August 2008

Predictive model of blood transfusion during CABG surgery in Pakistan

Sana Shoukat
Aga Khan University

Saqib A Gowani
Aga Khan University

Farhad Khimani
Aga Khan University

Faraz A Khan
Aga Khan University

Mohammad Zaman
Aga Khan University

See next page for additional authors

Authors
Sana Shoukat, Saqib A Gowani, Farhad Khimani, Faraz A Khan, Mohammad Zaman, and Hasanat Sharif

Predictive Model of blood transfusion during CABG Surgery in Pakistan

Sana Shoukat[1], Saqib A. Gowani[2], Farhad Khimani[3], Faraz A. Khan[4], Mohammad Zaman[5], Hasanat Sharif[6]

Medical Officer[1], Medical Students[2,3,4], Faculty of Health Sciences, Aga Khan University, Karachi, Department of Psychiatry[5], Aga Khan University, Karachi, Cardiothoracic Section, Department of Surgery[6]

Abstract

Objective: To determine predictors of need for transfusion of blood and blood products and create a clinical predictive model to reduce indiscriminate use of blood products during surgery.

Method: We conducted a retrospective chart review of 485 patients who underwent coronary artery bypass surgery from January 2004 to December 2004 at a Tertiary Care Hospital in Karachi, Pakistan. Independent predictors associated with transfusion were identified and a clinical prediction model developed.

Results: The transfusion rate was 37.1%. A predictive model was created based on the presence of pulmonary disease, diabetes mellitus, low ejection fraction and recent/ongoing myocardial infarction.

Conclusion: The study identifies some predictors of need for blood transfusion in patients undergoing Coronary Artery Bypass Grafting. However, prospective studies with a larger sample of patients are needed to determine other predictors and their applicability in patient selection across institutions (JPMA 58:421;2008).

Introduction

Coronary artery bypass-graft surgery (CABG) currently is the commonest cardiac operation performed in the adult population.[1] There have been great advances in perfecting this surgery leading to reduced number of complications. However, the complications related to blood transfusion are still high. According to international figures, use of blood transfusions for cardiac patients is as high as 10-40%, presumably higher in Pakistan considering the lack of blood conservation strategies.[2,3] The patients requiring blood transfusion make up more than one third of those going for elective CABG.[4]

Transfusion of blood or its products are reported as the most important factor associated with increased risk of postoperative morbidity and mortality following a coronary artery bypass graft surgery.[5,6] The risks associated with transfusion include infectious disease transmission, acute and delayed haemolytic reactions, transfusion-related acute lung injury and transfusion related immunomodulation.[7,8] These morbidities not only affect the patient's quality of life and risk of death after the procedure but also add a huge cost burden especially if a lifelong infection is acquired.

Blood conservation techniques including preoperative autologous blood donation (PABD), intraoperative use of antifibrinolytic drugs, hypervolaemic

haemodilution, preoperative erythropoietin administration and acute normovolaemic haemodilution are expensive and carry their own risks.[9,10] It is therefore imperative to have a model that selects patients for such procedures and patients who will eventually need a transfusion.

At the same time, risks related with use of blood in Pakistan are higher than the developed world. The prevalence of Hepatitis B exposure determined by Anti-HBc prevalence in healthy blood donors is reported to be as high as 17% and at the same time, not all blood bank facilities are well equipped for infectious disease detection in donors.[11,12] An average patient receiving two units of blood has a 10% chance of acquiring hepatitis C infection.[11] It is obvious that transfusion related risks are higher in the country than reported in the literature. To the best of our knowledge, no study has been conducted to explore the predictors for use of blood products in patients undergoing CABG in Pakistan.

Several studies have explored predictors for the use of blood and blood products in patients undergoing CABG. The various predictors include preoperative haemoglobin, red cell mass, body mass index, body surface area, female sex, age, extent of disease, number of diseased vessels, prior CABG, redo procedure, emergent operation, diabetes and renal disease, extent of acute normovolaemic haemodilution, use of cardiopulmonary bypass, ejection fraction albumin, preoperative antiplatelet or antithrombotic drugs and preoperative bleeding and prothrombin times[2,13-17] the above predicators cannot be applied to our population , as the demographics and outcome of surgery may be variable.

We aimed to determine the predictors of transfusion of blood and blood products in patients undergoing CABG in a tertiary care centre in Pakistan and develop a clinical prediction model for use of blood products in patients undergoing CABG.

Patients and Methods

After institutional ethics approval, data on consecutive patients who had undergone CABG surgery at a tertiary care hospital, from January 2004 to December 2004 was retrieved retrospectively. All patients undergoing CABG surgery during this time period at were included. Those with missing record files and unclear or incomplete information were excluded.

The study was conducted in a tertiary care teaching hospital (representing private sector) of Karachi, Pakistan. A total of 510 open-heart surgical procedures were performed during the study year at this institution. Blood-conservation methods used before surgery included discontinuation of anti-platelet and anticoagulant medication 1 week prior to surgery and screening for and correction of coagulation disorders. Blood-conservation methods used during surgery included the administration of antifibrinolytic agents (tranexamic acid and aprotinin). On routine, recycled pumped blood was used in all patients. Blood was transfused in patients with haemoglobin levels less than 10 mg/dl if off-pump and 7 mg/dl if on-pump.

Platelets and fresh frozen plasma was empirically given to any patient who had episode of bleeding post operatively.

The exposure variables were divided into continuous and categorical variables. The continuous variables included age (years), Body Mass Index (kg/m^2), preoperative haemoglobin (g/dl), preoperative platelet, preoperative prothrombin time, preoperative activated partial thromboplastin time, preoperative bleeding time, ejection fraction, cardio-pulmonary bypass duration (min) and aortic clamp duration (min).

The categorical variables included gender, use of anti-platelets, anticoagulant or antithrombotic agents (defined as more than 2 weeks of use of the agent prior to the surgery), coagulation defects (history of any coagulopathy or objective evidence of coagulation defect pre-operatively), smoking (ex and current smokers combined), renal dysfunction (defined as Cr>1.1 mg/dl), hypertension (history of hypertension and being on antihypertensive therapy at the time of surgery), peripheral vascular disease (defined as a history of claudication, ischaemic resting pain, vascular surgery or a non invasive vascular test showing > 50% obstruction of the lower extremity vasculator), carotid artery disease (Carotid doppler proven > 70% stenosis of carotid artery), diabetes mellitus (as history of diabetes mellitus, Type I or II, and being on medication at the time of surgery), pulmonary disease (known history of pulmonary disease or FEV1 < 1.5 L at the time of surgery), recent/ ongoing myocardial infarction (based on EKG changes and Trop I > 0.5 ng/ml), type of surgery defined as urgent, emergent or elective and catheterization during admission. All variables except gender and type of surgery were binomial variables defined as Yes/No.

The primary outcome measure was blood transfusion given intra-operatively or post-operatively.

Preoperative and peri-operative patient variables previously reported to be associated with the need for blood transfusion during CABG and other cardiac surgeries were determined along with variables which revealed a statistically significant association. Database accuracy was measured by re-abstracting a random sample of 10 percent of the medical records of CABG patients. In addition, all outlying values were compared to patients' records to identify and correct errors in the database.

SPSS 15.0 (copyright © SPSS Inc., 1989-2007) was used for statistical analysis.

Results were expressed as mean ± standard deviation for all continuous variables and frequency and percentage for categorical data. Univariate analysis was performed by using the independent sample t-test, Pearson Chi-square test and Fisher Exact test wherever appropriate to assess the unadjusted relationship between the predictor variables and the outcome. A p-value <0.05 was considered as statistically significant.

The initial model was derived by using all statistically significant (p<0.25, the standard criterion for selection of candidate variables to be used in multivariate analysis) predictor variables that were not confounding with other variables. The best fitting model was identified from different models, each derived from different predictor variables. The Hosmer and Lemeshow goodness-of-fit test was also used to determine the final model.[18]

Results

Among 485 patients 82.5% (n=400) were male and 17.5% (n=85) female. The mean age of the patients was 58. 5 ± 9.6 years. Mean Body Mass Index of the patient population was 26.6 ± 4.5 kg/m^2. Out of 485 CABG surgeries performed during the study period selected 68.9 %(n=334) were elective, 22.3% (n=108) were urgent and 8.9% (n=43) emergency.

Of the 485 patients undergoing CABG, 21.0% (n= 102) patients had acute coronary syndrome with 19.8% (n=96) having a recent or ongoing myocardial infarction at the time of presentation.

Hypertension was a common comorbid seen in 70.7% (n= 343) of the patients while 43.1% (n=209) had diabetes, 39.0% (n= 189) had dyslipidaemia, 4.5% (n=22) had renal disease, 1% (n=5) had carotid artery disease and 6.6 %(n=32) patients had pulmonary disease, whereas 2.1% (n=10) of the patients had a history of previous coronary bypass surgery. Mean preoperative haemoglobin and haematocrit level of the patients were 12.8 ± 1.8mg/dl and 38.6 ± 73.4% respectively. The mean International Normalized Ratio was 1.02 ± 0.13. 73.4% (n= 356) of the patients were exposed to some form of anteplatelet therapy prior to the surgery. Among this group, majority (95.2%) had taken aspirin. These medications were stopped in 68.2% (n= 331) patients at a mean of 5 days before the surgery was performed.

Majority of the procedures were carried out using the conventional technique, (only a small proportion (2.3%; n=11) used the off pump technique. Mean cardiopulmonary bypass time was 99.1 ± 31.9 minutes. Aortic Cross Clamp time was 59.9 ± 20.7 minutes. Intra-aortic Balloon Pump (IABP) use was found in 9.1% (n=44) cases. Blood or blood products were used in 37.1% (n= 180) of the patients.

The complications of surgery occurred in 9.9% (n=48) patients. 45.8% of these suffered from hemorrhage.

On univariate analysis presence of diabetes mellitus differed significantly between the patients who required blood transfusions and who did not. Also, ejection fraction, presence of pulmonary disease, prothrombin time, recent/ongoing myocardial infarction differed between the two groups, however, it was not significant. We found no interaction among the variables used in univariate analysis. The comparison of all variables between the two groups is shown in Tables 1 and 2.

We applied multiple logistic regression on all the significant variables to put together a predictive model for transfusion requirement during CABG. Hence, after removing all the confounded variables, a model consisting of diabetes mellitus, pulmonary disease, ejection fraction and recent/ongoing myocardial infarction were found as predicting factors for need of blood transfusion in patients undergoing CABG surgery (Table 3).

Table 1. Unadjusted relationship of continuous variables with transfusion (n=485)

Variable	Transfused (180,37.1)	Not transfused (305, 62.9)	p value
Patient variables			
Age (years)	58.9 ±9.3	58.3±9.7	0.52
Body Mass Index (kg/m^2)	26.9±5.0	26.5±4.1	0.42
Preoperative Hemoglobin (g/dl)	12.6±1.9	12.9±1.7	0.15
Preoperative Platelet (x10^9/l)	250.7±69.7	241.6±72.4	0.19
Preoperative Prothrombin Time (sec)	12.1±1.0	12.3±1.8	0.07
Preoperative Activated Partial Thromboplastin Time (sec)	30.6±5.3	30.2±6.0	0.48
Preoperative Bleeding Time (sec)	3.0±1.5	3.2±1.7	0.15
Ejection Fraction (%)	50.3±10.6	48.4±11.8	0.07
Perioperative variables			
Cardiopulmonary Bypass Duration (min)	101.1±35.3	97.9±29.7	0.31
Aortic clamp Duration (min)	60.7±24.1	59.4±18.5	0.53

Table 2. Unadjusted relationship of categorical variables with transfusion (n=485).

Variable	Transfused	Not transfused	Odds Ratio (OR)	Confidence Interval (95% CI)	P-value
Patient variables					
Gender					
Male	148 (82.2)	252 (82.6)	1.0		0.91
Female	32 (17.8)	53 (17.4)	1.0	0.6-1.7	
Preoperative variables					
Anti platelet usage					
No	55 (30.6)	74 (24.3)	1.0		0.13
Yes	125 (69.4)	231 (75.7)	0.73	0.5-1.1	
Anti coagulant usage					
No	154 (85.6)	253 (83.0)	1.0		0.45
Yes	26 (14.4)	52 (17.0)	0.82	0.5-1.3	
Thrombolytic usage					
No	1 (0.6)	2 (0.7)	1.0		0.89
Yes	179 (99.4)	303 (99.3)	1.2	0.1-13.1	
Coagulation defects present					
No	178 (98.9)	301 (98.7)	1.0		0.85
Yes	2 (1.1)	4 (1.3)	0.9	0.2-4.7	
Re-operation					
No	176 (97.8)	299 (98.0)	1		0.85
Yes	4 (2.2)	6 (2)	1.1	0.3-4.1	
Smoking					
No	114 (63.3)	195 (63.9)	1.0		0.89
Yes	66 (36.7)	110 (36.1)	1.0	0.7-1.5	
Renal dysfunction					
No	173 (96.1)	290 (95.1)	1.0		0.6
Yes	7 (3.9)	15 (4.9)	0.8	0.3-2.0	
Hypertension					
No	48 (26.7)	94 (30.8)	1.0		0.33
Yes	132 (73.3)	211 (69.2)	1.2	0.8-1.9	
Peripheral Vascular disease					
No	179 (99.4)	305 (100.0)			
Yes	1 (0.6)	0			
Carotid artery disease					
No	178 (98.9)	302 (99.0)	1.0		0.89
Yes	2 (1.1)	3 (1.0)	1.1	0.2-6.8	
Diabetes Mellitus					
No	91 (50.6)	185 (60.7)	1.0		0.03
Yes	89 (49.4)	120 (39.3)	1.5	1.0-2.2	
Pulmonary disease					
No	163 (90.6)	290 (95.1)	1.0		0.06
Yes	17 (9.4)	15 (4.9)	2.0	1.0-4.1	
Recent/ongoing Myocardial Infarction					
No	137 (76.1)	252 (82.6)	1.0		0.08
Yes	43 (23.9)	53 (17.4)	1.5	0.95-2.4	
Perioperative variables					
Type of surgery					
Elective	18 (10.0)	25 (8.2)	1.0		0.79
Emergency	39 (21.7)	69 (22.6)	1.2	0.7-2.4	
Urgent	123 (68.3)	211 (69.2)	1.0	0.6-1.5	
Catheterization during admission					
No	139 (77.2)	230 (75.4)	1.0		0.65
Yes	41 (22.8)	75 (24.6)	0.91	0.6-1.4	

Table 3. Final multiple logistic regression model selected for the prediction rule*

Variable	Odds ratio	95% CI	P value
Diabetes Mellitus	1.6	1.1-2.3	0.021
Pulmonary disease	2.1	1.0-4.4	0.048
Ejection fraction	1.0	1.0-1.0	0.028
Recent / ongoing Myocardial Infarction	1.5	1.0-2.4	0.071

Discussion

Variability of transfusion rate in different institutions has been demonstrated frequently in literature.[3] The differences have been attributed to adherence to different blood saving techniques and adherence to different guidelines, availability of products and quality of surgical care to the patients. The rate of 37.1% in our study setting is comparable to Karkouti et al where strict guidelines for blood conservation were employed.[19]

However, we found very few similarities with previous studies while looking at independent predictors of need for blood transfusion in our study. For instance, factors associated with reduced red cell volume including a low HB, Haematocrit and red cell mass have been significantly associated with need for blood transfusion in other studies.[13-15,19] This lack of association in our data could be attributed to low threshold of haemoglobin levels and haematocrit levels for blood transfusion practiced in our institution.

A lack of association of need of transfusion with sex was also different from other similar studies conducted in other countries. But this result must be interpreted with caution as the state of revascularization surgeries for females was drastically lower than those of males in the study. This could not have been controlled as fewer women than men suffer from serious heart disease to require cardiac revascularization procedures in a year.

The factors found to be significantly associated with need for blood products in our study are unrelated to each other and hence may add to the strength of the clinical predictive model. Ejection fraction being an independent predictor is not a novel finding and is consistent with other studies. A poorer outcome in patients with a low ejection fraction has previously been established and hence this group of patients becomes high risk for operative and postoperative complications.[20] A higher risk of blood transfusion with a low ejection fraction is a result of limited reserve of blood pumping power to meet the demands of vital end organs and hence early transfusion becomes essential.

A recent/ on going myocardial infarction could be explained partially by its effect on the ejection fraction and the overall efficiency of systemic circulation and partially by instability of vital signs as a result of a recent cardiovascular episode.

The other two factors, presence of pulmonary disease and diabetes mellitus are difficult to explain biologically but nonetheless were seen be independently associated with need for blood transfusion for the procedure. A compromise of vascularity and reserve of oxygenation of end organs remains a hypothesis.

The differences seen between our study and the rest of the literature is also attributed to major differences in the populations where these studies were conducted. Therefore, not all predictors significantly associated with transfusion in other settings could play a role in our setting of South Asian population.

What is important to note is that this study is the first of is kind ever done in a large tertiary care hospital of the South Asian region and has provided a clinical predictive model that will benefit surgeons and anaesthesiologists in decision making for transfusion for their patients. Hence they can rely on local experience along with international blood conservation guidelines, which may or may not be valid for our population. This study also highlights presence of high variability of transfusion practice, predictors of transfusion and predictive models across populations and institutions.

The retrospective study design and data from a single private tertiary care hospital are limitations of the study. Major differences exist in private and public hospitals and between different parts of the country and therefore limits the applicability of this model nationally. Also, predictive factors of use of whole blood and those of blood products may be potentially different but this was not assessed separately in our study. However, we found our results comparable with other similar studies conducted in which this separation of predictive models of different blood products was not assessed.[2,13,19]

Conclusion

Employing a clinical predictive model and following blood conservation guidelines can help to select the right patients who need transfusion during CABG surgery. The prediction rule comprises of presence of pulmonary disease, diabetes mellitus, ongoing/recent myocardial infarction and a low ejection fraction. This rule needs to be validated to assess its applicability. Gender differences in need of transfusion also need to be explored.

References

1. Steinbrook R. Public report cards--cardiac surgery and beyond. N Engl J Med 2006; 355: 1847-9.
2. Arora RC, Legare JF, Buth KJ, Sullivan JA, Hirsch GM. Identifying patients

at risk of intraoperative and postoperative transfusion in isolated CABG: toward selective conservation strategies. Ann Thorac Surg 2004; 78: 1547-54.

3. Stover EP, Siegel LC, Parks R, Levin J, Body SC, Maddi R, et al. 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.
4. Karthik S, Grayson AD, McCarron EE, Pullan DM, Desmond MJ. Reexploration for bleeding after coronary artery bypass surgery: risk factors, outcomes, and the effect of time delay. Ann Thorac Surg. 2004; 78: 527-34.
5. Koch CG, Li L, Duncan AI, Mihaljevic T, Cosgrove DM, Loop FD, et al. Morbidity and mortality risk associated with red blood cell and blood-component transfusion in isolated coronary artery bypass grafting. Crit Care Med 2006; 34: 1608-16.
6. Engoren MC, Habib RH, Zacharias A, Schwann TA, Riordan CJ, Durham SJ. Effect of blood transfusion on long-term survival after cardiac operation. Ann Thorac Surg 2002; 74: 1180-6.
7. Goodnough LT. Risks of blood transfusion. Crit Care Med 2003; 31: S678-86.
8. Madjdpour C, Heindl V, Spahn DR. Risks, benefits, alternatives and indications of allogenic blood transfusions. Minerva Anestesiol 2006; 72: 283-98.
9. Spahn DR, Casutt M. Eliminating blood transfusions: new aspects and perspectives. Anesthesiology 2000; 93: 242-55.
10. Linden JV, Kruskall MS. Autologous blood: always safer? Transfusion 1997; 37: 455-6.
11. Luby S, Khanani R, Zia M, Vellani Z, Ali M, Qureshi AH, et al. Evaluation of blood bank practices in Karachi, Pakistan, and the government's response. J Pak Med Assoc 2006; 56: S25-30.
12. Bhatti FA, Ullah Z, Salamat N, Ayub M, Ghani E. Anti-hepatits B core antigen testing, viral markers, and occult hepatitis B virus infection in Pakistani blood donors: implications for transfusion practice. Transfusion 2007; 47: 74-9.
13. Covin R, O'Brien M, Grunwald G, Brimhall B, Sethi G, Walczak S, et al. Factors affecting transfusion of fresh frozen plasma, platelets, and red blood cells during elective coronary artery bypass graft surgery. Arch Pathol Lab Med 2003; 127: 415-23.
14. Moskowitz DM, Klein JJ, Shander A, Cousineau KM, Goldweit RS, Bodian C, et al. Predictors of transfusion requirements for cardiac surgical procedures at a blood conservation center. Ann Thorac Surg 2004;77: 626-34.
15. Scott BH, Seifert FC, Glass PS, Grimson R. Blood use in patients undergoing coronary artery bypass surgery: impact of cardiopulmonary bypass pump, hematocrit, gender, age, and body weight. Anesth Analg 2003; 97: 958-63.
16. Shevde K, Pagala M, Kashikar A, Tyagaraj C, Shahbaz N, Iqbal M, et al. Gender is an essential determinant of blood transfusion in patients undergoing coronary artery bypass graft procedure. J Clin Anesth 2000; 12: 109-16.
17. Litmathe J, Boeken U, Feindt P, Gams E. Predictors of homologous blood transfusion for patients undergoing open heart surgery. Thorac Cardiovasc Surg 2003; 51:17-21.
18. Hosmer DW, Lemeshow S. Applied Logistic Regression: John Wiley & Sons New York 1996.
19. 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: 1193-203.
20. Christakis GT, Weisel RD, Fremes SE, Ivanov J, David TE, Goldman BS, et al. Coronary artery bypass grafting in patients with poor ventricular function. Cardiovascular Surgeons of the University of Toronto. J Thorac Cardiovasc Surg.