Original Article

Efficacy of cardiac resynchronization with defibrillator insertion in patients undergone coronary artery bypass graft: A cohort study of cardiac function

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ABSTRACT

Introduction: Cardiac resynchronization therapy (CRT) is a proven therapeutic method in selected patients with heart failure and systolic dysfunction which increases left ventricular function and patient survival. We designed a study that included patients undergoing coronary artery bypass graft (CABG), with and without CRT-defibrillator (CRT-D) inserting and then measured its effects on these two groups. **Patients and Methods:** Between 2010 and 2013, we conducted a prospective cohort study on 100 coronary artery disease patients where candidate for CABG. Then based on the receiving CRT-D, the patients were categorized in two groups; Group 1 (n = 48, with CRT-D insertion before CABG) and Group 2 (n = 52 without receiving CRT-D). Thereafter both of these groups were followed-up at 1–3 months after CABG for mortality, hospitalization, atrial fibrillation (AF), echocardiographic assessment, and New York Heart Association (NYHA) class level. **Results:** The mean age of participants in Group 1 (48 male) and in Group 2 (52 male) was 58 ± 13 and 57 ± 12 respectively. Difference between Groups 1 and 2 in cases of mean left ventricular ejection fraction (LVEF) changes and NYHA class level was significant (P > 0.05). Hospitalization (P = 0.008), mortality rate (P = 0.007), and AF were significantly different between these two groups. **Conclusions:** The results showed that the increase in LVEF and patient's improvement according to NYHA-class was significant in the first group, and readmission, mortality rate and AF was increased significantly in the second group.

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INTRODUCTION

Coronary artery disease (CAD) increases the risk of a myocardial infarction and angina pectoris and reduces left ventricular output that causes sudden death and congestive heart failure (CHF).[1] CAD is responsible for two-third of heart failures.[2,3] The main cause of CHF exacerbation is uncontrolled ischemic disease.[4,5] One in five deaths in U.S is due to CAD. According to American Heart Association statistics in 2006, the prevalence of cardiovascular disease in US was 81.1 million that 17.6 million of them had CAD and among patients who had CAD the incidence of CHF was 5.8 million.[6] Drug therapy for CAD has many side effects. Also, interventional or surgical treatments in patients with multiple stenosis lesion or multiple vessel diseases do not have long-term relief for the patient and most of them remain symptomatic and may require surgery to be repeated.[7] Several clinical trials have been proven beneficial effects of coronary artery bypass graft (CABG) for CAD treatment.[8,9]

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Although myocardial dysfunction improves after CABG, left ventricular contractile dysfunction remains after surgery.[10] Left ventricular dysfunction is an independent factor for predicting postoperative mortality in patients undergo CABG[11] that can reduce cardiac output or increased mortality after surgery.[12] Lots of patients with postoperative left ventricular dysfunction require mechanical or inotropic support.[12] Cardiac resynchronization therapy (CRT) is a proven therapeutic method in selected patients with heart failure and systolic dysfunction,[13,14] which increases left ventricular function and patient survival. Although yet it's difficult to identify patients that will cause a favorable response to this treatment.[15,16] CRT has been successful in the treatment of advanced heart failure but in treating atrial fibrillation (AF) that adds up to 25% of cases after device insertion has not been better than drug therapy. However, the role of CRT-defibrillator (CRT-D) in this issue and to prevent the fibrillation that it is an increasing factor for death in the heart failure patients is highlighted.[17] Also the causes of sudden death in patients with chronic heart failure respectively are: Electromechanical dissociation (30%), primary Brady arrhythmia (30%), ventricular tachycardia, and/or fibrillation (40%) indicating the necessity of the CRT with the defibrillator in preventing sudden death in these patients.[18] At least part of the reduction in mortality in CRT is due to the hemodynamic correction.[19,20] Traditionally, the treatment of ischemia in patients with ischemic cardiomyopathy is surgery, and they are re-evaluating the need for CRT-D after 3 months (60–90 days).[21,22] We designed a prospective cohort study that included patients undergoing CABG, with and without CRT-D inserting and then measured its effects on these two groups.

PATIENTS AND METHODS

Study design and population

Between 2010 and 2013, we conducted a prospective cohort study on 100 CAD patients who referred to our center and were candidate for CABG. Our sampling method was the census. New York Heart Association (NYHA) class level between II/III/IV, left ventricular ejection fraction (LVEF) ≤35%, QRS ≥120 ms (based on the electrocardiography) were the indications for receiving CRT-D and the patients who had a narrow QRS or NYHA class level I, were excluded from our study. Then based on the receiving CRT-D, the patients were categorized in two groups; Group 1 were 48 patients who received a CRT-D 24–48 h before CABG and Group 2 were 52 cases that underwent CABG without receiving a CRT-D. Thereafter both of these groups were followed-up at 1–3 months after CABG for mortality, hospitalization, AF, echocardiographic assessment, and NYHA class level. During the follow-up, Group 2 patients were also evaluated for requiring a CRT-D (based on the mentioned indications for receiving CRT-D). At one, two, and three times of follow-up. All patients in both groups were asked to refer to the clinic and filled questionnaires providing information concerning using of angiotensin converting enzyme (ACE) inhibitor, using of beta blocker.

Ethics

This study was approved by the Ethics Committee of our university. Also, all of the participants signed an informed written consent before entering to this study.

Statistical analysis

Statistical analysis was done with SPSS, version 19 (IBM Inc. Chicago Illinois, USA, 2010). Mean ± standard deviation and frequency was used for expressing quantitative and qualitative variables respectively. For comparisons of quantitative variables, we used Student's *t*-test, and qualitative variables were compared with Chi-square (or Fisher's exact test). $P < 0.05$ was considered significant.

RESULTS

Before the surgery

Finally according to the inclusion and exclusion criteria 100 patients were included in this project. The mean age of participants in Group 1 ($n = 48$) and in Group 2 ($n = 52$) was 58 ± 13 and 57 ± 12 respectively. There was not a statistical difference between these two groups in case of age ($P > 0.05$) and sex ($P > 0.05$) and both groups were matched in gender and age. [Table 1] represents some other baseline variables and characteristics of both groups. Based on this table both of the study groups are also matched in case of mean LVEF, and using of beta blocker and ACE inhibitor.

Table 1: Baseline characteristics of the group I and II

Baseline characteristics	Group 1	Group 2	Statistical difference between two group (*P*)
Mean LVEF[a]	22±6	26±8	0.3
Beta blocker (%)	80	79	0.4
ACE[b] inhibitor (%)	88	91	0.3

[a]Left ventricular ejection fraction, [b]Angiotensin converting enzyme

Table 2: Comparison of studied variables during the follow-up (in the row about LVEF changes, each column *n* was compared with the first ejection fraction)

Variables (%)	Group I				Group 2			
	Before the surgery	First month	Second month	Third month	Before the surgery	First month	Second month	Third month
LVEF[a] changes	26±6	5↑	10↑	5↑	24±6	0↑	5↑	0↑
NYHA[b] class level	III	II	I	I	III	III	II	II
Hospitalization	0	0	0	0	12	13	7	8
Mortality rate	0	0	0	0	-	0	0	8.6
Atrial fibrillation	0	0	0	0	0	0	0	23

[a]Left ventricular ejection fraction, [b]New York heart association

After the surgery

During the follow-up, no one of the Group 2 patients needed a CRT-D. Comparisons of two groups about LVEF changes, NYHA class level, hospitalization, the morality rate, and AF has been shown in Table 2. Mortality rate and AF was zero in Group 1 during the whole follow-up time. NYHA class level ($P = 0.005$) significantly decreased and ventricular ejection fraction changes ($P = 0.001$) significantly increased in Group 1. In Group 2, increase in LVEF changes was not statistically meaningful ($P = 0.5$) while NYHA class level significantly decreased ($P = 0.01$). Difference between Groups 1 and 2 in cases of LVEF changes and NYHA class level was significant ($P > 0.05$). Hospitalization ($P = 0.008$), mortality rate ($P = 0.007$), and AF ($P = 0.003$) was significantly different between these two groups.

DISCUSSION

The results showed that the increase in LVEF and patient's improvement according to NYHA-class was significant in the first group and readmission, mortality rate, and AF was increased significantly in the second group. All patients in the second group after 3 months were still remaining on the CRT placement list while none of the patients in the first group required CRT-D and readmission. No mortality and AF were reported in the first group. Implantable cardioverter defibrillator) reduces the risk of mortality due to arrhythmia that probably in the first phase after surgery is more likely in patient with low LVEF, two ventricular pacemaker reduces the risk of arrhythmias due to its positive effects on hemodynamics and modification of left ventricular function. Hemodynamic modification after CRT decreases the effects of stretching on myocardia[23] and balances the autonomic nervous system which can reduce postoperative arrhythmia and AF. Several studies have shown that biventricular pacemaker also reduces frequency of ventricular ectopia[24-27] this, in turn decreases the onset of sustained ventricular arrhythmia, so justifies the positive hemodynamic effects, antiarrhythmia, AF, and no need for readmission in patients with CRT-D in a quarterly survey.[28,29] Cleland *et al*. in a study that conducted on 813 patients with class 3–4 heart failure and average follow-up 29.4 months showed that in addition to reducing the mortality and hospital readmission, LVEF and NYHA – class improvement rate in patients who were treated with CRT along with medical therapy was much higher than that of patients who received only medical treatment.[13] These findings were consistent with the results of our study, but unlike our study, they didn't use defibrillator with CRT-D. In a study performed on 1520 patients with advanced heart failure by accident use of CRT-CRT-D and drug therapy, the results showed that hospitalization risk in both intra-cardiac device groups were less than drug therapy and this reduction is further in type of defibrillator.[30] Another study by BRISTOW in the U.S. in the year 2000 on 2200 patients with class 3–4 heart failure, showed that compared to the use of CRT, CRT-D and optimal pharmacological therapy, CRT-D and CRT are significantly more successful than oral treatment in lowering mortality (up to 25%).[18] The results of this study were consistent with ours so that the mortality rate in group 1 was significantly lower than Group 2. Lindenfeld *et al*. In a study on 1520 patients with class 3–4 heart failure in 2006 that compared using of CRT and CRT-D with maximum oral therapy. The study showed that CRT, CRT-D compared to oral therapy on a follow-up of 12 months were with lower rates of mortality and hospitalization.[31] The results were consistent with ours too so that in addition to increased mortality rate in Group 2, 23% of this group in comparison with Group 1 needed for readmission due to heart failure or arrhythmia in the first 3 months. The conventional treatment of patients with Ischemic CMP is surgery and after 3 months (60–90 days) they are investigating the need for CRT-D. But in this study the candidate patients initially inserted CRT-D during CABG surgery and in Group 2 the similar patients underwent the surgery

without CRT-D insertion. All patients were followed for 3 months. At the end, both two groups were compared. Increase in LVEF, patient's improvement according to NYHA-class, decrease in mortality rate and AF in Group 1 were significantly increased. Among the limitations of this study compared with the previous studies, low sample size and short time follow-up could be indicated that, fortunately, the interpretation of our results showed these limitations caused no significant difference.

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