Use of Blood Products and Diseased Ascending Aorta Are Determinants of Stroke After Off-Pump Coronary Artery Bypass Grafting

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Objective: **To examine the effect of blood products on the occurrence of stroke after coronary artery surgery.**

Design: **Institutional retrospective analysis.**

Setting: **University hospital.**

Participants: **One thousand three hundred fourteen patients undergoing coronary artery surgery.**

Interventions: **Off-pump coronary artery bypass grafting (OPCAB). Epiaortic ultrasound was performed in all patients.**

Measurements and Main Results: **Complete pre-, intra- and postoperative data including the number of transfused blood products as well as the timing, type, and course of stroke were available in all patients. Postoperative stroke occurred in 23 patients (1.8%). Logistic regression identified transfusion of platelets (3.6% *v* 1.1%, p = 0.003, OR 3.34, 95% CI 1.46-7.67) and diseased ascending aorta (3.0% *v* 1.2%, p = 0.022, OR 2.64, 95% CI 1.15-6.06) as independent predictors of stroke. When these variables were adjusted for CHA_2DS_2-VASc (p = 0.005, OR 1.44, 95% CI 1.12-1.86), only transfusion of platelets (p = 0.012, OR 2.91, 95% CI 1.26-6.70) was associated with stroke. Neither nadir hematocrit on the day of surgery nor nadir hematocrit during the perioperative period was an independent predictor of stroke. Chi-squared automatic interaction detection analysis identified solvent/detergent-treated plasma (Octaplas; Octapharma AG, Lachen, Switzerland) units >2 and platelet units >4 along with diseased ascending aorta as independent predictors of stroke. The stroke rate was 8.9% in patients receiving >2 units of Octaplas and having a diseased ascending aorta. In patients receiving ≤2 units of Octaplas, the stroke rate was as high as 3.8% in patients receiving >4 units of platelets.**

Conclusions: **The results of this study indicated that atherosclerosis of the ascending aorta as well as transfusion of platelets and/or Octaplas were independent predictors of stroke after OPCAB.**

KEY WORDS: stroke, off-pump, hematocrit, transfusion, coronary artery bypass grafting, CHA_2DS_2-VASc

STROKE IS ONE of the most deleterious and costly complications related to cardiac surgery, and special attention should be paid to identify its causes.[1] Old age, aortic arch atherosclerosis, systemic inflammatory response,[2] preoperative creatinine,[3] pre- and postoperative atrial fibrillation,[3,4] extracardiac arteriopathy,[3,5] use of cardiopulmonary bypass,[2,5] type of procedure,[5] pre- or perioperative use of intra-aortic balloon pump,[5,6] emergency procedure, prolonged cardiopulmonary bypass time, re-exploration for bleeding[6] and low postoperative hemoglobin levels[7] all have been associated with increased risk of stroke after adult cardiac surgery. In addition, red blood cell (RBC) transfusion,[3,5,7–9] and transfusion of other blood products[3,6] recently have been shown to be potentially associated with increased risk of stroke after cardiac surgery. However, the association of RBC transfusion[10] and perioperative anemia[10–12] with postoperative neurologic complications also has been denied. Thus, the role of different blood products and other risk factors in the occurrence of stroke after coronary artery bypass graft surgery (CABG) remain unclear. The main pitfall of many studies was that the status of the ascending aorta was not taken into account in the analysis of predictive factors for stroke. Indeed, identification of a diseased ascending aorta as well as a "no-touch" aorta policy should be considered in any analysis evaluating the mechanisms underlying the development of postoperative stroke. In order to overcome these potential biases, the authors planned the present study in a consecutive series of patients who underwent isolated off-pump coronary artery surgery (OPCAB), and in whom the revascularization strategy was planned according to the status of the ascending aorta evaluated by epiaortic ultrasound. The authors hypothesized that transfusion of blood products increased the risk of postoperative stroke.

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MATERIAL AND METHODS

Patient Population and Data Collection

This study included a series of 1,314 patients who underwent isolated OPCAB at the Division of Cardiothoracic and Vascular Surgery of the Oulu University Hospital, Oulu, Finland, from June 2006 to December 2013. Patients' characteristics and operative data are summarized in Table 1. Patients undergoing procedures other than isolated CABG were excluded from this study as their immediate and late outcome was likely to differ from those undergoing isolated OPCAB.

Complete pre-, intra-, and postoperative data were available in all of these patients as obtained from the institutional prospective electronic cardiac surgery registry. Additional data were collected retrospectively from patients' records including files of all departments of the authors' hospital, including the department of internal medicine and neurology. The number of transfused blood products such as RBCs, platelets, and solvent/detergent-treated plasma (Octaplas; Octapharma AG, Lachen, Switzerland) was retrieved from a prospective electronic hospital registry collecting data on any transfusion of blood products. Transfused blood product units were counted from the day of surgery to the discharge of the patient or to a maximum of 1 month after the surgery if the length of in-hospital stay was more than 1 month. Data on the amount of postoperative blood loss were retrieved from a prospective electronic registry of the intensive care unit. Risk factors were defined according to the EuroSCORE criteria[13] as well as the definition criteria of the stroke risk scoring methods $CHADS_2$ and CHA_2DS_2-VASc.[14,15] The latter scores have been derived and largely validated for prediction of stroke in patients with atrial fibrillation. Estimated glomerular filtration rate was

Table 1. Clinical and Operative Risk Factors and Postoperative Variables in 1,314 Patients Who Underwent Off-Pump Coronary Artery Bypass Surgery. The Association of These Variables and Any Immediate Stroke After Surgery at Univariate and Multivariate Analysis is Shown

	No Postop. Stroke No. 1291	Postop. Stroke No. 23	Univariate Analysis p Value	Multivariate Analysis OR, 95% CI
Baseline variables				
Age (years)	67.2 ± 9.2	69.8 ± 9.4	0.128	
Females	268 (20.8)	4 (17.4)	0.693	
Diabetes	371 (28.7)	11 (47.8)	0.046	
Hypertension	708 (54.8)	14 (60.9)	0.565	
Pulmonary disease	122 (9.5)	0 (0)	0.262	
Neurologic dysfunction	24 (1.9)	2 (8.7)	0.074	
History of stroke	44 (3.4)	2 (8.7)	0.171	
eGFR (mL/min/m^2)	86 ± 26	83 ± 30	0.522	
Baseline hemoglobin (g/L)	137 ± 16	126 ± 19	0.010	
Baseline hematocrit	0.40 ± 0.4	0.37 ± 0.5	0.006	
LVEF ≤50%	323 (25.7)	11 (47.8)	0.016	
Critical preoperative status	90 (7.0)	2 (8.7)	0.748	
Myocardial infarction <3 months	623 (48.3)	16 (69.6)	0.043	
Extracardiac arteriopathy	153 (11.9)	3 (13.0)	0.861	
Previous cardiac surgery	8 (0.6)	0 (0)	1.000	
Atrial fibrillation	139 (10.8)	6 (26.1)	0.020	
Previous PCI	98 (7.6)	1 (4.3)	0.559	
Urgent/emergency surgery	716 (55.5)	15 (65.2)	<0.0001	
Preoperative IABP	6 (0.5)	0 (0)	0.743	
Potent antiplatelets within 5 days	244 (18.9)	8 (34.8)	0.055	
$CHADS_2$	1.4 ± 1.1	2.1 ± 1.3	0.004	
CHA_2DS_2-VASc	2.9 ± 1.6	3.9 ± 1.6	0.001	
Operative variables				
Epiaortic ultrasound	1291 (100)	23 (100)	–	
Diseased aorta	387 (30.0)	12 (52.2)	0.022	2.641, 1.151-6.060
Aorta side-bite clamping	1165 (90.2)	18 (78.3)	0.057	
No. distal anastomoses	3.9 ± 1.0	3.7 ± 0.9	0.454	
Postoperative variables				
Atrial fibrillation	548 (42.4)	15 (65.2)	0.029	
Blood loss at 12 hours after surgery	517 ± 349	452 ± 282	0.321	
Nadir hemoglobin (g/L)	89 ± 12	84 ± 8	0.028	
Nadir hematocrit on day of surgery	0.29 ± 0.04	0.26 ± 0.04	0.007	
RBC transfusion	666 (51.6)	14 (60.9)	0.377	
RBC units	0.3 ± 0.4	0.5 ± 0.5	0.260	
Octaplas transfusion	315 (24.4)	11 (47.8)	0.010	
Octaplas units	1.0 ± 2.1	2.2 ± 2.9	0.097	
Platelet transfusion	325 (25.2)	12 (52.2)	0.003	3.340, 1.455-7.665
Platelet units	0.04 ± 0.21	0.17 ± 0.39	0.004	

NOTE. Binary variables are reported as counts and percentages; continuous variables are reported as means and standard deviation. Variables are according to the EuroSCORE criteria.[11]

Abbreviations: CI, confidence interval; eGFR, estimated glomerular filtration rate; IABP, intra-aortic balloon pump; LVEF, left ventricular ejection fraction; OR, odds ratio; PCI, percutaneous coronary intervention; potent antiplatelets, clopidogrel, prasugrel and ticagrelor; RBC, red blood cell.

estimated by the Modification of Diet in Renal Disease formula.[16] Data on late death were retrieved from the Central Statistical Office of Finland (Tilastokeskus), which collects the certificates of death of all inhabitants of Finland. The data for this study were provided up to December 31, 2013. The authors assumed that there were no missing data on the immediate and late death of this study population. No attempt to replace missing values was done.

Antithrombotic Treatment and Transfusion of Blood Products

During the study period, the authors' policy was to discontinue aspirin 7 days, clopidogrel 5 days, and warfarin 2 days before surgery when feasible. Aspirin was discontinued for 7 days during the first part of the study period until 2012 and later on was continued until surgery. Aspirin was restarted in all patients immediately after surgery.

Heparin (300 u/kg) was administered intravenously after sternotomy to maintain an activated coagulation time of more than 400 seconds, and it was neutralized at the end of the procedure by protamine sulphate (3.0 mg/kg). A further dose of protamine sulphate was given in case of bleeding during closure of the chest or within the first hours after surgery according to activated coagulation time. Aprotinin was not used in any of the patients. Tranexamic acid was administered intraoperatively at the discretion of the anesthesiologist.