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The impact of minor blood transfusion on the outcome after coronary artery bypass grafting

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ABSTRACT

Purpose: To investigate the impact of minor perioperative bleeding requiring transfusion of 1–2 red blood cell (RBC) units on the outcome after coronary artery bypass grafting (CABG).
Methods: Sixteen cardiac surgical centers contributed to the prospective European CABG registry (E-CABG). 1014 patients receiving 1–2 RBC units during or after isolated CABG were compared to 2264 patients not receiving RBCs.
Results: In 827 propensity score matched pairs, transfusion of 1–2 RBC units did not affect the risk of in-hospital/30-day death ($p = 0.523$) or stroke ($p = 0.804$). However, RBC transfusion was associated with an increased risk of acute kidney injury ($p = 0.008$), sternal wound infection ($p = 0.001$), postoperative use of antibiotics ($p = 0.001$), prolonged use of inotropes ($p < 0.0001$), use of intra-aortic balloon pump ($p = 0.012$), length of intensive care unit stay ($p < 0.0001$) and length of in-hospital stay ($p < 0.0001$). Matched paired analysis excluding pre- and postoperative critical hemodynamic conditions showed that RBC transfusion was associated with an increased risk of major complications except in-hospital/30-day death.
Conclusion: Minor perioperative bleeding and subsequent transfusion of 1–2 RBC units did not affect the risk of early death, but increased the risk of other major adverse events. Minimizing perioperative bleeding and prevention of even low-volume RBC transfusion may improve the outcome after CABG.

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1. Introduction

In cardiac surgery, perioperative bleeding and transfusion of red blood cells (RBCs) are known to be associated with major adverse events [1–4]. However, due to the complex nature of perioperative bleeding and factors affecting it, disentangling the independent roles of different bleeding-related issues in the development of postoperative complications is challenging and a subject of continuous investigation. A growing body of evidence suggests that major perioperative bleeding and transfusion of significant amounts of RBC units are associated with increased morbidity and mortality after cardiac surgery [2,5,6]. Nevertheless, the possible impact of minor perioperative bleeding and related transfusion of one to two RBC units on the outcome appears to be more elusive as contradictory results have been reported [2,5,7–14]. Transfusion rates have been shown to vary largely between institutions [15]. Transfusion of one to two RBC units is common [7,9] and can be considered discretionary and is therefore of clinical importance. The aim of the present study was to investigate the impact of minor perioperative bleeding requiring transfusion of one to two RBC units on the outcome after isolated coronary artery bypass grafting (CABG).

2. Material and methods

2.1. Patient population and data collection

The *E*-CABG registry is an on-going prospective, multicenter international registry enrolling patients undergoing isolated CABG in 16 centers of cardiac surgery in six European countries (Finland, France, Germany, Italy, Sweden and United Kingdom). Twelve of these centers are university hospitals, two centers are central hospitals and two centers are private hospitals with agreements with the regional health authorities. This registry is registered in Clinicaltrials.gov (Identifier: NCT02319083) and its detailed protocol along with the definition criteria have been published elsewhere [16]. Recruitment of patients was started from January 2015 and data on baseline, intraoperative and postoperative variables were prospectively collected in an Access (Microsoft Corporation, Redmond, Washington, USA) datasheet by researchers who were trained for data collection into this registry. Data were checked by researchers from each participating center before submitting dataset to the principal investigator for merging. External auditing of the data was not possible because of linguistic and geographical barriers. The principal investigator evaluated the databases for consistency by asking for missing and random data.

The present study included patients who underwent isolated CABG from January 1 to December 31, 2015. Since a preliminary analysis (described in detail in the Results section) showed that the best cutoff for perioperatively transfused RBC units in predicting early postoperative mortality was transfusion of ≥3 units of RBCs, we aimed to evaluate the impact of minor perioperative bleeding on patient outcome. Therefore, solely patients who received 0 to 2 RBC units perioperatively (during and after the operation until the discharge) were included in the further analyses. Patients receiving one to two RBC units were compared to those not receiving RBC transfusion.

Data on baseline characteristics, pre- and perioperative hemoglobin and hematocrit levels, postoperative drainage output at 12 h, and use of any type of blood products as well as on operative variables and postoperative adverse events were collected prospectively. Transfused RBC units were counted from the beginning of the operation to the discharge of the patient, i.e. during the entire hospital stay excluding possible preoperative transfusions. Transfused fresh frozen plasma (FFP), solvent/detergent-treated plasma (Octaplas, Octapharma AG, Lachen, Swizerland) and platelet units were counted from the time of chest closure until the discharge from the hospital. The operative risk was estimated by the EuroSCORE II [17]. Preoperative anemia was defined according to the World Health Organization definition criteria as hemoglobin level < 120 g/L in women and <130 g/L in men [18]. Critical preoperative state was defined as any of the following conditions: ventricular tachycardia or ventricular fibrillation or aborted sudden death, preoperative cardiac massage, preoperative ventilation before anesthetic room, preoperative inotropes or intra-aortic balloon pump (IABP), preoperative acute renal failure (anuria or oliguria <10 mL/h). Acute coronary syndrome was defined as any unstable angina, non-ST elevation or ST elevation myocardial infarction requiring myocardial revascularization during the index hospitalization.

2.2. Clinical management

In general, red blood cells (RBCs) were given intraoperatively to maintain a hemoglobin concentration > 7 g/dL, or a hematocrit >20% during cardiopulmonary bypass, or given postoperatively when hemoglobin was <8 g/dL. The need of perioperative administration of blood products such as FFP, Octaplas and platelets also was determined on an individual, patient-by-patient basis. There was no specific inter-institutional protocol regarding transfusion thresholds or blood management.

2.3. Outcome endpoints

The primary clinical outcomes of this study were in-hospital or 30-day mortality, stroke, acute kidney injury (AKI) and sternal wound infections. Secondary clinical outcomes were postoperative use of antibiotics, prolonged use of inotropes (>12 h), use of IABP (excluding preoperatively inserted IABP), intensive care unit (ICU) stay (days), in-hospital stay (days), atrial fibrillation and resternotomy for bleeding. Postoperative stroke was defined as any focal or global neurological syndrome occurring during the in-hospital stay caused by ischemia and/or hemorrhage not resolving within 24 h. AKI was stratified according to the Kidney Disease: Improving Global Outcomes (KDIGO) definition criteria [19]. Deep sternal wound infections or mediastinitis were graded according to the Centers for Disease Control and Prevention definitions of surgical site infections [20]. The definition criteria of the outcomes have been described in detail elsewhere [16].

2.4. Ethical considerations

This study was approved by the Institutional Review Board (IRB) of the participating centers. Informed consent was collected in Institutions where it was required by the internal IRB, otherwise it was waived.

2.5. Statistical analysis

Statistical analysis was performed using the SPSS v. 23.0 statistical software (IBM Corporation, Armonk, New York, USA). No attempt to replace missing values was made. Fisher's exact sum test, Chi-square test, Mann-Whitney and Kruskal-Wallis tests were used for univariate analysis. Correlation between continuous and ordinal variables was estimated by the Spearman's test. C-statistics were calculated to assess the predictive ability of continuous variables on outcome end-points. Youden's test was used to estimate the best cutoff value of continuous variables in predicting adverse events. As observational studies do not provide randomization, a propensity score matching method was employed to select two groups of patients not receiving any RBC transfusion and those receiving transfusion of one to two units of RBCs during the intra- and postoperative period with similar baseline and operative characteristics. The propensity score was estimated using a non-parsimonious logistic regression model with RBC transfusion as the dependent variable. The following variables were included as covariates: age, gender, body mass index, preoperative hemoglobin, estimated glomerular filtration rate, pulmonary disease, diabetes, stroke, poor mobility, extracardiac arteriopathy, atrial fibrillation, previous percutaneous coronary intervention, previous cardiac surgery, left ventricular ejection fraction, recent myocardial infarction, acute coronary syndrome types,