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Comparison of Surgical Results of Patients Undergoing On-pump and Off-pump Coronary Artery Bypass Grafting

On-pump ve Off-pump Koroner Arter Bypass Greft Ameliyatı Yapılan Hastaların Cerrahi Sonuçlarının Karşılaştırılması

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ABSTRACT

Aim: The aim of this study is to evaluate the clinical results of the patients undergoing off-pump and on-pump coronary artery bypass grafting (CABG) retrospectively in consideration of current literature.
Material and Methods: A total of 1672 patients undergoing CABG between October 2014 and August 2016 and having a postoperative sinus rhythm were enrolled in the study. Patients who underwent an additional procedure in addition to CABG and underwent open heart surgery except CABG were excluded from the study. Off-pump CABG was applied to 783 and on-pump CABG to 889 of 1672 patients.
Results: In comparison of operative data, duration of operation ($p<0.001$), number of bypasses to the coronary arteries ($p<0.001$), number of bypasses of the right coronary artery to the posterior descending artery ($p<0.001$), and diffuse coronary artery disease ($p<0.001$) were less in the off-pump CABG group and there was a statistically significant difference. In comparison of postoperative data, postoperative atrial fibrillation development ($p<0.001$), intubation time ($p<0.001$), intensive care unit stay ($p<0.001$), length of hospital stay ($p<0.001$), reexploration ($p=0.006$), vasopressor drug usage ($p<0.001$), positive inotropic drug usage ($p<0.001$), total drainage ($p<0.001$), blood and blood product used ($p<0.001$), and mortality rate ($p=0.001$) were less in the off-pump CABG group and statistically significant difference was found between groups.
Conclusion: In this study, we found that off-pump CABG has many advantages. In a selected group of patients having a coronary artery disease performing CABG in beating heart would avoid the patient from morbid and mortal negative effects of cardiopulmonary bypass.
Keywords: Off-pump; on-pump; coronary artery bypass; cardiopulmonary bypass.

ÖZ

Amaç: Bu çalışmanın amacı on-pump ve off-pump koroner arter baypass greftleme (KABG) yapılan hastaların klinik sonuçlarını retrospektif olarak güncel literatür ışığında değerlendirmektir.
Gereç ve Yöntemler: Çalışmaya Ekim 2014 ile Ağustos 2016 tarihleri arasında KABG uygulanan ve postoperatif sinüs ritmi olan toplam 1672 hasta dahil edildi. KABG yanında ek bir işlem uygulanmış ve KABG dışında açık kalp ameliyatı geçiren hastalar çalışma dışı bırakıldı. Toplam 1672 hastadan 783'üne off-pump KABG ve 889'una on-pump KABG uygulandı.
Bulgular: Operasyonel verilerin karşılaştırılmasında, operasyon süresi ($p<0.001$), koroner arter baypass sayısı ($p<0.001$), posterior desenden artere yapılan sağ koroner arter baypasslarının sayısı ($p<0.001$) ve yaygın koroner arter hastalığı ($p<0.001$), off-pump KABG grubunda daha azdı ve istatistiksel olarak anlamlı bir farklılık vardı. Ameliyat sonrası verilerin karşılaştırılmasında, ameliyat sonrası atriyal fibrilasyon gelişimi ($p<0.001$), entübasyon süresi ($p<0.001$), yoğun bakımda kalma süresi ($p<0.001$), hastanede kalma süresi uzunluğu ($p<0.001$), reeksplorasyon ($p=0.006$), vazopressör ilaç kullanımı ($p<0.001$), pozitif inotropik ilaç kullanımı ($p<0.001$), toplam drenaj ($p<0.001$), kullanılan kan ve kan ürünü ($p<0.001$) ve mortalite oranı ($p=0.001$) off-pump KABG grubunda daha azdı ve gruplar arasında istatistiksel olarak anlamlı bir farklılık olduğu bulundu.
Sonuç: Bu çalışmada off-pump KABG'nin birçok avantajı olduğu saptanmıştır. Koroner arter hastalığı olan seçilmiş bir hasta grubunda çalışan kalpte KABG uygulanması hastaları kardiyopulmoner baypassın morbidite ve mortaliteye neden olan negatif etkilerinden korur.
Anahtar kelimeler: Off-pump; on-pump; koroner arter baypass; kardiyopulmoner baypass.

INTRODUCTION

Performing coronary artery bypass grafting (CABG) surgery with cardiopulmonary bypass (CPB) had been the gold standard technique from the beginning of coronary artery surgery. However, due to the negative effects of CPB and the increasing age of patient population undergoing CABG leading to the increasing numbers of accompanying systemic diseases off-pump coronary artery bypass grafting (OPCAB) have been popular for the last two decades.

In the studies, hemostasis, neurological, renal and gastrointestinal functions deteriorated as a result of systemic inflammatory reaction initiated by the extracorporeal circuit, mechanical blood trauma, activation of various immunological cascades (complement, cytokines) as negative effects of CPB (1,2). In addition, it has been shown that aortic cannulation and cross clamp application in the on-pump coronary artery bypass grafting (ONCAB) technique may cause negative effects such as neurological and end organ damage as a result of microembolics (3).

In recent studies, it has been shown that CPB increases morbidity and mortality. These negative effects of CPB led surgeons to techniques that allow coronary bypass without CPB. As a result of different techniques, OPCAB recently gained popularity among surgeons. Devices developed for such surgeries and new anesthesia techniques have become applicable to the majority of patients undergoing CABG surgery. In this study, we aimed to compare the results of 1672 patients who were operated with OPCAB and ONCAB technique with the diagnosis of coronary artery disease retrospectively and to compare them with the literature review.

MATERIAL AND METHODS

A total of 1672 patients who underwent CABG operation and had preoperative sinus rhythm, were included in the study between January 2014 and August 2016. Patients with mechanical complications of myocardial infarction, such as a ventricular septum defect, papillary muscle rupture, and mitral valve regurgitation, and patients with cardiogenic shock persisting for a length of 24 hours were excluded from this study. Besides, combined procedures, impaired left ventricular function as assessed by angiography (ejection fraction <30%), patients requiring chronic dialysis, oliguria and anuria, a high-serum creatinine level (≥2.5 mg/dL), emergency surgery or reoperation, respiratory impairment, and coagulopathy not included in the study. Patients who underwent additional procedures with CABG operations and underwent open heart surgery other than CABG, were excluded from the study. Of these patients, 783 patients had OPCAB and 889 patients had ONCAB.

The study was approved by the local Ethics Committee of Düzce University Medical Faculty (date: 01.04.2019 and number: 2019/69).

In addition to the routine preoperative laboratory and radiological examination, each patient was applied respiratory function test. Bilateral carotid colored Doppler ultrasonography was applied to the patients older than 55 years old and having a unilateral or bilateral carotid sufl or a history of cerebrovascular accident. In case of determining a carotid artery disease, a selective carotid artery angiography was applied. With preoperative transthoracic echocardiography each patient was examined in terms of left ventricular ejection fraction, valvular anatomy, and cardiac spaces. OPCAB technique was preferred in the patients who had severe atheromatous plaques and severe calcification in the ascending aorta, who have high risk or contraindication of the use of CPB and aortic cross-clamp, have impaired renal function or chronic renal failure with a risk of embolization, rupture or dissection, who had cerebrovascular event, elderly, respiratory problems, systemic disease which increased the surgical risk or other comorbidities (4). ONCAB technique was preferred in the patients who had a poor vascular quality, had an intramyocardial target vessel, a target vessel disease was diffuse, and the target vessels were calcified and planned to undergo endarterectomy in the target vessels, hemodynamic instability, severely impaired left ventricular functions and previous myocardial infarction. Median sternotomy was performed for all CABG operations. The technique we use in OPCAB operations is described in detail by Yanagawa and Puskas (5). Two patients who underwent OPCAB surgery but were switched to emergency CPB due to intraoperative hemodynamic impairment were included in the CABG group under CPB. After cardiac arrest with antegrade and retrograde cold crystalloid cardioplegia and topical hypothermia, cardiac arrest was achieved with intermittent retrograde cold blood cardioplegia. Operations were completed under moderate (28 °C) hypothermia. In 1662 of 1672 patients undergoing CABG, left internal mammarian artery (LIMA) was used in left anterior descending artery position. In 10 patients, saphenous vein grafts were used because LIMA flow was not good. Saphenous vein grafts were used in the bypasses of the other coronary arteries. Hot blood cardioplegia was given before the cross clamp was removed. Preoperative and operative age, gender, body mass index, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, echocardiography findings, coronary angiography findings, coronary artery bypass count, coronary artery grafts used in bypass, duration of operation, aortic cross clamp and total CPB duration of ONCAB operations, total amount of cardioplegia used, postoperative vasopressor therapy, positive inotropic treatment, intra-aortic balloon pump need, intubation time, intensive care unit and hospital stay, total amount of red blood product, total amount of drainage, reexploration, development of postoperative atrial fibrillation (POAF) and hospital mortality were evaluated retrospectively.

Statistical Analysis

Statistical analyses were performed using the statistical program SPSS v.11.5 (SPSS Inc, Chicago, IL). Normality assumption of variables were determined using the Kolmogorov-Simirnov test. Student's t test was used for comparison of variables with normal distribution while Mann-Whitney U test was used for comparison of variables with non-normal distribution. Descriptive statistics for continuous variables were expressed as mean±standard deviation and median (minimum-maximum). Categorical data were presented in frequency and percentage, and compared using Pearson Chi-square or Fisher's Exact test, and p values of 0.05 or fewer were considered significant.

RESULTS

The mean age of cases was 58.3±8.7 years in the off-pump group and 59.5±9.7 in the on-pump group. Body mass index was 28.4±3.9 in the off-pump group and 28.5±4.3 in the on-pump group. While 53.8% of patients in the off-pump group had hypertension, this rate was 58.3% in the on-pump group. The standard EuroSCORE calculation was 3.6±2.7 in the off-pump group and 3.2±2.5 in the on-pump group. There was no significant difference in terms of preoperative features except age, left ventricular ejection fraction and EuroSCORE (Table 1).

In comparison of operative data, duration of operation (p<0.001), number of bypasses to the coronary arteries (p<0.001), number of bypasses of the right coronary artery to the posterior descending artery (p<0.001), and diffuse coronary artery disease (p<0.001) were less in the OPCAB group and there was a statistically significant difference between groups (Table 2).

In comparison of postoperative data, total drainage amount was 486.4±56.3 mL in the off-pump group while it was 696.4±34.7 mL in the on-pump group. Intra-aortic balloon pump usage rate was 1.1% in the off-pump group and 3.6% in the on-pump group. Reexploration rates were 1.1% in the off-pump group and 3.1% in the on-pump group. Mortality rates were 0.1% in the off-pump group and 1.7% in the on-pump group. In the comparison of postoperative data, POAF development (p<0.001), intubation time (p<0.001), intensive care unit stay (p<0.001), length of hospital stay (p<0.001), re-exploration (p=0.006), vasopressor drug usage (p<0.001), positive inotropic drug usage (p<0.001), intra-aortic balloon pump need (p=0.001), total drainage (p<0.001), blood and blood product used (p<0.001), and mortality rate (p=0.001) were less in OPCAB group, and statistically significant difference was found between groups (Table 3).

Table 1. Comparison of preoperative characteristics of patients in OPCAB and ONCAB groups

	OPCAB (n=783)	ONCAB (n=889)	p
Age (years)	58.3±8.7	59.5±9.7	0.008
Gender			
Male	345 (44.1%)	391 (44.0%)	0.974
Female	438 (55.9%)	498 (56.0%)	
Body mass index (kg/m^2)	28.4±3.9	28.5±4.3	0.620
Diabetes mellitus	381 (48.7%)	451 (50.7%)	0.398
Hypertension	421 (53.8%)	518 (58.3%)	0.064
Chronic obstructive pulmonary disease	193 (24.6%)	205 (23.1%)	0.446
Previous myocardial infarction	410 (52.4%)	473 (53.2%)	0.730
Left ventricular ejection fraction (%)	47.5±8.3	49.1±9.4	<0.001
Standart EuroSCORE	3.6±2.7 3 (0-7)	3.2±2.5 3 (0-8)	<0.001

OPCAB: Off-pump Coronary Artery Bypass Grafting, ONCAB: On-pump Coronary Artery Bypass Grafting, EuroSCORE: European System for Cardiac Operative Risk Evaluation, values were expressed as mean±standard deviation and median (minimum-maximum) for continuous variables, and n (%) used for categorical data.

Table 2. Comparison of operative properties of patients undergoing OPCAB and ONCAB

	OPCAB (n=783)	ONCAB (n=889)	p
Cross-clamp time (min)	NA	65.2±21.4 62 (31-82)	
Cardiopulmonary bypass time (min)	NA	97.1±26.9 86 (75-128)	
Operation duration (min)	137±35 132 (110-161)	231±49 226 (180-320)	<0.001
Total amount of cardioplegia used (ml)	NA	1518±437 1400 (1000-1600)	
Number of anastomoses performed			
2 and less	574 (73.3%)	346 (38.9%)	<0.001
3 and more	209 (26.7%)	543 (61.1%)	
Diffuse coronary artery disease	205 (26.2%)	498 (56.0%)	<0.001
Left internal mammary artery usage	782 (99.9%)	880 (99.0%)	0.024
Right coronary artery or right coronary posterior descending artery grafts	97 (12.4%)	786 (88.4%)	<0.001

OPCAB: Off-pump Coronary Artery Bypass Grafting, ONCAB: On-pump Coronary Artery Bypass Grafting, NA: not applicable, values were expressed as mean±standard deviation and median (minimum-maximum) for continuous variables, and n (%) used for categorical data.

Table 3. Comparison of postoperative characteristics of patients with OPCAB and ONCAB

	OPCAB (n=783)	ONCAB (n=889)	p
Vasopressor therapy (adrenalin, noradrenalin)	32 (4.1%)	147 (16.5%)	<0.001
Positive inotropic therapy (dopamine)	97 (12.4%)	246 (27.7%)	<0.001
Intra-aortic balloon pump	9 (1.1%)	32 (3.6%)	0.001
Total drainage (mL)	486.4±56.3 465 (150-850)	696.4±34.7 682 (175-925)	<0.001
Total amount of red blood product used (mL)	463.5±78.4 442 (225-625)	743.5±35.6 734 (250-850)	<0.001
Intubation time (hours)	6.1±1.6 4 (2-18)	11.7±3.4 9 (4-26)	<0.001
Intensive care unit stay (days)	2.2±1.3 1 (1-8)	3.5±1.5 2 (1-14)	<0.001
Hospital stay time (days)	5.1±2.6 4 (3-8)	7.4±3.8 5 (4-14)	<0.001
POAF development	79 (10.1%)	251 (28.2%)	<0.001
POAF development times (hours)	42.4±12.1 36 (24-46)	47.1±13.2 38 (22-42)	<0.001
Re-exploration	9 (1.1%)	28 (3.1%)	0.006
Mortality	1 (0.1%)	15 (1.7%)	0.001

OPCAB: Off-pump Coronary Artery Bypass Grafting, ONCAB: On-pump Coronary Artery Bypass Grafting, POAF: Postoperative atrial fibrillation, values were expressed as mean±standard deviation and median (minimum-maximum) for continuous variables, and n (%) used for categorical data.

DISCUSSION

In previous studies, OPCAB technique has many advantages over ONCAB technique. OPCAB technique reduces systemic inflammatory response caused by CPB, operative trauma, postoperative complication rate, length of rehabilitation, duration of intensive care unit stay, hospital stay, morbidity and hospital cost, but also decreases stroke, neurocognitive dysfunction, organ dysfunction and atrial fibrillation (AF), these benefits confirmed by clinical trials (6,7). In addition, OPCAB technique has shown advantages such as less blood loss, less blood transfusion requirement, need for less inotropic support, less morbidity, less mortality and less cost (8-12). The OPCAB technique will continue to be beneficial for the patient with the concomitant pathology of atherosclerotic plaques or the situation of a porcelain aorta. Other patient cohorts are those with further contraindications for the use of extracorporeal circulation as those with liver cirrhosis or evolving failure. There is no doubt, that the OPCAB technique will play its special role in the future. Long- term results by those groups who are using the latter in the majority of their patients, should clarify the current question, whether the OPCAB technology is detrimental to our patients or an enrichment of the surgical armamentarium.

The authors concluded that off-pump techniques may reduce early mortality in selected patients undergoing re-operative CABG; however, this does not persist into mid-term follow-up. OPCAB may also lead to intraoperative conversion and, although this did not affect outcomes in this study, these results are constrained by the limited data available. Furthermore, OPCAB may increase target vessel revascularization and, consequently, incomplete revascularization which, whilst not reflected in the short-term outcomes, requires longer-term follow-up in order to be fully assessed (13).

Patients with higher eGFR stages had statistically more reduced long-term survival, and this pattern was similar in the three treatment groups, also including the OPCAB group, who had the lowest survival in patients with eGFR stage 4. The authors concluded that patients with low GFR (Stages 3-4) undergoing ONCAB were at increased risk of early mortality. In contrast, there were no significant differences in operative mortality among eGFR groups in OPCAB patients. This 'off-pump advantage' on early outcomes was not observed at the long-term follow-up (14).

In addition to these two major trials several detailed questions in this matter were answered by various authors. Keeling and co-workers (15) analyzed the effect of off-pump versus on-pump coronary revascularization in patients with low ejection fraction. Between January 1, 2008 and June 30, 2011 data of 25667 patients with an EF of less than 0.3 according to the Society of Thoracic Surgeons National Data Base, who underwent primary non-emergent CABG were analyzed. 20509 had an ONCAB procedure and 5158 an OPCAB procedure. Propensity scores were estimated using 32 covariates and multivariate logistic regression was used to compare risk-adjusted outcomes between groups. The results showed that patients undergoing planned OPCAB were older, more frequently female and had a lower body mass index than those who underwent ONCAB. Unplanned conversion to CPB occurred in 270 (5.2% of the 5158 patients). OPCAB was associated with a significant lower adjusted risk of death (Odds Ratio (OR)=0.82, stroke (OR=0.67) and major adverse cardiac events (OR=0.75) and prolonged intubation (OR=0.78), postoperative transfusion rates were significantly lower in the OPCAB group (54.8% vs 51.6%). There were no adverse outcomes that occurred more commonly in OPCAB patients. The advantages associated with OPCAB were found in the

entire Society of Thoracic Surgeons National Database and among high-volume and low-volume OPCAB centres (15).

In recent studies, it has been shown that the complications related to CPB are higher in high-risk patients and consequently, mortality, morbidity and cost rates increase in these patient groups (16-19).

The CORONARY trial (20) is a large trial (n=4502 patients) designed to compare the two strategies. The final 5-year results showed similar outcomes with OPCAB and ONCAB. The difference between OPCAB and ONCAB in terms of number of grafts (3.0 vs. 3.2) and incidence of incomplete revascularization (11.8% vs. 10.0%) was only marginal. In the CORONARY, each procedure was performed by a surgeon who had expertise in the specific type of surgery (completion of more than 100 cases of the specific technique either off-pump or on-pump). A limitation of the CORONARY is that only patients at higher risk were enrolled and this aspect might limit the generalizability of the study findings.

In contrast, in the ROOBY trial (21), which enrolled 2203 patients, OPCAB has been recently reported to be associated with increased 5-year mortality (15.2% in the OPCAB group versus 11.9% in the ONCAB group, Relative Risk (RR)=1.28; 95.0% CI=1.03 to 1.58), and MACCE rates (31.0% in the OPCAB group versus 27.1% in the ONCAB group (RR=1.14; 95.0% CI=1.00 to 1.30). This trial has also demonstrated that the patency rate of the off-pump arm was lower than that of the on-pump arm on 12-month angiography. Such findings can be partially explained on the basis that the 53 participating surgeons enrolled on average only eight patients per year during the study period and had unacceptably high conversion rates to on-pump surgery (12.0%) and incomplete revascularization (18.0%). Moreover, in 60.0% of the cases, a resident was the primary surgeon again raising concerns about the relative inexperience translating into poor graft patency.

The survival advantage consistently associated with ONCAB over OPCAB has been attributed to the higher rates of incomplete revascularization, and worse graft patency with OPCAB compared with ONCAB observed in randomized trials and retrospective studies. Patients undergoing OPCAB have repeatedly been shown to receive fewer bypass grafts either than planned or than the number of diseased territories, in comparison with patients undergoing ONCAB. In a meta-analysis of 76 randomized trials reporting the number of grafts performed, OPCAB was associated with fewer grafts compared with ONCAB. The incidence of graft occlusion within 30 days was also higher in patients who underwent OPCAB compared with ONCAB in this meta-analysis (7.3% vs. 4.4%), and the rate of repeat revascularization within 1 year was higher after OPCAB (2.2% vs. 1.5%) (21). Our data confirm the higher rates of incomplete revascularization with OPCAB. These differences have been attributed to differential expertise bias in randomized and observational studies, due to the greater technical challenges of anastomosing a coronary artery on a beating heart, compared with the arrested heart in ONCAB. To address this, our study inclusion criteria specified surgical proficiency (experience of at least 100 on-pump or off-pump cases) for inclusion in each treatment arm. In this pool of relatively expert surgeons, OPCAB was still associated with fewer anastomoses and greater likelihood of incomplete revascularization, which we found to be an independent risk factor for late mortality in all patients.

In our study with literature compatible, better postoperative results were obtained in the OPCAB group. However, in this study, in the patients group with ONCAB; when the operative data were analyzed, the number of the bypassed veins, the number of bypasses to the right coronary posterior descending artery and the high number of patients with diffuse coronary artery disease suggest that it may be effective in the postoperative results. Ascione et al. (22) have shown that; AF, which is the most common arrhythmia type after CABG operations, develops significantly less in OPCAB patients. In our study, AF was less observed in OPCAB patients (10.1% vs 28.2%). In this study, the need for vasopressor therapy, the need for positive inotropic therapy, the need for intra-aortic balloon pump, the amount of chest tube drainage, the total amount of red blood product used, the duration of intubation, the duration of intensive care unit stay, hospital stay, reexploration, mortality and POAF development in patients with OPCAB was found statistically significantly lower than the patients who underwent ONCAB (23).

Finally, it has been argued that advances in technology and clinical practice, including optimal medical therapy, intraoperative epiaortic assessment, and CPB, have addressed more limitations of ONCAB surgery than OPCAB. We believe that these findings have clear implications for the optimal choice of procedure in the majority of patients undergoing surgical revascularization who do not have contraindications to CPB.

CONCLUSION

As a result, we think that OPCAB patient group has better postoperative results in terms of morbidity, mortality and cost, so it is safer to choose OPCAB technique for selected appropriate patient groups planned for CABG surgery as much as possible.

To conclude we could say that short term morbidity and mortality is less in very high-risk patients with off-pump, possibly because the procedure is shorter. It would be right to say that shorter the procedure, the better, especially for older, sicker patients. The length of the procedure is significantly shorter with off-pump than on-pump. However we suggest that the technique used should depend on the ease of the surgeon doing the operation as both the methods seem almost equally efficient according to the review otherwise. Certainly more data over large randomized trials is required before off-pump superiority over on-pump can be firmly established.

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