sırasında uygulanan prime stratejilerinin uzun vadeli klinik sonuçlarını anlamayı güçleştirmektedir. Bu nedenle, uzun takip süreli, metodolojik açıdan standartlaştırılmış ve prospektif çalışmaların gerçekleştirilmesi, hem klinik uygulamalara rehberlik edecek kanıtların elde edilmesini hem de prime solüsyonlarının potansiyel risk ve faydalarının doğru şekilde değerlendirilmesini sağlayacaktır. Bu derlemenin amacı, kardiyopulmoner bypass sırasında kullanılan prime solüsyonlarının organ fonksiyonları üzerindeki etkilerini incelemek ve konuya ilişkin kapsamlı bir bakış sunmaktır.

Anahtar Kelimeler: Kardiyopulmoner bypass, Prime solüsyonu, Organ fonksiyonu, Hemodilüsyon, Akut böbrek hasarı

ABSTRACT

Cardiopulmonary bypass (CPB) is a widely used technique in cardiac surgery, and the priming solutions employed during this process play a critical role in filling the circuit, maintaining hemodynamic balance, preserving electrolyte and fluid homeostasis, and optimizing organ perfusion. The composition of priming solutions including crystalloids or colloids, blood-based solutions, and added agents such as mannitol or albumin can directly influence hemodynamic responses, inflammatory processes, and organ function. Evidence suggests that priming strategies may significantly affect renal, neurological, pulmonary, and cardiac functions. Specifically, studies on renal function indicate that priming solutions can influence the risk of acute kidney injury (AKI). Neurological outcomes are also affected by the degree of hemodilution and the composition of the priming solution, potentially contributing to postoperative cognitive changes. Variations in priming composition have been observed to impact pulmonary and cardiac parameters, with strategies such as albumin supplementation potentially improving fluid balance and reducing postoperative complications. On the other hand, the renoprotective effects of agents like mannitol remain limited and inconsistent, while blood-based priming may enhance inflammatory responses. Studies evaluating the long-term effects of priming solutions on organ function are scarce. Most research has focused on short- to medium-term outcomes, with limited randomized controlled data on long-term results. Consequently, understanding the long-term clinical implications of different priming strategies remains challenging. The purpose of this review is to examine the effects of priming solutions used during cardiopulmonary bypass on organ function and to provide a comprehensive overview of the topic.

Keywords: Cardiopulmonary bypass, Priming solution, Organ function, Hemodilution, Acute kidney injury

Sorumlu Yazar/Corresponding Author: Harran University, Perfusion Technology, Şanlıurfa, Türkiye, gulsahcelik4861@gmail.com, ORCID: 0009-0001-2949-6287

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INTRODUCTION

Cardiopulmonary bypass (CPB) is a technique that temporarily replaces the functions of the heart and lungs during surgery, thereby maintaining systemic circulation and oxygenation, and is most commonly utilized in cardiac surgery. During CPB, an appropriate priming solution facilitates the preparation of the circuit, oxygenator, and pump, removes air from the arterial line, and ensures adequate hemodilution (1). The priming solution can influence the physicochemical properties and homeostatic balance of the blood and may also modify the metabolic response when CPB is applied in cardiac surgery. Therefore, selecting an appropriate priming fluid is of great importance for patients requiring CPB. Although numerous studies and debates on CPB priming solutions have been conducted over the past decades, a definitive consensus on the optimal solution has yet to be established (2). Due to surgical requirements, most cardiothoracic procedures still rely on CPB, and the selection of an appropriate priming fluid is a critical prerequisite for initiating bypass. In clinical practice, priming solutions are commonly classified into two main groups: crystalloids and colloids. Crystalloids typically consist of balanced electrolyte solutions, occasionally containing glucose, and often include additional agents such as mannitol. Colloids, on the other hand, may contain human albumin (HA), dextran, gelatin, or hydroxyethyl starch (HES) (3). The efficacy of these fluids during CPB is variable, with each presenting distinct advantages and disadvantages. For instance, the use of HES during CPB can significantly affect the coagulation system, whereas HA does not induce coagulation dysfunction compared to HES; however, the high cost of albumin should be considered. When crystalloids are used as priming fluids, hemodilution occurs, which can reduce the colloids' oncotic pressure and lead to interstitial edema. Although colloids can maintain oncotic pressure, their extravasation into the interstitial space may increase the risk of edema. Additionally, the use of colloids may contribute to non-surgical bleeding (4). Furthermore, the marketing authorization for HES infusion solutions was suspended by the European Commission in 2022 due to the increased risk of renal injury and mortality in critically ill patients with sepsis. Nevertheless, opinions regarding the use of HES have always varied. Studies have provided conflicting evidence concerning the optimal choice among colloids, crystalloids, and the different types of fluids within these categories for CPB (5).

This review encompasses the literature examining the effects of priming solutions on organ functions during CPB. The literature search was conducted using PubMed, Scopus, and Web of Science databases, covering English and Turkish articles published between 2000 and 2025. The search keywords included "cardiopulmonary bypass," "priming solution," "organ

function," "hemodilution," "acute kidney injury," "neurological outcomes," and "pulmonary function."

Inclusion criteria comprised randomized controlled trials, prospective and retrospective cohort studies, and systematic reviews. Animal studies, case reports, and publications without full-text access were excluded. Data from the selected studies were comparatively evaluated in terms of priming solution types, volume, additive components, and their effects on organ functions. Additionally, metabolic and inflammatory responses were included within the scope of the review. Based on a total of 30 publications, the compiled data aim to systematically assess the effects of priming solutions on neurological, renal, pulmonary, and cardiac functions, as well as on metabolic and inflammatory responses.

Types and Effects of CPB Priming Solutions

Crystalloid Solutions

Crystalloid solutions are low-molecular-weight fluids composed of water and electrolytes. The most common examples include Ringer's lactate and isotonic NaCl solutions. These solutions are frequently preferred due to their low cost and wide availability. However, when administered in large volumes, they may cause hemodilution, which can adversely affect organ perfusion.

Colloid Solutions

Colloid solutions contain high-molecular-weight components and have the capacity to maintain intravascular volume for a longer duration. The main colloid solutions used in CPB include:

- **Albumin:** A natural plasma protein, albumin helps maintain fluid balance by preserving oncotic pressure. However, its high cost and limited availability are notable disadvantages.
- **Dextran:** Dextran, a synthetic polysaccharide, increases intravascular volume. Nevertheless, its use at high doses may lead to adverse effects such as anaphylaxis and renal injury.
- **Hydroxyethyl Starch (HES):** HES provides prolonged intravascular volume support; however, its use is limited due to potential negative effects on renal function and the risk of coagulation disturbances (6).

Retrograde Autologous Priming (RAP)

Retrograde autologous priming involves filling the CPB circuit with the patient's own blood. This approach reduces hemodilution, preserves oncotic pressure, and decreases the need for blood transfusions. RAP can be particularly effective in patients with a small body surface area. However, due to technical challenges and potential complications, careful implementation is

required. The clinical significance of this priming strategy becomes evident through its effects on various organ systems, which are examined in detail in the following section with respect to neurological, renal, pulmonary, and cardiac functions, as well as metabolic and inflammatory responses.

Sanguineous (Blood) Priming

Sanguineous priming involves filling the CPB circuit with either the patient's own blood or donor blood. This approach reduces hemodilution and helps maintain oncotic pressure. However, it may alter the coagulation properties of the blood and enhance the inflammatory response. Therefore, its use is limited and requires careful patient selection.

Combined Priming Strategies

In recent years, priming strategies involving combinations of different types of priming solutions have been investigated. For instance, the concurrent use of crystalloid and colloid solutions may enhance hemodynamic stability and improve organ perfusion. Additionally, colloid solutions used in conjunction with retrograde autologous priming can more effectively preserve oncotic pressure (7).

Effects of Priming Solution Types on Organ Functions

Effects on Neurological Function

Neurological complications arising during CPB, such as delirium, postoperative cognitive dysfunction, and, less frequently, stroke, are associated with multifactorial mechanisms. Among these, microemboli, systemic inflammation, cerebral hypoperfusion, and the degree of hemodilution are particularly prominent. Priming solution strategies can directly influence some of these mechanisms, particularly by modulating hemodilution through priming volume and oncotic pressure (8). Prospective studies have demonstrated that lower levels of hemodilution reduce the incidence of early postoperative cognitive dysfunction compared to moderate hemodilution. These findings support the neurocognitive rationale for strategies such as low-volume or modified circuits, as well as retrograde autologous priming (RAP). Priming with the addition of albumin may help maintain oncotic pressure, reduce the risk of cerebral edema, and contribute to the continuity of cerebral perfusion. Several reviews and meta-analyses indicate that albumin use can mitigate the effects of hemodilution and result in a less pronounced positive fluid balance. However, evidence that these physiological benefits consistently translate into long-term cognitive outcomes remains limited.

Mannitol has the potential to reduce cerebral edema due to its osmotic and free radical–scavenging properties. Nevertheless, data regarding the clinical neurocognitive benefits of adding mannitol during CPB are heterogeneous. Existing randomized studies have primarily

focused on renal function and postoperative delirium, without demonstrating a significant advantage in cognitive function. Therefore, routine neuroprotective use of mannitol is not currently supported (9).

Effects on Renal Function

Priming solutions used during CPB are critically important with respect to the development of acute kidney injury (AKI), as hemodilution, inflammation, and perfusion changes can directly impact renal function (10). Crystalloid solutions, commonly preferred in CPB, rapidly increase intravascular volume; however, excessive use may lead to hemodilution, elevate the risk of renal hypoperfusion, and consequently increase the incidence of AKI (11). In contrast, colloid solutions help maintain oncotic pressure, ensuring more prolonged intravascular volume stability. Nevertheless, solutions containing hydroxyethyl starch (HES) have been reported to exert adverse effects on renal function and may increase the risk of AKI (12).

Albumin-containing priming solutions also contribute to the maintenance of intravascular volume; however, consistent evidence supporting their ability to improve renal function is lacking. Some studies have indicated that albumin use does not provide a significant advantage for renal function and, in certain cases, may even have adverse effects (13).

Mannitol can be added to the priming solution due to its osmotic diuretic properties and theoretically may offer renoprotective effects. Nevertheless, current clinical data do not definitively demonstrate that mannitol improves renal function or reduces the risk of AKI; in some cases, it may even impose additional burden (14).

In summary, the effects of priming solutions used during CPB on renal function are highly complex and vary depending on factors such as the type and volume of the solution and the patient's clinical condition. Therefore, the selection of the priming solution should be made carefully, and patients' renal function should be closely monitored throughout the perioperative period.

Effects on Pulmonary Function

Priming solutions used during CPB can directly impact pulmonary function, as factors such as inflammation, oxygen radicals, and hemodynamic changes may cause lung injury. Therefore, the type, composition, and volume of the priming solution selected during CPB play a critical role in determining postoperative lung function.

Crystalloid solutions rapidly increase intravascular volume, providing hemodynamic stability; however, excessive use may lead to hemodilution and consequently pulmonary hypoperfusion. This can increase the risk of postoperative pulmonary edema and ventilation-perfusion mismatch, particularly in elderly patients (15).

Colloid solutions help maintain intravascular volume for a longer duration by preserving oncotic pressure, theoretically offering an advantage in pulmonary perfusion. Nevertheless, colloid solutions containing hydroxyethyl starch (HES) have been reported to induce inflammation and edema in the lungs, and their use is therefore limited (16).

Albumin-containing priming solutions also help stabilize intravascular volume and maintain oncotic pressure, thereby supporting pulmonary function. However, studies on the long-term effects of routine albumin use during CPB on pulmonary function are conflicting; some reports indicate that it does not improve postoperative lung function and may even have adverse effects (17). Mannitol can be added to the priming solution due to its osmotic diuretic properties and may theoretically contribute to pulmonary fluid balance. Nevertheless, current clinical data indicate that mannitol does not consistently provide benefit to pulmonary function during CPB and, in some cases, may exacerbate pulmonary edema and ventilation-perfusion mismatch (18).

Effects of Cardiopulmonary Bypass on Cardiac Functions

The priming solutions used during CPB may directly affect cardiac functions through hemodilution, alterations in vascular resistance, and microcirculatory disturbances. Therefore, the composition and characteristics of the selected solution play a critical role in determining postoperative cardiac performance (19).

Crystalloid solutions are the most commonly preferred option in CPB, as they rapidly expand intravascular volume and help maintain fluid balance. However, excessive use may lead to hemodilution, which, in combination with microcirculatory dysfunction, can result in transient impairment of cardiac functions. Moreover, crystalloids may enhance inflammation and endothelial dysfunction, both of which can negatively influence postoperative cardiac performance (20). Colloid solutions maintain oncotic pressure, thereby allowing intravascular volume to remain stable for a longer duration and theoretically improving cardiac output and organ perfusion. However, HES-containing colloids have been reported to exert adverse effects on cardiac function by enhancing inflammation and inducing endothelial dysfunction; thus, the use of HES is limited (21). Albumin-containing priming solutions also stabilize intravascular volume by preserving oncotic pressure and may support cardiac function. Nevertheless, the literature presents conflicting findings regarding the routine use of albumin during CPB; while some studies report improvements in cardiac performance, others fail to demonstrate significant benefit (22).

Mannitol can be added to the priming solution due to its osmotic diuretic properties and may theoretically support cardiac function. However, current studies indicate that its effects are inconsistent and, in some cases, may adversely affect cardiac performance (23). The impact of

priming solutions on cardiac function during CPB varies depending on the type and volume of the solution as well as the patient's clinical condition. Therefore, the selection of the priming solution should be made carefully, and the patient's cardiac function should be closely monitored throughout the perioperative period (24).

To summarize the effects of different priming solution types on organ function, Table 1 presents a comparative overview of the impacts of various priming solutions used during cardiopulmonary bypass on neurological, renal, pulmonary, and cardiac functions.

Table 1. Effects of Different Priming Solutions on Organ Functions During Cardiopulmonary Bypass

Priming Solution Type	Neurological Function	Renal Function	Pulmonary Function	Cardiac Function
Crystalloids	May cause hemodilution; can increase risk of postoperative cognitive dysfunction if used in high volumes	Rapid intravascular volume expansion; excessive use may lead to renal hypoperfusion and increased AKI risk	May cause pulmonary hypoperfusion and edema if overused	Hemodilution may reduce microcirculation and transiently decrease cardiac performance; may increase inflammation
Colloids	Maintain oncotic pressure; may reduce cerebral edema	Maintain intravascular volume longer; HES may increase AKI risk; albumin effects inconsistent	Stabilizes intravascular volume; HES may promote pulmonary inflammation	Maintain intravascular volume and cardiac output; HES may have negative effects, albumin effect variable
Albumin	Preserves oncotic pressure; may reduce cerebral edema risk	Helps maintain intravascular volume; renal protective effects not consistently proven	Stabilizes intravascular volume; pulmonary effects variable	Maintains cardiac performance; evidence mixed
Hydroxyethyl Starch (HES)	Limited neurological effects; potential for hemodilution	May increase risk of AKI and coagulation disturbances	Potential pulmonary inflammation and edema	Can adversely affect cardiac function via inflammation and endothelial dysfunction
Retrograde Autologous Priming (RAP)	Reduces hemodilution; may lower early postoperative cognitive dysfunction	Decreases need for transfusion; effects on AKI not fully established	Preserves intravascular volume; pulmonary benefits possible	Maintains cardiac output by limiting hemodilution
Sanguineous Priming	Maintains oncotic pressure; potential for inflammatory response	Reduces hemodilution; careful monitoring needed for renal function	Preserves intravascular volume; may increase inflammation	Maintains cardiac performance; inflammatory effects must be monitored
Mannitol Addition	May reduce cerebral edema; neuroprotective effect inconsistent	Theoretical renal protection; clinical evidence limited and variable	May contribute to pulmonary fluid balance; benefits inconsistent	May support cardiac function; effects inconsistent

Metabolic and Inflammatory Responses

During CPB, prolonged contact of blood with the artificial circuit, surgical trauma, and ischemia-reperfusion mechanisms elicit a pronounced systemic inflammatory response (SIRS). The intensity of this response depends on circuit design, the composition of the priming solution, circuit volume/hemodilution degree, and the duration of surgery. In the early phase, increases are observed in multiple pro-inflammatory cytokines, particularly IL-6, as well as in complement activation products (C3a, C5a) and adhesion molecules; elevated levels of these biomarkers have been associated with postoperative organ dysfunction, prolonged intensive care stay, and increased morbidity (25).

The physiological effects of priming (pump priming) strategies occur via two main mechanisms: the priming volume and degree of hemodilution influence tissue oxygen-carrying capacity and blood viscosity, while the colloid osmotic pressure (COP) of the priming solution regulates capillary leakage and interstitial fluid accumulation, thereby modulating edema formation (26). Current evidence indicates that retrograde autologous priming (RAP) and reduced "minimal" circuit approaches decrease hemodilution and reduce transfusion requirements. However, high-quality and consistent evidence supporting RAP's ability to modulate inflammatory cytokine levels and achieve clinically significant reductions in inflammation remains limited (27).

In terms of priming solution composition, the use of albumin may limit interstitial edema through its colloid effect and potential glycocalyx stabilization, providing short-term advantages in fluid balance. However, large-scale randomized controlled trials and meta-analyses have not demonstrated a clear superiority of albumin priming in terms of mortality, AKI, or overall clinical benefit (28). Although HES solutions can provide colloid osmotic pressure, European regulatory authorities have suspended the use of HES products due to risks of renal injury and bleeding; these regulatory decisions are also reflected in clinical guidelines (29). Regarding electrolyte and acid-base balance, the chloride load and buffer content of the priming solution can influence perioperative acidosis or hyperchloremia. Balanced crystalloids (acetate- or lactate-buffered) have been reported to improve the perioperative acid-base profile compared to saline-based solutions; however, their impact on hard clinical outcomes such as mortality or renal failure remains uncertain (30).

Table 2 summarizes the metabolic and inflammatory effects of different priming solution strategies used during cardiopulmonary bypass in a more comprehensible and comparative manner.

Table 2. Metabolic and Inflammatory Effects of Different Prime Solutions During Cardiopulmonary Bypass

Prime Solution Type	Metabolic Responses	Inflammatory Responses
Crystalloids (Saline, Balanced Solutions)	High chloride load → hyperchloremia, metabolic acidosis; balanced solutions may improve acid-base profile	Hemodilution and circuit exposure can increase cytokine/complement activation
Albumin	Maintains oncotic pressure; may limit interstitial edema, metabolic advantage is short-term	May provide anti-inflammatory effect via glycocalyx stabilization; no proven superiority on mortality/AKI
Hydroxyethyl Starch (HES)	Provides colloid osmotic pressure; reports of increased lactate/metabolic stress; high risk of kidney injury	May increase pro-inflammatory response and endothelial dysfunction; usage is restricted
Retrograde Autologous Priming (RAP)	Reduces hemodilution, preserves oxygen-carrying capacity; may provide metabolic stability	Theoretically reduces inflammatory response; clinical evidence is limited
Sanguineous Priming	More stable electrolyte and acid-base balance; lower risk of metabolic acidosis	May trigger transfusion-related inflammatory response
Mannitol Addition	Osmotic diuresis and free radical scavenging; may reduce metabolic stress	May limit inflammatory response via antioxidant properties (evidence inconsistent)

CONCLUSION

Priming solutions used during cardiopulmonary bypass exert multidimensional effects on hemodynamic stability, organ perfusion, and metabolic-homeostatic processes. Different solution types, including crystalloids, colloids, albumin, hydroxyethyl starch, blood-based priming, and retrograde autologous priming strategies, produce distinct effects across various organ systems.

From a neurological perspective, both the degree of hemodilution and the composition of the priming solution can influence postoperative cognitive function. Certain strategies may reduce the risk of cerebral edema, whereas the neuroprotective effects of additives such as mannitol are heterogeneous and clinically inconsistent.

Renal function, particularly the risk of acute kidney injury, varies according to the type and volume of priming solution as well as the patient's clinical condition. Excessive use of crystalloids can lead to hemodilution and subsequent renal hypoperfusion, while colloid- and albumin-containing solutions maintain intravascular volume for a longer duration. In contrast, HES has well-documented adverse effects on renal function and carries a risk of coagulopathy. Mannitol may theoretically provide renoprotective benefits, but current clinical evidence is limited and inconsistent.

Pulmonary function is directly influenced by hemodynamic changes and inflammation. Colloids and albumin may theoretically provide benefits by maintaining intravascular volume, whereas HES has the potential to exacerbate inflammation. The effects of mannitol on pulmonary function remain clinically uncertain.

Cardiac function is affected by hemodilution, changes in vascular resistance, and microcirculatory disturbances. Priming with colloids and albumin can support cardiac output; however, excessive use of crystalloids and HES-associated inflammation may negatively impact cardiac performance. The effects of mannitol are heterogeneous and can be detrimental in certain circumstances.

Metabolic and inflammatory responses vary depending on the type of priming solution used, its osmolarity, and the buffering system it contains. Certain priming strategies may limit hemodilution and cytokine release, whereas blood-based priming can enhance the inflammatory response. Balanced crystalloids tend to improve the acid-base profile; however, their impact on hard clinical outcomes remains unclear.

Overall, priming solutions employed during cardiopulmonary bypass exert complex and multidimensional effects on organ function. Existing studies primarily focus on short- and medium-term outcomes, with long-term clinical effects being less well investigated. Therefore, individualized and patient-specific selection of priming strategies is crucial for maintaining hemodynamic stability, protecting organ function, and balancing inflammatory and metabolic responses. Future long-term, prospective, and methodologically standardized studies will help clarify the clinical benefits and risks associated with different priming strategies.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Ethics Approval and Consent

Ethical approval was not required since it was a review article.

Conflict of Interest

No conflict of interest was declared by the authors.

Author Contributions

Gülşah Celik Korhan: Article hypothesis, Literature review, Writing.

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