Blood Transfusion in ICU after Cardiac Surgery: A Lower Hemoglobin Level is Tolerated Liberal Versus Conservative Packed RBCs Transfusion after Open Heart Cardiac Surgery

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Abstract

Background: In patients undergoing cardiac surgery, currently RBC transfusion has been associated with adverse outcome. Evidence regarding optimal blood transfusion practice in those patients is lacking.

Objectives: To challenge the hemoglobin transfusion trigger of <9gm/dl compared to a trigger level of 7gm/dl.

Design: A prospective randomized controlled Study.

Setting: 19 beds post cardiac surgical Intensive care unit in a tertiary care hospital.

Patients and Methods: All patients who had open heart cardiac surgery were randomized immediately after admission to ICU into liberal (transfusion trigger is Hb <9.0 gm/dL) or conservative (transfusion trigger is Hb <7.0 gm/dL) strategy. Primary end points were 30 days all cause mortality and lab parameters of tissue perfusion (Lactate and ScVO2). Secondary end points were clinical complications and length of ICU or hospital stay.

Results: There was a non significant decrease in 30 days mortality in the conservative strategy compared to liberal strategy (5.8% vs. 7.4% respectively, p=0.08). No statistical significant difference in the perfusion parameters, clinical complications or length of ICU or hospital stay was noted between the 2 groups. Subgroup analysis of the CABG patients showed similar results.

Conclusion: Hemoglobin level of 7.0gm/dL as a transfusion trigger is not associated with any deleterious effect on 30 days mortality or tissue perfusion nor had any increase in clinical complications.

Key Words: Blood transfusion liberal – Conservative open heart – Cardiac surgery.

Introduction

IN 2001, Spiess [1] referred to current transfusion practices as “a silent epidemic.” His description is still accurate. Cardiac surgery is associated with a high rate of allogeneic blood transfusion, varying from 40% to 90% in most reports [2-4]. In 2006, almost half of all patients undergoing coronary bypass grafting in the United States received blood transfusions, and the probability of receiving blood is greater when procedures are more complex.

The rationale for perioperative red blood cell (RBC) transfusion is based on the observation that anemia is an independent risk factor for morbidity and mortality after cardiac operations [5,6]. However, transfusions have been associated with high rates of morbidity and mortality in critically ill patients, [7] and some recent studies have shown worse outcomes, including increased occurrence of renal failure and infection, as well as respiratory, cardiac, and neurologic complications, in transfused compared with non-transfused patients after cardiac surgery [8,9]. The association of blood transfusion with infection is presumably the result of immunosuppressive effects. Blood was used to decrease the incidence of rejection in the early days of kidney transplantation, and transfusion has been associated with cancer recurrence and death in patients with malignancy [1].

Rawn [10] stated that ischemic complications (myocardial infarction, neurologic and renal injury) were not decreased with blood transfusion regardless of the patient's nadir hematocrit or comorbidities. The lack of benefit from blood transfusions in decreasing these complications might be explained because hemoglobin levels rarely limit oxygen delivery given the transfusion triggers that predominate in cardiac surgery [11]. Possible mechanisms for the contribution of transfusion to ischemic complications include pro inflammatory effects and storage defects. Stored red
blood cells are 2,3-DPG deficient and consequently less adept at unloading oxygen and less deformable, possibly leading to sludging and capillary occlusion.

The findings in previous studies that a transfusion of RBCs may affect long-term survival have made physicians reluctant to transfuse patients. This applies to those cases where the physician has an option not to transfuse. It does not apply to those patients with larger bleeding and rapidly decreasing hemoglobin, where transfusion is life-saving. The clinical dilemma applies when patients are stable, do not have an infection, renal dysfunction, or congestive heart failure but have a depressed Hb level. Should that patient receive an RBC transfusion to facilitate post-operative mobilization and discharge? [12]

There is a lack of evidence regarding optimal blood transfusion practice in patients undergoing cardiac surgery [13]. In an effort to conserve a limited and expensive resource and to minimize the injury caused by transfusion therapy, the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists have joined forces and, with impressive effort, have produced a clinical practice guideline. Their guideline emphasizes that the benefits of transfusion have not been adequately demonstrated and that existing evidence is an imperfect guide to transfusion decisions. They suggest a transfusion trigger of hemoglobin <7g/dL in postoperative cardiac surgery patients (class IIa recommendation). In addition, they suggest (class IIb recommendation) that it is “not unreasonable to transfuse red cells in certain patients with critical noncardiac end-organ ischemia (eg, central nervous system and gut) whose hemoglobin levels are as high as 10g/dL, but more evidence to support this recommendation is required.” [12]

In a comparative trial of 428 patients undergoing elective coronary artery bypass graft (CABG) surgery, Bracey et al. reported that reducing the hemoglobin trigger to 8g/dL did not adversely affect patient outcomes and resulted in lower costs [14].

The experience with Jehovah Witnesses demonstrates that when a commitment is made to avoid blood transfusion, the effort is successful in the vast majority of cases. Recognition that blood transfusion poses significant risk for what is frequently an uncertain benefit can inspire a similar level of commitment.

In our Cardiac Surgical ICU we used to apply the hemoglobin level of 9.0gm/dL as a transfusion trigger for most post-operative patients. In the view of limited blood resources and increasing demands, we conducted this randomized study aiming to decrease this trigger to the level of 7.0gm/dL.

Patients and Methods

Patients:

Inclusion criteria: All patients scheduled for elective cardiac surgery at the Heart center, King Faisal specialized hospital and research center, Riyadh, Kingdom of Saudia Arabia between 1st of April 2010 till 31st of October 2010, were enrolled in the study immediately on admission to cardiac surgical intensive care unit (CSICU) from the operating room. This included patients who were undergoing CAGB surgery or cardiac valve replacement or repair, alone or in combination.

Exclusion criteria: Age younger than 18 years; emergency procedure defined as surgery performed within 1h of decision to operate; root, ascending or descending thoracic aortic procedures; left ventricular aneurysm resection; inability to receive blood products; enrollment in another study; chronic anemia (preoperative hemoglobin concentration less than 10g/dL); low platelet count (preoperative platelet count less than 150x10^9 / L); pregnancy; neoplasm; congenital heart defect; hepatic dysfunction (total bilirubin value higher than 1.5mg/dL); end-stage renal disease (receiving chronic dialysis therapy); Patients who received 6 or more units of RBC were excluded. The 6U of RBC clinically represents, together with plasma, more than half the blood volume in most patients and indicates a lifesaving transfusion; and refusal to consent.

The study protocol was approved by the hospital research center and ethical committee and informed consent was obtained from either the patient or the next of kin before enrollment in the study.

In all patients, clopidogrel and oral anticoagulants were stopped at least 5 days before surgery. Patients were transferred from the operating room to the ICU after recovery from anesthesia while still receiving invasive mechanical ventilation with intermittent positive pressure with a tidal volume of 6-8mL/kg, positive end expiratory pressure of 5 to 8cmH2O, and fraction of inspired oxygen of 0.6 to 1 to keep arterial oxygen saturation above 95%. Patients were weaned from the ventilator after exhibiting complete recovery from anesthesia, hemodynamic stability with no evidence of significant bleeding, core temperature higher than 36°C, and adequate blood gas values. All patients were monitored with an arterial and central venous
catheter; some also received a pulmonary artery catheter. Patients were discharged from the ICU to a step-down unit on the second postoperative day if they met institutional discharge criteria.

**Study design:**

Prospective randomized controlled trial. Patients were randomly assigned to a liberal or a conservative transfusion strategy. Sealed, opaque envelopes arranged in a computer-generated random order were prepared, where they were opened sequentially to determine the patients' treatment assignments group. Transfusion guidelines for both study groups were developed from information obtained in a national survey of critical care practitioners in Canada [15] and a pilot study [16].

Patients assigned to the conservative strategy received blood transfusion when the hemoglobin concentration fell below 7.0g per deciliter and the hemoglobin concentration following the transfusion was maintained in the range of 7.0 to 7.9g per deciliter. Among patients assigned to the liberal strategy of transfusion, the hemoglobin concentration was maintained more than 9.0g per deciliter, with a threshold for transfusion of 9.0g per deciliter. In both groups, no further units were given if the goal hemoglobin was obtained (7.0 and above for the conservative strategy and 9.0 and above for the liberal strategy). Compliance with the two transfusion protocols was monitored by daily measurements of hemoglobin concentrations in each patient.

The physicians caring for the patients were instructed to administer transfusions, one unit at a time, and to measure a patient's hemoglobin concentration after each unit was transfused. We provided suggestions for the use of fluids and vasoactive drugs, (Nitroglycerin and sodium nitroprusside were administered intravenously as vasodilators, milrinone as an inodilator, dopamine as an inotrope, and norepinephrine and epinephrine as vasopressors) when necessary, and advice when a transfusion was not indicated by the study protocol. All other management decisions were left to the discretion of the patients’ physicians. Attending physicians could administer RBC transfusions outside the rules of the protocol if they considered the patient's status to be life-threatening, as in hemorrhagic or other forms of circulatory shock; such an event was considered a protocol deviation.

Adherence to the transfusion protocols was required only during the patient's stay in the intensive care unit.

**Base line assessment and data collection:**

At the time of randomization, demographic and clinical data as well as the information needed to calculate the predicted risk of surgery using the standard Euro-SCORE (European System for Cardiac Operative Risk Evaluation) [17] were obtained for each patient.

Preoperative laboratory values were recorded and included hemoglobin, hematocrit, prothrombin time, activated partial thromboplastin time, creatinine level, bilirubin level, and platelet counts. Surgical information was also collected on the type of surgical procedure, duration of bypass, duration of cross-clamping, number of RBC units transfused, administration of other blood products, amount and type of fluids administered, and clinically important events such as bleeding or hemodynamic instability.

During the ICU stay, clinical data were collected daily. Hemoglobin was measured every 12 hours until ICU discharge. Levels of serum, troponin, electrolytes and bilirubin were measured once daily. Blood gases (arterial and venous) and lactate were measured every 4 hours till extubation then twice daily till ICU discharge. Clinical and laboratory data for the Simplified Acute Physiology Score II [18] and for the Acute Physiology and Chronic Health Evaluation II score [19] were recorded using the worst value within the first 24 hours after ICU admission.

Data were also recorded regarding hemodynamic status, need for vasoactive drugs and other medications, need for mechanical ventilation, need for dialysis, and other forms of organ dysfunction. During the hospital stay, data were collected regarding the use of RBC transfusion, hemoglobin goals, and complications. After discharge from the ICU, clinical outcomes were evaluated on the regular ward. Respiratory complications were defined as prolonged need for mechanical ventilation (≥48 hours) and development of pneumonia or acute respiratory distress syndrome (ARDS) defined by standard criteria [20]. Pneumonia was diagnosed if the patient had a new, persistent, or progressive lung infiltrate on chest radiograph and if at least 2 of the following criteria were present: Temperature 38°C or greater, leukocytosis greater than 12 000 cells/L, leukopenia less than 3000 cells/L, purulent endotracheal secretions with a Gram stain showing more than 25 neutrophils and fewer than 10 epithelial cells per field [20]. In patients receiving mechanical ventilation and with clinical suspicion of nosocomial pneumonia, bronchial secretions for cultures were obtained with a
protected pulmonary specimen through the endotracheal tube.

Cardiac complications included cardiogenic shock, tachyarrhythmia, or postoperative cardiac ischemia. Cardiogenic shock was defined as the presence of tachycardia, hypotension, and poor perfusion associated with SCVO$_2$ less than 65% or metabolic acidosis (decrease in base deficit >4) or an increase in lactate level (> 18.02 mg/dL) in the absence of a cause other than heart failure.22 An electrocardiogram was performed daily during the ICU stay. Postoperative cardiac ischemia was considered if troponin I values were greater than 5 ng/mL during the first 72 hours, if creatine kinase MB level was elevated to at least 5 times the upper limit of normal (>30ng/mL), if new pathological Q waves appeared, if coronary artery occlusion was angiographically documented, or if there was imaging evidence of new loss of viable myocardium.

Renal function was evaluated daily using the RIFLE (renal risk, injury, failure, loss, end-stage kidney disease) classification.24 The need for renal replacement therapy was recorded.

Neurologic complications were diagnosed if the patient presented with delirium or stroke, which was characterized by a new focal deficit with a compatible image on computed tomography.

Infectious complications included septic shock, defined by standard criteria; mediastinitis, defined as a superficial or deep infection of the sternotomy wound with positive findings on cultures obtained from the wound; and pneumonia as described above. Inflammatory complications were diagnosed if the patient had vasodilatory shock, associated with a cardiac index greater than 4.0L/min per square meter.

Bleeding was defined as clinically important when blood loss exceeded 3mL/kg/h for 2 consecutive hours after ICU admission and/or patients needed reoperation. Operative mortality was considered as death from all causes in the 30 days after surgery.

Outcome measures:
The primary outcomes were: 30-day all-cause mortality, and parameters of tissue perfusion namely: arterial lactate and ScVO$_2$. Secondary outcomes included respiratory, cardiac, renal, neurologic, and infectious complications; bleeding requiring reoperation; and ICU and hospital lengths of stay. These clinical complications were selected because of the established association between these complications and blood transfusion and their known association with mortality.6,13,14,15

We also evaluated the incidence of RBC transfusions and the number of units transfused, predictive factors for RBC transfusions, and the effects of transfusion on patient outcomes.

Statistical analysis:
We compared baseline characteristics, follow-up measures, and clinical outcomes according to the randomized study group assignment. Continuous variables were compared using a $t$-test where numbers were large and not strongly skewed; otherwise a Mann-Whitney U was performed, and categorical variables using Pearson $x^2$ or Fisher exact. Comparisons of hemoglobin concentration over time were made using analysis of variance with repeated measures followed by the least-squares difference test to discriminate differences. Results are expressed as means with $\pm 1$ standard deviation or medians with interquartile ranges (IQRs). We calculated unadjusted 30-day Kaplan-Meier survival estimates, dividing patients by transfusion strategy and by number of transfused RBC units, using a log-rank test. A 1-sided $p$-value less than .05 was considered statistically significant. Statistical analyses were performed using SPSS version 18.0 (SPSS Inc, Chicago, Illinois).

Results

Study population:
Between the 1st of April 2010 till the end of October 2010, all cardiac surgical patients ($n=123$) were screened for eligibility for the study. 16 patients were excluded: 2 emergency cases, 3 had aortic root surgery, 4 patients had pre-operative renal failure with dialysis, 7 patients received more than 6 units of packed RBC's in the operating room and one patient needed packed RPC's transfusion before we can obtain the consent. 107 patients were assigned to either liberal ($n=54$) or restrictive ($n=53$) transfusion strategy groups. In the liberal strategy group, there were no cases of protocol deviation. Two patients in the restrictive-strategy group were considered to have deviated from protocol because they received 1 RBC unit outside the protocol trigger to address hemodynamic instability.

There were no significant differences in any baseline characteristics between the two groups (Table 1).
ICU course:

There was no statistical significant difference in the hemoglobin concentration between the liberal or conservative transfusion groups on admission to ICU, Table (1).

The hemoglobin concentrations were significantly higher in the liberal transfusion group compared to conservative group starting from day 1 post operatively till discharge from ICU.

As expected, more patients in the liberal strategy group received a blood transfusion than in the conservative strategy group (45% vs. 14% respectively, \( p < 0.01 \)). The total number of transfused RBC units was 98 in the liberal-strategy group and 16 in the restrictive-strategy group (\( p < 0.01 \)). Most transfusions were given in the first 2 days after surgery. The liberal-strategy group received a mean of 4.1 ± 1.1 RBC units per patient while the conservative strategy group received a mean of 2.3 ± 0.3 RBC units per patient (\( p < 0.01 \)).

Table (1): Base line characteristics of both groups.*

<table>
<thead>
<tr>
<th></th>
<th>Liberal transfusion group (n=54)</th>
<th>Conservative transfusion group (n=51)</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex, no. (%)</td>
<td>32 (63)</td>
<td>30 (56)</td>
<td>0.08</td>
</tr>
<tr>
<td>Age, yr</td>
<td>60.3 ± 17.5</td>
<td>62.1 ± 18.2</td>
<td>0.1</td>
</tr>
<tr>
<td>Body mass index a</td>
<td>31.5 ± 6</td>
<td>29.6 ± 5.8</td>
<td>0.5</td>
</tr>
<tr>
<td>APACHE II score †</td>
<td>22.1 ± 8.7</td>
<td>23 ± 9.1</td>
<td>0.06</td>
</tr>
<tr>
<td>MODS‡</td>
<td>7.1 ± 3.2</td>
<td>7.4 ± 3.8</td>
<td>0.9</td>
</tr>
<tr>
<td>Comorbid conditions, no. (%):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>36 (70.5)</td>
<td>38 (70.4)</td>
<td>0.07</td>
</tr>
<tr>
<td>Diabetes</td>
<td>18 (35.3)</td>
<td>22 (40.7)</td>
<td>0.2</td>
</tr>
<tr>
<td>Renal disease</td>
<td>7 (13.7)</td>
<td>7 (12.9)</td>
<td>0.3</td>
</tr>
<tr>
<td>Smoking</td>
<td>15 (29.4)</td>
<td>14 (25.9)</td>
<td>0.09</td>
</tr>
<tr>
<td>COPD</td>
<td>3 (5.9)</td>
<td>2 (3.7)</td>
<td>0.6</td>
</tr>
<tr>
<td>IHD</td>
<td>20 (39.2)</td>
<td>21 (38.9)</td>
<td>0.09</td>
</tr>
<tr>
<td>LVEF &lt;40%</td>
<td>8 (15.7)</td>
<td>10 (18.5)</td>
<td>0.7</td>
</tr>
<tr>
<td>EuroSCORE, median</td>
<td>4</td>
<td>5</td>
<td>0.5</td>
</tr>
<tr>
<td>Preoperative laboratory values:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>12.2 ± 0.9</td>
<td>11.7 ± 1.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>36.6 ± 2.5</td>
<td>34.1 ± 2.9</td>
<td>0.09</td>
</tr>
<tr>
<td>aPTT, s</td>
<td>79.3 ± 5.1</td>
<td>81.2 ± 3.4</td>
<td>0.4</td>
</tr>
<tr>
<td>Prothrombin time, s</td>
<td>16.4 ± 1.6</td>
<td>16.2 ± 3.1</td>
<td>0.8</td>
</tr>
<tr>
<td>Platelet count, x10 / µL</td>
<td>89 ± 10</td>
<td>96 ± 9</td>
<td>0.3</td>
</tr>
<tr>
<td>Creatinine level, mg/dL</td>
<td>1.2 ± 0.8</td>
<td>1.3 ± 1.1</td>
<td>0.08</td>
</tr>
<tr>
<td>Leukocyte count, x10 / µL</td>
<td>10.3 ± 1.5</td>
<td>11.9 ± 0.9</td>
<td>0.6</td>
</tr>
<tr>
<td>Preoperative drug exposure, no. (%):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>23 (45.1)</td>
<td>26 (48.1)</td>
<td>0.06</td>
</tr>
<tr>
<td>Heparin</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Type of surgery, no. (%):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single valve</td>
<td>15 (29.4)</td>
<td>17 (31.4)</td>
<td>0.07</td>
</tr>
<tr>
<td>Multiple valves</td>
<td>14 (27.4)</td>
<td>13 (24.1)</td>
<td>0.06</td>
</tr>
<tr>
<td>CABG</td>
<td>17 (33.3)</td>
<td>17 (31.5)</td>
<td>0.08</td>
</tr>
<tr>
<td>CABG with valve (s)</td>
<td>5 (9.8)</td>
<td>7 (13)</td>
<td>0.1</td>
</tr>
<tr>
<td>Redo surgery</td>
<td>22 (43.1)</td>
<td>21 (38.9)</td>
<td>0.09</td>
</tr>
<tr>
<td>CPB time, min</td>
<td>129 ± 21.3</td>
<td>127 ± 23.4</td>
<td>0.6</td>
</tr>
<tr>
<td>Aortic cross clamp time, min</td>
<td>98 ± 16.7</td>
<td>94 ± 13.6</td>
<td>0.7</td>
</tr>
<tr>
<td>Intra-operative transfusion §:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRBC’s</td>
<td>2</td>
<td>3</td>
<td>0.1</td>
</tr>
<tr>
<td>FFP</td>
<td>2</td>
<td>2</td>
<td>0.9</td>
</tr>
<tr>
<td>Platelets</td>
<td>6</td>
<td>4</td>
<td>0.7</td>
</tr>
</tbody>
</table>

* : Plus-minus values are means ± SD.

† : APACHE II denotes the Acute Physiology and Chronic Health Evaluation. The patients were assessed on the day of admission to the ICU. The range of scores for this test is 0 to 71, with higher scores indicating more severe illness.

‡ : MODS, multiple organ dysfunction score; COPD, chronic obstructive pulmonary disease; IHD, ischemic heart disease; EuroSCORE, European System for Cardiac Operative Risk Evaluation; IQR, interquartile range; LVEF, left ventricular ejection fraction; aPTT, activated partial thromboplastin time; CPB, cardiopulmonary bypass; PRBC’s, packed RBC’s; FFP, fresh frozen plasma

Abbreviations: MODS, multiple organ dysfunction score; COPD, chronic obstructive pulmonary disease; IHD, ischemic heart disease; EuroSCORE, European System for Cardiac Operative Risk Evaluation; IQR, interquartile range; LVEF, left ventricular ejection fraction; aPTT, activated partial thromboplastin time; CPB, cardiopulmonary bypass; PRBC’s, packed RBC’s; FFP, fresh frozen plasma
There were no differences between the groups in the transfusion of fresh frozen plasma (23% vs. 19%, \( p=0.11 \)), platelets (8% vs 6%, \( p=0.92 \)), or cryoprecipitate (4% vs. 4%, \( p=0.97 \)) during their stay in the ICU. The use of medications, including vasoactive drugs; the administration of fluids and daily fluid balance; and the use of pulmonary artery catheters were similar in both groups throughout the stay in the intensive care unit. The use of other interventions such as dialysis, mechanical ventilation, and surgical procedures was also similar.

**Outcome measures:**

The primary end points were 30 days all-cause mortality and parameters of tissue perfusion: Lactate and ScVO\(_2\). There was no statistically significant difference in the 30 days all-cause mortality between the two strategies (7.4% in the liberal group vs. 5.8% in the conservative group, \( p=0.08 \)), Fig. (1).

The same also occurred with tissue perfusion parameters: There was no statistical significant difference in the level of lactate or in the ScVO\(_2\) concentration between the liberal and conservative transfusion groups during the ICU course, Figs. (2-A&2-B).

There was no significant difference between the liberal and conservative strategies in rates of cardiogenic shock (5% vs. 9%, \( p=0.42 \)), ARDS (2% vs. 3%, \( p=0.99 \)), or acute renal failure requiring dialysis or hemofiltration (5% vs. 4%, \( p=0.99 \)).

There were no significant differences in the occurrence of cardiac complications (21% vs. 24%, \( p=0.27 \)), respiratory complications (11% vs. 11%, \( p=0.82 \)), neurologic complications (6% vs. 6%, \( p=0.96 \)), infectious complications (10% vs. 12%, \( p=0.58 \)), or severe bleeding requiring reoperation (4% vs. 5%, \( p=0.97 \)). There were also no differences in lengths of ICU stay (3 ± 1.1 days vs. 3 ± 0.9 days; \( p=.94 \)) or hospital stay (9 ± 2.3 days vs. 9 ± 1.9 days, \( p=0.45 \)).

The patients who had CABG surgery were analyzed separately, 24 patients in the liberal strategy group (17 CABG alone and 7 CABG with valve surgery), compared to 22 patients in the conservative strategy group had CABG (17 CABG alone and 5 CABG with valve surgery), \( p=0.78 \). Two patients only in each group died by day 30 (3.7% vs. 3.9% respectively, \( p=0.94 \)), Fig. (3).
The perfusion parameters also didn’t show statistical significant difference between the 2 strategy groups. Fig. (4-A & 4-B).

The incidences of various complications in the subgroup of CABG patients were also in the same range compared to their incidences in the whole study population. There was no statistical significant difference in the incidences of various complications between the 2 strategies in CABG subgroup of patients.

**Effects of RBCs transfusion on outcomes:**

In total, 31 patients (29%) received an RBC transfusion. Patients who received RBC transfusions were older (mean, 61.3 ± 12.7 vs. 58.5 ± 14.2 years \( p=0.03 \)) and more likely to be smokers (55% vs. 39%, \( p<0.01 \)). They had a higher mortality (16% vs. 2.7%, \( p<0.001 \)), a higher EuroSCORE values (median, 5 vs. 3; \( p<0.01 \)), lower preoperative hemoglobin levels (11.3 ± 2.3g/dL vs. 13.2 ± 1.8g/dL, \( p<0.05 \)) and, longer cardiopulmonary bypass duration (123 ± 14.6 vs. 103.5 ± 10.9 minutes, \( p=0.03 \)). After admission to the ICU, patients who received an RBC transfusion had higher Acute Physiology and Chronic Health Evaluation II scores (15 ± 3 vs. 9.4 ± 4.1, \( p<0.01 \)) and Simplified Acute Physiology Score II values (20.3 ± 6.5 vs. 17.6 ± 7.1, \( p<0.01 \)) compared with those who did not. Patients who received RBC transfusions had longer lengths of ICU stay (median, 4 vs. 3 days; \( p<0.01 \)) and hospital stay (median, 14 vs. 10 days, \( p<0.01 \)) compared with non-transfused patients.

**Discussion**

Our results showed that using hemoglobin level of 7gm/dL as a threshold for transfusion is associated with non-significant decrease in 30 days mortality and not associated with impaired perfusion parameters or increased incidence of complications compared to using the hemoglobin threshold of 9gm/dL in ICU patients having cardiac surgery.

The issue of blood transfusion trigger has been one of the controversies among medical practitioners. In a prospective randomized controlled clinical trial of 838 critically ill patients (not including patients undergoing cardiac surgery), Hebert et al. showed that a restrictive strategy of red blood cell transfusion was as effective as and possibly superior to a liberal transfusion strategy [26]. Not only that but he supported a causal link between blood transfusion and adverse outcomes in critically ill patients. When patients were randomized to liberal (transfusion threshold of hemoglobin <1 0g/dL) or restrictive (transfusion threshold <7g/dL) transfu-
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This controversy is more confusing among cardiac surgery patients early in their post-operative ICU course especially that the Guidelines from the Society of Thoracic Surgeons and Society of Cardiovascular Anesthesiologists emphasize the lack of evidence on transfusion triggers after cardiac surgery [12]. However, Hajjar et al. suggested that, in cardiac surgery, a restrictive transfusion strategy targeting a hematocrit of 24% is as safe as a liberal strategy targeting a hematocrit of 30%, with respect to a composite end point of 30-day mortality and inpatient clinical complications. Moreover, regardless of the treatment strategy, the number of transfused RBC units was an independent risk factor for worse outcomes, including mortality [27]. A subsequent subgroup analysis of patients with cardiovascular disease in the Transfusion Requirements in Critical Care (TRICC) trial showed a trend toward increased survival in the liberal transfusion group, but transfusion also resulted in a statistically significant increase in pulmonary edema and multi organ system dysfunction [28]. In a similar retrospective study, Murphy et al. [29] showed that RBC transfusion was strongly associated with Infection and with postoperative ischemic morbidity, hospital stay, increased early and late mortality, and hospital costs. This study joins a decade of observational studies demonstrating an association between red blood cell transfusion and adverse outcomes in cardiac surgery [9,30-32]. In a dose-dependent and often durable manner, red blood cell transfusion in cardiac surgery patients has been linked as an independent variable to an increase in infectious complications, myocardial infarction, stroke, renal failure, prolonged ventilation, atrial fibrillation, hospital length of stay, and mortality.

A number of randomized, controlled clinical trials have addressed the hypothesis that oxygen delivery should be increased or maintained at high levels to minimize the effects of tissue hypoxia caused by disease processes that interfere with oxygen delivery or the body’s ability to extract oxygen. One meta-analysis [33] found that oxygen delivery was increased when oxygen therapy was initiated preoperatively, but this benefit was not observed in studies that evaluated patients admitted to the intensive care unit. The historic rationale for blood transfusion includes the purported benefit of improved oxygen delivery. Tissue hypoxia occurs in healthy adults at hemoglobins as low as 5 to 6g/dL (hematocrits of 15 to 18) [34,35]. In all the previous studies, the transfusion thresholds exceeded 1.0g per deciliter; therefore, it was not possible to make inferences about optimal strategies for red-cell transfusion. In spite, there has been a specific concern about the adverse effects of anemia in patients with ischemic heart disease [6]. Two large cohort studies found that an increasing severity of anemia was associated with a disproportionate increase in mortality rates among patients with ischemic heart disease [5,36]. Moreover, some studies in patients with anemia and myocardial infarction seem to suggest that transfusion may be beneficial [37]. Wu et al. [38] published an analysis based on Medicare administrative data that showed an improvement in survival for patients >65 years of age treated for acute myocardial infarction if they received blood transfusions when their admission hematocrit was <30.

On the other hand, subsequent studies based on clinical data suggested that blood transfusion was a risk factor for death and myocardial infarction in patients with acute coronary syndromes [39]. Rao et al. [40] found this association to be significant for patients who received blood for hematocrits <25%. Although the immediate impact on survival is significantly greater, transfusion with as little as 1 unit of red blood cells has been associated with decreased 10-year survival after coronary artery bypass grafting [31]. In a retrospective analysis of 11963 patients who underwent isolated CABG surgery, Koch et al. showed that perioperative RBC transfusion was associated with a dose-dependent increased risk of postoperative cardiac complications, serious infection, renal failure, neurologic complications, overall morbidity, prolonged ventilator support, and in-hospital mortality [32].

Another two small studies in patients undergoing CABG surgery suggested that different transfusion strategies gave similar outcomes [41,42]. A systematic review of transfusion [43] identified five randomized, controlled clinical trials that compared clinical outcomes after the implementation of two transfusion strategies. Two of them were in patients undergoing bypass surgery [41,42] and another pilot study [16] did not find differences between the transfusion strategies but were too small to yield clinically useful inferences. Dardash et al. [44] couldn’t associate RBC transfusions with...
a risk for increased long-term mortality in CABG patients when 8U or less is transfused during the hospital stay. Instead, it indicates that patient-related factors, such as pre-operative renal function and Hemoglobin levels, affect survival.

In our study, as expected, the conservative strategy patients received fewer RBC units than the liberal-strategy patients and, consequently, had lower mean hemoglobin levels during the study. Interestingly, this didn't result in a higher incidence of mortality or clinical complications among neither the whole study population nor the CABG subgroup of patients. Presumably this occurred because the conservative strategy did not result in tissue hypoxia. This is supported by the lack of difference in lactate levels and ScVO₂ between the 2 groups during the study period.

Limitations of our study include that it was performed in a single referral center for cardiac surgery, which could compromise the generalizability of our findings. Another limitation is the lack of blood leuko depletion in our study, but again could limit generalizability. Some studies, [45,46] but not all, [47] have suggested better outcomes in critically ill patients who receive transfusion of leuko-depleted RBCs. The potential higher risk associated with use of non leuko-depleted blood in our study may be compensated for by the relatively young age of the RBCs, the result of routine active selection of fresh blood (stored less than 10 days) for patients undergoing cardiac surgery at our institution. In one study, [48] transfusions with blood stored for more than 14 days were associated with a significant increase in morbidity and mortality in patients undergoing cardiac surgery.

Conclusions:

The use of conservative transfusion strategy is as safe as the liberal strategy in post operative cardiac surgical patients regarding the 30 days mortality, perfusion parameters and clinical complications.

References

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