On-pump versus off-pump coronary artery bypass surgery in patients with preoperative anemia

Domenico Paparella, MD,[a] Pietro Guida, PhD,[b] Giuseppe Scrascia, MD, PhD,[c] Vitantonio Fanelli, MD,[d] Marco Contini, MD,[d] Salvatore Zaccaria, MD,[c] Giuseppe Labriola, MD,[e] Carmine Carbone, MD,[f] Florinda Mastro, MD,[a] and Valerio Mazzei, MD[f]

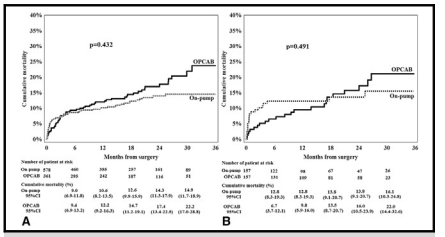
ABSTRACT

Objectives: The study objective was to evaluate the effects on early outcome and midterm survival of performing coronary artery bypass grafting with the off-pump technique in comparison with cardiopulmonary bypass (on-pump) in patients with preoperative anemia.

Methods: Consecutive adult anemic patients (preoperative hemoglobin <13.0 g/dL in men and <12.0 g/dL in women) resident in Puglia region who underwent isolated coronary artery bypass grafting between January 2011 and November 2013 were considered. Vital status was ascertained from the date of surgery to December 31, 2013. Odds ratio and hazard ratio (HR) were estimated. Propensity score methods were used to control for confounders.

Results: Of 939 anemic patients (234 female, aged 71 ± 9 years), 361 underwent operation with the off-pump technique and 578 underwent operation with the on-pump technique. Patients undergoing off-pump coronary artery bypass had a shorter intensive care unit length of stay, lower blood transfusion rate, and postoperative reduction in creatinine clearance. During a median follow-up of 18 months, 126 patients died: 46 in hospital (35 on-pump) and 80 after discharge (33 on-pump). In comparison with the off-pump technique, the on-pump technique had greater hospital mortality (odds ratio, 2.57; $P = .028$) and 30-day incidence of fatal events (HR, 2.67; $P = .026$). After a period without risk differences between groups (1-6 months; HR, 0.79; $P = .618$), a lower mortality in those undergoing the on-pump technique was detected (after 6 months HR, 0.35; $P = .014$). All results were confirmed in the 157 pairs of patients matched for propensity score, anemia grade, and surgery center.

Conclusions: In patients with low levels of preoperative hemoglobin, off-pump coronary artery bypass was associated with lower early morbidity and mortality but a greater risk of mortality during follow-up compared with on-pump coronary artery bypass. (J Thorac Cardiovasc Surg 2015;149:1018-26)



In anemic patients, the initial advantages of OPCAB are counterbalanced by worse survival during follow-up.

Central Message

Preoperative anemia is a risk factor for mortality and adverse outcome in patients undergoing coronary artery surgery. In anemic patients, OPCAB is associated with reduced operative mortality/morbidity; however, the initial advantages are counterbalanced by decreased survival during follow-up compared with on-pump surgery.

Perspective

The presented data impose 2 different considerations. First, the performance of CPB should be optimized to reduce short-term adverse events in anemic patients. The use of miniaturized CPB equipment, with reduced hemodilution and transfusion requirements, may lead to improved outcome. Second, OPCAB technique should provide documented complete and adequate myocardial revascularization to improve long-term survival.

See Editorial page 962.

Supplemental material is available online.

Coronary artery bypass grafting (CABG) is a widely performed operation. It can be executed with the use of cardiopulmonary bypass (CPB) (on-pump) or off-pump coronary artery bypass (OPCAB), which has been developed to decrease perioperative complications related to the use of CPB.[1,2] The optimal surgical strategy remains controversial without clear differences in early and long-term outcomes in randomized controlled trials.[3-8] Recent observational and randomized studies have suggested that certain high-risk patient subgroups are more likely to benefit from an OPCAB approach, avoiding the deleterious effects of CPB.[9,10] On the other hand, some studies have documented that the initial beneficial effects of OPCAB are counterbalanced by a worse survival during follow-up, probably because of a higher rate of incomplete revascularization or inaccurate anastomosis.[11,12]

From the Division of Cardiac Surgery,[a] Department of Emergency and Organ Transplant, University of Bari Aldo Moro, Bari, Italy; Puglia Health Regional Agency,[b] Bari, Italy; Department of Cardiac Surgery,[c] Vito Fazzi Hospital, Lecce, Italy; Department of Cardiac Surgery,[d] Villa Verde Hospital, Taranto, Italy; Department of Cardiac Surgery,[e] Santa Maria Hospital, Bari, Italy; and Department of Cardiac Surgery,[f] Mater Dei Hospital, Bari, Italy.

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Address for reprints: Domenico Paparella, MD, Division of Cardiac Surgery, Department of Emergency and Organ Transplant (D.E.T.O.), University of Bari "Aldo Moro," Piazza Giulio Cesare 11, 70100 Bari, Italy (E-mail: domenico.paparella@uniba.it).

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Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CI = confidence interval
CPB = cardiopulmonary bypass
euroSCORE = European System for Cardiac Operative Risk Evaluation
HR = hazard ratio
ICU = intensive care unit
OPCAB = off-pump coronary artery bypass
OR = odds ratio

Preoperative anemia is associated with a number of comorbidities, including advanced age, female gender, small body surface area, poor left ventricular ejection fraction, renal function impairment, congestive heart failure, unstable angina, and others,[13,14] all of which are recognized risk factors for adverse outcome after cardiac surgery. Postoperative morbidity and mortality after cardiac surgery, specifically after CABG, are higher in anemic patients,[13-16] and when preoperative anemia is added to risk classification scores, it improves their discrimination ability.[17] Differences in postoperative outcomes between on-pump and OPCAB techniques have not been studied in patients with preoperative anemia. The aim of the present study was to compare in-hospital morbidity and short-term and midterm survival in patients with preoperative anemia undergoing on-pump coronary artery bypass or OPCAB surgery.

MATERIALS AND METHODS

Study Population

Preoperative, intraoperative, and postoperative information on consecutive adult patients who underwent isolated CABG from January 1, 2011, to November 30, 2013, were gathered from the Puglia Regional Adult Cardiac Surgery Registry. The study is an initiative of the Health Regional Agency of Puglia region, which has been described.[18] Briefly, by implementing an accurate database including prospectively clinical information and details on cardiac surgical procedures, the aims of the study were the evaluation of short- and long-term results of heart operations performed at the 7 adult cardiac surgery centers in the Puglia region (University of Bari–Policlinico Hospital Coordinating Centre, Anthea Hospital in Bari, Santa Maria Hospital in Bari, Villa Bianca Hospital in Bari, Villa Verde Hospital in Taranto, Vito Fazzi Hospital in Lecce, and Città di Lecce Hospital in Lecce). The study was conducted in accordance with the Declaration of Helsinki. According to institutional review board policy, it was determined that the research did not require informed consent. Hospital mortality risk prediction was carried out for each patient according to the European System for Cardiac Operative Risk Evaluation (euroSCORE) II model.[19] Anemia was classified according to the preoperative hemoglobin level evaluated on the day of surgery. Patients with anemia according to the World Health Organization criteria were included.[20] Men with a hemoglobin level of 13.0 g/dL or greater and women with a hemoglobin level of 12.0 g/dL or greater were excluded. Anemia was classified as (1) mild if hemoglobin was 11.0 to 12.9 g/dL in men and 11.0 to 11.9 g/dL in women; (2) moderate if hemoglobin was 8.0 to 10.9 g/dL in both genders; or (3) severe if hemoglobin was less than 8.0 g/dL in both genders. Two of 7 cardiac surgery units of region were excluded from the analysis because of systematic missing preoperative hemoglobin values.

Surgical Management

The conventional surgical approach was median sternotomy in most of the CABG procedures. Heparin was injected as a single bolus of 300 U/kg in on-pump procedures and 150 U/kg in OPCAB to obtain an activated clotting time of 400 and 300 seconds, respectively. An additional heparin bolus of 5000 units was injected if the activated clotting time decreased below these targets. After surgery, protamine sulfate was administered to neutralize heparin (1 mg protamine/100 U of heparin in on-pump procedures and 0.8 mg/100 U of heparin in OPCAB). CPB was established with aortic cannulation and right atrial cannulation with 2-stage cannula. Deep pericardial suture, heart stabilizer, intracoronary shunts, or snares were used to stabilize the heart and allow bloodless anastomoses according to the surgeon's preference. Patients with hemoglobin values less than 8 g/dL received transfusions after the induction of anesthesia. Indications for intraoperative homologous blood transfusion were hemoglobin less than 7 g/dL or hematocrit less than 0.21 to 0.22, and the postoperative cutoff was hemoglobin less than 8 g/dL or hematocrit less than 0.23 to 0.24.

End Point

The primary outcome was hospital mortality, defined as death occurring at any time after surgery during the hospital period in which the operation was performed. The secondary end point was hospital morbidity. The coprimary end point was midterm mortality. Vital status and dates of death to December 31, 2013, were obtained for resident in Puglia by linking regional Health Information System to the registry on the basis of an encrypted patient identifier. Follow-up was considered to be administratively censored on December 31, 2013, and was at least 1 month for all patients (maximum, 36 months).

Statistical Analysis

Data are shown as mean values ± standard deviation, and categoric variables are given as percentages. Because of the low number of patients with severe anemia, 2 anemia grades were analyzed: mild and moderate to severe. Intraoperative conversion from off-pump to on-pump CABG was analyzed according to the intention-to-treat principle based on the initial treatment assignment group (OPCAB). Preoperative patients' characteristics and individual risk factors were analyzed using a mixed model with centers fitted as random so that possible differences in data across surgical units could be considered. To control for selection bias as a result of nonrandom treatment assignment, the propensity analysis method was used to estimate the probability of being assigned to on-pump surgery.[21] A multivariate mixed logistic regression model was developed including all risk factors and preoperative variables associated with the type of surgery. We matched participants, stratified by anemia grade, on the basis of closest propensity score (<0.15 in matched pairs). We used an automated matching procedure that for each OPCAB case selected 1 on-pump case that fulfilled the matching criterion. Patients were initially matched within the same cardiac surgeon, with the remaining patients who were matched by center.

In the entire sample, in-hospital mortality was analyzed by using mixed logistic regression analysis adjusting for linear predictor of propensity score.[21] For the propensity analysis that required statistical methods appropriate for matched data, a conditional logistic regression model was used considering the pairs of selected patients. Odds ratios (ORs) for in-hospital mortality were estimated (on-pump vs OPCAB). The cumulative mortality curves, based on Kaplan–Meier analyses stratified by type of surgery, were compared with the Wilcoxon test. Survival analysis was performed by using Cox proportional hazards model with stratification by surgical center. Because of significant evidence against the proportional hazards assumption for the overall survival from surgery, we estimated separate hazard ratios (HRs) for each of the following time intervals