Elective Coronary Artery Bypass Graft Surgery Using Reduced Homologous Blood Transfusion

Azaltılmış Homolog Kan Transfüzyonu Kullanılarak Elektif Koroner Arter Baypas Greft Ameliyatı

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ABSTRACT

Substantial blood loss following by anemia may be a common event during the pre-, peri- and postoperative period of cardiac surgery. Despite the goodness and life-saving of allogenic blood transfusion, it is not accepted by healthcare professionals due to the transmission of viral infections and increased risk of morbidity and mortality. This study aimed to review blood conservation strategies in use leading reduction of homologous blood transfusion, to evaluate the hemoglobin threshold for elective surgeries, to define transfusion trigger point in practice. The finding showed that a decrease in homologous blood transfusion using transfusion management is well accepted worldwide. Various blood conservation strategies could be mitigated anemia by applying hemostatic agents, hemoglobin substitutes, blood salvage systems, the reduction of blood loss related to diagnostic testing, prescription of erythropoietin and restrictive blood transfusion triggers in hospitalized patients. Strategies such as blood loss reduction, hemostatic agents and erythropoietin result in higher hemoglobin levels had some limitations and not been found to reduce blood transfusions or to improve clinical practice and outcomes. Other blood management ways in the surgical procedure include perioperative blood loss reduction using diathermy, hypotensive anesthesia, tourniquet, aminocaproic acid and desmopressin as the anti-fibrinolytic agents. Lowering the hemoglobin threshold considered as the way to decrease morbidity or mortality rate among the patients without vigorous cardiac disease. Therefore, it is crucial to plan prior to a predicted occurrence in the case of anemia or blood loss including elective surgery, pregnancy, and chemotherapy, to organize early screening and management of anemias via the bloodless medicine programs in the clinical setting.

Keywords: Homologous blood Transfusion; coronary artery bypass graft surgery; CABG

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ÖZET

Anemiyi takiben önemli kan kaybı, kalp cerrahisinin öncesi, periferi ve postoperatif döneminde yaygın bir olay olabilir. Allojenik kan transfüzyonunun iyiliği ve hayat kurtarıcı olmasına rağmen viral enfeksiyonların bulaşması ve morbidite ve mortalite riskinin artması nedeniyle sağlık profesyonelleri tarafından kabul edilmemektedir. Bu çalışma, homolog kan transfüzyonunun azaltılmasına yol açan kullanımdaki kan koruma stratejilerini gözden geçirmeyi, elektif ameliyatlar için hemoglobin eşiğini değerlendirmeyi, uygulamada transfüzyon tetik noktasını tanımlamayı amaçladı. Bulgu, transfüzyon yönetimi kullanılarak homolog kan transfüzyonunda bir azalmanın dünya çapında kabul gördüğünü gösterdi. Hastanede yatan hastalarda hemostatik ajanlar, hemoglobin ikameleri, kan kurtarma sistemleri, tanısal testlere bağlı kan kaybının azaltılması, eritropoietin reçete edilmesi ve kısıtlayıcı kan transfüzyon tetikleyicileri uygulanarak çeşitli kan koruma stratejileri anemi hafifletilebilir. Kan kaybını azaltma, hemostatik ajanlar ve eritropoietin gibi stratejilerin daha yüksek hemoglobin seviyeleri ile sonuçlanması bazı sınırlamalara sahipti ve kan transfüzyonlarını azalttığı veya klinik uygulama ve sonuçları iyileştirdiği bulunmadı. Cerrahi prosedürdeki diğer kan yönetimi yolları, anti-fibrinolitik ajanlar olarak diatermi, hipotansif anestezi, turnike, aminokaproik asit ve desmopressin kullanılarak perioperatif kan kaybının azaltılmasını içerir. Şiddetli kalp hastalığı olmayan hastalarda morbidite veya mortalite oranını düşürmenin yolu olarak kabul edilen hemoglobin eşiğinin düşürülmesi. Bu nedenle, elektif cerrahi, gebelik ve kemoterapi dahil olmak üzere anemi veya kan kaybı durumunda, öngörülen bir olaydan önce planlama yapmak, klinik ortamda kansız tıp programları aracılığıyla anemilerin erken taramasını ve yönetimini organize etmek çok önemlidir.

Anahtar Sözcükler: Homolog kan Transfüzyonu; koroner arter baypas greft ameliyatı; KABG

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INTRODUCTION

The bloodless operating field also called bloodless surgery is one of the most important health measures that includes pre-, peri- and postoperative care (1, 2). The invasive nature of surgical procedures such as cardiac surgery causes substantial blood loss as well as repeated blood transfusions during and after the operation (3). The most common method in hospitalized patients is allogeneic blood transfusion (ABT) that is associated with diverse transfusion concerns with an increased rate of patients who refuse the blood transfusions.

Coronary artery bypass grafting (CABG), concomitant body temperature reduction and cardiopulmonary bypass (CPB) are tendered major practical challenges to physicians and anesthetists especially in Jehovah's witnesses (JW) (3). The JW is a religious group of people who are refused to accept blood transfusions including whole blood, platelets (PLTs), red blood cells (RBS), white blood cells (WBC), or plasma products due to their faith (1).

Improvement of minimally invasive cardiac surgery including CABG without CPB or minimally invasive direct coronary artery bypass grafting (MIDCAB) is considered as a promising tool in caring of the patients with inaccessible stenotic or obstructed left anterior descending coronary arteries (LAD) and multi-vessel disease and reduction of repeated blood transfusions (2). There is a general desire in the reduction of blood products used for each patient due to the increased mortality and morbidity rate as well as subsequent adverse outcomes of blood transfusion (3). On the other hand, bloodless care programs are different between institutions leading to the emergence of unique treatment paradigms that need to be centered (4-9). Indeed, several retrospective evaluations reported from single institutions with a focus on liberal versus restrictive transfusion practices in CABG (10-15). Therefore, quick screening, anemias management, early detection of patient demands concerning transfusions in multidisciplinary medical and surgical care and comparing the outcomes of blood conservation programs in competition with the general blood practices in cardiac surgery are essential.

This study was aimed to find out the approaches of practical blood maintenance, to measure the lower hemoglobin level in optional procedures, to evaluate blood transfusion trigger point in different practices, to identify limitations in clinical practice and to estimate the safety of a multimodality blood maintenance over to the common practice of substantial transfusion.

Patient outcomes after cardiac surgery

Anemia considered the single and most common predictor of perioperative erythrocyte transfusion (16). Patient blood management (PBM) applies as a practical tool in anemia treatment to minimize repeated transfusion of RBCs. To limit the transfusion of blood products in the perioperative period of some patients, PBM is an essential tool in safe cardiac surgery (8). Similar or improved outcomes have been observed among the cardiac surgical JW patients to those who accept blood (6, 17). It has been reported that JW showed similar consequences including shorter length of stay (LOS), fewer obstacles, and better one-year and twenty-year survival compared to those who received transfusions (5).

A hazard-adjusted and predilection score-matching model has been applied to evaluate and compare bloodless and blood transfusion methods in all inpatients and controls as well as surgical patients resulting in lower mortality rates in the bloodless method and lower total and direct hospital charges (9). There is no significant difference in total cost between the patients with or without blood transfusion from surgery to release providing certain treatment and management of preoperative anemia in CABG (8). The cost in the diagnosis and materials subgroups were significantly fewer in the WJ cohort than in the controls due to lack of postoperative diagnostic tests and declined blood set charges (8).

Risks of Allogeneic RBC transfusion

- Infectious risks including bacterial, parasitic, viral or prion transmission.
- Noninfectious risks including febrile, allergic or anaphylactic and hemolytic transfusion reactions, transfusion-associated circulatory overload (TACO), transfusion-related acute lung injury (TRALI), Post-transfusion purpura, Urticarial reaction

Blood conservation methods in clinical practice

Despite the recently applied technical and pharmacologic blood conservation methods, the most persistent and remained complications in open-heart surgery are bleeding and allogeneic transfusion as well as transmission of viral infections, transfusion-related diseases and reaction (18, 19). The application of blood conservation methods is essential to limit homologous blood use or to completely avoid transfusions that are well accepted worldwide by healthcare professionals (19).

Implementation of a successful health care strategies and programs involves the integrated technical and pharmacologic blood conservation measures as the following ways (15):

- preoperative patient preparation
- use of hemostatic agents (acute normovolemic hemodilution) and hemoglobin substitutes
- application of blood recover techniques
- blood loss reduction due to diagnostic testing
- improvement of surgical skills, as well as limiting blood loss using diathermy, hypotensive anesthesia
- optimize coagulation status using pharmacologic agents including aprotinin, amicar, desmopressin acetate, etc.
- minimize unnecessary transfusions or use of restrictive blood transfusion triggers
- maximize autologous blood generation using pharmacologic agents including erythropoietin, vitamins/minerals (15, 20)

These strategies help to decrease blood loss resulting in higher hemoglobin levels, but their role in blood transfusions reduction or clinical outcomes improvement has not been. Another way that is connected with decreased morbidity or mortality rate especially in patients without active cardiac disease considered to be Lowering the hemoglobin threshold (20). Therefore, other blood conservation strategies are needed to be examined in clinical outcomes improvement of CABG patients. Some of evidence base blood conservation approaches were abridged in Table 1.

Table 1. Summary of evidence base blood conservation approaches and their pros and cons

Strategy	Function	Pros and Cons
Acute blood loss reduction approaches		**Pros**
• Antifibrinolytic agents • Tranexamic acid or epsilon aminocaproic • Aprotinin • Desmopressin • Recombinant activated factor VII • Artificial oxygen transporters • Postoperative cell retrieve • Blood transfusion from sterile surgical drains in cardiac surgery	Improved hemostasis Increased oxygen transport Implementation of acute normovolemic hemodilution	• Risk mitigation of perioperative and recurrent bleeding in cardiac surgery and patients with congenital coagulation faults • Prevention of transfusions and risk of disease transmission **Cons** • Thrombosis • About artificial oxygen carrier, interference with laboratory measures and Vasoreactivity after application of hemoglobin substitutes
Subacute anemia prevention approaches		**Pros**
• Blood loss reduction after diagnostic testing • Application of closed blood sampling methods and small-volume sampling tubes • Use of Erythropoietin • Limiting RBC transfusion	Iatrogenic blood loss reduction RBC generation in bone marrow after Erythropoietin Elevated hemoglobin threshold	• Elevated hemoglobin level • Short change time in test results • Patients' time saving **Cons** • Increase in Retrograde arterial embolization after closed blood methods • Insufficient volume of blood in small-volume sampling • Thrombosis after Erythropoietin application • Possible death in active cardiac disease cases obtaining restrictive RBC transfusion

Safety and effectiveness of blood-saving on outcomes in CABG

An increase in postoperative morbidity and mortality rate and decreased long-term survival has been considered as perioperative blood transfusion complications in patients undergoing CABG (10, 21-23). It has been indicated that risk for postoperative complications increases by transfusion of small volumes of blood (11-13, 24). A dose-dependent association between transfusion and developed morbidity rate after CABG has been observed by several studies (25). It has also been shown that transfusion was individualistically associated with an increase in risk factors of morbidity such as organ dysfunction as well as mortality (25-28). The tolerated rate of perioperative hemoglobin level without a blood transfusion has been reported to be as low as 6 g/dl but there is controversy among different studies (29). The transfusion rates have been decreased using a simple practice with a transfusion endpoint of hemoglobin level less than 8 g/dl in patients during the postoperation without any effect on consequence (14). In another retrospective report focusing on morbidity and mortality rate of CABG after application of a wide range blood conservation program, the blood transfusion rate has been diminished from 35% to 16% (24). A highly effective transfusion rate of 10.6% has been reported by using a multimodality approach of blood conservation in cardiac surgery (21). These disagreements considered as one of the most imperative restrictions of blood conservation in CABG cases (29). The safety of acute anemia acceptance in the blood conservation practice with no adverse effect on the outcome has been reported by several studies (30-33). In a randomized trial of CABG cases from several centers in addition to a restrictive method to RBC transfusion by preserving hemoglobin at 7 to 9 g/dl or by preserving hemoglobin at 10 to 12 g/dl no alteration in mortality rate was not observed between the groups (34). It has been found that a restrictive transfusion approach has not worse effect on outcome in the cardiac surgery cases (21). A statistically substantial association was observed between blood preservation and better outcome concluding the advantage of a blood preservation practice over the common transfusion practice (21).

Effect of Mini-cardiopulmonary bypass (CBP) on blood conservation approach in CABG

The adverse effects associated with CPB could be reduced using minimized extracorporeal circulation or a fastened circuit system with nominal priming volume (35). Challenges regarding CPB adverse effects in cardiac operations caused to manage the standard equipment (non-heparin-based well-matched treatments, new group centrifugal impels), characteristics of the materials comprising the CPB circuit, priming volume, oxygenator, and the anticoagulation (36). Excessive hemodilution considered as a consequence of CBP and impairment of homeostasis leading cause of a decrease in coagulation and fibrinolytic proteins (35, 37). The mini-cardiopulmonary bypass (MCPB) technique and MCPB equipment have been applied to reduce the negative effects of blood transfusion including hemodilution, the air–blood interface after cardiac surgery and conventional cardiopulmonary bypass (CCPB) system (38). The MCPB and other challenges for improvement of CPB quality have been established to create new competitive techniques even with off-pump cardiac surgery (39).

DISCUSSION

The autologous blood transfusion has been systematically reviewed by AuBuchon in 1989 (40). Risks in CABG patients including transfusion reactions, blood product sensitization, and infectious disease transmission increase with homologous blood transfusions through and after cardiac procedures (41). The preoperative autologous blood donation has been introduced as a practical method for the decrease in homologous blood transfusions in cardiac surgery (42). In a study conducted by Yoda et al, the volume of predonated autologous blood has been determined to eliminate homologous blood transfusion in scheduled off-pump CABG (42). In another study performed by Guarino by et al bloodless surgery was introduced as a feasible method in geriatric patients under the supervision and management of specialized multidisciplinary teams (1). Another study, blood management improved surgical outcomes in JW patients undergoing OPCAB for the first time (3). In Sorm et al study, a less invasive coronary artery bypass surgery using external tourniquet occlusion or intraluminal-left anterior descending shunt has been applied as a bloodless technique in CABG (2). Qvrum et al applied a simple and low-cost blood preservation program for consecutive patients undertaking elective coronary artery bypass surgery without homologous blood transfusion (13). They performed pre-bypass removal of autologous heparinized blood intraoperatively, then the volume lasting in the oxygenator reinfused to the patients after the extracorporeal circulation (13). Autotransfusion of mediastinal blood has been caused to evade the infusion of homologous RBCs (13). In a comparative study, different factors including transfusion of packed cells (PC) and fresh frozen plasma (FFP), hospital length, charges, and postoperative problems were compared between two bloodless and classic groups of CABG patients (43). Application of bloodless method significantly reduced the adverse effect of blood transfusion such as post-transfusion infection, allergic and immunological reactions (43). In a CABG based blood management strategy, the number of patients transfused with RBC, postoperative hemorrhage, respiratory support duration, and ICU stay was significantly reduced in the blood conservation group (44).

Reducing the size of the blood transfusion device leads to a reduction in the amount of blood-biomaterial and reduction in the initial volume required for less hemodilution (45). Not only the institutional differences are influential in the frequency and number of transfusion practice, but individual differences also play an important role in this regard (46). Due to the various institutional and patient factors, it is inconceivable to define a distinct transfusion program (46).

On the other hand, several variables associated with the preoperative and intraoperative period including body surface area, preoperative hematocrit, red blood cell mass, total crystalloid volume, conventional circuit, and 24 h postoperative bleeding have been introduced as the most significant transfusion risk factors (44). The main target of several structured blood management programs was to apply bloodless methods, to reduce transfusion without patient safety involvement and to apply novel techniques resulting in less hemodilution (44-46). Therefore, blood loss reduction by applying appropriate blood conservation procedures help CABG surgery to be performed with less adverse outcomes and lower costs from surgery to release.

In a study performed by Budak et al for the blood conservation, the rate of patients transfused with RBC reduced by 26.8% compared to 56% in the control (44). Moreover, blood transfusion rate, postoperative depletion, ICU stay and respiratory were significantly less in the blood conservation cases (44). There are some strategies to reduce homologous blood transfusions in cardiac patients including hemodilution or hemostatic drugs, blood pre-donation methods, erythropoietin for RBC generation and artificial blood substitutes, the collection of autologous platelet-rich plasma before and during the operation, the remaining extracorporeal pump volume returning, and intraoperative or mediastinal auto-transfusion after operation (20, 47-50). Plenty of reports exist regarding the undesired outcomes of homologous blood transfusion such as allergic and febrile reaction, an acquired immunodeficiency syndrome (AIDS), the transmission of hepatitis, and bacterial sepsis in cardiac patients (51-55).

Pre-donation has been introduced as one of the safest methods for elective surgical procedures including cardiac surgery resulting in a reduction of homologous blood use (56-58). The results of 18 days' donation resulted in an average of 1.97 units of blood with 22 g/L (2.2 g/dL) mean decrease in hemoglobin level (56-58). The average of homologous transfusion units has been decreased to 1.1 units in the pre-donation group compared with 2.05 in the control group. Findings of other pre-donation programs in patients undergoing elective cardiac procedures showed a 75% reduction of homologous blood products in the pre-donation group compared with 21% in the control group (58). Other practical aspects that have been mentioned to reduce the rate of exposure to blood transfusion include crystalloid priming of the extracorporeal circulation, postoperative or intraoperative auto-transfusion and residual pump volume reinfusion (48-50). After the first clarification of pre-donation and storage of autologous blood by Grant in 1921 for an elective surgical procedure (59), the safety and efficacy of autologous blood pre-donation in the cardiac procedure have been demonstrated in several studies (56, 60-65). Yoda et al showed that the 800 ml predonated volume was sufficient to avoid homologous blood transfusions in 100% of the patients compared to 400 ml predonated volume in 63% of cases (42).

In the case of diagnostic testing, reduction of blood loss as a logical intervention could be helped in the reduction of anemia in patients with serious illness. Another constricting transfusion practice is a lower hemoglobin threshold which has been introduced by large clinical trials for transfusion reduction (34, 66-70). Blood salvage and reinfusion have been considered as the way of blood conservation if blood loss was considerable but it is associated with risk of septic contamination as well as the machine inaccessibility in some included centers (71). Different variables involved in blood transfusion need after cardiac operations. Elective coronary, valve, and even thoracic aneurysm could be easily performed using modern blood conservation methods without applying blood transfusion or aprotinin therapy. Topical aprotinin efficacy has been examined by Regan et al in the pericardial cavity and on the mediastinal tissues (72). They showed that aprotinin therapy leads to reduce in bleeding in treated patients compared to the control group (72). A chance for intra-pericardial infusion has been provided by topical aprotinin resulted in established postoperative bleed rather than prophylaxis (72). Qvrum et al designed a blood preservation practice for 121 sequential patients with elective coronary artery bypass surgery in order to reduce the hazards related to the transfusion of homologous blood and blood products, cost, prevention of homologous transfusions, and increase safety (73). They reduced homologous red cell infusion by application of simple and low-priced programs for blood conservation including pre-bypass autologous blood elimination, reinfusion of the volume residual in the oxygenator and auto-transfusion (73). In order to decrease the occurrence of hepatitis and other impediments, Beall et al tried to limit transfusion and application of blood in cases of blood obligatory (74). They applied open-heart operation using nonrefundable plastic oxygenators with an exact focus on a group of 157 patients without the need for blood (74). They concluded that the application of approaches like this could be reduced possible transfusion reactions and blood therapy complications such as homologous serum hepatitis (74).

The efficacy of topical use of aprotinin has been introduced by other studies in terms of postoperative blood loss reduction in patients undergoing cardiac operations (75). Another report regarding topical aprotinin suggested that antifibrinolytic action in order to aprotinin leads to stabilizes fibrin sealing of the surgical wound and after the closure of the thoracic cavity (76, 77). Belcher et al found that blood use in surgery such as coronary artery disease could be reduced and it is proper to avoid bank blood transfusion with its attendant hazards and expense in coronary artery operations. It could be concluded that this form of resource-saving cause blood availability for high-risk surgeries (78). Previously studied ways such as tourniquet and diathermy application have demonstrated as a useful method among sickle cell patients (79). Given that allogeneic transfusion is related to adverse outcomes, the Serious Hazards of Transfusion (SHOT) system has been established to collect statistics regarding the serious outcomes following allogeneic blood transfusion (80, 81). In order to replace or decrease perioperative allogeneic blood components along with decrease costs and blood shortages, evaluation of efficacy and cost-effectiveness of alternative interventions are essential. Several alternatives have been introduced to reduce blood loss and need for allogeneic blood including cell salvage (auto-transfusion) as intraoperatively and/or postoperatively, a preoperative autologous donation (PAD), acute normovolaemic haemodilution (ANH) (82). Other alternatives proposed by several studies to reduce operating losing blood include antifibrinolytic drugs [aprotinin, tranexamic acid (TXA) as a serine protease inhibitor, ε-aminocaproic acid (EACA)], and fibrin sealants (FSs) (83, 84). Reviewed findings from various studies have been a focus on patient consequences, supply use and charges of homologous blood-lowering alternatives (85).

Several conclusions have been drawn from the available evidence in this regard. However, it should be noted that these conclusions limited to several findings discussed in reviewed studies about the reliability and feasibility of the applied approaches, which may affect the superiority and strength of the findings. Besides, conclusions on the cost-effective bloodless approaches are mainly based on unintended evaluations and comparisons of findings on a specific population undertaking elective surgery with moderate to major blood loss in different studies. All of the reviewed aspects regarding different bloodless methods may not be generalizable to the world population and may also limit to a specific geographic area.

Results from various studies for bloodless methods have mainly focused on the following implications; in most cases, cell salvage method has been suggested as a practical and cost-effective alternative to the allogeneic blood transfusions at least for patients without clinical reason to avoid allogeneic blood transfusion compared to PAD in the short time. According to the conclusions derived from a systematic review on the UK, PAD and ANH has been considered to be more affordable than cell salvage in patients with the predicted life expectancy of more than 5 years and stroke has been considered as an adverse outcome in either surgery or transfusion for the longer-term investigations with any significant differences between allogeneic and autologous transfusion techniques (85). They mainly focused on the nine transfusion strategies to diminish perioperative allogeneic blood transfusion including cell salvage, PAD, EPO [recombinant human erythropoietin (rHuEPO)], PAD plus EPO, ANH, cell salvage plus ANH, AFs or antifibrinolytic (aprotinin, TXA, EACA), FSs (fibrin sealants) and restrictive transfusion thresholds or protocols (85). Cell salvage plus AFs, FSs or EPO has also been recommended to be more cost-saving than allogeneic blood transfusion (85). The efficacy and cost-effectiveness of the washed intraoperative cell salvage were highly recommended than postoperative cell salvage in cardiac surgeries than unwashed postoperative cell salvage applied in orthopedic procedures (85). Based on the statistical evaluations, the application of cell salvage would be halved the amount of allogeneic blood used in each operation annually.

In conclusion, choosing the most effective, simplest and likely least costly blood conservation strategies would be helped cardiac patients to be well-cured. Further efforts and investigations including high-quality RCTs are required to report short- and long-term patient outcomes, to manage and define transfusion trigger point in clinical practice, to evaluate the prospective roles of other blood conservation approaches according to surgical procedure, timing and techniques of different bloodless strategies and finally to realize the restrictions and the ways to progress in clinical practice.

Conflict of interest

No conflict of interest was declared by the authors.

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