The Effect of Pump on Early Postoperative Mortality and Cerebrovascular Accident in Coronary Bypass Surgery Patients

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ABSTRACT

Introduction: This study investigated the mortality rates during the postoperative early period (one month) in patients who underwent on- or off-pump coronary artery bypass grafting (CABG) and explored the effects of cardiopulmonary bypass (CPB) on early mortality and cerebral accident.

Patients and Methods: This study comprises a total of 260 subjects that underwent CABG surgery in our clinic. Patients who underwent CABG were grouped according to two different surgical techniques: the first group (Group 1) consisted of patients who underwent CABG using CPB and cross-clamp (on-pump); the second group (Group 2) consisted of patients who underwent CABG by beating heart (off-pump) technique. Proximal anastomoses were performed using side clamps in all cases.

Results: Postoperative follow-up was conducted on patients until Day 30 for mortality. We encountered four dead cases and six cerebrovascular accidents.

Conclusion: The rates of cerebral accidents (2.4% vs. 2.1%) and deaths (1.8% vs. 1%) have the same ratios and are not statistically significant in on-pump CABG surgeries compared with off-pump CABG surgeries.

Key Words: Coronary artery disease; coronary artery bypass; off-pump coronary artery bypass; heart-lung machine; mortality; stroke

Açık Kalp Cerrahisinde, Pompanın Erken Postoperatif Mortalite ve Serebrovasküler Olay Üzerine Etkisi

ÖZET

Giriş: Bu çalışma, son gelişmelerle pompatlı/pompasız koroner arter bypass grafting (KABGO) uygulanan hastalarda, postoperatif erken dönemde (bir ayda), kardiyopulmoner baypas (KPB)”ın erken mortalite ve serebrovasküler olay üzerine etkileri araştırıldı.

Hastalar ve Yöntem: Çalışmamız, kliniğimizde koroner arter bypass greftleme ameliyatı yapılan toplam 260 olguyu içermektedir. KABGO uygulanan hastalar iki farklı cerrahi tekniğe göre gruplandırıldı. Birinci grup (Grup 1), CPB ve X klem (on-pump) kullanılarak KABGO uygulanan hastalardan oluştu. İkinci grup (Grup 2), atan kalp (off-pump) tekniği ile KABGO uygulanan hastalardan oluştu. Proksimal anastomozlar tüm olgularda yan klem kullanılarak yapıldı.

Bulgular: Hastalar postoperatif otuzuncu güne kadar mortalite açısından takip edildi. Dört ölüm olgu ve altı serebrovasküler olaya karşı karşıya kaldık.

Sonuç: On-pump KABGO ameliyatlarında off-pump KABGO ameliyatlarına kıyasla serebral kaza oranları (%2.4’e karşı %2.1) ve ölüm (%1’e karşı %1.8) benzer oranda görülün istatistiksel olarak anlamlı değildir.

Anahtar Kelimeler: Koroner arter hastalığı; koroner arter bypass operasyonu; off pump koroner arter bypass operasyonu; kalp akciğer makinesi; mortalite; felç

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INTRODUCTION

Coronary artery bypass grafting (CABG) surgery is one of the most frequently performed surgeries in the world. It has risks for central nervous system complications and mortality. Conventional CABG is performed using a cardiopulmonary bypass (CPB) device and is called as on-pump CABG, whereas the CABG performed without CPB is called off-pump CABG (beating heart).

On-pump CABG is considered the gold standard, but this method has physiological outcomes including the activation of the complement system, as well as thrombocytopenia, immune suppression, and inflammatory response, which can lead to organ dysfunction. Nevertheless, the manipulation of ascending aorta during cannulation (cannulation and cross-clamping) poses a risk for embolization and stroke.

Some studies emphasize that the mortality and morbidity rates of off-pump and on-pump coronary artery bypass surgeries are different, particularly in high-risk patients (1). There are studies reporting the differences between these two CABG techniques in terms of the incidence of renal insufficiency, postoperative cognitive exposure, prolonged mechanical ventilation, blood loss, and prolonged duration of hospital and intensive care unit stays (2-5 days). However, in recent years, developments in CPB have led to improvements in surgical experience and patient management. We have encountered improvements in cooperation among specialists, such as cardiac surgeons, clinical perfusionists, anesthetists, and other technicians.

This study investigated the mortality and cerebral accident rates in the postoperative early period (one month) in patients who underwent on/off-pump CABG and explored the effects of CPB on early mortality and cerebral accidents.

PATIENTS and METHODS

This study has been approved by Institutional Review Board.

Clinical Characteristics of Patients

This study comprises a total of 260 subjects that underwent CABG surgery in our clinic. Their medical history was questioned, and detailed physical examination was performed in all patients. Transthoracic echocardiography (TTE) (Acuson, Mountain View, Acuson Sequoia C256, Siemens, GERMANY), standard preoperative laboratory analyses, pulmonary function test (Spirobank Spirometry, MIR medical International Research Product, ITALY), and bilateral carotid artery Doppler ultrasonography (Toshiba XARIO prime ultrasound, JAPAN) were performed in our clinic. Ascending aorta, thorax, and aortic arch calcification were evaluated by standard telegram prior to the surgery. During surgery, the ascending aorta and the beginning of the aortic arch were examined by manipulation. Patients with plaque detected during manipulation were not included in this study because their medical treatments were changed.

Clopidogrel (Plavix® 75 mg, Sanofi Aventis, FRANCE) and acetylsalicylic acid were respectively discontinued five and three days before surgery in patients who will undergo on-pump (with cross-clamp) CABG. Clopidogrel and acetylsalicylic acid (Coraspin® 100,150, 200 mg, Bayer Turk, TURKEY) were respectively discontinued five days and one day before surgery in patients who will undergo off-pump CABG.

Blood glucose concentration in patients with type 2 diabetes was regulated using regular insulin before and after surgery. The blood glucose levels of the patients were kept below 200 mg/dL.

Dyslipidemia in study participants was defined as fasting serum total cholesterol level ≥ 40 mg/dL, triglyceride level ≥ 200 mg/dL, low-density lipoprotein cholesterol level ≥ 160 mg/dL, and/or high-density lipoprotein cholesterol level < 40 mg/dL, as well as receiving or not receiving active drug therapy (6). Serum cholesterol level was measured by enzymatic methods.

Serum samples were collected in standard tubes containing ethylenediaminetetraacetic acid as anticoagulant. These serum samples were analyzed via Cell-Dyne 3700 (Abbott, Abbott Park, IL, USA) device. The weight (SECA, Vogel & Holke, Hamburg, GERMANY) and height (SECA, Vogel & Holke, Hamburg, GERMANY) of the participants were measured, and body mass index (BMI) was calculated prior to the surgery. The distribution of BMI according to ages in groups is presented in Figures 1 and 2.

Patients who underwent CABG under emergency conditions, CABG surgery for the second time, CPB-supported off-pump CABG, and valvular and coronary artery surgeries in the same session, as well as those with chronic renal insufficiency and...
undergoing dialysis patients, were excluded from this study to create a homogeneous group. Data were collected retrospectively. The stage approach was applied in patients with carotid artery disease over 70% and under 100%, and carotid artery surgery was delayed until one month after CABG.

**Study Groups**

Patients who underwent CABG were grouped according to two different surgical techniques. The first group (Group 1) included those that underwent CABG by using CPB and the cross-clamp (on-pump) technique. The second group (Group 2) consisted of patients who underwent CABG by the beating heart (off-pump) technique. A side clamp was used for proximal anastomosis in all cases.

In a study about CPB duration, it was found that the prolonged CPB duration independently increased mortality and morbidity after CABG. Mean duration was 115 min in CABG patients participating in the study. To make a more balanced comparison between groups, the patients who underwent CABG by the beating heart technique (off-pump) were included.

Beating heart operation indications in our clinic: the proper diameter of the coronary artery, the epicardial view of the coronary arteries, and the cardiac performance are good enough to allow for cardiac manipulation. Otherwise, on-pump surgery is preferred. This choice obviously increases the number of anastomoses in on-pump surgery.

To create homogeneous groups, dialysis patients (or patients with creatinine level higher than 2 g/dL), patients whose surgery procedure has been changed because aortic pathology was seen during surgery, patients who underwent surgery under emergency conditions, patients who underwent redo-CABG, and patients who underwent surgery without touching the ascending aorta or underwent left internal mammarian artery (LIMA)-LAD CABG were not included in the study.

**Surgical Procedure**

Isolated CABG was performed in all patients who participated in this study. Fentanyl, midazolam, and pancuronium bromide were administered for the induction of anesthesia. Standard median sternotomy was applied. Vascular conduits (LIMA, saphenous vein and radial artery) were prepared. Heparin sodium (Nevparin® 5000 IU/mL Mustafa Nevzat, TURKEY) was administered (at a dose of 300 IU/kg). CPB, cross-clamp, standard aortic cannula, and two-stage venous cannula were applied. Jostra-Cobe (Model 043213 105, VLC 865, SWEDEN) heart-lung machine was used. Crystalloid cardioplegia during surgery and hot shot cardioplegia at the end of the surgery were used in all patients. LIMA was used in all cases, but the right internal artery was not. Great saphenous vein and radial artery have been the preferences for conduit. Meticulous aseptic technique was used in all operations. Unnecessary electrocautery and luxury perfusion (unnecessary CPB that enhances postoperative complications) were avoided. Heparinization was performed by administering 150 IU/kg heparin in patients who underwent the beating heart technique. Octopus and Starfish were applied in distal anastomoses.

In on-pump and off-pump techniques, a side clamp was used for proximal anastomoses. Several data about surgery are demonstrated in Table 1.

**Postoperative Care**

Cefazolin sodium (Cefamezin®-IM/IV, Zentiva, TURKEY), which is being used as standard prophylactic antibiotic in our clinic, was administered at a dose of 1 g/30 min before surgery and continued at 8 h intervals for 72 h after surgery. Acetylsalicylic acid (Coraspin® 300, Bayer Turk, TURKEY) was commenced at a dose of 300 mg/d together with enteral nutrition in all study participants. Blood glucose levels in diabetic patients were strictly regulated after surgery by using insulin glargine at a dose of 100 IU/ml (Lantus® flacon, Sanofi Aventis, FRANCE) and human soluble regular insulin at a dose of 100 IU/ml (Humulin-R® flacon, Lilly, TURKEY). Insulin infusion was not avoided. Blood glucose concentration was kept below 200 mg/dL in all diabetic patients.

Patients stayed at the cardiovascular surgery (CVS) intensive care unit for 48 h. They were admitted to the CVS clinic within 72 h after their drains and arterial catheters were removed. The patients were discharged from the hospital 6-12 d after surgery and were followed up until the 30th postoperative day for mortality and cerebral accident.

**Statistical Analysis**

Statistical analyses were made by SPSS (SPSS Inc., Chicago, IL, USA). Pearson’s chi-squared analysis was used in the analysis of the statistical significance of nonparametric data between the groups, and Fisher’s exact test was used for nonparametric data.
in case the observed between-group values were lower than expected. Although parametric data were shown as minimum, maximum, and mean ± standard deviation, independent Student’s t-test was used in the statistical significance of parametric data between the groups. If two-tailed p value was lower than 0.05 (p< 0.05), it was considered statistically significant (Table 1).

RESULTS

Subject Characteristics
The minimum and maximum ages of all participants were 29 and 89 years (mean ± standard deviation: 62.8 ± 9.7 y), respectively. Among the patients in our study, 166 (63.8%) were male and 94 (36.2%) were female. The number of patients receiving an antidiabetic agent was 123 (47.3%), and the number of patients with hypertension (HT) was 210 (80.8%). There were 69 (26.5%) patients with chronic obstructive pulmonary disease (COPD) and 109 smokers (41.9%). A total of 18 (6.9%) patients have histories of stroke, 1 patient (0.4%) with right carotid artery stenosis (70% ≤ lesion < 100%), 2 patients (0.8%) with left carotid artery stenosis (70% ≤ lesion < 100%). In our study, the number of patients who underwent CABG with CPB was 164 (63.1%), and the number

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°F: p value as Student’s t-test result,
°F: p value as Pearson’s chi-squared test result,
°F: Student’s t-test was made according to these values,
°F: Fisher’s exact test was used because the observed values were below the expected values.
BMI: Body mass index, SD: Standard deviation, PAD: Peripheral artery disease, COPD: Chronic obstructive pulmonary disease, CABG: Coronary artery bypass grafting.
of patients who underwent beating heart technique was 96 (36.9%). Mortality was observed in four patients (1.5%) in the postoperative period.

Groups Characteristics

Males in Group 1: Two (1.9%) dead cases were shown, and the mean ± standard deviation preoperative EF was 52.5 ± 9.4. The mean ± standard deviation age was 62.4 ± 10.3 y, the mean ± standard deviation body mass index (BMI) was 28.2 ± 4.6 kg/m², and the mean ± standard deviation number of bypass grafting performed in CABG was 3.5 ± 0.8. The number of patients with history of cerebrovascular accident (CVA) before surgery, right carotid artery stenosis (70% ≤ lesion < 100%), and left carotid artery stenosis (70% ≤ lesion < 100%) was nine (8.4%), zero (0%), and two (1.9%), respectively. There were 67 (62.6%) smokers, 82 (76.6%) hypertensive patients, 29 (27.1%) patients with COPD, 7 (6.5%) patients with PAD, 28 (26.2%) patients receiving oral antidiabetic agent, and 12 (11.2%) patients receiving parenteral antidiabetic agents. The mean ± standard deviation preoperative leukocyte count was 8.27 ± 6.1, and the mean ± standard deviation preoperative thrombocyte count was 247.9 ± 74.9.

Females in Group 1: One (1.8%) dead case was shown. The mean ± standard deviation age was 64.1 ± 7.9 y, the mean ± standard deviation BMI was 31.8 ± 5.1 kg/m², the mean ± standard deviation preoperative EF was 56 ± 9.8, and the mean ± standard deviation number of bypass grafting performed in CABG was 3.7 ± 0.8. Two patients (3.5%) have CVA histories before surgery, one patient (1.8%) has right carotid artery stenosis (70% ≤ lesion < 100%), and no patient (0%) has left carotid artery stenosis (70% ≤ lesion < 100%). It was observed that there were 54 (94.7%) hypertensive patients, 5 (8.8%) smokers, 8 (14%) patients with COPD, 2 (3.5%) patients with PAD, 21 (36.8%) patients receiving oral antidiabetic agent, and 17 (29.8%) patients receiving parenteral antidiabetic agent. The mean ± standard deviation preoperative leukocyte count was 7.89 ± 2.5 and the mean ± standard deviation preoperative thrombocyte count was 278.9 ± 112.

Males in Group 2: No (0%) death cases were encountered after surgery. The mean ± standard deviation age was 61.5 ± 9.5 y, the mean ± standard deviation BMI was 28.1 ± 3.8, the mean ± standard deviation preoperative EF was 56.3 ± 7.5, and the mean ± standard deviation number of bypass grafting performed in CABG was 2.7 ± 1. Five patients (8.5%) have CVA histories, zero patients (0%) have right carotid artery stenosis (70% ≤ lesion < 100%), and no patient (0%) has left carotid artery stenosis (70% ≤ lesion < 100%). There were 33 smokers (55.9%), 42 hypertensive patients (71.2%), 18 patients (30.5%) with COPD, 2 patients (3.4%) with PAD, 19 patients (32.2%) receiving oral antidiabetic agent, and 3 patients (5.1%) receiving parenteral antidiabetic agent. The mean ± standard deviation preoperative leukocyte count was 8.51 ± 2.1, and the mean ± standard deviation preoperative thrombocyte count was 256.7 ± 71.8.

Females in Group 2: One (2.7%) dead case was shown after surgery. The mean ± standard deviation age was 63.9 ± 10.8 y, the mean ± standard deviation BMI was 32.2 ± 5.6, the mean ± standard deviation preoperative EF was 51.5 ± 10, the mean ± standard deviation number of bypass grafting performed in CABG was 2.5 ± 0.8. Two patients (5.4%) have CVA histories before surgery, no patient (0%) has right carotid artery stenosis (70% ≤ lesion < 100%), and no patient (0%) has left carotid artery stenosis (70% ≤ lesion < 100%). There were 4 smokers (10.8%), 32 hypertensive patients (86.5%), 14 patients (37.8%) with COPD, 1 patient (2.7%) with PAD, 11 patients (29.7%) receiving oral antidiabetic agent, and 12 patients (32.4%) receiving parenteral antidiabetic agent. The mean ± standard deviation preoperative leukocyte count was 8.1 ± 2, and the mean ± standard deviation preoperative thrombocyte count was 249 ± 64.1.

The patients were followed up until the 30th postoperative day for mortality and cerebral accident. We encountered four dead cases and six cerebrovascular accidents. The distribution of mortality in all participants is presented in Figure 3.

DISCUSSION

Conventional CABG is performed using a CPB device and is called on-pump CABG, whereas the CABG performed without CPB is called off-pump CABG. On-pump CABG is described as the gold standard; however, this method has some physiological outcomes, including thrombocytopenia, complement system activation, immune suppression, and inflammatory response, which lead to organ dysfunction. The manipulation of the ascending aorta during cannulation has risk for embolization and stroke.

Figure 3. Distribution of mortality in all participants.
Puskas et al. reported that beating heart CABG (off-pump) has become the preferred technique because of similar number of revascularization, improved time until hospital discharge, and decreased number of patients with low cardiac output compared with conventional CABG (on-pump CABG) \(^9\). Supporting these data, some authors reported that off-pump CABG might reduce perioperative morbidity compared with on-pump CABG \(^9\).

Conventional CABG is characterized by precise coronary anastomoses performed by using CPB. However, providing blood-free surgical area and performing precise anastomosis using CPB brings along unfavorable effects for the patient including blood trauma, inflammatory response, negative nonpulsatile flow, potential air embolus, and debris embolization arising from the aorta \(^10\). Off-pump CABG was considered a technique for removing the unfavorable effects of CPB.

Dalen et al. retrospectively reviewed patients who underwent CABG surgery in Sweden in a mean period of 7.1 years \(^11\). They emphasized that patients who underwent off-pump or on-pump surgery had similar outcomes in terms of long-term survival, mortality, re-hospitalization due to myocardial infarction (MI), heart failure, and stroke. Hueb et al. prospectively followed 155 patients who underwent off-pump CABG and 153 patients who underwent on-pump CABG surgery for five years and found no difference between off-pump CABG and on-pump CABG in terms of mortality, MI, revascularization, recurrence of angina, and stroke \(^12\).

Recently, CABG is increasingly being performed in many high-risk patients. The benefits of off-pump CABG are obvious in terms of complications due to CPB and aorta. Recent studies have demonstrated improvements in high-risk patients who underwent off-pump CABG \(^13-16\).

Off-pump CABG and the gold standard on-pump CABG have been compared both in large retrospective observational studies and in randomized controlled studies. The results of studies on both techniques revealed comparable outcomes. However, small, prospective, randomized, controlled studies are lacking. One study has reported that these other studies are incapable of demonstrating early- and late-term results concerning incomplete revascularization, decreased long-term graft patency, increased recurrent revascularization, and survival. This has encouraged researchers who are against off-pump CABG to promote the discontinuation of this technique. There are studies stating that those who have doubt about the applicability and benefit of off-pump CABG ignore statistically significant studies that demonstrate similar long-term outcomes and more comfortable hospital care periods than on-pump CABG \(^17-22\).

Selnes et al. followed 75 patients who underwent off-pump CABG and 152 patients who underwent on-pump CABG for 6 years and reported that long-term cardiac and cognitive outcomes are generally similar \(^23\). Van Dijk et al. performed 282 off-pump CABG surgeries by using the octopus stabilizer device and emphasized that it is not different from CPB in terms of five-year survival rate, MI, angina recurrence, stroke, revascularization, and cognitive functions \(^24\).

Van Dijk et al., Roy et al., Legare et al. and Parolari et al. compared the short-term outcomes of on-pump and off-pump CABG and found no comparable differences \(^25\). Beckermann et al. stated that off-pump CABG is superior to on-pump CABG owing to mildly better hospital discharge rates and lower incidence of some postoperative complications particularly atrial fibrillation, psychotic syndromes, and renal dysfunction \(^1\).

In their large-series studies, Plomondon et al. reported that off-pump CABG is superior to on-pump CABG in terms of early morbidity and mortality rates \(^26\).

In this study, it was observed that the rate of death and cerebral accident in hospitals or within 30 postoperative days was the same (i.e., statistically insignificant) in the on-pump CABG group (Group 1) compared with the off-pump group (Group 2). The preoperative evaluation of EF by transthoracic ECHO was not different between the groups. It was observed that EF was over 50% in two of three cases that died and below 50% in the other case in Group 1. EF was below 50% in one patient who died in Group 2. Although the mortality in Group 1 was due to low cardiac output syndrome in two cases and due to multiple organ failure in one case, mortality was due to catastrophic CVA in Group 2. Even though postoperative stroke was not the cause of any postoperative death in the on-pump CABG group, stroke was considered the cause of mortality in the off-pump CABG group. Two of the cases that died in Group 1 were under the age of 70, and one was over the age of 70. By contrast, the case that died in Group 2 was over the age of 80. The mean number of bypass grafting was found to be statistically significantly higher in the on-pump group versus the off-pump group. However, it was determined that three grafts were used in two of the three patients who died in the postoperative period in Group 1, and four grafts were used in the other case. By contrast, three grafts were used in the case that died in the postoperative period in Group 2.

**CONCLUSION**

In this study, no statistically significant difference was determined between on-pump CABG and off-pump CABG in terms of early postoperative mortality rate and cerebral accident rate during 30 postoperative days. The results can be summarized under two topics: the number of bypass grafting performed in on-pump CABG surgeries is statistically significantly higher than the number of bypass grafting performed in off-pump CABG surgeries; the rates of cerebral accident (2.4% vs. 2.1%) and death (1.8% vs. 1%) have the same ratios and are not statistically significant in on-pump CABG compared with off-pump CABG \(^1,2\). In recent years, developments
in CPB have improved the surgical experience and patient management. Additionally, we have observed improvements in the cooperation of specialists, such as cardiac surgeons, clinical perfusionists, anesthetists, and other technicians. These improvements help surgical teams achieve better results. We believe that current on-pump CABG surgery is as safe as off-pump CABG for patients who meet the criteria mentioned in our study.

Study Limitations

All study participants are Caucasians and do not represent other ethnic groups. The present study does not comprise patients with renal insufficiency, dialysis patients, or redo-CABG cases.

CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: FA
Analysis/Interpretation: MÖ
Data Acquisition: FA
Writing: MÖ
Critical Revision: FA
Final Approval: All of authors

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