Primary Isolated CABG Restrictive Blood Transfusion Protocol Reduces Transfusions and Length of Stay

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Abstract

Background: Cardiac surgeries use 10%–15% of red blood cells transfused in the United States, despite benefits of limiting transfusions. We sought to evaluate the the feasibility and impact of a restrictive transfusion protocol on blood use and clinical outcomes in patients undergoing isolated primary coronary artery bypass grafting (CABG). Methods: Blood conservation measures, instituted in 2012, include preoperative optimization, intraoperative anesthesia and pump fluid restriction with retrograde autologous priming and vacuum-assisted drainage, use of aminocaproic acid and cell saver, intra- and postoperative permissive anemia, and administration of iron and lowdose vasopressors if needed. Medical records of patients who underwent isolated primary CABG from 2009–2012 (group A; n=375) and 2013–2016 (group B; n=322) were compared. Results: CABG with grafting to 3 or 4 coronary arteries was performed in 262 (70%) and 222 (69%) patients and bilateral internal thoracic artery grafting in 202 (54%) and 196 (61%) patients in groups A and B, respectively. Mean preoperative and intraoperative hematocrit was 40.3% and 40.7%, 28.9% and 29.4% in groups A and B, respectively. Total blood transfusion was 24% and 6.5%, intraoperative transfusion 10% and 1.2%, postoperative transfusion 19% and 5.3% ($p<0.0001$ for all) in groups A and B, respectively. Median postoperative length of stay was 5.0 days in group A and 4.5 days in group B ($p = .02$), with no significant differences between groups in mortality or morbidity. Conclusions: A restrictive transfusion protocol reduced blood transfusions and postoperative length of stay without adversely affecting outcomes following isolated primary CABG.

Introduction

Cardiac surgical procedures account for 10% to 15% of the 15 million units of red blood cells (RBCs) transfused in the United States annually.[1] More than 32% of patients undergoing coronary artery bypass grafting (CABG) receive a transfusion.[1] Blood transfusions and re-exploration for bleeding have been shown to increase mortality and major morbidity after cardiac surgery.[2-8] Despite the potential risks from transfusions, prevalence of transfusions varies widely nationwide.[9] Transfusion guidelines set forth by the Society of Thoracic Surgeons (STS) in 2007[10] and again in 2011[11] have not resulted in substantially decreased blood use in cardiac operations.[1] The purpose of this study was to assess a multifaceted blood conservation and transfusion protocol developed and applied at a community hospital cardiac surgery program.

Methods

Perioperative blood conservation measures were established in our institution in 2012. Medical records that included transfusion data and clinical outcomes of patients who underwent isolated primary CABG from 2009 to 2012 (group A) and 2013 to 2016 (group B) were compared. Most operations were performed by a single surgeon (RA). Clinical outcomes (mortality, morbidity, and postoperative length of stay) and transfusions were measured as endpoints. Groups were compared using simple descriptive statistics and a chi-square test or Wilcoxon rank sum test as appropriate. A p-value $<.05$ was considered significant.

Blood Transfusion Protocol Guidelines

Preoperative

Preoperative procedures included optimizing the patient's condition. Medically stable patients were released and readmitted electively. All blood thinners were withheld before operation: enoxaparin sodium for at least 24 hours, rivaroxaban and apixaban for at least 3 days, and antiplatelet drugs (clopidogrel and ticagrelor) for 5 to 7 days. Erythropoietin was administered if hematocrit was <30%, especially in patients with renal failure whose surgery could be scheduled electively.

Intraoperative

During surgery, pre-pump anesthesia fluid was restricted to 400 cc. Cardiopulmonary bypass fluid was limited to 300 cc with the help of retrograde autologous priming and vacuum-assisted drainage. Aminocaproic acid was administered to all patients, and cell saver was routinely used. Meticulous surgical technique with regard to homeostasis was paramount.

Postoperative

Fluid was cautiously administered, and permissive anemia to a hematocrit of 21% was tolerated if the patient was hemodynamically stable. Sodium ferric gluconate and low-dose vasopressors were administered if needed. As part of our protocol, quick re-exploration was adopted for high chest tube drainage.

Results

Patients

The study included 697 patients who underwent isolated primary CABG, 375 in group A and 322 in group B. CABG with grafting to 3 or 4 coronary arteries was performed in 262 (70%) and 222 (69%), and bilateral internal thoracic artery grafting was used in 202 (54%) and 196 (61%) of patients from groups A and B, respectively. Two hundred and seventy six (74%) and 243 (75%) patients were male, diabetes was present in 135 (36%) and 158 (49%) patients, hypertension in 337 (90%) and 312 (97%) patients, and severe left ventricular dysfunction in 63 (17%) and 48 (15%) patients, in groups A and B, respectively (Table 1).

Outcomes

There were no statistically significant differences in operative outcomes between the 2 groups. Mortality occurred in 2 patients (0.5%) and 1 patient (0.3%) (p= 0.7), renal failure in 3 patients (0.8%) and 2 patients (0.6%) (p= 0.75), bleeding in 4 patients (1.1%) and 3 patients (0.9%) (p= 0.8), infection in 2 patients (0.5%) and 1 patient (0.3%) (p =0.7) in groups A and B, respectively. Median postoperative length of stay decreased in group B compared to group A, (4.5 days in group B vs 5.0 days in group A;p =.02) (Table 2).

Prevalence of Blood Transfusions

Mean preoperative hematocrit was 40 ± 4.5% and 41 ± 4.7%, and mean intraoperative hematocrit was 29 ± 5.1% and 29 ± 4.7% (group A and B). Total blood transfusion decreased from an average of 24% to 6.5%, intraoperative transfusion from 10% to 1.2%, and postoperative transfusion from 19% to 5.3% (groups A and B) (p< 0.0001 for all [Table 3]).

Adoption of quick re-exploration for bleeding did not increase overall rate of return to the operating room (4 patients [1.1%] group A and 3 patients [0.9%] group B), but did lower the need for transfusions even in the subset of patients who were bleeding (all 3 patients [100%] in group A and only 1 patient [33%] in group B).

In group A, 41 (11%) patients received blood products intraoperatively, and of these, 6 (15%) received only 1 unit, 6 (15%) received only fresh frozen plasma and/or platelets, and 8 (20%) received red blood cells (RBCs) in addition to other products. In addition, in group A, 73 (19%) patients received blood products postoperatively, and of these, 57 (78%) received RBCs, with 27 (47%) patients receiving only 1 unit. In group B, on the other hand, 4 (1.2%) patients received blood intraoperatively, all RBCs with 2 (50%) receiving only 1 unit. In group B, 18 (5.6%) patients received blood postoperatively, with 12 (67%) receiving RBCs, and of these, 6 (50%) received only 1 unit.

Discussion

Blood transfusions and re-exploration carry substantial risk for postoperative morbidity and mortality and should be used prudently.[2-8,12,13] In a study of over 18,000 patients at Cleveland Clinic from 2000 to 2010, Vivacqua et al noted that transfusion and reoperation for bleeding were independently associated with increased risk of mortality and morbidity, respectively (8.5% vs 1.8%).[8] Mehta and colleagues noted a risk-adjusted mortality of 5.9% for bleeding post CABG in patients who required re-exploration compared to 2.0% for others.[4] Ranucci et al showed higher mortality (14.2% vs 3.4%; p = .001) and greater morbidity in patients requiring surgical re-exploration compared to patients who did not.[5] In addition, the amount of packed red blood cells was associated with significantly increased morbidity and mortality (0.25% increase for each unit transfused). In a study that included almost 5400 patients, Frojd et al noted a twofold increase in early postoperative mortality and an increase in risk of mortality beyond 90 days in patients requiring re-exploration for bleeding.[3] In an international prospective study of patients undergoing urgent CABG with acute coronary syndrome on antithrombotic agents, Stone et al noted that patients receiving > 4 units of packed red blood cells was an independent risk factor for mortality for up to 1 year after CABG.[6]Freeland and colleagues[14] noted that blood transfusion is an independent predictor of acute kidney injury in cardiac surgical patients. Several studies have linked transfusions to potentially lethal complications, including infection and lung damage.[15-18]

The landmark paper in 1979 by Cosgrove and colleagues[19] showed that blood transfusions during myocardial revascularization could be reduced to 6%. In his 2015 commentary, Svensson noted several important factors for achieving low prevalence of transfusions, including tolerating lower hematocrits on-pump and use of cell saver, among others.[20] He pointed out, however, that over time there has been an increase in transfusions, perhaps attributable to greater use of anticoagulant and antiplatelet agents and reduced concern regarding transfusion-related infections.

Although the Society of Thoracic Surgery established guidelines in 2007[10] and 2011[11] for blood transfusions, prevalence of transfusions in patients undergoing CABG increased from 12% in 1999 to 32% in 2010[1] and is likely associated with older age, increased comorbidities, and the complexity and multiple component aspect of surgical procedures. Nevertheless, only a small percentage of team members, including perfusionists, anesthesiologists, and even surgeons, reported reading the guidelines, implementing them, or altering practice habits.[1,21]

Cost effectiveness and value-based medicine have become a cornerstone of our health care system. Cardiac surgery accounts for a noteworthy proportion of the 14 million annual RBCs transfused in the United States.[9,22] Shanders et al noted the cost of transfusions to be US $1,158 per unit (2007 value) when indirect overhead and acquisition costs are included, and even higher when transfusion-related complications are considered.[23] In addition, the postoperative length of stay in the current study, was significantly reduced to 4.5 days in the blood restricted group, adding further cost savings as suggested and corroborated by others.[24,25]

The lack of adherence to conservation measures may be because of the assumption that restricting red blood cell use could be detrimental and undermine patient safety. This is contrary to the findings of several studies demonstrating the use of blood conservation techniques without adverse consequences.[26-28] Magruder and colleagues[29] noted significant variation in blood transfusion practices even after risk adjustment, suggesting that transfusion practices may be physician- rather than patient-driven.

Blood transfusions can be lifesaving and are more likely needed in patients at higher risk of blood loss, such as those undergoing reoperations, complex aortic, or valvular surgeries. As stated in the Introduction, the reported prevalence of transfusions for primary CABG is more than 32%, and the objective of this study was to concentrate on the subset of patients in whom transfusion reduction could be accomplished safely. A significant reduction in blood use for isolated primary CABG following implementation of perioperative conservation guidelines was observed, with no negative impact on patient safety or outcome. Transfusions decreased intraoperatively and postoperatively, resulting in a statistically significant decline in overall prevalence of transfusions and postoperative length of stay.

These findings can likely be extended to other surgeries as well. Yaffee and colleagues assessed a conservation strategy for aortic valve replacement, emphasizing permissive anemia and minimization of hemodilution (also through use of autologous priming and vasopressors).[30] They found a 14.9% decrease (82.9% to 68.0%) in the number of patients transfused with RBCs, as well as a 54.4% reduction in overall mean blood product transfusions, with no increase in mortality or major complications.[30]

Limitations

The main limitations of the current study are the retrospective nature of the study, with most cases performed by a single surgeon, and the population sample not being random, although it did include all isolated primary CABG patients during the 2 study periods. In addition, the protocol was implemented as a unit, so we could not analyze which techniques were more successful than others. For example, several of the protocol measures, such as cessation of blood thinners and use of aminocaproic acid and cell saver, were part of our practice to varying degrees during the first study period because their efficacy in reducing transfusions had been previously proven. The purpose of the protocol was to reduce transfusion rates, with the understanding that some variables could be more impactful than others. The study did not test any of these variables independently. However, a major change during the second period was tolerance of anemia both intraoperatively and postoperatively. Commonly, during the first period (group A), the hematocrit "trigger point" for transfusion was 26% compared with 21% for the second period (group B).

Some may argue that this study was underpowered to demonstrate improved outcomes from a restrictive transfusion protocol. First, the low risk of blood transfusion-related complications would require a much larger sample to demonstrate any meaningful difference. Second, outcomes typically measured with coronary revascularization would not necessarily capture some of the potential long-term transfusion-related complications. Third, the purpose of this study was to demonstrate the feasibility and safety of implementing a transfusion reduction practice in one of the most commonly performed cardiac operations, not to prove or disprove the risks of blood transfusions already well documented in the literature. Finally, there is a fundamental flaw with such an argument. When subjecting a patient to a treatment or intervention, the burden of proof should be on the intervening rather than the non-intervening group. To our knowledge, there are no studies demonstrating improved outcomes with transfusions. Should patients undergo an operation or receive chemotherapy with no proven benefit? Blood products are a scarce resource,[31,32] and exhausting them without a proven justification in an era of evidence-based medicine imposes a moral question. Should we transfuse a stable patient post-CABG merely for a predetermined hematocrit trigger point, while it could be life saving for another patient?

Two key issues are at hand. First is the realization and acceptance of the team caring for the patient that a blood transfusion does not lead to better outcomes and may actually be detrimental. Second, and perhaps more challenging, is taking ownership and interest in reducing blood use. This would require buy-in from all team members. At our facility, the primary caretaker is the surgeon, who must approve or deny all transfusion requests. This could be more challenging in other settings with multiple services (such as intensivists, residents, etc.), mandating strict adherence to a protocol agreed on by all.

Clinical Inferences

A stricter and more restrictive approach in transfusing patients after isolated coronary revascularization is called for owing to the lack of clinical evidence that transfusions lead to better outcomes, blood transfusions carrying potential risks of early and delayed complications, blood products being a limited resource that could be life saving for other patients, and cost factor in this era of increased cost awareness.

Conclusions

Adherence to a restrictive protocol can significantly reduce blood transfusions and postoperative length of stay in patients undergoing isolated primary CABG without adversely affecting outcomes. The current study warrants further investigation into using a restrictive transfusion protocol as a quality metric for isolated coronary revascularization.

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Table 1. Patient Characteristics

Characteristic	**Group A 2009–2012 (n=375)**	**Group B 2013–2016 (n=322)**	p-**Value**
Male	276 (74%)	243 (75%)	.8
Diabetes	135 (36%)	158 (49%)	.0005
Hypertension	337 (90%)	312 (97%)	.0002
Severe LV dysfunction	63 (17%)	48 (15%)	.5

Characteristic	Group A 2009–2012 (n=375)	Group B 2013–2016 (n=322)	p-Value
CABG x 3-4	262 (70%)	222 (69%)	.8
Bilateral ITA grafts	202 (54%)	196 (61%)	.06

Values are n (%). CABG x 3-4 = coronary artery bypass grafting with grafts to 3 or 4 coronary arteries; ITA = internal thoracic artery; LV = left ventricular; NS = not significant.

Table 2. Outcomes

Outcome	Group A 2009–2012 (n=375)	Group B 2013–2016 (n=322)	p-Value
Mortality (30 days)	2 (0.5%)	1 (0.3%)	.7
Renal failure	3 (0.8%)	2 (0.6%)	.7
Bleeding	4 (1.1%)	3 (0.9%)	.8
Infection	2 (0.5%)	1 (0.3%)	.7
Postoperative length of stay, days	4.0/5.0/7.0	3.0/4.5/7.0	.02

Values are n (%) or 15th/50th/85th percentiles.

Table 3. Hematocrit and Prevalence of Transfusion

Variable	Group A 2009–2012 (n=375)	Group B 2013–2016 (n=322)	p-Value
Mean hematocrit (%)			
Preoperative	40.3 ± 4.48	40.7 ± 4.66	.24
Intraoperative	28.9 ± 5.11	29.4 ± 4.67	.18
Transfusion			
Total	90 (24%)	21 (6.5%)	<.0001
Intraoperative	38 (10%)	4 (1.2%)	<.0001
Postoperative	71 (19%)	17 (5.3%)	<.0001

Values are mean ± SD or n (%). NS = not significant; SD = standard deviation.