**ORIGINAL ARTICLE**

# Multivariate predictors of blood transfusion in patients undergoing coronary artery bypass graft in Mashhad, Iran

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## Abstract

**Background:** Determining the factors associated with increased risk of transfusion in coronary artery bypass graft (CABG) surgery can help to decrease the rate of transfusion. This study was performed to determine the rate of blood transfusion in our CABG surgeries and the clinical and demographic variables associated with increased risk of blood transfusion.

**Methods:** Data were prospectively collected from patients undergoing CABG surgery in Emam Reza Hospital affiliated to Mashhad University of Medical Sciences in Mashhad, Iran from March 2005 and April 2006. Patients' variables including age, sex, height, weight, body mass index, surface body, estimated blood volume and preoperative hemoglobin concentration in relation to the need for blood transfusion were evaluated.

**Results:** Transfusion rate was 77.6%. Whole blood transfusion rate was more than that of packed red blood cells. In 70% of patients, transfusion was 1-2 units. The prediction rule included surgeon and height of patients.

**Conclusion:** This study and other transfusion guidelines help to change individual physician behavior and restrict factors in relation to the need for blood transfusion in CABG, such as hemoglobin. These changes result in a major reduction in the transfusion rate.

**Keywords:** Mitomycin –C; Epithelial cell; Cornea; Balanced salt solution

## Introduction

There has been a marked decrease in blood consumption for coronary artery bypass graft (CABG) surgery because of improvements in surgical, anesthesia and blood conservation techniques. Nevertheless, the incidence of blood transfusion in CABG surgery remains high.[1] Various factors such as red blood cells, platelets and coagulation factors, platelet dysfunction and activation of the coagulation, and fibrinolytic system predispose patients to preoperative transfusion.[2,3] Factors such as sex, age, preoperative hemoglobin concentration, surgeon, etc. are associated with the risk of transfusion.[2] The objectives of this study are to determine the rate of blood transfusion in our CABG surgeries and clarify the clinical and demographic variables associated with increased risk of blood transfusion.

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## Materials and Methods

We obtained data prospectively from patients undergoing CABG surgery at the Emam Reza Hospital affiliated to Mashhad University of Medical Sciences between March 2005 and April 2006. Patients who received blood after the first two postoperative days were not included in because in cases of prolonged hospital stay, some delayed transfusions would have been administered for reasons not related to surgery such as gastrointestinal bleeding.[1] More than 1000 open heart surgeries including about 500 CABG are

performed at this hospital every year by three surgeons. In addition to antibody screening, three units of packed red blood cells (RBCs) are cross-matched before CABG surgery for all patients. Blood conservation techniques used before surgery included discontinuation of anticoagulant medication one week before surgery and screening for coagulation disorders. Aspirin antiplatelet drug continued until surgery. Blood conservation techniques during surgery included the use of a non-hematic prime solution for the bypass pump, the intraoperative salvage of antilogous blood from the operative field, and the return of blood from the extracorporeal circuit after cardiopulmonary bypass. All the patients received heparin to achieve an activating clotting time more than 400 seconds during cardiopulmonary bypass. CABG procedure was performed in on- or off–pump. After cardiac surgery, all the patients were admitted to the postoperative cardiac unit where the patient to nurse ratio was 1:1 for the first 24 hours after surgery and were discharged from this unit to a regular hospital ward within 24 hours. The guideline for blood transfusion in this institute was Hct < 30% for patients undergoing CABG surgery. Preoperative patient variables that have previously been shown to be associated with the need for blood transfusion during CABG surgery were included. These are often factors associated with low preoperative RBC volume (Table 1).[1,2,4]

The initial analyses confirmed based on packed RBCs or whole blood transfusion during CABG surgery or after the first two postoperative days. The SPSS software (version 11.5) was used for the statistical analyses. Categorical variables were summarized as frequencies and percentages. Continuous variables had normal distributions and summarized as means and standard deviations (SD). A bivariate analysis (using the Chi-Square statistic for categorical variables and t test for continuous variables) was first carried out to assess the unadjusted relationship between the predictor variables and transfusion. A p value < 0.05 was considered significant. For the multivariate analysis of risk, logistic regression models were used. The initial model was derived, using all statistically significant predictor variables except hemoglobin (Table 2). Because some patients had missing values for hemoglobin, it was not included in the model. The appropriate model for the prediction rule was identified through Hosmer-Lemeshow Goodness-of-Fit test.

## Results

575 patients with CABG surgery were included in the analyses. Table 2 shows the patients' characteristics.

**Table 1:** Predictor variables.[1]

| Variable | Definition and unit of measurement |
|---|---|
| Preoperative Hb | Continuous variable (gr/dl) |
| Age | Continuous variable (years) |
| Sex | Binominal variable (male/female) |
| Height | Continuous variable (m) |
| Weight (Wt) | Continuous variable (kg) |
| Body mass index (BMI) | Continuous variable ($kg/m^2$) |
| Body surface area (BSA) | Continuous variable incorporating Ht and Wt (obtain from nomogram) |
| Estimated blood volume (EBV) | Continuous variable incorporating sex, Ht, Wt:<br>Men: EBV= 0.3669 $Ht^3$+0.03219 Wt+0.6041<br>Women: EBV= 0.3561 $Ht^3$+0.03308 Wt+0.1833 |
| Surgeon | Nominal variable ( classified as no 1-3) |

**Table 2.** Unadjusted relationship of continuous variables with transfusion.

| Variable | Numbers | Transfused | Not transfused | P value |
|---|---|---|---|---|
| Sex | | | | |
| Men | 395 | 294 (74.4%) | 101 (25.6%) | 0.008 |
| Women | 180 | 152 (84.4%) | 28 (15.6%) | |
| Surgeon | | | | |
| No 1 | 304 | 216 (71.1%) | 88 (28.9%) | |
| No 2 | 129 | 103 (79.8%) | 26 (20.2%) | < 0.001 |
| No 3 | 142 | 127 (89.4%) | 15 (10.6%) | |

446 patients (77.6%) received blood. Of those who received blood, 152 (34.1%) received 1 unit; 163 (36.5%), 2 units; 87 (19.5%), 3 units; 29 (6.5%), 4 units; 14 (3.1%), 5 units; and 1 (0.2%), 7 units. An average of 1.6 (SD=1.2) units of blood was transfused preoperatively per patient. The average unit of blood transfusion in patients receiving blood was 2.1 (SD=1.1) units. From all patients transfused, 91.7% received whole blood and 53.6% packed RBCs. The unadjusted relationships of the predictor variable to the risk of transfusion were shown in Tables 2 and 3. All variables except age and BMI were significantly related to the risk of transfusion. Of the several logistic regression models developed, the one identified as the best model for the prediction rule was surgeon and height. First and second surgeons had odds ratio of 0.26 and 0.36, respectively (Table 4 and Figure 1). It was also observed that with 1 cm rise in the patient's height, a decrease in transfusion rate would occur with the odds ratio of 0.97 (Table 4 and Figure 1).

Because surgeon is a categorical variable, two were considered as indicators, and the third surgeon as a reference. The other models that examined the impact of replacing weight and height with derived variables including blood volume, BMI and BSA were also considered. Sex was included in the model that assessed blood volume (even though blood volume was derived from the patients' sex, height, and weight) to determine whether sex is related to the risk of transfusion independent of its effect on blood volume. In this model, height replaced the blood volume variable.

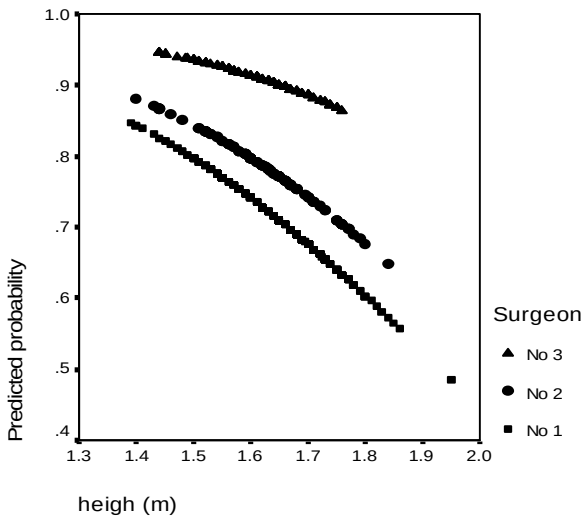


**Fig 1:** Prediction rule based on surgeon and height.

## Discussion

The use of blood transfusion on cardiac surgical intervention varies from 10-100% despite published transfusion guideline.[5,6] This variability is mostly due

**Table 3:** Unadjusted relationship of categorical variables with transfusion.

| Variable | Total numbers (N= 575) | Transfused (77.6%, N= 446) | Not transfused (22.4%, N= 129) | P value |
|---|---|---|---|---|
| Hb (gr/dl) | 13.7±1.2 | 13.5±1.3 | 14.1±1.2 | 0.018 |
| Age (years) | 58±10 | 58±10 | 57±11 | 0.392 |
| Weight (kg) | 71±12 | 70±12 | 73±11 | 0.022 |
| Height ( m) | 1.63±0.09 | 1.63±0.09 | 1.65±0.08 | 0.001 |
| BMI (kg/m$^2$) | 26.5±3.7 | 26.5±3.8 | 26.6±3.5 | 0.855 |
| BSA | 1.75±0.2 | 1.74±0.21 | 1.78±0.18 | 0.022 |
| EBV | 4.4±0.7 | 4.3±0.7 | 4.6±0.6 | < 0.001 |

**Table 4:** Final multiple logistic regression model selected for the prediction rule.

| Variable | Coefficient (β) | Standard error | Wald Chi- Square | P value | OR | 95% CI |
|---|---|---|---|---|---|---|
| Surgeon | | | 15.326 | <0.001 | | |
| No 1 | -1.341 | 0.345 | 15.112 | < 0.001 | 0.262 | 0.133- |
| No 2 | -1.011 | 0.396 | 6.525 | 0.011 | 0.364 | 0.514 |
| | | | | | | 0.167- |
| | | | | | | 0.790 |
| Height (cm) | -0.033 | 0.12 | 6.897 | 0.009 | 0.968 | 0.945- |
| | | | | | | 0.992 |
| Constant | 7.607 | 2.045 | | | | |

Abbreviations: CI = Confidence interval, OR = Odds ratio.

to differences in transfusion practice. Although surgical bleeding after open heart surgery is a common problem as reflected by the substantial use of blood products, the individual physician and institutional behavior rather than patient comorbidity or blood loss have been identified as the main reasons for blood transfusion.[1,7] To improve transfusion practice in heart surgery, several guidelines for transfusion and blood conservation have been published.[1,7-10] In spite of this, transfusion of allergenic blood in cardiac surgery is a major health problem; 10 to 20% of all donated units of blood are consumed during cardiac surgery.[5,6,11,12] Transfusion of allergenic red blood cells is associated with well-documented mortality and morbidity after cardiac surgery.[6,12-15] Excessive bleeding after cardiac surgery occurs because of alterations in the homeostatic system pertaining to dilutional thrombocytopenia, excessive hemeostatic activation, and exposure to long acting anti-platelet or antit-hrombotic agents.[6]

There has recently been a marked reduction in the use of blood components for CABG surgery because of improvements in surgical techniques such as off-pump CABG, anesthesia and blood conservation techniques. Therefore, according to recent reports, about one-third of patients with CABG surgery require allergenic blood.[1,9,15] In this study, the overall rate of preoperative transfusion in patients having CABG surgery was 77.6%. This rate of transfusion can be decreased by the modification of transfusion habits, using transfusion and blood conservation guidelines.[1,6,7,11] In our institute, the rate of whole blood consumption was more than packed RBCs. At present, whole blood consummation has limited the clinical indication so that the major indication is massive hemorrhage. There is a progressive loss of the labile coagulation factor V and factor VIII when blood is stored at 1° to 6°. Therefore, in the cases of the need to replace coagulation factor, one can use packed RBCs along with fresh frozen plasma (FFP). If one wants to increase the velocity of infusion, packed RBCs with FFP, crystalloid or colloid solutions can be diluted.[16-18] In this study, 70% of the patients who needed blood transfusion received 1-2 units of blood. This fact shows that the velocity of infusion and the rate of bleeding are not often urgent. Therefore, packed RBCs could be used instead of whole blood in the majority of patients. Average units of blood transfusion were 1.6 (±1.2) units per patient, which is similar to that in other studies.[9,19-21]

The previous studies showed that hemoglobin and weight were inversely related to the risk of transfusion, age being directly related to the risk of transfusion, and woman were at higher risk of transfusion than men.[1,2,11,14,22] BSA, BMI and blood volume are variables derived from weight and height that are inversely related to the risk of transfusion.[2,6,11,23] The surgeon performing the procedure and institutional behavior has been identified as the main reason for transfusion.[1,7] All variables of this study, except age and BMI were related to the risk of transfusion in unvaried analysis (Table 1). Perhaps the absence of the relation between age and risk of transfusion was due to the lower age average in this study than in other reports.[2,8] It seems that the influence of sex on the risk of transfusion is due to the smaller blood volume of women.[1] There was no difference in the rate of transfusion in men compared to women. The rate of transfusion in men was 10% more than that in women. In another study, 64.2% rate of transfusion in men and 17.6% in women have been reported.[1] The transfusion trigger hemoglobin concentration or hematocrit below which anaesthesists consider RBC transfusions varies from patient to patient, but for cardiac patients, this should be set between 7 and 9 g/dl (Hct= 20-25%).[1,6,9,10,12] Hemoglobin concentration less than 10 gr/dl (Hct < % 30) was used as a trigger for blood transfusion. This concentration is more than that in other reports. It was also considered that 70% of patients with blood transfusion consumed 1-2 units of blood. It is known that transfusion of one unit of blood in an adult raises the hematocrit about 1% to 3%.[17] So with the use of lower trigger hematocrit concentration for blood consumption, a marked decrease in the rate of transfusion will occur. First and second surgeons had odds ratio of 0.26 and 0.36, respectively (Table 4 and Figure 1). Therefore, the rate of transfusion in the first and second surgeons in comparison to the third one decreased 84% and 64%, respectively. It was also observed that with 1 cm rise in the patient's height, a decrease in transfusion rate would occur with the odds ratio of 0.97 (Table 4 and Figure 1).

Our study limitations were first, the patients who were enrolled that underwent non-elective as well as elective CABG surgeries. Non-elective cases had a higher risk for blood transfusion.[1,21,23] Second, we did not have the discharge Hb concentration of patients who received blood. The fact that discharge hemoglobin of patients was lower than that of those who did not receive blood suggests that patients had been appropriately transfused.[1]

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## References

**1** Karkouti K, Cohen MM, McCluskey SA, Sher GD. A multivariable model for predicting the need for blood transfusion in patients undergoing first-time elective coronary bypass graft surgery. *Transfusion* 2001;**41:**1193-1202.

**2** Parr KG, Patel MA, Dekker R, Levin R, Glynn R. Multivariate Predictors of Blood Product Use in Cardiac Surgery. *J Cardiothorac Vasc Anesth* 2003;**17:**176-181.

**3** Marietta M, Facchini L, Pedrazzi P, Busani S, Torelli G. Pathophysiology of Bleeding in Surgery. *Transplant Proc* 2006;**38:**812–814.

**4** Body SC, Birmingham J, Parks R, Ley C, Maddi R, Shernan SK, Siegel LC, Stover EP, D'Ambra MN, Levin J, Mangano DT, Spiess BD. Safety and efficacy of shed mediastinal blood transfusion after cardiac surgery: a multicenter observational study. Multicenter Study of Perioperative Ischemia Research Group. *J Cardiothorac Vasc Anesth* 1999;**13:**410-6.

**5** Stover EP, Siegel LC, Parks R, Levin J, Body SC, Maddi R, D'Ambra MN, Mangano DT, Spiess BD. Variability in transfusion practice for coronary artery bypass surgery persists despite national consensus guidelines: a 24-institution study. Institutions of the Multicenter Study of Perioperative Ischemia Research Group. *Anesthesiology* 1998;**88:** 327-33.

**6** Arora RC, Le´gare´GF, Buth KJ, Sullivan JA, Hirsch GM, M. Identifying Patients at Risk of Intraoperative and Postoperative Transfusion in Isolated CABG: Toward Selective Conservation Strategies. Ann Thorac Surg 2004; 78: 1547-55.

**7** Shander A, Moskowitz D, Rijhwani TS. The safety and efficacy of "bloodless" cardiac surgery. *Semin Cardiothorac Vasc Anesth* 2005; **9:**53-63.

**8** Van der Linden P, De Hert S, Daper A, Trenchant A, Jacobs D, De Boelpaepe C, Kimbimbi P, Defrance P, Simoens G. A standardized multidisciplinary approach reduces the use of allogeneic blood products in patients undergoing cardiac surgery. *Can J Anaesth* 2001;**48:**894-901.

**9** Nydegger U. Transfusion dependency in cardiac surgery–update 2006. *Swiss Med Wkly* 2006;**136:** 781-788.

**10** Murphy GJ, Angelini GD. Indications for Blood Transfusion in Cardiac Surgery. *Ann Thorac Surg* 2006;**82:**2323–34.

**11** Moskowitz DM, Klein JJ, Shander A, Cousineau KM, Goldweit RS, Bodian C, Perelman SI, Kang H, Fink DA, Rothman HC, Ergin MA. Predictors of Transfusion Requirements for Cardiac Surgical Procedures at a Blood Conservation Center. *Ann Thorac Surg* 2004;**77:**626–34.

**12** Diprose P, Herbertson MJ, O'Shaughnessy D, Deakin CD, Gill RS. Reducing allogeneic transfusion in cardiac surgery: a randomized double-blind placebo-controlled trial of antifibrinolytic therapies used in addition to intra-operative cell salvage. *Br J Anaesth* 2005;**94:**271-278.

**13** Spiess BD. Transfusion of blood products affects outcome in cardiac surgery. *Semin Cardiothorac Vasc Anesth* 2004;**8:**267-81.

**14** Banbury MK, Brizzio ME, Rajeswaran J, Lytle BW, Blackstone EH. Increases the Risk of Postoperative Infection after Cardiovascular Surgery. *J Am Coll Surg* 2006;**202:**131-138.

**15** Koch CG, Li L, Duncan AI, Mihaljevic T, Loop FD, Starr NJ, Blackstone EH. Transfusion in Coronary Artery Bypass Grafting is Associated with Reduced Long-Term Survival. *Ann Thorac Surg* 2006; **81:**1650-7.

**16** Levy JH, Tanaka KA, Steiner ME. Evaluation and management of bleeding during cardiac surgery. *Curr Hematol Rep* 2005;**4:**368-72.

**17** Boral LI,Weiss ED, Henry JB: Transfusion medicine. In: Henry JB, ed. Clinical diagnosis and management by laboratory methods. 20th ed, Philadelphia: WB Saunders Company; 2001; p.735-745, 758.

**18** Allen MB, Component Preparation and Storage. In: Hillyer CD, et al. Blood Banking and Transfusion Medicine. 1st ed: Churchill Livingstone; 2003. P. 154.

**19** Renton MC, McClelland DB, Sinclair CJ. Use of blood products in cardiac surgery. *Perfusion* 1997;**12:**157-62.

**20** Leal SR, Jiménez PI, Márquez JA, Flores JM, Muñoz JM, Fernández JM. Supply of blood to heart surgery patients. Can transfusion habits be changed? *Medicina Clínica Med Clin (Barc)* 1996;**106:**368-71.

**21** Liu B, Belboul A, Larsson S, Roberts D. Factors influencing haemostasis and blood transfusion in cardiac surgery. *Perfusion* 1996;**11:** 131-43.

**22** Surgenor DM, Wallace EL, Churchill WH, Hao SH, Chapman RH, Collins JJ Jr. Red cell transfusions in coronary artery bypass surgery (DRGs 106 and 107). *Transfusion* 1992; **32:**876.

**23** Magovern JA, Sakert T, Benckart DH, Burkholder JA, Liebler GA, Magovern GJ Sr, Magovern GJ Jr. A model for predicting transfusion after coronary artery bypass grafting. *Ann Thorac Surg* 1996;**61:**27-32.