



Comparison of Treatment Outcomes in Off-pump Coronary Artery Bypass Graft and Medical Therapy in Patients with Triple-vessel Coronary Artery Disease and Severe Ventricular Dysfunction

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ABSTRACT

**Introduction:** Heart failure is a major hazard for public health. Despite recent advance in medical therapy, there is not enough information on the outcome of off-pump coronary artery bypass (OPCAB) and medical therapy on the patients with severe ventricular dysfunction and triple-vessel (CAD). This study aimed to compare treatment outcomes and mortality rate in patients undergoing off-pump coronary artery bypass (OPCAB) surgery and medical therapy who presented with severe ventricular dysfunction and triple-vessel coronary artery disease (CAD).

**Materials and Methods:** This retrospective cohort study was conducted on patients with severe ventricular dysfunction and triple-vessel CAD during 2010-2011 in the Imam Ali Hospital of Kermanshah University of Medical Science. Patients were divided into two groups of medical therapy (group one) and OPCAB (group two). Follow-up data were collected after 30 months. Survival estimation was performed using Kaplan-Meier survival analysis and Cox regression model.

**Results:** Of the 276 enrolled patients, 139(50.4%) underwent group one and 137(49.6%) group two. Study groups were homogenous in baseline characteristics, with the exception of hyperlipidemia (P=0.005). A significant difference was observed in cardiac mortality rates between the study groups (hazard ratio: 0.260; 95% confidence interval: 0.105-0.644; P=0.004). However, no significant difference was observed between the groups regarding the frequency of admission due to decompensate heart failure (P=0.17). In addition, the rate of admission due to acute coronary syndrome (ACS) in the first group was higher than the second group, significantly (P=0.001). Level of ejection fraction (EF) had a significant increase after coronary artery bypass graft (CABG) (28.50) compared to the preoperative stage (27.59) (P=0.042). However, no significant increase in the level of EF was observed in the first group before and after medical therapy (27.28 and 27.20, respectively) (P=0.83).

**Conclusion:** According to the results of this study, the mortality rate associated with OPCAB was lower compared to medical therapy, ACS and EF enhancement in patients with triple-vessel CAD and severe ventricular dysfunction.

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Introduction

Heart failure is a major hazard for public health, and despite recent advancement in medical therapy, it is still associated with high rates of morbidity and mortality (1, 2). Coronary artery disease (CAD) is known as a major risk factor for

heart failure (3), as well as the main cause of mortality in developing and industrial countries (4, 5). Treatment of choice for patients with CAD is medical therapy or revascularization (6). The guidelines proposed by the American Heart Association

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have implemented the advanced methods of treatment in medical and surgical therapies for patients with CAD and heart failure (7).

Several randomized clinical trials have compared the effects of coronary artery bypass graft (CABG) and medical therapy on patient with left ventricular (LV) dysfunction and CAD.

According to the literature, survival of CAD patients could enhance significantly after coronary revascularization (8-14). However, patients with LV dysfunction are at a higher risk of surgery with lower survival rates compared to those with normal ventricular function (12). In this regard, one randomized trial assessed the myocardial viability of patients with CAD and LV dysfunction who received medical therapy with or without CABG. According to the results, there was no significant difference between myocardial viability and treatment methods in terms of mortality rate (15).

Previous clinical studies have indicated that in comparison with medical therapy, CABG could produce superior outcomes in patients with triple-vessel CAD, left main artery involvement, and other complications caused by CAD (8-11). Furthermore, these studies compared the effects of conventional CABG and medical therapy.

To date, no studies have evaluated the effects of OPCAB and medical therapy on the mortality rate of patients with severe ventricular dysfunction and triple-vessel CAD. This is considered as a limitation in the literature since OPCAB is a less invasive method that commonly decreases the incidence of intraoperative complications.

This study aimed to compare treatment outcomes including Survival, hospital admission, ejection fraction (EF) in patients with severe ventricular dysfunction and triple-vessel CAD after OPCAB and medical therapy.

## Materials and Methods

### Study design

This retrospective cohort study was conducted on patients with triple-vessel CAD and severe ventricular dysfunction during 2010-2011. We identified the patients with ejection fraction (EF) of  $\leq 35\%$  who were amenable to CABG from all the patients undergoing cardiac catheterization in our medical center. Exclusion criteria were the presence of heart valve disease, acute myocardial infarction, percutaneous coronary intervention, and recommendation for medical therapy.

In total, we reviewed 296 medical records, 20 of which were excluded due to the inaccessibility of the contact information, and 276 cases were included in the final sample size. Patients ( $n=276$ ) had the same indications before treatment and were recommended for CABG by their surgeon or cardiologist. Based on the preference of the patients, they were divided into

two groups. In group one, patients ( $n=137$ ) received medical therapy due to unwillingness for surgery, and patients in the second group ( $n=139$ ) underwent OPCAB.

### Data collection and management

Relevant baseline variables (Table 1) were collected retrospectively from patient files, coronary angiography, and echocardiography and recorded in standard forms, which were preserved in the databank of our medical center. Moreover, results of CABG and medical therapy procedures were recorded for all the patients.

### Coronary revascularization and medical therapy

In this study, medical therapy was performed using blockers, angiotensin-converting-enzyme inhibitors, aspirin, and lipid-lowering agents and all of them treated with the same protocol. OPCAB was carried out by a single surgeon in accordance with the international surgery techniques using Medtronic Octopus stabilizer device for coronary stabilization and deep pericardial traction sutures for cardiac displacement and presentation.

Conventional immobilization techniques, such as deep pericardial suture, esmolol and Octopus T-300, were used to provide better access to lateral and posterior target vessels. Moreover, patients were administered with heparin 100 mg/kg in order to maintain the activated clotting time (ACT) at 200-400 seconds. Before anastomosis, the target coronary artery was temporarily occluded proximally and distally using fine bulldog clamps or looped 5-0 Vylene sutures. Also, phenylephedrin was administered intravenously to maintain the blood pressure at 70-90 mmHg. If possible, the left internal mammary artery and saphenous vein conduits were used as well.

### Follow-up procedures

Ascertainment of clinical events was obtained by the research associates in patient follow-ups at one and six month, and then annually during 30 months (mean duration of follow-up:  $931 \pm 13$  days). To equalize the study groups, the dates of surgery and catheterization (plus the mean time of CABG [ $43.3 \pm 34.4$  days]) were considered as the beginning of the follow-up for the second and first group, respectively. Predominant follow-up tools were questionnaires and contact information of the patients, and all-cause mortality was regarded as the clinical endpoint of the study.

### Data analysis

Data analysis was performed in SPSS V.17 for Windows (SPSS Inc., Chicago, IL, USA). Frequencies of baseline variables were determined using the Chi-square test, and survival curves of both study

Table 1. Baseline characteristics

Variables	Medical Therapy (n=137)	*CABG (n=139)	P-value
Age (years)	62±9.003	61±9.063	P=0.329
Smoking Habits	35%	38.1%	P=0.619
Hypertension	48.2%	47.1%	P=0.904
Diabetes Mellitus	36.5%	37.4%	P=0.901
Hyperlipidemia	21.6%	37.2%	P=0.005
<b>**NYHA Heart Failure Class</b>			
Class One	29.9%	36.7%	P=0.387
Class Two	70.1%	63.3%	P=0.252
Angina Pectoris	94.2%	95%	P=0.794

\*CABG: Coronary Artery Bypass Grafting, \*\*NYHA: New York Heart Association

groups were created based on the Kaplan-Meier method. In addition, we used a log-rank test to determine the differences between the study groups. Unadjusted relative risk of mortality was calculated using the univariate Cox proportional hazard model. Adjusted relative risk of mortality was calculated using the multivariate Cox proportional hazard model for both groups in order to control the factors significantly associated with the selected treatments (e.g., age, smoking habits, hypertension, hyperlipidemia, diabetes mellitus, and angina).

Proportional hazard assumption was examined by determining the correlation between OPCAB and other covariates in Cox regression analysis model. Moreover, hazard ratios (HRs) and confidence intervals (CIs) of OPCAB were calculated. In this study, P value of less than 0.05 was considered significant, and all the reported P values were two-sided.

Results

Baseline characteristics

Out of 276 patients enrolled in this study, 139 (50.4%) and 137 (49.6%) were placed in groups one and two, respectively. Baseline clinical characteristics of the sample population are presented in Table 1. In general, the study groups were homogenous in terms of baseline characteristics. Mean age of the patients in groups one and two was 60.8±0.77 and 62.06±0.77 years, respectively. With regard to the gender, 78.4% and 77.4% of the patients in groups one and two were male, respectively. History of peripheral arterial disease was reported in one patient in the first group and none of the patients in the second group. Moreover, renal failure was reported in none of the studied patients. Among the similar baseline clinical characteristics were smoking

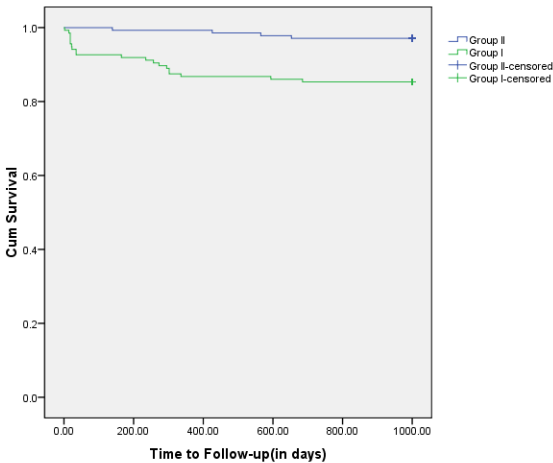


Figure 1. Kaplan-Meier Estimate of Time of Mortality in Groups One and Two

habits, hypertension, diabetes mellitus, and angina pectoris. In addition, heart failure class was similarly distributed in the two groups although the prevalence rate of hyperlipidemia was higher in the second group (37.2%) compared to the first group (21.6%) (P=0.005).

Survival analysis

In total, 27(9.8%) patients succumbed to cardiac deaths, 21(77.8%) and 6(22.2%) of whom were in the first and second groups, respectively. A significant difference was observed in the rate of cardiac mortality between the two study groups (HR: 0.260; 95% CI: 0.105-0.644; P=0.004). Furthermore, the results of Kaplan-Meier survival analysis were indicative of a significant difference between the two groups in this regard (P=0.002) (Figure 1). Unadjusted Cox regression analysis for the overall study cohort revealed a significant correlation between the incidence of diabetes mellitus and cardiac mortality (P=0.042) (Table 2). However, the results of adjusted Cox regression analysis were indicative of no significant variables in the model (Table 2).

In this study, no significant difference was observed in the frequency of admissions due to diastolic heart failure between group one (once: 7.8%, twice: 18.1%, three times: 6%, four times: 0.9%, and no admission: 67.2%) and group two (once: 9%, twice: 9%, three times: 4.5%, and no admission: 77%) (P=0.17). Additionally, a statistically significant difference was reported in the frequency of admissions due to ACS between group two (once: 5.3%, twice: 1.5%, and no

Table 2. Results of adjusted and unadjusted Cox regression analysis for different variables

Variables	Unadjusted *OR	95% **CI	P-value	Adjusted OR	95% CI	P-value
Smoking Habits	1.001	0.44-2.23	0.99	1.162	0.505-2.67	0.72
Hypertension	1.076	0.505-2.28	0.85	0.892	0.402-1.97	0.77
Hyperlipidemia	1.803	0.836-3.88	0.13	1.68	0.750-3.79	0.20
Diabetes Mellitus	2.204	1.03-4.71	0.04	2.19	0.98-4.87	0.05

\*OR: Odds Ratio, \*\*CI: Confidence Interval.

admission: 93.2%) compared to group one (once: 16.4%, twice: 7.8%, and no admission: 75.9%) ( $P=0.001$ ).

### Effects of clinical variables

According to our findings, EF level significantly increased from 27.59 preoperatively to 28.50 after CABG ( $P=0.042$ ), while no significant increase was reported in this regard in group one before (27.28) and after (27.20) medical therapy ( $P=0.83$ ).

### Discussion

In the present study, we evaluated the 30-month survival rate associated with OPCAB and medical therapy in patients with severe ventricular dysfunction and triple-vessel CAD. According to our findings, despite the presence of severe LV dysfunction and triple-vessel CAD, OPCAB resulted in a higher survival rate compared to medical therapy after 30 months of follow-up (Figure 1).

Results of unadjusted Cox regression regarding the treatment methods were indicative of a significant difference between the study groups in terms of the combined endpoints of cardiovascular death (HR: 0.260; 95% CI: 0.105-0.644;  $P=0.004$ ). According to the results of Kaplan-Meier analysis and log-rank test, mean of survival in groups one and two in the present study was estimated at 878 and 983 days, respectively ( $P=0.002$ ). Therefore, it could be concluded that patients who underwent surgical operation had a lower mortality of cardiovascular causes compared to the patients receiving medical therapy only. In other words, medical therapy could not be a proper treatment for patients with severe ventricular dysfunction and triple-vessel CAD.

In the literature, several studies have evaluated the survival rate of patients with CAD, and the results have confirmed that CABG could prolong the life of these patients more significantly compared to medical therapy (16-18).

In one study, O'Connor et al. stated that CABG is associated with higher survival compared to medical therapy in patients with ischemic cardiomyopathy (19). In another study by Velazquez et al., patients with ischemic heart disease were enrolled for propensity score analysis, including 624 patients receiving medical therapy and 139 patients undergoing CABG. After 10 years of follow-up, mortality rate in the CABG group was lower and the rate of symptom improvement was higher compared to the medical therapy group (20).

In their research, Elefteriades et al. evaluated CABG outcomes in patients with severe LV dysfunction. Moreover, they analyzed the data of 83 patients with LVEF of  $\leq 30\%$  who underwent CABG,

and the results indicated that CABG could be a safe approach to improve the quality of life in these patients (21). Findings of the current research are consistent with the aforementioned studies. It is also noteworthy that in our medical center, the surgical operation on the patients was performed using the off-pump technique, which is distinctive in comparison with other medical centers.

In the present study, unadjusted Cox regression models revealed a significant correlation between the incidence of diabetes mellitus and cardiac mortality ( $P=0.04$ ). In this regard, previous studies have reported diabetes mellitus to be a major risk factor for CAD patients and CABG candidates in Iran (22, 23), which is in line with the results of the current study.

According to the results of the present study, there was a statistically significant increase in the mean EF value after OPCAB ( $P=0.042$ ). However, no significant difference was observed in group one before and after medical therapy ( $P=0.83$ ).

EF is considered as a remarkable predictor of short-term and long-term survival rate in patients after CABG (24). Although low EF could be an important risk factor in patients undergoing CABG, the results of the current study indicated that CABG not only reduced mortality in patients with EF of  $<30\%$ , but it also improved the level of EF after OPCAB. Therefore, it could be concluded that this modality plays a pivotal role in the reduction of heart failure symptoms, as well as the improvement of LV function and survival after OPCAB. This finding is consistent with the results obtained by Nardi et al. (25) conducted on 302 patients with EF of 0.35. After a 10-year follow-up, patients with low EF presented with excellent long-term results after CABG (25).

The results of the current study carried out in our medical center were correspondent with other medical centers in the terms of mortality rate and symptom improvement. One of the limitations of the present study was that we were not able to evaluate preoperative myocardial viability in the patients, and further investigation is required in this regard.

### Conclusion

According to the results of this study, OPCAB was superior to medical therapy in term of mortality rate, ACS, and EF enhancement in patients with triple-vessel CAD and severe ventricular dysfunction. It is recommended that future studies compare the long-term outcomes in these two procedures.

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# Conflicts of interest

The authors declare no conflicts of interest.

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