Transfusion and Blood Stream Infections after Coronary Surgery

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Manuscript word count: 2000 words

Abstract word count: 131 words

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Abstract

The aim of this study was to evaluate the impact of blood transfusion on blood stream infections. This study included 2764 patients who underwent isolated coronary artery bypass grafting (CABG). Blood cultures were drawn in 27.9% of patients and were positive in 3.5% of them. Blood transfusion before blood cultures were drawn (4.7% vs. 1.2%, OR 3.75, 95%CI 1.11-12.67) and deep sternal wound infection/mediastinitis (20.0% vs. 2.8%, OR 7.43, 95%CI 2.72-20.32) were independent predictors of positive postoperative blood culture. Positive blood culture increased the risk of 5-year mortality (among patients with blood cultures drawn: 44.7% vs. 19.6%, adjusted HR 2.10, 95%CI 1.18-3.71). Exposure to blood products may increase the risk of blood stream infection after cardiac surgery. Positive blood cultures after CABG are associated with poor late survival. These findings require validation in prospective studies.

Keywords: Coronary artery bypass; transfusion; blood culture; bacteremia; blood stream infection.

Introduction

Perioperative bleeding has a negative impact on the outcome after cardiac surgery. However, it is difficult to disentangle the individual impact of perioperative anemia from that of blood products on the outcome of these patients [1]. The adverse effects of red blood cell (RBC) transfusion may partly be related to an increased risk of blood stream infections secondary to transfusion-related immunomodulation or contamination [2,3]. This issue has been investigated in the present study.

Materials and methods

This study includes 2764 patients who underwent isolated coronary artery bypass grafting (CABG) from June 2006 to December 2013 at the Oulu University Hospital, Finland. This study was approved by the Institutional Review Board. Variables were defined according to the EuroSCORE criteria [4]. Cefuroxime 1.5-3.0 gr i.v was used for antibiotic prophylaxis. Blood cultures were obtained routinely in patients with body temperature >38.0°C or any clinical sign of infection. Data on transfused blood products and blood cultures were retrieved from electronic hospital registries. Data on concomitant antibiotic use was recorded. Positive postoperative blood culture was the primary outcome of this study. Early or late postoperative death was the secondary outcome. Other outcomes are listed in Table 1. Date of death were retrieved on January 2016 from the Finnish National Registry, Statistics Finland.

Statistical analysis was performed using SPSS statistical software (version 24.0, IBM Corporation, Armonk, New York, USA). Multiple imputation method with 5 datasets was used for missing data. Logistic regression with the backward stepwise method including pre-, intra, and postoperative variables with a $p<0.2$ in univariable analysis was used to identify predictors of positive blood cultures. The effect of positive blood culture on survival was assessed using the Kaplan-Meier method with the log-rank-test and the Cox proportional hazards method and adjusted for relevant baseline risk factors. The proportional hazards assumption was checked with log-log-survival plots. $P<0.05$ was considered statistically significant.

Results

Blood cultures were drawn from 772 patients (27.9%) after a mean of 2.6±2.0 days (range, 0-14 days) from surgery. Blood cultures were positive in 27 cases (3.5%). Antibiotic treatment was going on at the time of positive blood culture in 28.0% of the cases and in 22.9% of the cases with negative blood culture ($p=0.63$). The growth of *Staphylococcus epidermidis* was detected in ten cases, *Staphylococcus aureus* in seven, *Candida albicans* in two, *Staphylococcus hominis* in one, *Enterococcus faecium* in one, *Enterococcus faecalis* in one, *Klebsiella pneumonia* in one, *Micrococcus luteus* in one, *Prevotella* in one, *Pseudomonas aeruginosa* in one, *Sphingomonas paucimobilis* in one and coagulase-negative staphylococci in one case. In one case, both *Staphylococcus aureus* and *Staphylococcus epidermidis* were identified in the blood cultures. Among patients with positive blood cultures, three (11.1%) underwent a resternotomy for bleeding, six (22.2%) had deep sternal wound infection/mediastinitis and three (11.1%) had concomitant infection of a central venous catheter. Twenty-four patients (88.9%) received RBC transfusion before a positive blood culture.

Among patients who had blood cultures drawn, RBC transfusion before blood cultures were drawn (p=0.012), emergency surgery (p=0.047) and deep sternal wound infection/mediastinitis (p<0.001) were associated with an increased risk of positive postoperative blood cultures in univariable analysis. Logistic regression showed that RBC transfusion (4.7% vs. 1.2%, OR 3.75, 95%CI 1.11-12.67), and sternal wound infection/mediastinitis (20.0% vs. 2.8%, OR 7.43, 95%CI 2.72-20.32) were independent predictors of positive postoperative blood culture. Transfusions of platelets (4.0% vs. 3.2%, p=0.554) and Octaplas (4.4% vs. 3.0%, p=0.301) did not increase the risk of positive blood culture.

Regarding the secondary outcome, 536 patients died after a mean length of follow-up of 5.5±2.5 years. Adjusted analysis including patients with or without blood cultures drawn showed that patients who had positive blood culture (HR 2.23, 95%CI 1.26-3.94; compared to those who had blood culture drawn; HR 2.10, 95%CI 1.18-3.71) and those who had negative blood culture (HR 1.63, 95%CI 1.20-2.22) had a higher risk of late mortality compared to patients who did not have blood culture drawn (5-year mortality: 44.7%, 19.8%, and 13.3%, respectively, log-rank p<0.001). Such an increased risk persisted also after excluding patients who died within 30 days from surgery (5-year mortality: 37.8%, 15.3%, 11.2% respectively, log-rank p=0.001; positive blood culture: HR 2.43, 95%CI 1.28-4.59; negative blood culture: HR 1.26, 95%CI 1.03-1.54).

Discussion

This study showed that the yield of blood culture after CABG is rather low, but identification of blood stream infection is associated with an increased risk of late mortality (Fig. 1). This analysis showed that RBC transfusion and deep sternal wound infection/mediastinitis were independent predictors of positive postoperative blood cultures after CABG. Among patients with positive blood cultures, only three patients (11.1%) did not receive RBC transfusion before blood culture was drawn. Transfusion of platelets and Octaplas was not associated with an increased risk of positive blood culture.

The increased risk of blood stream infection in patients with deep sternal wound infection/mediastinitis after cardiac surgery is intuitively related to the severity of this postoperative complication. Still blood cultures yielded positive findings in a limited number of thems (22.2%).

The association between blood transfusion and positive blood cultures is a novel finding. Prior pooled studies demonstrated an increased risk of infection after blood transfusion [5,6]. Although the negative immunomodulation effect of blood transfusion in surgical patients cannot be ruled out [2], contamination from RBC donors can be a source of blood stream infection. A recent study identified viable bacteria in 35% of RBC fractions from self-reported healthy donors [3], with a large prevalence of *Staphylococcus epidermidis*. However, it is unclear whether blood transfusion may directly contribute to postoperative infection, or rather perioperative anemia and suboptimal oxygen delivery may trigger surgical site infections [7].

This study showed that the yield of blood culture (3.5%) was lower than the one (9.8%) observed in a general cardiac surgery population [8]. However, herein we evaluated a homogenous patient series undergoing isolated CABG, which was less exposed to direct contamination of intra-cardiac structures and artificial prostheses, and theoretically at lower risk of blood stream infections.

The retrospective nature of this study is a limitation of this study. However, data on blood cultures, laboratory parameters, blood products and date of death are from prospective institutional and national registries. Furthermore, the association between positive blood cultures and RBC transfusion is not substantiated either by a direct proof of bacterial contamination of transfused RBCs or absence of any other source of infection. Therefore, the present findings should be viewed as hypothesis generating on the possible role of perioperative anemia, suboptimal oxygen delivery and exposure to blood products as triggers of postoperative blood stream infections.

In conclusion, RBC transfusion and deep sternal wound infection/mediastinitis are predictors of blood stream infection after CABG. Positive postoperative blood culture are associated with a remarkably increased risk of early and late mortality.

Declaration of conflict of interests: None to declare.

Funding: This study was not financially supported.

References

[1] Loor G, Rajeswaran J, Li L, Sabik JF 3rd, Blackstone EH, et al. The least of 3 evils: Exposure to red blood cell transfusion, anemia, or both? J Thorac Cardiovasc Surg 2013;146:1480-7.

[2] Spinella PC, Sparrow RL, Hess JR, Norris PJ. Properties of stored red blood cells: understanding immune and vascular reactivity. Transfusion 2011;51:894-900.

[3] Damgaard C, Magnussen K, Enevold C, Nilsson M, Tolker-Nielsen T, Holmstrup P, et al. Viable bacteria associated with red blood cells and plasma in freshly drawn blood donations. PLoS One 2015;10:e0120826.

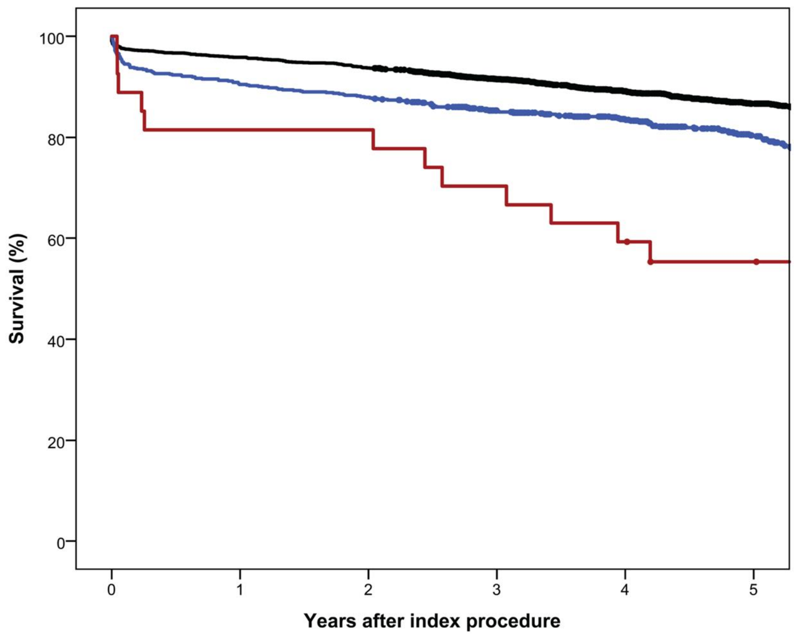
[4] Nashef SA, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardiothorac Surg 1999;16:9-13.

[5] Marik PE, Corwin HL. Efficacy of red blood cell transfusion in the critically ill: a systematic review of the literature. Crit Care Med 2008;36:2667-74.

[6] Rohde JM, Dimcheff DE, Blumberg N, Saint S, Langa KM, Kuhn L, et al. Health care-associated infection after red blood cell transfusion: a systematic review and meta-analysis. JAMA 2014;311:1317-26.

[7] Qadan M, Akça O, Mahid SS, Hornung CA, Polk HC Jr. Perioperative supplemental oxygen therapy and surgical site infection: a meta-analysis of randomized controlled trials. Arch Surg 2009;144:359-66.

[8] Copeland-Halperin LR, Stodghill J, Emery E, Trickey AW, Dort J. Clinical predictors of positive postoperative blood cultures. Ann Surg 2017 (in press).



No. at risk						
No blood culture	1992	1909	1867	1690	1430	1195
Negative blood culture	745	674	655	589	509	401
Positive blood culture	27	22	22	19	16	13

Figure 1. Kaplan-Meier estimates of survival in the study cohorts.

Table 1. Baseline and operative data in the study cohorts. Univariable and multivariable analyses were performed only in the cohort of patients who had blood culture drawn.

Variables	*Overall cohort 2764 pts*	*Missing data*	*Blood culture not drawn 1992 pts*	*Negative blood culture 745 pts*	*Positive blood culture 27 pts*	*Univariable analysis P-value*	*Multivariable analysis OR, 95%CI*
Baseline characteristics							
Age (years)	67.0 (9.1)		67.3 (8.9)	66.3 (9.7)	68.5 (9.1)	0.388	-
Females	582 (21.1)	0	451 (22.6)	127 (17.0)	4 (14.8)	0.761	-
Anemia	662 (24.0)	3 (0.1)	436 (21.9)	215 (28.9)	11 (42.3)	0.081	-
Estim. glomerular filtration rate<60 mL/min1.73 m^2	350 (26.7)	10 (0.4)	221 (11.1)	124 (16.7)	5 (19.2)	0.789	-
Diabetes	788 (28.5)	0	531 (26.7)	250 (33.6)	7 (25.9)	0.408	-
Stroke	95 (3.4)	0	71 (3.6)	24 (3.2)	0	1.000	-
Extracardiac arteriopathy	265 (9.6)	0	177 (8.9)	83 (11.1)	5 (18.5)	0.236	-
Prior cardiac surgery	46 (1.7)	0	33 (1.7)	13 (1.7)	0	1.000	-
Recent myocardial infarction	1319 (47.7)	0	869 (43.6)	434 (58.3)	16 (59.3)	0.917	-
Left ventricular ejection fraction≤50%	699 (25.3)	104 (3.8)	444 (23.2)	244 (33.6)	11 (44.0)	0.300	-
Critical preoperative state	217 (7.9)	0	121 (6.1)	91 (12.2)	5 (18.5)	0.329	-
Operative variables							
Emergency operation	198 (7.2)	0	96 (4.8)	95 (12.8)	7 (25.9)	0.047	-
Off-pump surgery	1510 (54.6)	0	1074 (53.9)	424 (56.9)	12 (44.4)	0.199	-
Bilateral int. mammary a. grafts	221 (8.0)	0	146 (7.3)	74 (9.9)	1 (3.7)	0.505	-
Early outcomes							
30-day death	89 (3.2)	0	48 (2.4)	38 (5.1)	3 (11.1)	0.168	-
Intensive care unit stay (days)	2.2 (2.5)	0	1.6 (1.4)	3.6 (3.6)	5.6 (6.1)	<0.001	
Low-cardiac output	383 (13.9)	0	233 (11.7)	147 (19.7)	3 (11.1)	0.266	-
Stroke	58 (2.1)	0	28 (1.4)	30 (4.0)	0	0.619	-
Resternotomy for bleeding	181 (6.5)	0	108 (5.4)	70 (9.4)	3 (11.1)	0.765	-
Deep sternal wound infection/mediastinitis	72 (2.6)	0	42 (2.1)	24 (3.2)	6 (22.2)	<0.001	7.434, 2.720-20.324
Surgery for gastrointestinal complications	32 (1.2)	0	9 (0.5)	21 (2.8)	2 (7.4)	0.168	-
Acute kidney injury*	457 (16.5)	52* (1.9)	217 (10.9)	233 (31.9)	7 (30.4)	0.884	-
Red blood cell transfusion	1758 (63.5)	0	1177 (59.1)	488** (65.5)	24** (88.9)	0.012	3.746, 1.107-12.672
Platelets transfusion	826 (29.9)	0	525 (26.4)	289 (38.8)	12 (44.4)	0.554	-
Octaplas transfusion	738 (26.7)	0	467 (26.4)	259 (34.8)	12 (44.4)	0.301	-

Data are reported as mean and standard deviation (in parentheses) or counts and percentages (in parentheses); * according to KDIGO classification, patients on preoperative dialysis excluded; **: before blood culture were drawn; OR: odds ratio; CI: confidence interval.