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Prediction of Changes in Left Ventricular Ejection Fraction after Off-Pump Coronary Artery Bypass Grafting Surgery by Myocardial Perfusion Single-Photon Emission Computed Tomography

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ABSTRACT

Introduction: Left ventricular ejection fraction (LVEF) is considered to be the single most important prognostic factor in patients with previous myocardial infarction. LVEF is not improved in all patients after coronary artery bypass grafting (CABG). This study aimed to assess the possibility of prediction of LVEF changes after CABG using myocardial perfusion gated signle photon emission computed tomography (GSPECT).
Materials and Methods: Overall, 48 patients with mean LVEF of 30.2% (±4.7) underwent Echocardiography and GSPECT after injection of Tc-99m- MIBI at rest. Myocardial uptake was evaluated in 17 myocardial segments and was compared with age and gender matched normal data pool. The risks and benefits of CABG were explained to the patients and 16 cases (15 male and 1 female) with the mean age of 61.1 years (±10.8) accepted to undergo off-pump CABG. All the patients were followed-up for at least six months and echocardiography and GSPECT were repeated at the end of follow up.
Results: The mean LVEF was increased from of 31.1% (±3.5) to 34.5% (±3.6) after surgery ($P<0.001$). Delta LVEF was defined as ΔLVEF=LVEF (before CABG) - LVEF (after CABG). ΔLVEF was within the range of 0-8% with the mean of 3.4% (±2.5). The number of non-viable myocardial segments was not significantly different between patients with ΔLVEF ≥ 5% and those with smaller changes. Myocardial perfusion was estimated for all segments, and the mean global uptake was defined by adding the mean uptake in all segments, divided by 17. The mean global uptake was 53.1% in our patients. Regression analysis revealed that ΔLVEF after CABG can be predicted reliably using the following formula: ΔLVEF= -33.8 + (0.77 × mean global uptake) ($P<0.01$).
Conclusion: Our study showed that change of LVEF after CABG can be predicted reliably using mean global uptake in preoperative myocardial perfusion SPECT at rest.

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Introduction

Coronary artery disease (CAD) is a principal cause of morbidity and mortality in human beings. The treatment strategy used for patients with CAD can be based on disease-related risks and may

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range widely from medical treatment to angioplasty or coronary artery bypass grafting (CABG) (1). The incidence of cardiovascular disease (CVD) is increasing rapidly, worldwide (2).

Left ventricular ejection fraction (LVEF) is a major determinant of survival in patients with CAD. Patients with low ejection fraction (EF) and multi-vessel disease (with viable myocardium) undergoing revascularization have by far lower mortality and morbidity rates than those with no myocardial viability (3).

This issue accentuates the importance of preoperative myocardial viability assessment which can prevent ineffective high-risk cardiac surgery. There are numerous diagnostic methods for the study of viability such as MRI, thallium scan, technetium-99m-methoxy-isobutyl-isonitrile (MIBI), and 18FDG positron emission tomography (PET) (3, 4). One can choose any of these diagnostic modalities considering their sensitivity and accuracy. Other factors such as history of allergic reactions to the contrast material and concerns about ionizing radiation might be critical for choosing the appropriate modality (5).

Although stress imaging is not mandatory for viability assessment, stress myocardial perfusion single photon emission computed tomography (SPECT) could provide vital diagnostic and prognostic information. Besides, myocardial stunning can also occur after significant stress-induced myocardial ischemia (6, 7). Additionally, electrocardiogram-gated SPECT (GSPECT) by ^{99m}Tc for myocardial perfusion imaging (MPI) could provide important data about left ventricular (LV) function.

Specification of normal myocardial function in a fixed perfusion defect may be a sign of viable myocardial tissue in patients with CAD (8). However, in case of observing motion and thickening abnormalities in a segment, presence of viable tissues cannot be rejected (9). Stunned or hibernating myocardium areas may have either normal or abnormal motions; nevertheless, they may regain function after successful revascularization (10).

Trinitroglycerin (TNG) administration can improve myocardial perfusion and lower the rate of false negative defects due to myocardial stunning. This study was conducted on CABG candidates with left ventricular systolic dysfunction, clinical heart failure, CAD and EF less than 35%. We aimed to evaluate short-term outcomes of off-pump CABG using MPI SPECT with and without oral TNG (as a predictor of improvement in ventricular function) in the aforementioned patients.

Materials and Methods

This before-after study was conducted on a group of patients with 75% diameter stenosis in at least one of the three major epicardial coronary vessels undergoing cardiac catheterization at Ghaem General Hospital, affiliated to Mashhad University of Medical Sciences, Mashhad, Iran from 2004-2006. The inclusion criteria were EF less than 35% in patients' echocardiography and class III symptoms of heart failure according to New York Heart Association criteria.

Two out of 50 patients, who had been chosen through convenience sampling, died before SPECT imaging, and a subset of 48 patients was studied (Figure 1). The death circumstances were acquired from hospital records or by conducting telephone interviews with the assigned physician or family members.

Baseline variables such as demographics, physical examinations, biochemical lab tests, clinical data, chest X-rays and 12-lead electrocardiograms were recorded at the first admission in the nuclear medicine department. All the data was collected by one observer using structured checklist.

Gated myocardial perfusion SPECT was performed at rest on all the patients. On the first day, 20mCi of Tc-99m-MIBI was injected intravenously and GSPECT imaging was done one hour after, using a 32-step and 25 sec/image acquisition protocol. The next day basal blood pressure was recorded and a TNG pearl was administered; blood pressure was re-recorded 10 minutes later. In case of systolic pressure of >140 mmHg, another pearl of TNG was administered and 20mCi of Tc-99m-MIBI was injected intravenously. GSPECT was re-performed one hour after applying the same protocol.

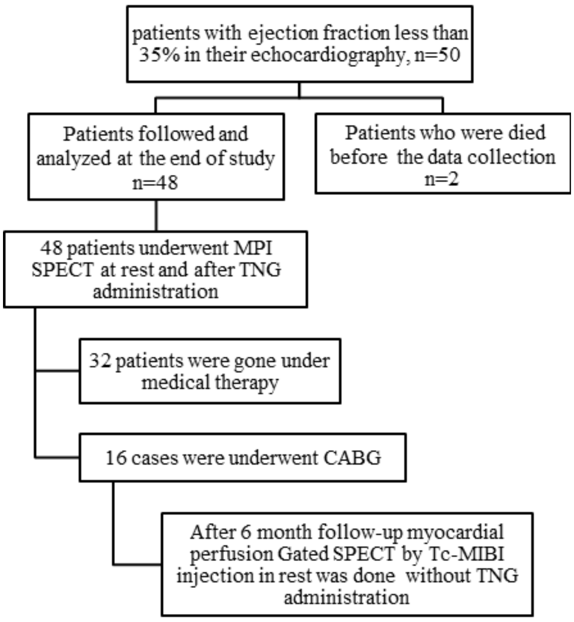

Figure 1. Flow chart for the selection and exclusion of the studied patients

Siemens Syngo software was used for reconstruction of images and all the images were interpreted by two experienced nuclear physicians. American Heart Association (AHA) 17-segment model was used for interpretation of MPI. Additionally, using QPS software (Cedars Sinai Hospital, USA) and 17-segment model, myocardial perfusion was estimated for all segments (comparing to normal data pool) and a "mean global uptake" was defined by adding mean uptake to all segments divided by 17.

The patients were re-examined by a cardiovascular surgeon, and CABG was offered to patients meeting the appropriate diagnostic and surgical criteria for bypass surgery. Sixteen out of 48 patients, underwent off-pump CABG and 32 patients received medical therapy.

Standard cardiac surgical and anesthesia methods and techniques were adopted using off-pump bypass surgery by a single surgeon. Follow-up was done through telephone interviewing in all the patients, six months after revascularization.

Follow-up data for each patient was obtained using a standardized checklist including history of admission to the CCU, history of admission to cardiac departments, myocardial infarction or death. The mean follow-up time was 6.2 months after revascularization.

MPI SPECT at rest, was re-conducted on revascularized patients at the end of the follow-up. LVEF was estimated after CABG in gated images. The difference in LVEF before and after CABG was calculated in MPI images as delta LVEF. Delta LVEF was defined as: ΔLVEF=LVEF (before CABG) - LVEF (after CABG).

The study was approved by the ethics committee of Mashhad University of Medical Sciences and informed consent was obtained from all the patients.

Statistical Analysis

Descriptive analysis was performed for all the variables. Man-Whitney U test (Independent t-test) and Wilcoxon signed-rank test were performed to compare the quantitative variables; moreover, $\chi 2$ test was employed for dichotomous variables.

SPSS software version 11.5 was used for the statistical analyses. Kolmogorov–Simonov test and linear regression were performed to assess normality of the data and to predict changes in LVEF, respectively (P-value<0.05).

Results

Overall, forty-eight patients (42 male and 6 female) with mean age of 61.23(±8.17) were studied. Indeed, sixteen patients underwent CABG and 32 patients were treated with medical therapy. Demographic characteristics of patients in CABG and medical treatment groups are demonstrated in Table 1.

Mean LVEF in baseline GSPECT (no TNG) was 27.50% (±5.24), which increased to 33.33% (±10.75) after CABG (P=0.68), while the corresponding LVEF by echocardiography were 30.21% (±4.7) and 32.30% (±5.93), respectively (P=0.001).

The study also showed that preoperative LVEF improved in GPECT images after TNG administration. However, postoperative LVEF did not increase after TNG administration (Table 2). This finding confirms the effect of CABG on preventing myocardium stunning.

The mean (±SD) follow-up time in this longitudinal study was 6.21±1.47 months. During the six-month follow-up of 16 CABG patients,mean number of admission times to cardiac departments was 0.54±1.61 and mean CCU admission times were 1.88±2.69.

Preoperatively, the mean uptake of the 17 segments without TNG administration and after TNG administration were 53.4±2.8 and 56.2±3.2, respectively (P=0.003).

Postoperatively, the mean uptake of the 17 segments with and without TNG administration were 55.34±0.12 and 54.2±0.75, respectively (P=0. 19).

Additionally, the mean baseline uptake of the 17 segments before and after CABG were 53.4%±2.8 and 54.2%±0.75, respectively (P=0.10). To predict the amount of change in LVEF (ΔLVEF) after CABG using different variables, linear regression analysis was performed. The model was statistically significant (P=0.010)

Table 1. The characteristics of patients at the beginning of the study.

Characteristic	Medical therapy (N=32)	CABG (N=16)	P value
Mean Age# (SD)	61.28(9.2)	61.13(9.3)	0.95[a]
Male/Female ratio *	27/5	15/1	0.33[b]
Three Vessel Disease*	27(64.3%)	15(35.7%)	0.35[c]
Two Vessel disease*	5(83.3%)	1(16.7%)	
Mean Number of Infarcted Segments*	6.29	3	0.056[b]
Baseline LVEF*	28.4±4.2	27.50±5.24	0.34[c]

Analysis was done by [a] Independent t test; [b] Man- Whitney u test; [c] Chi square test; *No (%) or (%); # Age in years

Table 2. The comparison between pre-operative mean global uptake of ^{99m}Tc-MIBI with and without TNG administration (first row) and comparison between mean global uptakes before and after CABG without TNG administration (2[nd] row).

	TNG	Mean(%) ± SD	P value
Before CABG	+	56.2±3.2	P=0.003[a]
	-	53.4±2.8	
After CABG	-	54.2±0.752	P=0.10[b]

The analysis was done using [a]wilcoxon test and [b] Mann-Whitney u test

According to this study, LVEF after CABG can be predicted using mean global uptake in preoperative ^{99m}Tc-MIBI myocardial perfusion SPECT at rest (Figure 2) as follows: ΔEF= -33.785 + [0.769*] (* Mean uptake of all segments without TNG administered).

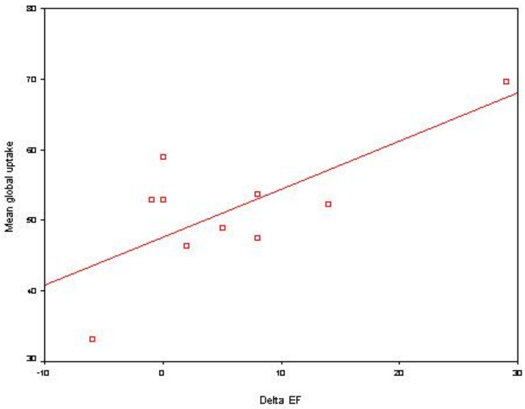

Figure 2. The amount of change in LVEF after CABG versus pre-operative mean global uptake of rest ^{99m}Tc-MIBI SPECT. ΔLVEF= -33.8 + (0.77 × mean global uptake); R^2=0.52; P=0.01

Discussion

Although patients with severe CAD and heart failure can be treated with CABG, it is not beneficial for all patients. Considering perioperative mortality, careful selection of patients for CABG is of utmost importance.

It is shown that LVEF is the most decisive prognostic factor for mortality in these patients, therefore; one of the main objectives of CABG is to improve LVEF. Our study showed that *ΔLVEF* can be predicted by mean global LV uptake of Tc-99m-MIBI at rest.

In a study by Leoncini et al., functional recovery after revascularization was examined using baseline and low dose dobutamine (LDD) GSEPCT. They proposed that low dose dobutamine GSPECT achieved better accuracy in predicting segmental functional recovery as compared with GSPECT at rest. Moreover, the positive and negative predictive values of LDD GSPECT were similar to low dose dobutamine echocardiography(12). However, they did not predict LVEF which is the main prognostic factor in patients with CAD.

Another study by Santiago on a total of 1,680 segments from 84 patients using thallium-201 GSPECT myocardial perfusion imaging, demonstrated significant correlations between perfusion and wall motion, perfusion and wall thickening, as well as wall motion and wall thickening. They also found a significant correlation between the severity of ischemia and transient stunning through either wall motion ($P<0.05$) or wall thickening ($P<0.005$) evaluation (13). This finding shows association between perfusion and viability.

Other modalities were used for viability assessment as well. PET imaging was employed with 13NH3 to assess blood flow. Additionally, 18FDG was adopted to evaluate the metabolic activity of myocardium, which was proven to be an accurate method for predicting potential reversibility of wall-motion abnormalities after surgical revascularization (1).

Another study on patients with ischemic cardiomyopathy employed dobutamine technetium-^{99m}Tc-sestamibi GSPECT to examine the possibility of change in LVEF induced by dobutamine. It was found that this method can predict EF improvement after revascularization. In that study, 37 patients underwent resting and dobutamine sestamibi GSPECT before revascularization and after intervention to assess the global functional changes. Improvement was detected using the cut-off value of 5 EF units; improvement was noted in 19 patients after revascularization. Dobutamine GSPECT was successful in predicting EF improvement after revascularization with a sensitivity rate of 79% and specificity rate of 78% in that study. The increase in EF during dobutamine was a good predictor of EF improvement after revascularization. The aforementioned study showed that GSPECT imaging data can be used for the evaluation of myocardial viability and prediction of EF improvement after revascularization in patients with ischemic cardiomyopathy (14).

Our study showed that global LV uptake did not increase postoperatively following TNG administration in patients with mean LVEF≤35%. This finding suggests that in patients with nonviable myocardium, TNG administration was not associated with improved uptake.

Hachamovitch studied prognostic value of stress/rest SPECT in 5183 consecutive patients who were followed-up for the occurrence of cardiac death or myocardial infarction. With the mean follow-up duration of 642 ± 226 days, they found 3.0% cardiac death rate and 2.3% myocardial infarction rate. Myocardial perfusion SPECT yields incremental prognostic information about identification of cardiac death (15). Also, in another large observational series with a long-term follow-up, it was found that the survival chance of the patients with significant ischemia and without extensive scar increased through early revascularization.

In contrast, the survival of patients with minimal ischemia was superior with medical therapy without early revascularization (16). These studies showed correlation between myocardial uptake and patients' prognosis.

Myocardial ^{99m}Tc-sestamibi activity correlates well with the extent of viable myocardium and predicts regional function improvement after CABG. This finding is the basis for the use of sestamibi as a myocardial viability agent (10).

In the present study, we demonstrated that myocardial MIBI uptake at rest with and without TNG administration could be used for assessment of myocardial viability.

Patients with significant ischemia and without extensive scars in SPECT were likely to obtain survival benefit from early revascularization. In severe ischemic heart failure, MRI hyper-enhancement is also performed as a marker of myocardial scar, the results of which closely agree with PET data. Although hyper-enhancement correlated with areas of decreased flow and metabolism, it seems to identify scar tissue more frequently than PET, reflecting higher spatial resolution (17,18).

Although impact of selection bias and missing covariates cannot be ignored in this study, a complete follow-up of the patients and performing off-pump bypass surgery by one surgeon were among its strengths.

Conclusion

This study suggests that using rest SPECT with or without TNG administration is a reliable method to demonstrate myocardial viability. It was also found that LVEF after CABG can be predicted using mean global uptake in preoperative ^{99m}Tc-MIBI myocardial perfusion SPECT at rest.

Conflict of Interest

The authors declare no conflict of interest.

Acknowledgments

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