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# Transfusions and early outcomes in anaemic patients undergoing off- or on-pump coronary artery bypass grafting

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## Abstract

We retrospectively compared transfusion rates and early outcomes in 1621 consecutive patients with preoperative anaemia undergoing off-pump coronary artery bypass grafting (OPCAB) or on-pump coronary artery bypass grafting (ONCAB) surgery using a propensity score analysis with inverse probability of treatment weighting. Endpoints were transfusions, early morbidity, and mortality. Surgeries were performed by 45 dedicated OPCAB and/or ONCAB surgeons during the 10-year study period. Operative data did not differ significantly between study groups with the exception of a more frequent use of bilateral internal mammary artery revascularization approach in OPCAB patients than ONCAB patients. OPCAB was associated with fewer transfusions and lower risk for the need of postoperative renal replacement therapy, but higher risk of wound infections than ONCAB. Perioperative stroke risk and 30-day and 1-year mortality did not differ significantly between the groups. Our data in a 'real-world setting' indicate that in patients with preoperative anaemia both ONCAB and OPCAB are feasible surgical approaches regarding early morbidity and mortality.

**Keywords:** Anaemia • Coronary artery bypass grafting • On-pump cardiopulmonary bypass grafting • Off-pump cardiopulmonary bypass grafting • Transfusions

## INTRODUCTION

In cardiac surgery, preoperative anaemia is diagnosed in about 20% of patients [1]. Anaemia is associated with increased risk of acute kidney injury (AKI), stroke, infections and early mortality [1]. However, it remains currently unclear whether anaemia itself or increased transfusions of red blood cells (RBCs) trigger these adverse outcomes [2, 3]. Randomized controlled trials (RCTs) demonstrated that off-pump cardiopulmonary bypass grafting (OPCAB) surgery is associated with significantly fewer RBC transfusions than on-pump cardiopulmonary bypass grafting (ONCAB) [4]. We hypothesized that in patients with preoperative anaemia these differences in transfusions, and probably in clinical outcomes, would be even more distinct than in patients without anaemia.

## METHODS

This retrospective cohort analysis of prospectively collected data included consecutive patients who underwent isolated OPCAB or ONCAB at our institution between January 2009 and December 2019. Patients with preoperative anaemia were selected from the entire group of patients who underwent coronary artery bypass grafting at our institution. Patients with concomitant or any

previous cardiac surgery, low ejection fraction (<30%), preoperative dialysis, haemodynamic instability (preoperative cardiogenic shock), emergency status and patients undergoing minimally invasive direct coronary artery bypass grafting were excluded. An inclusion criterion was, according to the WHO definition, a haemoglobin (Hb) concentration below 12 g/dl (females) or 13 g/dl (males). A total of 1621 patients were finally included in our data analysis (OPCAB = 1188; ONCAB = 433). The study was approved by the local ethics committee on 20 April 2020 (AZ 2020-628).

Surgery was performed as described before [5]. During the 10-year study period, 45 dedicated OPCAB and/or ONCAB surgeons performed the operations, with ONCAB and OPCAB procedures being done by 34 and 43 surgeons, respectively. Emergency surgery was, according to institutional standards, the only exclusion criterion for OPCAB surgery. In the OPCAB group, cell saving was used as a replacement for cardiotomy suction during the grafting procedure. For patients ≤70 years, the institutional transfusion threshold was an Hb value of ≤8–9 g/dl. However, the threshold was raised to ≤9–10 g/dl in patients who required high inotropic support or were aged 70 years and over. During cardiopulmonary bypass, the critical value for RBC transfusions was an (expected) Hb of 7–8 g/dl. End points were RBC transfusions, early morbidity and mortality.

Because of the nonrandomized group assignment, we generated a propensity score (PS) for each patient. For the creation of

**Table 1:** Baseline characteristics in unweighted and weighted study populations

Parameter	Unweighted patients, n = 1621			Weighted, n = 3249		
	ONCAB, n = 433	OPCAB, n = 1188	SMD (%)	ONCAB, n = 1629	OPCAB, n = 1620	SMD (%)
Age (years), mean ± SD	71.1 ± 9.4	71.0 ± 9.3	1.1	71.1 ± 8.3	71.1 ± 9.3	0.0
Sex, females, n (%)	110 (25.4)	287 (24.2)	3.9	390 (24.0)	396 (24.4)	-1.3
Body mass index (kg/m <sup>2</sup> ), mean ± SD	27.9 ± 5.0	27.9 ± 4.6	0.0	27.9 ± 4.8	27.9 ± 4.7	0.0
Diabetes mellitus, n (%)	209 (48.3)	575 (48.4)	-0.3	780 (47.9)	785 (48.4)	-1.4
Hypertension, n (%)	376 (86.6)	1069 (90.0)	-15.9	1462 (89.7)	1446 (89.3)	1.8
Stroke, n (%)	22 (5.1)	67 (5.6)	-2.3	97 (6.0)	90 (5.6)	2.3
Myocardial Infarction, n (%)	161 (37.2)	371 (31.2)	18.0	536 (32.9)	534 (32.9)	0.0
COPD, n (%)	61 (14.1)	106 (8.9)	24.5	165 (10.1)	167 (10.3)	-0.9
LVEF (%), mean ± SD	55.3 ± 10.3	53.8 ± 11.5	13.7	54.9 ± 11.0	54.9 ± 10.4	0.0
eGFR (ml/min/1.73 m <sup>2</sup> ), mean ± SD	65.7 ± 24.5	65.7 ± 24.5	0.0	65.9 ± 25.2	65.7 ± 24.4	0.8
PAOD, n (%)	95 (21.9)	225 (18.9)	10.6	322 (19.8)	321 (19.8)	0.0
Three-vessel disease, n (%)	380 (87.8)	1017 (85.6)	8.8	1397 (85.8)	1396 (86.2)	-1.6
EuroSCORE II (%), mean ± SD	2.80 ± 3.50	3.39 ± 3.60	-16.6	3.01 ± 3.19	3.00 ± 3.94	0.3
Current/previous smokers, n (%)	187 (43.2)	465 (39.1)	11.7	647 (39.7)	650 (40.1)	-1.1
NYHA class, mean ± SD	2.26 ± 0.80	2.42 ± 0.76	-20.5	2.30 ± 0.77	2.30 ± 0.82	0.0
Haemoglobin (g/dl), mean ± SD	11.6 ± 1.1	11.6 ± 1.1	0.0	11.6 ± 1.0	11.6 ± 1.1	0.0
<b>Medication</b>						
Beta-blocker use	334 (77.1)	880 (74.1)	9.6	1234 (75.8)	1215 (75.0)	2.6
Aspirin use, n (%)	338 (78.1)	908 (76.4)	5.6	1261 (77.4)	1246 (76.9)	1.7
ACE-inhibitor use, n (%)	254 (58.7)	623 (52.4)	17.7	869 (53.3)	875 (54.0)	-2.0
AT-blocker use, n (%)	66 (15.2)	276 (23.2)	-26.2	348 (21.4)	342 (21.1)	1.0
Clopidogrel use, n (%)	89 (20.6)	229 (19.3)	4.5	322 (19.8)	319 (19.7)	0.4
<b>Operation priority</b>						
Elective, n (%)	382 (88.2)	1116 (93.6)	-31.2	1507 (92.5)	1497 (92.4)	0.5
Urgent, n (%)	123 (11.8)	72 (6.1)	31.2	122 (7.5)	124 (7.6)	-0.5

COPD: chronic obstructive pulmonary disease; eGFR: estimated glomerular filtration rate; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; ONCAB: on-pump coronary artery bypass grafting; OPCAB: off-pump coronary artery bypass grafting; PAOD: peripheral arterial occlusive disease; PS: propensity score; SD: standard deviation; SMD: standardized mean difference; ACE: angiotensin converting enzyme; AT: angiotensin II.

the PS, we used the multivariable logistic regression model with the type of surgery (ONCAB or OPCAB) as the binary dependent variable. The model comprised all baseline covariates of Table 1. After the PS was established, we applied inverse probability of treatment weighting [6]. Post-weighting balance in covariates was evaluated using standardized mean differences. To compare continuous and categorical perioperative outcome data, the Mann-Whitney *U*-test and Fisher's exact test were applied, respectively. Clinical outcome data are presented as relative risks and 95% confidence intervals. To account for multiple testing, the Benjamini and Hochberg false discovery rate method was considered to adjust the *P* values as previously described [7]. The false recovery rate was set at 5%. *P* values <0.05 were considered statistically significant. We performed all analyses using IBM SPSS Statistics version 24 (IBM Corporation, Armonk, NY, USA).

## RESULTS

In the weighted study population, all baseline characteristics assessed were well-balanced (Table 1). The percentage of transfused patients and the number of transfused RBC units were significantly lower in the OPCAB group than in the ONCAB group (Table 2). Likewise, prolonged mechanical ventilatory support, prolonged intensive care unit (ICU) stay, and the risk of stroke and haemofiltration were significantly lower in the OPCAB group than in the ONCAB group. However, use of the bilateral internal mammary artery (BIMA) revascularization approach and readmission for wound infection were significantly higher in the

OPCAB group than in the ONCAB group. Thirty-day and 1-year mortality did not differ significantly between study groups (Table 2). After applying the Benjamini and Hochberg FDR method, prolonged mechanical ventilation, prolonged ICU stay and the perioperative risk of stroke became nonsignificant.

## DISCUSSION

Data challenge our primary hypothesis that, in the condition of preoperative anaemia, the difference in the number of patients transfused would be more distinct between the two surgical strategies. Due to the dilutional effect of CPB, the high transfusion rate of almost 100% in our anaemic ONCAB patients was an expected finding. However, the high transfusion rate of 90% in our OPCAB patients was unexpected and probably, at least in part, due to the liberal transfusion trigger in our elderly patients.

Preoperative anaemia is regarded as an important risk factor in cardiac surgery [1]. Whether the slightly lower transfusion rate in our OPCAB group can explain differences in renal complications between OPCAB and ONCAB surgery remains unclear. Notably, in a subgroup of a meta-analysis of high-risk patients in RCTs, OPCAB was associated with significantly lower transfusion rates and lower risks of postoperative AKI than ONCAB [4]. The higher risk of wound infections in our OPCAB group was an unexpected finding. However, inherent to the strategy of non-aortic or less-aortic touch OPCAB surgery, more patients in the OPCAB group underwent a BIMA approach than those in the ONCAB group [8].

**Table 2:** Perioperative and postoperative outcomes in the 2 inverse probability of treatment weighting groups with preoperative anaemia

	ONCAB, n = 1629	OPCAB, n = 1620	RR (95% CI) <sup>b</sup>	P-Value
Operation time (min) <sup>a</sup>	190 (161; 230)	194 (166; 223)	–	0.65
Peripheral anastomoses <sup>a</sup>	3 (2; 3)	3 (2; 3)	–	0.53
Revascularization ratio <sup>a</sup>	1.00 (0.67; 1.33)	1.00 (1.00; 1.00)	–	0.25
BIMA approach, n (%)	96 (5.9)	268 (16.5)	0.32 (0.25; 0.40)	<0.001
Haemoglobin <sub>min</sub> (g/dl) <sup>a</sup>	9.2 (8.6; 9.8)	9.2 (8.7; 9.8)	–	0.34
Red blood cell units <sup>a</sup>	5 (4; 8)	4 (2; 5)	–	<0.001
No red blood cell unit transfusion, n (%)	18 (1.1)	163 (10.3)	0.08 (0.06; 0.16)	<0.001
Mechanical ventilation >24 h, n (%)	142 (8.7)	108 (6.7)	1.34 (1.03; 1.73)	0.029
Intensive care unit stay >48 h, n (%)	510 (31.3)	450 (27.8)	1.19 (1.02; 1.38)	0.028
Haemofiltration, n (%)	136 (8.3)	91 (5.6)	1.53 (1.17; 2.02)	0.002
Stroke, n (%)	41 (2.5)	24 (1.5)	1.68 (1.01; 2.79)	0.045
Mediastinitis, n (%)	10 (0.6)	12 (0.7)	0.78 (0.34; 1.82)	0.57
In-hospital stay, days <sup>a</sup>	12 (11; 14)	12 (11; 14)	–	0.69
Readmission for wound infection, n (%)	19 (1.2)	44 (2.7)	0.42 (0.24; 0.72)	0.002
Readmission for thoracic wound infection, n (%)	8 (0.5)	31 (1.9)	0.25 (0.12; 0.54)	<0.001
Thirty-day mortality, n (%)	35 (2.1)	21 (1.3)	1.68 (0.97; 2.91)	0.06
One-year mortality, n (%)	136 (8.5)	125 (7.8)	1.10 (0.85; 1.41)	0.48

<sup>a</sup>Median with 25th and 75th percentiles.

<sup>b</sup>Reference: OPCAB group.

BIMA: bilateral internal mammary artery; CI: confidence interval; ONCAB: on-pump coronary artery bypass grafting; OPCAB: off-pump coronary artery bypass grafting; RR: rate ratio.

A recent meta-analysis showed that BIMA grafting, particularly in diabetic patients, is associated with an increased risk of wound healing impairment and postoperative infections [9].

In our study, differences in RBC transfusions and early morbidity outcomes between OPCAB or ONCAB patients did not translate into significant group differences of 30-day or 1-year mortality. Data support results of the aforementioned meta-analysis of RCTs in the subgroup of high-risk patients [4].

Strengths of our study are the relatively large and homogeneous study cohort and use of the statistical inverse probability of treatment weighting approach. Limitations are the retrospective and monocentric study design, and the study group differences regarding the use or non-use of a CPB system and the no- or less 'aortic touch' approach, the latter resulting in an increased BIMA use [5, 8]. Thus, we cannot definitively exclude the possibility that non-considering perioperative data for the PS such as BIMA use has biased study results. However, our data more reflect the 'real-world' situation rather than randomized trials which accurately balance groups in this regard.

In conclusion, the number of transfused anaemic patients was statistically significant, but only modestly lower in OPCAB surgery than in ONCAB surgery. The type of surgery was also associated with risks of AKI and infections. Since early mortality did not differ significantly between groups, our data indicate the feasibility of both surgical approaches.

**Conflict of interest:** none declared.

## Data availability

Data will be available upon reasonable request.

## Reviewer information

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