Management of intraoperative fluid balance and blood conservation in adult cardiac surgery

[1]Eleftheriadis S, [2]Stamoulis K, [2]Ieropoulos Ch, [2]Flossos A

ABSTRACT

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The reduction of homologous blood transfusions remains an important goal. The actual blood loss and the positive fluid balance during cardiac operations involving CPB result in a fall in the haematocrit and represent major risk factors for blood transfusions. Methods and techniques which lead to a decrease of haemodilution are important when aiming at fewer transfusions in such operations. Considering volume load as modifiable, a number of efforts have been made to reduce the resulting positive fluid balance under CPB. The minimization of the prime volume with or without the use of hyperoncotic solutions is crucial in the attenuation of haemodilution. The beneficial effect of minimized circuits on inflammation and haemodilution and the retrograde autologous priming of the cardiopulmonary bypass circuit have a positive result in a reduce need for allogeneic blood. Autologous blood cell salvage and intraoperative autotransfusion decreases requirements for homologous blood. Experience in these techniques increases their effectiveness and reduces their possible dangers. A multimodal approach and change in physician transfusion practices is deemed necessary for reducing homologous blood transfusion during cardiac operations.

The reduction of blood transfusions is considered to be an important and relevant goal as described in numerous reviews [1]. Minimizing transfusion has become desirable for all patients. Behavioral and simple interventions appear to be effective in changing physician transfusion practices and reducing blood utilization [2]. Cardiac surgery has been identified as a major consumer of donor blood products. In a recently published report by the Society of Thoracic Surgeons and the Society of Cardiovascular Anaesthesiologists[3], a number of variables were identified as important indicators of risk for transfusion: advanced age, low preoperative red blood cell volume (preoperative anaemia or small body size), preoperative antiplatelet or antithrombotic drugs, complex procedures or emergency operations, and non-cardiac patient comorbidities. In the same report, careful review revealed a number of interventions that were likely to reduce blood transfusion, including limitation of antithrombotic drugs, use of drugs that increase preoperative blood volume (eg, erythropoietin) or decrease post-operative bleeding (eg, antifibrinolytics), selective use of off-pump coronary artery bypass graft surgery, use of autologous predonation and normovolemic haemodilution, and routine use of a cell-saving devices. Existing guidelines underline the significance of a

[1] Cardiac Anaesthesia Unit, University Hospital of Alexandroupolis, Greece
[2] Cardiac Anaesthesia Unit, University Hospital of Larissa, Greece

multimodal approach to blood conservation, with the high-risk patients receiving all available peri-operative interventions under appropriate institution-specific transfusion algorithms [3,4]. Nevertheless and despite its worldwide approval, the application of conservation or alternative therapies for transfusion has been slow[5,6]. It seems that in order to change practices, appropriately designed clinical trials are still needed to determine the relative effectiveness of different interventions [2].

During cardiac operations under CPB, the combination of two factors, namely the actual blood loss and the positive fluid balance associated with CPB, result in a fall in haematocrit and the consequent transfusion of allogeneic blood. The importance of clinical evaluation to avoid unnecessary transfusion has been highlighted[7]. This review focuses on the intraoperative methods and techniques available to the anesthesiologist for blood sparing during cardiac operations. The reader can seek elsewhere for blood saving techniques and alternatives to blood transfusion which can be applied throughout the peri-operative period and in a wide spectrum of surgeries.

Haemodilution in cardiac operations with extracorporeal circulation

The application of CPB alone leads to an acute dilutional anaemia, impacting insignificantly on the number of circulating erythrocytes. The administration of fluids during the pre-bypass period has an additive effect. The inevitable dilution of the red blood cell mass, occurring on initiation of CPB, becomes a primary determinant of transfusion practices, as clinically, the actual value of the haemoglobin concentration or the haematocrit significantly affect the decision to transfuse[8,9]. Nevertheless, recommendations for transfusion, often referred to as the "transfusion triggers", are not supported by high-level evidence[2,10]. In case of iatrogenic haemodilution, the value of a specific haemoglobin or haematocrit level as the indicator for transfusion becomes less appropriate. But as accurate estimates of blood loss and intravascular blood volume are difficult or impossible,

other measurements may be needed. These measurements include whole body oxygen-carrying capacity, oxygen consumption, oxygen extraction ratios, and oxygen delivery. In many reports, female sex and low body surface area have been recognized, among others, as independent predictors of erythrocyte transfusion in cardiac surgery patients[11-14]. When compared to a male population with normal somatometric values, blood loss and initiation of CPB are both expected to affect haemoglobin concentration to a greater degree in the above group of patients. These observations underline the significance of the degree of haemodilution on the amount of blood product usage. One of the most important factors in achieving blood conservation in cardiac surgery is the acceptance of haemodilution[15].

During cardiopulmonary bypass, oxygenation and systemic perfusion are provided under conditions of heparinization, haemodilution and reduced blood viscosity, nonpulsatile blood flow and hypothermia. This situation creates a number of physiological consequences that affect systemic physiology and blood formed elements[16]. Adequate oxygen delivery to tissues may be well maintained with haematocrit well below normal baseline levels. Past studies showed that haemoglobin values of 5.0 g/dL under dilution provide adequate oxygen delivery during CPB [17,18] and a study performed in patients immediately after CPB showed no change in myocardial lactate extraction or production even with elective haemodilution to the same haemoglobin level[19]. In practice, these observations create feelings of reassurance and shift the so-called "trigger value" towards a lower haematocrit. At the same time it leaves greater scope for subjectivity, when a decision to transfuse must be taken. This seems to be of greater importance for female and low body surface area patients, as they are more prone to haemodilution. Under these circumstances, clinicians have to estimate the degree of anaemia that is tolerated by the patient with measurements other than the change of haemoglobin or haematocrit values. Lack of these measurements leads to adoption of "triggers" and may explain to a degree the higher inci-

dence of blood product usage in easily haemo-diluted patients.

Considering volume load as modifiable, a number of efforts have been made to reduce the resulting positive fluid balance during surgical procedures under CPB. These studies focused on the minimization of the prime volume with or without the use of hyperoncotic solutions, the retrograde autologous priming of the cardio-pulmonary bypass circuit, the application of cell salvage techniques, and the use of mechanical support by filters for plasma concentration.

Reduction in prime volume

Low prime volume is crucial in the attenuation of haemodilution. As prime volume stands at the core of this well recognized problem of cardiac surgery, numerous efforts have been made to minimize the circuit. Conventional circuits need volumes of more than 1.400ml for the pump and oxygenator, while newer integrated circuits combine centrifugal pump and oxygenator thus reducing the necessary volume to 450ml. It is needless to say that techniques such as retrograde autologous priming and hyperoncotic prime (*see below for details*) aim to reduce both prime and "extra" volume on pump. In one retrospective study of 970 patients undergoing elective CABG a significant reduction in red blood cell transfusion rates was found with minimized circuits (MC) compared to conventional circuits[20]. Another group of researchers published two prospective studies including surgeries of valve replacement and reported at least a 50% reduction in transfusion rates with the use of minimized circuits[21,22]. Cardiac surgery for Jehovah's Witness patients is a challenge as they not only reject homologous transfusion but also blood that has been separated from their own circulatory system i.e. autologous transfusion. This challenge is greater for paediatric patients. In one report, open-heart surgery was performed in three Jehovah's Witness infants with a body weight between 3.1 and 4.5kg without transfusion of blood components. This was achieved by using a low-volume CPB circuit (priming volume of 200mL), de-signed to decrease the degree of haemodilution [23].

In cardiac surgery, CPB and circuits are considered to provoke systemic inflammatory response by complement activation and preinflammatory cytokine release[24]. Existing data support that minimized circuits reduce inflammatory reaction, activation of coagulation and fibrinolysis[25]. The beneficial effect of these circuits on inflammation and haemodilution seems to have a positive result on the number of transfusions, leading to less use of allogeneic blood[26,27]. On the other hand, a randomized control study of 204 patients undergoing CABG found no decrease in transfusion requirements with the use of a minimized circuit[28]. The authors stated that the possible transfusion benefits from minimized circuits must be balanced against possible risks including air embolism, and lack of cardiotomy suction associated with this technology. Currently, a number of circuits are commercially available and this technology is spreading quickly as more and more team members (anaesthesiologists, perfusionists and surgeons) are trained. Nevertheless, the impact of these circuits on transfusion, inflammatory response and outcome must be further investigated. Finally, the use of low prime and minimized extracorporeal bypass circuits to reduce the fall in haematocrit during CPB is classified in the report by the Society of Thoracic Surgeons and the Society of Cardiovascular Anaesthesiologists as Class IIb level of evidence, i.e. that their use is **not unreasonable** for blood conservation[3].

Hyperoncotic cardiopulmonary bypass prime

Haemodilution and the consequent fall in colloid osmotic pressure (COP) with the initiation of CPB, was shown to play a key role in the development of post pump organ dysfunction. As COP falls, the microvascular blood pressure is less responsive, causing imbalance of microvascular net filtration and reduction in the removal of interstitial fluid by the lymphatics, thus leading to oedema formation. Rise in extravascular lung water (EVLW) and myocardial

oedema contribute to cardiopulmonary dys-function[29-31]. The disorder has a problematic course in ICU and bad outcome. Although there has been much discussion over the last 30 years of the optimal priming composition for the CPB circuit in order to avoid or at least to ameliorate post-pump organ dysfunction, the subject is still controversial. No beneficial effects regarding clinical parameters and outcome could be de-monstrated in the majority of studies using colloidal prime compositions[32-34]. Reasons for this may be that the COP of the hyperoncotic priming solutions used was still less than phy-siological in many studies, and that the cardio-plegia used was crystalloid. Currently in many centres, blood cardioplegic solution is drained from the reservoir (blood cardioplegia), and, if hyperoncotic priming is agreed, the fall of COP may be avoided.

An improved clinical performance score and a reduced post-operative hospital stay for patients treated with a colloidal CPB prime were demon-strated in only one study[35]. Although cardio-plegia was with crystalloid, the study was able to demonstrate a significant increase of COP before its administration. In a later study with hydroexylstarch (HES) versus crystalloid, the fall in COP, the degree of positive fluid balance, and weight gain were significantly less in the HES group[33]. There was also an improvement in haemodynamic parameters and in functional respiratory variables such as $AaDO_2$ and Qs/Qt. As the number of the patients was small however and in good clinical condition, the study was unable to show an improved outcome. Despite the improved intra-operative fluid balance, there was no change in haemo-globin and haematocrit values 2 and 4 hours post-operatively. Furthermore, there was a trend towards increased calculated blood lost in the HES group. Unfortunately, the study does not provide information about the intra-operative course of these parameters or about the peri-operative blood transfusions. Presently, it cannot be concluded that hyperoncotic priming solutions and attenuation of fall of colloid osmotic pressure show any beneficial effect on blood product usage in cardiac surgery.

Retrograde Autologous Priming (RAP) of the cardiopulmonary bypass circuit

RAP of the CPB circuit is a blood conservation method developed to limit the degree of haemo-dilution occurring during extracorporeal circula-tion. This concept was first described in 1960 [36] and revived in the late 1990s[37]. The technique involves the replacement of the crystalloid prime with the patient's own blood. After arterial and venous cannulae are inserted, the crystalloid prime is slowly drained into a recirculation bag. Up to 1L of the circuit volume can be displaced by the patient's own blood immediately before the onset of CPB [37]. A 1000-mL blood transfer bag is con-nected to the venous line. Transfer is performed in three basic steps. First, crystalloid is dis-placed from the arterial line. Blood is allowed to flow by pressure gradients from the aorta and through the arterial line and filter, displacing crystalloid prime into the blood transfer bag. Next, the crystalloid in the venous reservoir and oxygenator is similarly displaced using pressure gradients from the aorta. Finally, the entire prime from the venous line is displaced into the bag at the onset of CPB. Approximately 300 mL of volume in the CPB circuit is replaced during each of these steps. The entire RAP process is completed in 5–8 min. Sequestered prime in the blood transfer bag can be reinfused after processing via a cell saver system. This technique maintains colloid osmotic pressure and reduces extravascular lung water compared with standard priming techniques.

Caution needs to be taken if the displaced crystalloid is collected and excluded from the circuit with a vacuum assisted venous drainage system. On at least one occasion, this resulted in massive systemic air embolism through a patent foramen ovale, and vacuum-assisted venous drainage should not be used in such ca-ses for retrograde autologous priming[3]. Hae-modynamic instability is not rare and can develop when blood is drained from the patient into the arterial and venous lines. Transient hypotension occurring during the period until the pump reaches an adequate flow for organ perfusion, may be treated with phenylephrine bolus or infusion and crystalloids. Crystalloid

administration reduces the RAP effect. If these measures are unsuccessful, the RAP process must be terminated. In general, the technique induces hypovolemia in the system patient-circuit and the perfusionist must be cautious so that organ perfusion is not adversely affected. Usually, perfusionists are introduced to the RAP technique during a training period.

A number of studies have demonstrated clinical efficacy of RAP in reducing the number of patients transfused or in decreasing total blood product usage[37-39]. However in a recent study, only a minimal reduction in PRC use was observed when RAP was routinely applied as a blood conservation modality[40]. The study included 257 patients in the RAP group and 288 in the non RAP group. Forty-four percent of patients in the RAP group received packed red cells versus 51% of patients in the non RAP group and patients with a larger initial red cell mass appeared to derive a greater benefit from this technique. The results of this study are limited by its retrospective character. In a later analysis, the same group of investigators found a decrease in the incidence of post-operative cardiac arrest in the RAP group and no evidence of any increase in other adverse events, suggesting that RAP is a safe technique[41]. Other investigators observed no effect of RAP on post-operative or total transfusion require-ments[42,43], but on one occasion, they conclu-ded that by reducing crystalloid fluid admini-stration and fall of COP during CPB, RAP reduced post-pump EVLW accumulation and weight gain[43]. These clinical trials were limi-ted by the small randomized sample sizes (10-57 patients in the RAP group) and by the ex-clusion of patients at highest risk for peri-operative transfusion.

To determine the effect of different prime volumes on the typically observed post-operati-ve hyperdynamic response, patients under CPB with large prime volume (2.350ml) versus small (1.400ml) were studied[44]. In the small prime group, COP was higher and associated with decreased degrees of positive fluid balance and an attenuated hyperdynamic response. With the on-bypass haematocrit aimed at 22% to 23%, autologous blood was predonated by 16 patients

in the small prime group but by none in the large prime group. The authors concluded that reduction in blood bank products can be obtained with small prime volumes. In two other randomized trials, retrograde autologous priming caused a significant reduction in the frequency of allogeneic blood transfusion com-pared with usual practice[45,46]. Finally, retro-grade autologous priming of the CPB circuit is classified in the report by the Society of Thoracic Surgeons and the Society of Cardio-vascular Anaesthesiologists as Class IIb level of evidence, i.e. **not unreasonable** for blood con-servation[3].

Red cell saving

Autologous blood cell salvage is practiced routinely worldwide in cardiac[4] and other high-risk surgery[1]. Cell saver makes the pa-tient's own blood available for transfusion. Intraoperative autotransfusion involves reco-very of patient's shed blood from surgical wounds, washing and/or filtering before re-infusion. The report by the Society of Thoracic Surgeons and the Society of Cardiovascular Anaesthesiologists states that **routine use** of red cell saving is **helpful** for blood conservation in cardiac operations using CPB, except in patients with infection or malignancy. (Class A, level of evidence A)[3]. A cell-saving device gives the advantage of being able to collect blood both when the patient is heparinized and during periods where no heparin effect is present (eg, during the preparation of the internal thoracic artery). Reinfusion can be performed continu-ously during and after surgery. Currently, this device can quickly process very small amounts of blood, requires low priming volumes and offers blood of high quality. Several reports document the safety of red blood cell saving and support its routine use in cardiac surgery to reduce blood transfusion[47-54]. It has been shown that cell saver in combination with intra-operative autologous blood donation decrease transfusion requirements in small sized patients (mean body weight of 45 kg)[55]. In a recent study, patients scheduled for CABG were ran-domized into an autotransfusion group (n=98) receiving autotransfused washed blood from

intraoperative cell salvage and postoperative mediastinal fluid cell salvage, and a control group (n=102) receiving stored homologous blood only. Patients in the autotransfusion group were significantly less likely to receive a homologous blood transfusion and received significantly fewer units per patient. There was no difference between the groups in terms of postoperative blood loss, fluid requirements, blood product requirements, or in the incidence of adverse clinical events. Autotransfusion did not produce any significant derangement of thromboelastograph values or laboratory measures of clotting pathway function (prothrombin time, activated partial thromboplastin time, fibrinogen, and fibrinogen D-dimer levels) when compared with the effect of homologous blood transfusion[56]. It seems that the concern about transfusion of cytokines through autologous shed blood[57] is diminished as modern salvage is associated with reduced circulating markers of systemic inflammation[58-61].

After weaning from CPB, perfusionists drain the circuit into the saving apparatus so that the number of wasted red cells is limited. Salvage of pump blood is not an unreasonable means of blood conservation (level of evidence C)[2] and is routinely performed in many centres. In one prospective randomized trial, residual blood from pump processed with an autotransfusion system was better than unprocessed when complement activation, coagulation factors and the stimulation of IL-6 and IL-8 were taken into account[62]. The better post-operative clinical course of the patients in the processed blood group was attributed to the reduced load of retransfused activated mediators. Most surgeons agree that discarding the residual pump blood wastes a potentially valuable resource. However, extensive use of cell salvage systems to process the contents of the extracorporeal circuit after discontinuation of CPB may lead to loss of coagulation factors and platelets, resulting in a bleeding diathesis[63]. The impact of pump salvage on the requirement for allogeneic blood transfusion also remains unclear as existing studies cannot draw firm conclusions[64-66]. It is noteworthy that new data is challenging the belief that salvage is contraindicated in malignancy, as savers in combination with leucocyte depletion filters or irradiation of salvaged blood have been reported as beneficial in oncologic surgery[67-69].

Aspiration of mediastinal blood from the operative field during adult cardiac surgical procedures using a cardiotomy suction device and direct reinfusion is not only routinely performed but life-saving ("sucker by-pass"). However, "uncontrolled" cardiotomy suction during prolonged cardiopulmonary bypass (longer than 3 hours) may be associated with increased postoperative bleeding[70]. Cardiotomy suction in combination with a cell-saving apparatus is routinely practiced worldwide. In most cases, blood from the field is processed by the saver when there is no heparin effect (before its administration and after reversal with protamine). During heparinization, direct reinfusion of cardiotomy blood is performed. However, preference for the method of autotransfusion during CPB is not evidence-based. According to available evidence, only a weak recommendation for autotransfusion during CPB, either with cell saving or with cardiotomy suction, can be made (level of evidence C)[3]. Finally, direct reinfusion of shed mediastinal blood from postoperative chest tube drainage is not recommended as a means of blood conservation and may cause harm (Level of evidence B). In cases of extensive postoperative bleeding, the collected blood must be processed by a saver in order to be reinfused. In conclusion, with the usual red blood cell saving protocols, about half of the blood suctioned from the patient is ultimately reconstituted.

Filters for plasma concentration

Filters to remove the excess fluid associated with the priming volume needed for CPB are usually employed in cardiac surgery. Haemoconcentration is the separation of plasma fluid liquid and low molecular solute substances, in particular electrolytes, from diluted blood applying the principle of ultrafiltration. A separate membrane holds blood components and proteins. No absolute contraindication is known for haemoconcentration. Potential side effects include infections, haemolysis and embolism. To

avoid haemolysis, it is recommended that filters must not to be run up dry and must be primed before running. Priming volume, depending on the type of device, varies from 15-100ml. The driving force for filtration is the transmembrane pressure. During haemofiltration (HF), addition of crystalloid to the circuit is often needed to maintain adequate circulating volume. In consequence, the effect of haemofiltration (HF) on haemodilution is counteracted by the "extra" volume on pump. The effect of this technique on the reduction of total body water and the number of transfusions are inconsistent. In a study of 60 patients randomly assigned to HF versus standard CPB, there was no difference in allogeneic blood product usage[71]. One prospective randomized study showed no difference in the amount of the transfused allogeneic blood, while at the same time a significant reduction in postoperative blood loss and a reduction in the transfusion of fresh frozen plasma was found[72]. Another retrospective study of 61 patients who were treated with conventional filters in comparison with 57 patients who were treated with CPB alone showed a trend toward decreased bleeding in the HF group for high-risk adult cardiac procedures[73]. This effect of HF on bleeding seems to be related to a removal of inflammatory mediators and improvement in haemodynamic indices. The effect of HF on inflammatory response seems more prominent with modified filters. In a randomized study of 97 patients comparing a modified filter to conventional CPB, there was no difference in blood loss between the two groups, although there was a significant reduction in adhesion molecules and cytokines in the filter group[74]. Haemofiltration is advantageous for paediatric patients[3], but further analysis is beyond the scope of this review.

Presently, as the impact of HF on the number of transfusions is unclear, the **routine use** of ultrafiltration during or immediately after CPB is considered **not helpful** for blood conservation in adult cardiac operations. (Class III, level of evidence B)[3]. Nevertheless, experienced perfusionists decide to proceed to HF in certain cases during CPB or near the completion of CPB for indications such as excessive haemo-

dilution and a large positive fluid balance, reduced response to diuretics and unavailability of a saver.

Restriction of parenteral fluids

As has already been mentioned, limiting haemodilution in cardiac operations involving CPB is an important goal aiming at fewer transfusions. Reduction in prime volume and MC, RAP and HF are of positive value in these operations mainly because they reduce the augmentation of extracellular volume. Pharmaceutical support with diuretics is commonly practiced for plasma concentration during these operations. The importance of the avoidance of excessive parenteral administration of fluids is recognized and many practitioners make an effort to limit the extent of positive fluid balance. Surprisingly, data about intra-operative fluid restriction protocols are unavailable.

Conclusion

Presently, many peri-operative interventions are available for blood conservation in patients undergoing cardiac surgery. A multimodal approach, particularly for the high-risk patient, is deemed necessary. Of primary importance is the intra-operative control by the anaesthesiologist of the extent of positive fluid balance. Appropriately designed clinical trials to determine the effectiveness of intra-operative interventions and the support offered on the decision to transfuse by new monitoring modalities are needed. It appears that there is still scope for change in physician transfusion practices and new evidence may play a significant role in changing these practices.

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ΕΠΙΚΟΙΝΩΝΙΑ:

Chronis Ieropoulos: UNIVERSITY HOSPITAL OF LARISSA, Mezourlo - Larissa 41110, GREECE

τηλ. +302410-681368, +306970-885256

e-mail: Ieropoulos@gmail.com

Key words: cardiac anesthesia, transfusion, cardiopulmonary bypass, cell salvage