Original Article

Increased Demand for Blood Transfusion in Cardiac Surgery, Simple but Unsolved Common Problem

Mahnoosh Foroughi[1], Majid Golestani Eraghi[2], Zahra Ansari Aval[1], Hanieh Majidi[1]

Abstract

Background: Despite the general concern about the safety of blood transfusion and mounting evidence exist for more restrictive practice; there is no national consensus guideline and uniformity of institutions for blood transfusion associated with coronary artery bypass graft surgery in Iran. The aim of this study is an assessment of current transfusion practice and compares it with one decade ago.

Materials and Methods: The authors retrospectively analyzed the data of all patients undergoing elective surgery (first time operation) during one year, in two different decade interval (2003 and 2015) in a tertiary heart center.

Results: A total of 801 patients were evaluated and compared (n=249 in 2015, n=552 in 2003). There is a significant increase in the use of blood transfusion in both operating room and at ICU than the last decade (60.6% vs. 42.4%, p<0.001, and 54.4% vs. 39.9%, p <0.001, respectively). The incidence of preoperative anemia was four times higher in patients who received transfusion, compared to those who did not, in both groups. With compared to the past, the patients are older, have less preoperative hematocrit, more diabetic, more need to intra-aortic balloon pump, shorter operation time, and less postoperative bleeding.

Conclusion: With advanced knowledge about transfusion complications and conservative approach to transfusion practice, the need to blood transfusion is increased in current cardiac operations in our center, due to association of more co-morbidity.

Keywords: Blood conservation, Coronary artery bypass grafting, CPB

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1. Cardiovascular Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Tracheal Diseases Research Center, National Research Institute of Tuberculosis and Lung Diseases

Corresponding Author: Mahnoosh Foroughi, MD, Cardiovascular Research Center, Sa'adat Abad, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
Email: m_foroughi@sbmu.ac.ir

Introduction

The growing evidence indicating inevitable blood transfusion during cardiac surgery is dose dependent and associated with increase morbidity and mortality. In addition to systemic inflammatory response due to cardiopulmonary bypass, leukocyte containing blood transfusion induces immune modulation, stimulates to release more inflammatory cytokines (IL6, IL12, TNFα) and procalcitonin, and lower level of anti-inflammatory marker like IL10. Any effort to reduce blood products are valuable (1-6).

The presence and synergistic effect of constant factors such as: acute hemodilution, the complexity of the cardiac surgeries and patients factors (comorbidities, preoperative anemia, age,

small body size, female gender and non-elective surgery) may explain high rate of blood transfusion during cardiac surgery (1, 2, 7).

Preoperative anemia, blood loss, and nadir of hematocrit (Hct) are risk factors of perioperative blood transfusion (2, 5). Although blood transfusion is often life-saving, but there is a growing body of evidence suggests an association between blood transfusion and increased morbidity, mortality, waste of resources, in addition to significant cost (4, 8-11). Several pharmacological agents and mechanical methods in the perioperative setting have been introduced to reduce perioperative transfusion, but the lower safe limit of hematocrit (Hct) in cardiac surgery patients was not described.

The objective of present study was to explain the transfusion management and physicians practice during one decade in a tertiary cardiac center in Iran and its comparison with other countries.

Methods

The surgical and anesthetic procedures were same during this decade. Standard monitoring was instituted before surgery (arterial pressure, central venous pressure, electrocardiogram, urinary catheter and nasal temperature). The surgical staffs were the same during the study period.

Study Population

The study was designed as a retrospective cross-sectional study in a tertiary educational referral hospital in Tehran, Iran. Patients who underwent elective primary coronary artery bypass grafting (CABG) using cardiopulmonary bypass (CPB) in 2003 and 2015 (one decade interval) were studied based on inclusion and exclusion criteria. All other types of cardiac procedures, off-pump CABG, combination of CABG with other cardiac surgeries and preoperative blood transfusion were excluded. The Research Ethics Committee approved the use of anonymous data and the need for individual patient consent form was waived.

Data Collection

The authors performed a retrospective review of prospectively collected data. All demographic, clinical and paraclinical date, laboratory findings, cardiovascular risk factors such as, hypertension, smoking, diabetes mellitus, previous myocardial infarction, operative details (time of CPB and aortic clamp, the number of grafted vessels, need to intra-aortic balloon pump (IABP), exploration for bleeding), 30-days survival and transfusion therapy were collected.

Transfusion Guideline

Hct level was measured at preoperative admission, after arterial line placement, 10 minutes after initiation of CPB, every 30 minutes during CPB, before termination of CPB, and every 30 min. after CPB in the operating room, upon arrival and every four hours in the ICU from the first day after surgery (and more frequently in bleeding, or unstable patients). Except to life-threatening bleeding, an absolute indication for blood transfusion, transfusion decision was based on Hct and was constant during this decade: an Hct level of 20–22% during CPB. After CPB weaning and return of remained blood, patients were transfused for Hct ≤27%. The Hct threshold for blood transfusion was 26–28% in the ICU. If the patient's status showing signs of hemodynamic instability, or excessive bleeding, the cardiac intensivists could administer blood transfusion outside this policy. However, blood transfusion was not allowed for an Hct 30%, or greater. When blood was ordered for transfusion, the blood bank provided the oldest available matching unit for each request. Leucodepletion has not been used for transfused blood.

Return to operating room was considered, if the patient had sustained hemodynamic instability not responding to an intravenous fluid with increasing requirement for inotropic support in the setting of excessive chest bleeding. The transfusion protocol was followed by all care givers.

Statistical Analysis

Dichotomous and categorical variables were presented as percentages and were tested by the Chi-square test. Continuous variables were expressed as mean±SD and one way analysis of variance was performed to compare the means among the groups. Statistical analyses were performed using SPSS version 12.0 (SPSS Inc, Chicago, Illinois) and $P<0.05$ was considered statistically significant.

Results

Study Population

Based on our criteria, 801 adult patients who had undergone CABG (n= 552 in 2003 and n=249 in 2015) were eligible for the study and 66 patients were excluded due to incomplete data record. Preoperative demographic characteristics, intraoperative data and postoperative variables are summarized in Tables1and 2 respectively.

Baseline Hct concentration showed a significant decrease during this interval. The prevalence of anemia (according to WHO definition cutoff values for women: 12 g/L and men: 13 g/L) had increased significantly from 17.9% in 2003 to 31.6% in 2015 (p=0.00), with no gender tendency. The incidence of preoperative anemia was four times higher in patients, who received transfusion compared to those who did not, in both groups (3.7% *vs*. 18.2%, p= 0.00).

Duration of surgery and CPB time and excessive postoperative hemorrhage need to exploration in patients of 2015 were significantly less than patients of 2003 (table 2). There was a significant decrease in the total number of distal grafts, but it does not seem clinically different. There were no differences between the groups in mediastinal drainage and length of ICU and hospital stay. Hospital mortality had not significant differences between the groups. There were no

Table 1: Preoperative demographic data of patients.

Groups	2015 (N=249)	2003 (N=552)	P value
Male (%)	190 (76.3%)	387 (70.1%)	0.07
Age (years)	60.7± 9.3	59± 9.9	0.02*
Hyperlipidemia (%)	90 (37.3%)	246 (44.6%)	0.06
Hypertension (%)	133 (53.6%)	269 (48.8%)	0.2
Diabetes mellitus (%)	91 (37%)	160 (29%)	0.02*
Family history for CABG (%)	43 (18.1%)	108 (19.6%)	0.6
Anemia (%)	78 (31.6%)	98 (17.9%)	0.000*
Active smoking (%)	86 (35.1%)	189 (34.2%)	0.8
Myocardial infarction (%)	76(30.8%)	139 (25.2%)	0.1
Blood Urea Nitrogen (mg/dL)	40.2±19	22±11.1	0.000*
Creatinine (mg/dL)	1.2±0.7	1.2±0.5	0.6
Fasting blood sugar (mg/dL)	134±65	120±54	0.001*
Hematocrit (%)	40±4.7	41.8±4.8	0.000*
β blockers (%)	202 (83.1%)	354 (64%)	0.000*
Aspirin (%)	181 (73.3%)	117 (21.7%)	0.000*
ACEI (%)	168 (68%)	302 (56%)	0.002*
Diuretics (%)	52 (20.9%)	78 (14.5%)	0.03*

Table 2: Operative and postoperative data.

Groups	2015 (N=249)	2003 (N=552)	P Value
Ejection Fraction (%)	45.3±10.7	46.4±10.6	0.1
Graft number	3.1±0.7	3.4±0.8	0.000*
Clamp time(minute)	59.5±18.9	68.5±18.5	0.000*
Pump time(minute)	105.8±29.3	113.4±30.7	0.001*
IABP (%)	35(14.7%)	31(5.6%)	0.000*
Bleeding (%)	9 (3.7%)	78 (14.1%)	0.000*
Hospital mortality (%)	6 (2.4%)	8 (1.4%)	0.3

Table 3: Intra and postoperative blood transfusion data.

	2015 (N=249)	2003 (N=552)	P value
Operative transfused packed cell (%)	152(62%)	233(42.4%)	0.000*
Operative transfused packed cell(mean)	1.2±1.3	0.5±0.7	0.000*
ICU transfused packed cell(mean)	1.1±1.5	0.7±1.3	0.001*
ICU transfused packed cell (%)	218 (29.9%)	134 (54.5%)	0.000*
Totally blood transfusion(intra and postoperative transfusion)	195(80.6%)	350(64.5%)	0.000*

intraoperative deaths in either group. Preoperative withdrawal of autologous blood is not performed due to anemia and short hospital-stay before operation.

Transfusion

Intra-and postoperative blood transfusion data are shown in Table 3. While the incidence of transfusion was increasing from 42.4% in 2003 to 62% in 2015, the blood units administered per patient also increased from a mean of 0.5 units in 2003 to 1.2 units in 2015. In 2003 group, a total number of 755 units of packed red blood cell were used for transfusion, 324 units were transfused during operation and 431 units in the postoperative period. This data had increased to 602 and 316, respectively, in 2015 group.

The significant association between female gender and increased need to transfusion was only seen in 2003 group during operation (male/female: 33.5% vs. 63.4%, p=0.000). Table 4 shows gender differences in blood transfusion requirement and anemia prevalence. There were no association between coexisting diseases and patients, who were treated with blood transfusion.

Group differences according to transfusion

Left ventricular ejection fraction was comparable in patients who received blood transfusion and who did not in both groups. Patients who received perioperative blood transfusions had more distal anastomoses than patients who did not in 2003 group (p= 0.02) with no significant difference in 2015 group (p=0.3). The duration of CPB had a significant effect on the magnitude of blood transfusion (p=0.006). Chest tube drainage has no important difference between the groups. According to WHO definition of anemia, it had increased prevalence in both genders during this decade. The

Table 4: Sex differences in need to blood transfusion.

variable	gender	2015 (n=249)	2003(n=552)	P value
Intraoperative transfusion	Male	58.6%	33.5%	0.00
	Female	72.9%	63.4%	0.18
ICU transfusion	Male	52.7%	37.7%	0.04
	Female	60.3%	45.1%	0.00
Anemia (%)	Male	23.9%	13.3%	0.001
	Female	7.7%	4.6%	0.007

incidence of re-exploration (in most cases for excessive bleeding) is much higher in patients receiving more blood.

Discussion

There was a significant increase in the use of blood transfusion during coronary surgery in a tertiary heart center after one decade, despite increasing evidence suggesting potential adverse events of blood transfusion. The patients of 2015 group were older with more co-morbidity such as diabetes and anemia. The management of coronary artery disease was changed during this interval. The operation time get shorter than the past with less exploration for bleeding with no increase in hospital death in the presence of more co-morbidity.

The prevalence of CABG is decreased to <50% due to introduced percutaneous intervention methods, less invasive treatment options, and fewer surgery recommendation.

Our center does not have limitation of blood transfusion resources and transfusion is free of charge for patients and hospitals in Iran. The government pays all the cost, without contribution from hospitals, reassurances and patients. There is less concern of blood supply issues for our relative young population in comparison with old-age population in other countries (14).

There was a universal concept of improved cardiac output and oxygen delivery by blood transfusion (2, 3, 6, 15) and usually physicians notice Hct threshold during perioperative blood loss without notice clinical symptoms. It seems fear from detrimental physiologic effects of severe anemia may be responsible for inappropriate high-transfusion rate. A lot of studies confirmed even in critical care and cardiac surgery patients the restrictive strategy (transfusion threshold with Hb<7gr/dl) is as safe as liberal strategy with no more adverse outcome (2, 16-17).

There is an increasing evidence that relying on a single parameter without clinical signs of acute anemia, or oxygen deprivation (such as, tachycardia, hypotension, high oxygen-extraction ratio, low mixed venous oxygen saturation, and echocardiographic guided indices) may not be accurate for blood transfusion (2-4, 6, 8, 14, 16). There is a common conclusion in all of them: the less blood transfusion is better. Why does not it happen in practice?

The higher morbidities of patients with cardiac surgery and the complexity of the procedure augment this disparity (4, 5, 13, 16-21) which is even present in results of dose dependent relationship between transfusion units and morbidity/mortality (2, 8, 11-13, 17, 18, 22-24). The discrepancy is true for duration of storage blood and adverse outcome after cardiac surgery too (11, 13, 25-27). The published results of a study in more than 5000 cardiac surgery patients in 72

centers among 16 countries showed the rate of blood transfusion was 9–100% in intraoperative period, and 25-87% in postoperative period during 1996–2000 (14). The significant differences in transfusion practice were observed in different countries and between centers of each country. It was reported according to American College of Physicians Transfusion Guidelines, 76% of transfusions were deemed to be inappropriate. They found US patients are much more likely to receive blood, despite having similar rates of anemia and bleeding to non-US study populations with no better outcomes (28).

In a similar designed study, an observational cohort of 102470 patients with inclusion criteria of our study in 2008 at 798 cardiac centers in the US showed the blood transfusion rate was 56.1% (7.8–92.8%). They found that more use of blood transfusion at academic hospitals and those in lowest quartile of surgery volume (<115 operation/year) (9). In a comparable study on 3,374 CABG operations in 25 cardiac centers in UK (68% of UK adult cardiac surgery centers), the mean use of packed cell was 2.98 units (range 0–32) in 2010. Only 12% of cardiac centers had protocol for optimization of preoperative Hct before elective cardiac surgery (11). Straten et al. studied the data of more than 10,000 isolated CABG during 10 years; one third of them had transfusion (18).

The lowest safe limit of Hct level, where the benefits of transfusion outweigh the risks is unknown. The authors believe the main cause in failure to achieve a consensus about transfusion during cardiac surgery is the presence of numerous studies with opposite results. The known responsible factors are preoperative characteristics of patients, operative characteristics, hospital factors and surgeons' hemostatic practices. Attention to these aspects may help to identify patients at a high risk for transfusion and facilitate optimization leading to reduced perioperative blood transfusion (2, 6, 9, 13, 18, 22, 29-31).

It is presumed that the most important parameter is physician education to accept and believe in practice that restrictive transfusion strategy is safe and possibly more beneficial. It is the time to change the current practice behavior and accept permissive anemia, and make transfusion decisions based on clinical assessment of evidence of ischemia.

Both preoperative anemia and blood transfusion are associated with adverse outcomes. Today patients with more illnesses are undergoing cardiac surgery with more need to transfusion. It makes difficult to assess a cause and effect relationship between transfusion and outcome, as it may be secondary to the transfusion indication and not the blood itself (1, 2, 8, 32-34). It was suggested preoperative anemia in patients with higher comorbidities are less tolerated (30, 35).

The different dogmas persist in the field of ischemic heart disease. It was thought that these patients were less tolerant to anemia, due to decreased oxygen delivery to myocardium (36). The aim of blood transfusion is to restore adequate tissue oxygen delivery (13). It has been observed that blood transfusion in cardiac surgery increases oxygen delivery, while oxygen consumption remains stable (15). Some of evidence showed despite augmenting oxygen transport capacity, the stored blood transfusion may not necessarily contribute to improvement in microcirculatory oxygenation, and even may cause tissue ischemia and organ dysfunction (13, 20, 21). Some studies suggested blood transfusion in the setting of acute coronary syndrome (ACS) was a risk factor for mortality and MI, while nadir hematocrit as low as 25% may be tolerated in otherwise stable patient with ACS (17, 28).

The relationship of Hct level to perioperative myocardial ischemia is not clear, since the balance of oxygen supply/demand during CPB is affected by dilutional anemia, reduced vascular resistance, and increased blood viscosity (37, 38). According to the recent STS guideline, hematocrit level as low as 20% is safe in cardiac surgery with CPB due to associated hypothermia and increased viscosity (2, 39). The studies had shown lower Hct than this threshold is associated with adverse outcome, and interruption of myocardial metabolism recovery in early postoperative period (16,19,23,35,37).

The results of Austrian benchmark study confirmed 98% of all transfusions in surgical patients are secondary to pre-operative anemia, important surgical blood loss and refusal with a more restrictive hemoglobin threshold for transfusion (38).

In agreement with these findings, a study of 14,259 cardiac surgical procedures (during 2006-2010) used a multidisciplinary approach, with the aim of reduction in blood transfusion. The incidence of blood transfusion was decreased significantly with improvement in patients' outcome (10). More other studies had the similar results with up to 75% reduction of unnecessary blood transfusion (6,13,40). This event was not happened at this Center, by increased rate of anemic patients, without preoperative anemia correction and doubt about restrictive transfusion safety. It may confirm unnecessary increased transfusion rate, potentially unnecessary cost and care, even if it is not deleterious.

The findings should be considered in the context of the following limitations. Due to the nature of a database and its design, some important factors unavailable in this database included length of storage of the blood, the nature of preoperative anemia, and lack of blood leukodepletion in our study.

The study is the first to compare blood transfusion practice, after one decade in cardiac surgery patients as single center experience. The selection criteria used and the design of the study resulted in a sample that is very likely to represent the transfusion practices of most academic hospitals in Iran. The findings of this study may have important clinical implications. The results will help to convince the medical community to adopt a positive attitude toward the practice of blood conservation in cardiac surgery; believe that tolerance of anemia is a safe strategy and emphasize to treat preoperative anemia (and delay of surgery if necessary), as physician practices are slow to change.

Conclusion

Re-evaluation of transfusion practice in patients of cardiac surgery is suggested due to safety concerns about stored blood. To reduce the need for blood transfusion during cardiac surgery, adopting restrictive strategy and evaluation of the patient's clinical situation are the important factors. A protocol assessment of patients for preoperative optimization of Hct prior to elective cardiac surgery is suggested. It seems that blood conservation policy is a belief before being a mandatory protocol.

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Conflicts of Interest

The authors declare that they have no conflict of interest.

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