The Heart Surgery Forum #2011-1179
15 (5), 2012 [Epub October 2012]
doi: 10.1532/HSF98.20111179

Online address: http://cardenjennings.metapress.com

Managing Port-Site Bleeding during Less Invasive Coronary Artery Bypass Grafting

Dr. Kiani

Soroosh Kiani, MD,[1] Mary-Lynn Brecht, PhD,[2] Katherine Lovinger, MS,
[2]Robert S. Poston, MD[1]

[1]Division of Cardiothoracic Surgery, University of Arizona School of Medicine, Tucson, Arizona, USA;
[2]UCLA Integrated Substance Abuse Programs, Los Angeles, California, USA

ABSTRACT

Introduction: Robotic-assisted coronary artery bypass grafting (r-CABG) requires the placement of ports bluntly through the chest wall. When removed, these ports create bleeding sites that can be difficult to detect and treat. This study evaluated whether a topical hemostatic agent placed locally within these sites helps to reduce bleeding and blood product requirements.

Methods: We retrospectively analyzed outcomes for r-CABG cases where 5 mL of a flowable hemostatic agent was injected locally within all port sites (hemostat group, n = 62) compared with patients whose port sites were untreated (controls, n = 131). Outcomes included chest tube output, red blood cell (RBC) transfusions, length of hospital stay, and the risk of reoperation for bleeding. Analyses were adjusted for risk factors known to influence bleeding and Society of Thoracic Surgeons (STS) risk score as a weighted composite of variables, which controls for patient and clinical variables.

Results: The 2 study groups had similar baseline characteristics and underwent the same r-CABG procedure. The hemostat group had significant reductions in RBC transfusion (24.2% versus 40.8% receiving blood; P = .026; 0.44 versus 1.39 U transfused postoperatively, P = .024). After adjustment for bleeding risks (using STS risk score), differences in transfusions remained significant. Reoperation rates for bleeding, length of stay, chest tube drainage, and intraoperative transfusions were not significantly different in the 2 groups.

Conclusions: There was significantly reduced postoperative bleeding and less exposure to blood products in the hemostat group. These findings suggest that undetected bleeding from sites used for port access serves as an underappreciated source of morbidity after r-CABG.

INTRODUCTION

Coronary artery bypass grafting (CABG) is a common operation, with more than 230,000 patients undergoing this procedure in 2007 [Roger 2011]. Techniques and outcomes of CABG have improved over time [Ferguson 2002; Sedrakyan 2006], with increased survival reported for selected patients undergoing CABG via sternotomy by grafting the internal mammary artery (IMA) [Loop 1986; Malenka 2005]. The use of robotic-assistance for CABG (r-CABG) enables grafting of one or both IMA vessels without a sternal incision. Expert centers have reported reduced length of hospital stay and time to return to work for patients undergoing r-CABG compared to the traditional approach [Mohr 1999; Mohr 2001; Morgan 2004].

The adoption of r-CABG has not been widespread, despite growing access to the robot [Robicsek 2008], in part because of concerns about the safety of this technique [Desai 2010]. One issue that affects safety is the inability to detect and treat bleeding through small incisions compared with full sternotomy. In contrast to traditional techniques, minimal access thoracic surgery usually requires 8 to 15 mm diameter ports to be inserted bluntly through muscle layers in the chest wall. Disruption of vessels within the local tissue space created by these ports causes a unique source of bleeding that does not easily tamponade on its own. Although not usually brisk, limited visualization and access to these tracts makes bleeding challenging to diagnose and treat.

Topical hemostats are an established part of the surgeon's armamentarium to control bleeding during surgery. Intraoperative use of a hemostatic agent with cross-linked gelatin granules and recombinant human thrombin (FLOSEAL Hemostatic Matrix, Baxter, Deerfield, IL, USA) has been shown to reduce bleeding during spinal, nasal cavity, and cardiac surgical procedures [Oz 2000; Renkens 2001; Jameson 2006; Côté 2010]. However, there has been no investigation into the use of this or any other topical hemostatic agent to control port-site bleeding. Given the ability of gelatin to swell and tamponade bleeding in confined spaces, we hypothesized that application of this particular hemostatic agent within port sites would reduce bleeding after r-CABG.

PATIENTS AND METHODS

Study Design

This was a retrospective sub-study of a prospective observational analysis of patients undergoing r-CABG at a single institution that was approved by the local institutional review board. In this sub-study, patients who underwent r-CABG from May 3, 2008, to June 9, 2009, and who did not receive flowable hemostatic (control group) were compared with patients that received a dose of hemostatic agent within the

Received December 9, 2011; accepted April 24, 2012.

Correspondence: Robert S. Poston, MD, Cardiothoracic Surgery, PO Box 245071, Tucson, AZ 85724-5071; 520-626-7951; fax: 520-694-6101 (e-mail: postonlab@gmail.com; soroosh@bu.edu).

tissue tracts created by the port sites between June 11, 2009, and April 15, 2010 (hemostat group). The flowable hemostatic agent was not used on port sites prior to June 2009.

Patient Selection

All study participants gave written informed consent prior to surgery. The primary inclusion criterion was the presence of diseased coronary targets suitable for grafting via a mini-thoracotomy ± percutaneous coronary intervention (PCI).

Surgical Procedure and Bleeding Management

After securing one-lung ventilation, 2 8.0 mm ports were placed in the third and seventh intercostal spaces (ICS) at the midaxillary line. A third 12.0 mm port for the camera was placed in the fifth ICS. The robot (Intuitive Surgical, Mountain View, CA, USA) was connected to these ports and used to harvest one or both IMA with CO_2 insufflation at 8 to 10 mmHg pressure.

Distal anastomoses were completed manually via small thoracotomy on the beating heart using stabilizing devices (Medtronic, Inc, Minneapolis, MN, USA). Systemic heparin was administered prior to coronary occlusion. Cardiopulmonary bypass was initiated via femoral artery and vein cannulation based on ischemia or unstable hemodynamics. If a hybrid strategy was used, PCI was performed in a separate setting using 6F guiding catheters with pre- and post-dilation of coronary lesions at the discretion of the operator. Drug-eluting stents were implanted in these patients, and aspirin and clopidogrel were administered prior to PCI.

After removal of the 8.0 mm ports from the third and seventh ICS, if a specific bleeding site from the port track was identified, it was treated surgically (n = 1). The hemostatic agent was placed into the track sites of ports in the third and seventh ICS under direct camera visualization so that transmural placement of the applicator tip used to inject the hemostatic agent was confirmed prior to administering the 5 cc dose. The applicator was then slowly withdrawn while injecting the hemostat into each track site. When a topical hemostatic agent was deemed suitable to address bleeding from other sites (eg, epicardial veins, IMA bed), additional hemostatic was delivered to the site of bleeding, maintained at the site for 2 minutes with gentle approximation, and the excess gently irrigated away. The hemostatic agent was prepared according the manufacturer's instructions, and reapplication was permitted if bleeding persisted. Because the camera port in the fifth ICS was extended into a 2- to 3-inch mini-thoracotomy incision, standard surgical hemostatic techniques were used for this port.

Transfusions were provided according to a previously published algorithm [Poston 2006].

Outcomes

Patients who did not receive topical hemostatic treatment of their port sites were used as controls. The hemostatic group was compared with the control group for the percentage of patients transfused (intraoperatively and postoperatively), total number of red blood cell (RBC) units administered (intraoperatively and postoperatively), length of hospital stay, and risk of reoperation for bleeding. Total output from the chest tube was compared between groups.

Statistical Analysis

Summary statistics were computed for treatment groups. For continuous variables, the mean and standard deviation were calculated. For categorical variables, the frequencies and percentages were computed. Baseline differences between groups were assessed using unpaired *t* tests or chi-square tests. Differences between hemostatic and control groups were assessed using a general linear model to compare means of RBC measures and chest tube output and using logistic regression for transfusion rate. A general linear model was also used to examine differential effects of the hemostatic agent on postoperative RBCs by selected patient characteristics (gender, race, age, hybrid procedure, and surgery type). These analyses examined the effects of the hemostatic agent with no adjustment for risk and also with adjustment for the Society of Thoracic Surgeons (STS) risk score as a weighted composite of variables, which controls for patient and clinical variables.

RESULTS

Out of a total of 193 patients who underwent r-CABG during the study interval, there were 62 hemostatic-treated patients and 131 control patients. Most patients were men (70%), mean age was 65 years (standard deviation [SD], 12 years), and 36% underwent the hybrid procedure and received aspirin and clopidogrel prior to surgery (Table 1). The groups differed slightly in age at baseline (mean age of 62 years in the hemostatic group compared with 66 years in the control group, $P = .016$). Other baseline characteristics were similar in the 2 groups ($P = .098$ to $.832$).

Table 1. Baseline Characteristics*

Patient Characteristic	Control (N = 131)	Hemostat (N = 62)	All Patients (N = 193)
Female, %	31	29	30
Age, y	66.3 (12.5)	61.7 (11.5)	64.8 (12.4)
Race, %			
White	88.5	80.7	85.9
Black	4.6	8.1	5.7
Hispanic	3.9	3.2	3.7
Other	3.1	8.1	4.7
BMI, kg/m^2	29.5 (5.1)	29.7 (5.7)	29.5 (5.3)
Hybrid procedure[a], %	35	37	36
Multiple vessel CABG, %	55	60	56
STS risk score	0.02 (0.03)	0.01 (0.03)	0.02 (0.03)

*Data presented as mean (standard deviation) unless otherwise indicated. BMI indicates body mass index; CABG, coronary artery bypass grafting; STS, Society of Thoracic Surgeons.

[a]CABG + percutaneous coronary intervention.

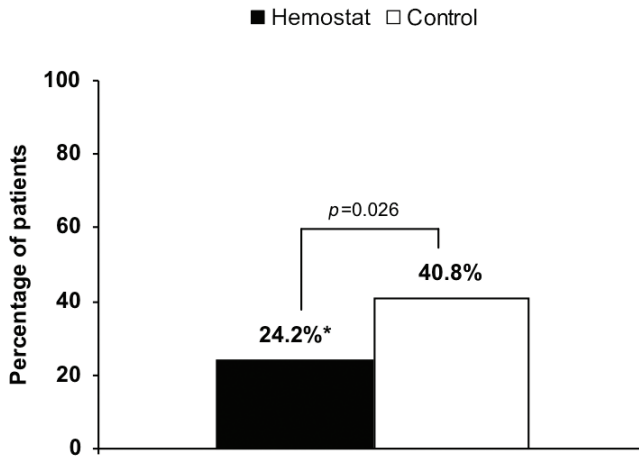

Figure 1. Red blood cell (RBC) transfusion rates. RBC transfusion rate (as a percentage of cohort) of the hemostat (black) and control (white) groups.

A significantly lower rate of RBC transfusion was observed in the hemostatic group compared with the control group (unadjusted rate, 24.2% versus 40.8%; *P* = .026; odds ratio [OR], 2.16; 95% confidence interval [CI], 1.09 to 4.25; Figure 1). This difference remained significant after adjusting for STS risk score (*P* = .046; OR = 2.02; 95% CI, 1.01 to 4.02). The reduction in transfusions in the hemostatic group compared with the control group was observed postoperatively (0.44 versus 1.39 units; *P* = .024; Table 2), but not intraoperatively (0.45 versus 0.45 units, *P* = .978). The postoperative difference in RBC transfusion between groups remained significant after adjusting for STS risk score (*P* = .035). Of those patients who were transfused, most patients received 1 unit (Figure 2), and no patients in the hemostatic group received > 7 units compared with 6 patients (5%) in the control group. Non-significant interaction effects (of hemostatic versus control groups by patient characteristic) observed in mean postoperative RBC transfused were an indication that the topical hemostatic results in lower mean RBC across a range of patient characteristics. The mean chest tube output was 1423 mL (SD = 763 mL) in the hemostatic group and 1579 mL (SD = 1192 mL) in the control group (*P* = .345; Table 2); though the resulting effect size (d = .15) may be of clinical interest, the difference was not statistically significant in this sample. After adjusting for risk factors, chest tube output was not statistically significantly different in the 2 groups. Platelets, fresh-frozen plasma, and cryoprecipitate were rarely utilized and with similar frequency in both study groups (data not shown).

Table 2. Red Blood Cell Transfusions and Chest Tube Drainage*

Outcome	Hemostat Group	Controls	*P*
Total chest tube drainage, mL	1423 (763)	1579 (1192)	.345a, .343b
Intraoperative RBC, units	0.45 (1.35)	0.45 (1.25)	.978a, .652b
Postoperative RBC, units	0.44 (1.10)	1.39 (3.18)	.024a, .035b
Total RBC, units	0.89 (1.92)	1.83 (3.62)	.056a, .101b

*Values are unadjusted mean (standard deviation). RBC indicates red blood cell transfusions.

[a]Hemostat versus control.

[b]Hemostat versus control after adjustment for Society of Thoracic Surgeons risk score.

The reoperations for bleeding rates were 1.6% in the hemostatic-treated patients and 3.1% in the control patients (*P* = .50 after adjustment for STS risk score). Mean length of stay was similar in both groups (5.5 days [SD = 5.1 days] versus 6.5 days [SD = 6.1 days], *P* = .28).

No adverse events related to hemotstatic agent use were observed.

COMMENT

In this study, assignment to the hemostatic group was associated with significantly less exposure to blood products and reduced postoperative bleeding in comparison to control patients undergoing r-CABG without treatment of the port sites. Patients treated with the topical hemostatic were transfused 24% of the time, compared with 41% of the control patients, and had fewer RBC units transfused postoperatively. Although this study was not a randomized comparison, the 2 study groups had similar baseline characteristics and followed the same r-CABG protocol with the exception of whether their port-site tracks were treated with a flowable hemostatic. There was a substantial clinical benefit of a single local injection of 5 cc of a hemostatic agent, focused primarily on only 2 port sites. This finding underscores that undetected bleeding from these port sites has likely been an underappreciated cause of bleeding and transfusion after r-CABG and other cardiac procedures that require port access.

R-CABG has demonstrated great potential to reduce the invasiveness of CABG and provide surgical care that is more

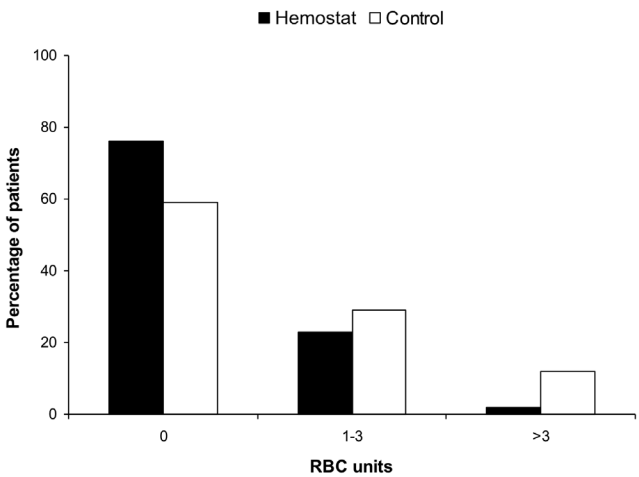

Figure 2. Distribution of postoperative red blood cell (RBC) units transfused. Distribution of postoperative RBC units transfused (as a percentage of cohort) for the hemostat (black) and control (white) groups.

"patient-centered," reducing length of hospital stay and time to return to work [Mohr 1999; Morgan 2004; Mohr 2001]. However, unforeseen bleeding risk has hampered enthusiasm of many "early adopters." Our use of hemostatic agents during the course of this study to reduce bleeding reflected the "trial and error" process that accompanies procedures such as r-CABG with no established "best practices" from which we could draw. Though not as rigorous of a study design as a randomized trial, this and other similar analyses have great merit if they are able to help improve the safety and acceptance of r-CABG. Previous studies in patients undergoing conventional cardiac surgery have reported that this hemostatic agent provides effective hemostasis with 97% of patients achieving hemostasis within 10 minutes [Koch 2006a] and that the rate of transfusions was reduced by 18% [Oz 2000; Koch 2006a; Nasso 2009]. In our study, the reduction in transfusions after hemostatic treatment was reported in all r-CABG patients, regardless of risk factors. Indeed, this benefit occurred despite full heparinization, as all patients had an ACT time that exceeded 300 seconds around the time that the hemostatic was applied to their track sites. The efficacy of the hemostatic agent in heparinized patients has been previously reported [Oz 2000] and is due to high concentration of thrombin, which can convert fibrinogen into fibrin in the absence of platelet function, and also to gelatin granules which swell and cause a local tamponade effect.

Hemostasis is important during cardiac surgery because uncontrolled bleeding resulting in blood transfusions is associated with increased mortality, morbidity, length of hospital stay [Koch 2006a; Koch 2006b; Murphy 2007; van Straten 2010], and total costs. An additional risk of bleeding following r-CABG is the need to return to the operating room and convert to a full sternotomy. Many patients that undergo r-CABG have specifically chosen this option to avoid the increased morbidity and recovery time after surgery associated with a sternotomy [Morgan 2004; Mohr 2001] and can be very distressed by such an event. In addition, emergency conversions to a sternotomy to address occult bleeding can negatively impact morale of the intensive care unit and operating room teams that are involved in the implementation of this program. In light of the numerous reverberations associated with bleeding after r-CABG, methods to reduce bleeding and transfusions are likely to improve the safety and broaden the acceptance of this procedure.

A steep learning curve is experienced when r-CABG is introduced into a unit [Bonatti 2009]. The current study collected data after learning curve plateau, and sensitivity analysis showed no time trend effect on RBC outcomes (data not shown) [Poston 2008]. Even though the robot has become available in more than 1400 US hospitals, concerns about safety and reproducibility have limited the adoption of r-CABG to fewer than 20 programs [Robicsek 2008]. It is likely that anecdotes of returning to the operating room for conversion to a full sternotomy to control port site bleeding have contributed to the controversy surrounding this procedure. Though our study suggests that this challenge can be addressed with modifications such as the use of topical hemostatic, we observed a low rate of reoperation in both groups with no significant difference in length of stay or reoperations for bleeding. However, the numerical reductions compared to the control group may be clinically significant due to the risks related to reoperations and the costs associated with both reoperations and length of stay.

There were limitations with our study, including the non-randomization of patients. Additionally, a reduction of bleeding from sites other than ports may have contributed to the observed effect of decreased bleeding in this study. In addition, perioperative bleeding was not rigorously measured by weighing intraoperative sponges or by measuring hemoglobin concentration of chest tube output. Additionally, the moderate sample size provided relatively lower power to detect small effects, which, nevertheless, could be of both statistical and clinical importance if maintained across large samples. Though propensity matching was not utilized due to study design, the STS risk score, a weighted composite of risk-related factors, was utilized to adjust for potential risk differences in this non-randomized study.

Although a similar use of this hemostatic has been documented for other robotic procedures [Ahlering 2005; Kaul 2007; Ho 2009], this is the first published report of the use of this agent during r-CABG. This study highlights the effectiveness of topical hemostatic in providing hemostasis and reducing the need for transfusions. As experience increases, we and others will continue to describe how the many challenges of r-CABG will be overcome so that the learning curve can be shortened for future adopters.

ACKNOWLEDGMENTS

Baxter BioScience provided funding for data analysis.

The authors would like to thank Mandy Suggitt, on behalf of Baxter Bioscience, Mary Anne MacMillan, RN, BSN, CNOR, and Huub Kreuwel, PhD, of Baxter BioScience for their editorial support.

DISCLOSURES

This study was funded by NIH Grant #RO1 HL084080 awarded to the senior author, Robert S. Poston, MD. Statisticians were provided with additional remuneration from Baxter Bioscience for data analysis specific to this project. Authors had control of the design of the study, methods used, outcome parameters and results, analysis of data, and written manuscript.

REFERENCES

Ahlering TE, Eichel L, Chou D, Skarecky DW. 2005. Feasibility study for robotic radical prostatectomy cautery-free neurovascular bundle preservation. Urology 65:994-7.

Bonatti J, Schachner T, Bonaros N, et al. 2009. Effectiveness and safety of total endoscopic left internal mammary artery bypass graft to the left anterior descending artery. Am J Cardiol 104:1684-8.

Côté D, Barber B, Diamond C, Wright E. 2010. FloSeal hemostatic

matrix in persistent epistaxis: prospective clinical trial. J Otolaryngol Head Neck Surg 39:304-8.

Desai PH, Tran R, Steinwagner T, Poston RS. 2010. Challenges of telerobotics in coronary bypass surgery. Expert Rev Med Devices 7:165-8.

Ferguson TB Jr, Hammill BG, Peterson ED, DeLong ER, Grover FL; STS National Database Committee. 2002. A decade of change—risk profiles and outcomes for isolated coronary artery bypass grafting procedures, 1990-1999: a report from the STS National Database Committee and the Duke Clinical Research Institute. Society of Thoracic Surgeons. Ann Thorac Surg 73:480-9.

Ho H, Schwentner C, Neururer R, Steiner H, Bartsch G, Peschel R. 2009. Robotic-assisted laparoscopic partial nephrectomy: surgical technique and clinical outcomes at 1 year. BJU Int 103:663-8.

Jameson M, Gross CW, Kountakis SE. 2006. FloSeal use in endoscopic sinus surgery: effect on postoperative bleeding and synechiae formation. Am J Otolaryngol 27:86-90.

Kaul S, Laungani R, Sarle R, et al. 2007. da Vinci-assisted robotic partial nephrectomy: technique and results at a mean of 15 months of follow-up. Eur Urol 51:186-91.

Koch CG, Khandwala F, Li L, Estafanous FG, Loop FD, Blackstone EH. 2006a. Persistent effect of red cell transfusion on health-related quality of life after cardiac surgery. Ann Thorac Surg 82:13-20.

Koch CG, Li L, Duncan AI, et al. 2006b. Transfusion in coronary artery bypass grafting is associated with reduced long-term survival. Ann Thorac Surg 81:1650-7.

Loop FD, Lytle BW, Cosgrove DM, et al. 1986. Influence of the internal-mammary-artery graft on 10-year survival and other cardiac events. N Engl J Med 314:1-6.

Malenka DJ, Leavitt BJ, Hearne MJ, et al. 2005. Comparing long-term survival of patients with multivessel coronary disease after CABG or PCI: analysis of BARI-like patients in northern New England. Circulation 112(9 Suppl):I371-6.

Mohr FW, Falk V, Diegeler A, Autschback R. 1999. Computer-enhanced coronary artery bypass surgery. J Thorac Cardiovasc Surg 117:1212-4.

Mohr FW, Falk V, Diegeler A, et al. 2001. Computer-enhanced "robotic" cardiac surgery: experience in 148 patients. J Thorac Cardiovasc Surg 121:842-53.

Morgan JA, Peacock JC, Kohmoto T, et al. 2004. Robotic techniques improve quality of life in patients undergoing atrial septal defect repair. Ann Thorac Surg 77:1328-33.

Murphy GJ, Reeves BC, Rogers CA, Rizvi SI, Culliford L, Angelini GD. 2007. Increased mortality, postoperative morbidity, and cost after red blood cell transfusion in patients having cardiac surgery. Circulation 116:2544-52.

Nasso G, Piancone F, Bonifazi R, et al. 2009. Prospective, randomized clinical trial of the FloSeal matrix sealant in cardiac surgery. Ann Thorac Surg 88:1520-6.

Oz MC, Cosgrove DM 3rd, Badduke BR, et al. 2000. Controlled clinical trial of a novel hemostatic agent in cardiac surgery. The Fusion Matrix Study Group. Ann Thorac Surg 69:1376-82.

Oz MC, Rondinone JF, Shargill NS. 2003. FloSeal Matrix: new generation topical hemostatic sealant. J Card Surg 18:486-93.

Poston RS, Tran R, Collins M, et al. 2008. Comparison of economic and patient outcomes with minimally invasive versus traditional off-pump coronary artery bypass grafting techniques. Ann Surg 248:638-46.

Poston RS, White C, Gu J, et al. 2006. Aprotinin shows both hemostatic and antithrombotic effects during off-pump coronary artery bypass grafting. Ann Thorac Surg 81:104-11.

Renkens KL Jr, Payner TD, Leipzig TJ, et al. 2001. A multicenter, prospective, randomized trial evaluating a new hemostatic agent for spinal surgery. Spine (Phila Pa 1976) 26:1645-50.

Robicsek F. 2008. Robotic cardiac surgery: time told! J Thorac Cardiovasc Surg 135:243-6.

Roger VL, Go AS, Lloyd-Jones DM, et al. 2011. Heart disease and stroke statistics—2011 update: a report from the American Heart Association. Circulation 123:e18-e209.

Sedrakyan A, Wu AW, Parashar A, Bass EB, Treasure T. 2006. Off-pump surgery is associated with reduced occurrence of stroke and other morbidity as compared with traditional coronary artery bypass grafting: a meta-analysis of systematically reviewed trials. Stroke 37:2759-69.

van Straten AH, Bekker MW, Soliman Hamad MA, et al. 2010. Transfusion of red blood cells: the impact on short-term and long-term survival after coronary artery bypass grafting, a ten-year follow-up. Interact Cardiovasc Thorac Surg 10:37-42.