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Decision Making and Results of Coronary Artery Bypass Grafting for Patients with Poor Left Ventricular Function

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ABSTRACT

Background: The aim of this study is to determine the results of coronary artery bypass surgery in patients with a low ejection fraction. Between January 2007 and January 2011, 3556 consecutive patients who underwent coronary artery bypass grafting at the Cardiovascular Surgery Clinic at Sifa University Hospital, Izmir, Turkey, were analyzed retrospectively.

Methods: The patients were divided into 2 groups. Patients undergoing isolated first-time elective coronary bypass surgery were classified according to their preoperative ejection fraction; Patients in Group I had an ejection fraction between 20% and 35% with poor left ventricular function (n = 1246; 695 men and 551 women; mean age, 62.25 ± 5.72 years, range, 47-78 years). Control patients in Group II underwent elective coronary artery bypass grafting at the same time and had left ventricular ejection fraction between 36% and 49% (n = 2310; 1211 men and 1099 women; mean age, 61.83 ± 8.12 years, range, 41-81 years). The mean follow-up time for all patients was 24 ± 9.4 months (range, 12-48 months). Patients were followed postoperatively at the end of the first month and every 6 months. The left ventricular ejection fraction was assessed by transthoracic echocardiography.

Results: The mean number of distal anastomoses, myocardial infarction, and mean age was not significantly different between the 2 groups; however, cross-clamp time was longer in Group I. Patient recovery time was significantly longer in Group I. Morbidity (14.5% in Group I versus 7.4% in Group II, $P < .005$) and mortality (1.76% versus 0.30%, $P < .005$) were higher in Group I. During late follow-up, the 2-year survival rate (85.1% versus 94.5%) and 2-year event-free rate (77.6% versus 86.9%) were significantly lower in Group I when compared to Group II. Postoperative left ventricular ejection fraction values were significantly superior in Group I compared to Group II.

Conclusion: Coronary artery bypass grafting can be safely performed in patients with low ejection fraction with minimal postoperative morbidity and mortality. The viable myocardium could be reliably determined by positron emission tomography. Low ejection fraction patients could greatly benefit from coronary bypass surgery regarding postoperative ejection fraction, increased long-term survival, improvement in New York Heart Association classification, and higher quality of life.

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INTRODUCTION

Coronary artery bypass grafting (CABG) was introduced as a treatment for ischemic atherothrombotic coronary disease more than 40 years ago. However, due to the ongoing technological evolution of this procedure and changes introduced in the clinical treatment of the disease, a continuous assessment of the results is required by observation and critical analysis of its use in clinical practice. Between 2007 and 2011, Sifa University Hospital in Izmir, Turkey, performed 3556 CABG procedures without valve replacement.

Postoperative complications can jeopardize the success of the CABG procedure. A study of complications of CABG reported that 73% of octogenarian patients, as well as 41% of the population of the study experienced at least 1 complication [Alderman 1983]. The most frequent complications were atrial fibrillation, acute renal dysfunction, bleeding, need for hemotransfusion, and nosocomial infections [Pigott 1985; Scott 1994].

The aim of this study was to assess baseline clinical patient characteristics in hospital mortality rates before hospital discharge and predictive factors for mortality and morbidity in patients with low ejection fraction.

METHODS

Data on CABG procedures performed from January 2007 to January 2011 were collected from the patients' medical charts in Sifa University Hospital in Izmir. This study included 3556 patients with coronary artery disease undergoing CABG. The patients were divided into 2 groups. Patients undergoing isolated first-time elective coronary bypass surgery were classified according to their preoperative ejection

Table 1. Demographic, Clinical, and Procedural Data for Study Patients*

	Group 1 (n = 1246, ejection fraction 20%-35%)		Group 2 (n = 2310, ejection fraction 36%-49%)		
Parameters	Patient Number	%	Patient Number	%	*P*
Age, y (mean ± standard deviation)	62.25 ± 5.72		61.83 ± 8.1		.1114
Female sex	518	41.60	1099	47.58	.03
Unstable angina	342	27.44	651	28.18	.914
Recent myocardial infarction	72	5.77	129	5.58	.591
Heart failure	386	30.97	392	16.96	.0001
Three vessel disease	1089	87.39	1450	62.77	.0001
Risk factors					
Smoking	568	45.58	914	39.56	.003
Arterial hypertension	609	48.87	1156	50.05	.72
Morbid obesity	215	17.25	447	19.35	.83
Dyslipidemia	650	52.16	1774	76.79	.001
Family story	275	22.07	395	19.09	.047
Peripheral vascular disease	176	14.12	182	7.87	.001
Stroke	156	12.52	169	7.31	.001
Comorbidity					
Recent myocardial infarction	609	48.87	812	35.15	.001
Diabetes mellitus	650	52.16	853	36.92	.001
Chronic obstructive lung disease	447	35.87	484	20.95	.001
Chronic renal failure	81	6.50	95	4.11	.001
New York Heart Association class (mean ± standard deviation)	3.3 ± 3.8		2.8 ± 4.6		.001
Preoperative ejection fraction (Ort ± standard deviation)	33.6 ± 6.7		45 ± 4.8		.0001
Left main coronary artery lesion	375	30.09	685	29.65	.012

fraction (EF). Group I had poor left ventricular function (n = 1246; EF 20% to 35%, 695 men and 551 women; mean age 62.25 ± 5.72 years, range, 47-78 years). Group II had EF 36% to 49% (n = 2310; 1211 men and 1099 women; mean age 61.83 ± 8.12 years, range, 41-81 years). The mean follow-up time for all patients was 24 ± 9.4 months (range, 12-48 months). Patients were followed postoperatively at the end of the first month and every 6 months.

Postoperative left ventricular ejection fraction (LVEF) was assessed by transthoracic echocardiography. The groups were compared with operational data, postoperative complications, and postoperative LVEF. We performed positron emission tomography (PET) scanning to demonstrate the viable myocardium in 104 patients with LVEF was less than 25%. The patients who had no viable myocardium were excluded. Functional improvement was evaluated using echocardiography and gated scintigraphy both at rest and exercising.

Echocardiographic Study

LVEF was calculated by using Simpson's method and biplane data for each measurement of transthoracic echocardiography (Hewlett-Packard ultrasound imaging system, Palo Alto, CA, USA). Endocardial borders were traced at end diastole and end systole and the surfaces were generated using an algorithm. Papillary muscle was included for end systolic measurements. An average of 3 cardiac cycles were obtained for all the echocardiographic measurements. Intra- and inter-observer variability by measuring EF were 1.2% and 2.0%, respectively [Tavli 1992].

Surgical Technique

All patients were on 5 mg midazolam intramuscular and 1 gr Cefazolin intravenous before the operation and continued in repeated doses (twice a day) until chest tube removal. In case of infection, a swab was taken from the wound and following the outcome of cultures and targeted antibiotics were administered. The sternotomy was done via a standard midline skin incision. Internal thoracic arteries (ITAs) were harvested as a pedicle with the surrounding tissue and accompanying vein. Arteries were obtained with diathermy and the use of clips. The ITAs were divided after 3 minutes of systemic heparinization and left in a sponge soaked with

Table 2. Mortality and Complications after Coronary Artery Bypass Grafting*

	Group 1 (n = 1246, ejection fraction 20%-35%)	Group 2 (n = 2310, ejection fraction 36%-49%)	*P*
Number of distal anastomosis	3.72 ± 3.6 (1-4)	3.48 ± 4.2 (1-5)	.093
Time of cross-clamp, min	39.6 ± 14.3	31 ± 24.3	.001
Time of perfusion, min	72.7 ± 26.2	69.3 ± 34.6	.003
Positive inotropic support	47.4%	31.9%	.0001
Intraaortic balloon pump	3.52%	0.12%	.0001
Using Grafts			
Left internal thoracic artery	1042 (83.62%)	2275 (98.48%)	.0003
Safein ven	204 (16.38%)	35 (1.52%)	.0001
Radial artery	—	—	—
Blood transfusion	3.4 ± 2.7	3.1 ± 1.4	.001
Days in intensive care unit	1.8 ± 2.3	1.2 ± 2.1	.001
Total days in hospital	6.2 ± 5.8	5.1 ± 3.6	.001
Preoperative use of levosimendan	6.05%	0.00%	.0001
Intubation time, h	12.67 ± 4.8	7.86 ± 9.2	.0001
Reoperation for bleeding	0.4%	0.6%	.016
Arrhythmias needing treatment	35%	18%	.0001
Cerebrovascular events	0.4%	0.5%	.213
Early mortality (first 7 days)	17 (1.34%)	5 (0.21%)	.0001
Cumulative mortality in hospital	22 (1.76%)	7 (0.30%)	.0001

*Data are presented as n (%) or mean ± standard deviation.

papaverine, while the distal end was clamped with a small bulldog clamp. The pleural spaces were always open, and the pericardium was incised to avoid any tension on the arterial conduits. Chest drains were positioned in 1 or bilateral pleural spaces and in the mediastinum. The sternum was reapproximated with steel wire, and subcutaneous tissues were closed with 2 layers of continuous absorbable sutures and skin with continuous intra-coetaneous absorbable suture.

Statistical Analysis

Continuous data are displayed as a means with standard deviation. Categorical data are expressed as proportions. Categorical variables were analyzed using the chi-squared test or Fisher's exact test when appropriate. Multiple Cox regression analysis was performed to assess the impact of the following possible risk factors: viability and LV-function. In all studies, P values < .05 were considered statistically significant. Calculations were performed using the SPSS 16 package (IBM; Chicago, IL, USA).

RESULTS

The mean number of distal anastomoses, acute myocardial infarction, and mean age was not significantly different between the 2 groups; however, cross-clamp time was longer in Group I. Patient recovery was significantly slower in Group I. Morbidity (14.5% in Group I versus 7.4% in Group II, $P < .005$) and in-hospital mortality (1.76% versus 0.30%, $P = .0001$) were higher in Group I. During late follow-up, the 2-year survival rate (85.1% versus 94.5%) and 2-year event-free rate (77.6% versus 86.9%) were significantly inferior in Group I when compared to Group II. LVEF was significantly decreased in Group I ($P = .0001$). Early mortality was related to heart failure ($P = .0001$) (Table I). In Group I, early mortality was 17 patients (1.34%, $P = .001$) and in-hospital mortality was significantly higher (1.76% in Group I versus 0.30% in Group II) (Table 2). Early and cumulative mortality and arrhythmia complications with regard to levels of EF in all patients after CABG are shown in Figure 1.

The cross-clamp time, perfusion time, and blood transfusion were significantly higher in patients in Group I ($P < .05$) (Table 2). Time of cross-clamp, time of perfusion, and reoperation of bleeding were significantly higher in patients with poor EF (EF < 35%) (Figure 2).

Incidence of stroke, current smoking status, family story, diabetes mellitus, chronic renal failure, peripheral arterial disease, and congestive heart failure were significantly different in Group I compared to Group II ($P < .05$) (Table 3).

The incidence of major adverse cardiac and cerebral vascular events (MACCE), such as myocardial infarction, death, or stroke, were statistically significantly increased in Group I ($P < .05$). A probable risk factor for MACCE was a history of peripheral atherosclerosis and heart failure. A possible risk factor for MACCE was low EF before surgery (Table 1). Left

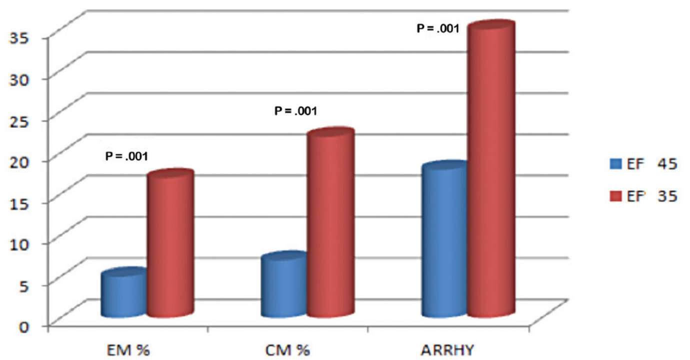

Figure 1. Comparison of complication with levels of ejection fraction in patients after coronary artery bypass grafting (CABG). EM indicates early mortality; CM, cumulative mortality; ARRHY, arrhythmia needs treatment.

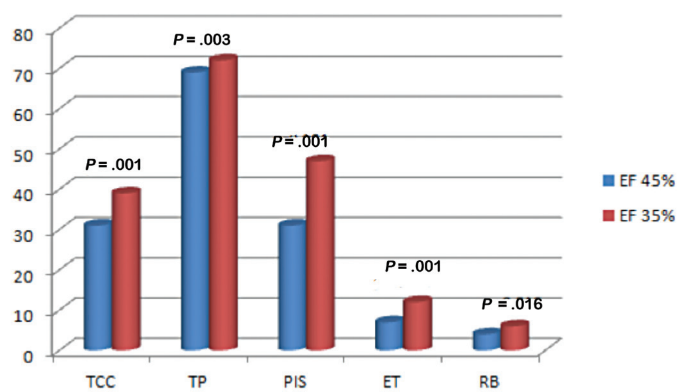

Figure 2. Comparison of procedures with levels of ejection fraction during and after coronary artery bypass grafting (CABG). TCC indicates time of cross clamp; TP, time of perfusion; PIS, positive inotropic support; RB, reoperation for bleeding.

Table 3. Preoperative Factors Affecting 30-Day Mortality in Patients with Coronary Artery Bypass Grafting*

Parameters	Mortality (n = 28)	Healthy (n = 3528)	*P*
Left main coronary artery lesions	42.4%	18.4%	.001
Intraaortic balloon pump use	86.2%	0.68%	.0001
Time of perfusion (mean ± standard deviation)	145.26 ± 45.36	71.15 ± 24.12	.0001
Time of cross-clamp (mean ± standard deviation)	76.23 ± 89	36.14 ± 65	.0001
Peripheral artery disease	64.8%	16.5%	.001
Arrhythmias	72.4%	44.6%	.018
Current smoking status	84.5%	56.7%	.018
Cerebrovascular disease	24.2%	0.74%	.001
Chronic heart failure	88.4%	22.6%	.001
Left internal thoracic artery use	72.8%	94.5%	.0001
Diabetes mellitus (type 1)	92.8%	86.7%	.01
Chronic renal failure	28.9%	2.3%	.0001

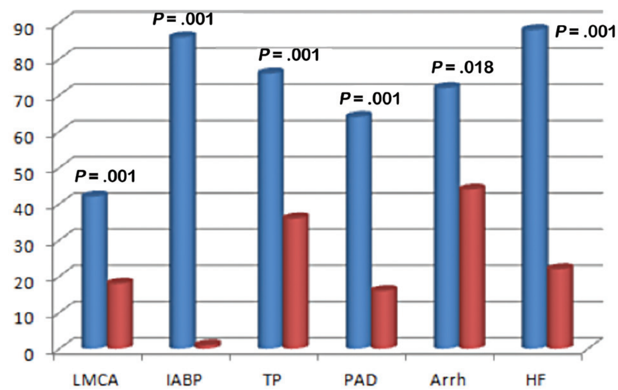

Figure 3. Comparison of parameters in mortal (M) and healthy (H) patients. LCMA indicates left main coronary artery; IABP, intraaortic balloon pressure; TP, time of perfusion; PAD, periferic artery disease; Arrh, arrhythmia; HF, heart failure.

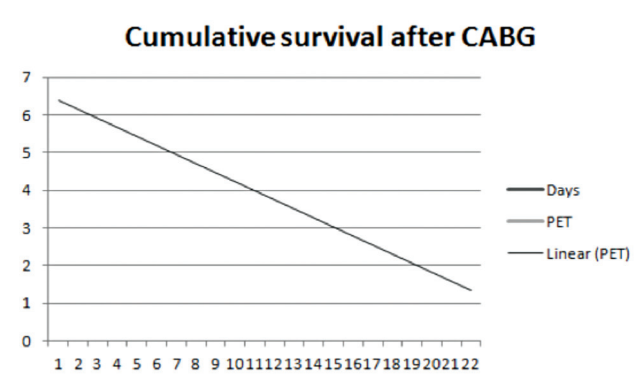

Figure 4. Relationship between positron emission tomography (PET) and cumulative survival after coronary artery bypass grafting (CABG).

main coronary artery, intraaortic balloon pump, time of perfusion, and peripheral arterial disease and heart failure were significantly higher in patients with low EF. Cox-regression analysis revealed an influence of preoperative viability assessment via PET ($P < .05$) of preoperative left ventricular function ($P = .05$) on short-term survival (Table 1; Figure 3).

In the case of death, probable risk factors estimated using multivariate logistic regressions were higher heart failure (NYHA class IV) and low EF preoperatively ($P < .05$) (Table 1). Peripheral artery disease, arrhythmia, or a history of myocardial infarction were possible risk factors.

Preoperative assessment of myocardial viability via PET identifies patients who will benefit most from CABG. Postoperative survival of patient selection by viability assessment via PET is shown in Figure 4.

DISCUSSION

Despite all the developments in invasive treatments for coronary artery stenosis with impaired ventricular function in patients with coronary artery disease, the benefits of non-surgical treatment options for patients and physicians is far from satisfactory [Topkara 2005]. One of the treatment options for coronary artery disease patients with impaired left ventricular function is surgical treatment and is emphasized by many authors to be superior to other treatment options [Elefteriades 1995; Shapira 1995; Lslamoglu 2002; Hovnanian 2010]. Alderman and his colleagues reported that in patients with a LVEF value below 35%, the 5-year survival rate is 43% with medical therapy and 63% with surgical therapy [Alderman 1983]. Di Carli and his colleagues performed a similar study assessing symptoms of angina and published that surgical treatment is superior [Di Carli 1998].

There is no consensus in the literature about which patients will benefit and the degree of benefit from surgical treatment. Patients with symptoms of angina benefit more compared to patients with left ventricular insufficiency from operation [Lansman 1993]. Some of the other studies demonstrated that live hibernating myocardium-specific tests such as PET imaging or dobutamine stress echocardiography is noteworthy when applied in the preoperative selection of the patients [Afridi 1998]. Some of the other centers concluded that convenient structure of coronary artery for grafting was enough for surgical revascularization, and live tissue research was not performed in any of the patients [Elefteriades 1998; Lslamoglu 2002; Langenburg 1995].

There are publications, however, reporting that patients with no viable myocardium observed at PET imaging have no improvement in functional capacity and angina after surgery [Di Carli 1998]. Lslamoglu and colleagues did not apply any viability test to the preoperative patients and performed surgery according to the results of ventriculography and echocardiography [Lslamoglu 2002]. They concluded that the sole determinant was suitable coronary arteries for grafting documented by angiography.

All of our patients were investigated by PET imaging for viable myocardial tissue with LVEF value between 20% and 25%. We did not use the PET imaging in patients with LVEF value above 25% because it is not cost effective. The assessment of myocardial viability by nuclear imaging techniques has become an important aspect of the diagnostic and prognostic work-up of patients with ischemic heart disease. Noninvasive imaging such as PET has been reported as a useful tool for the determination of tissue viability and hence for the prediction of reversibility of regional left ventricular dysfunction and mortality [Boehm 2010].

CABG was performed only on patients with viable myocardial tissue. Christakis and colleagues have shown that under emergency conditions, the most important factor that affected early mortality in patients with low LVEF was a value below 20% [Christakis 1992]. Lslamoglu and colleagues also reported that factors that affected early mortality in patients with LVEF value less than 20% were advanced age, diabetes mellitus, hypertension, severe angina, and functional class III-IV

[Lslamoglu 2002]. In this study, the female gender has not been an effective factor. In addition, cross-clamp time longer than 60 minutes and the use of IAB*P* have been identified as perioperative factors affecting mortality. Selim Isbir and colleagues reported increased pulmonary artery pressure and right ventricular failure as the most important factors affecting mortality [Selim Isbir 2003]. Hausman and colleagues also showed that increased left ventricular end-diastolic pressure, decreased cardiac index values, and patients in class IV according to the NYHA classification were factors affecting mortality in patients with low LVEF [Hausmann 1997]. In Topkara and his colleagues' study, advanced age, female gender, hepatic failure, renal failure, congestive heart failure, emergency surgery, myocardial infarction starting 6 hours before the procedure, and previous cardiac surgery were regarded as risk factors in patients with LVEF value below 20%. Additionally, LVEF value less than 35% is also mentioned as an independent risk factor [Topkara 2005]. In Mickleborough and colleagues' study, advanced age, class IV functional capacity, and unfavorable coronary artery disease for grafting were reported as important factors [Mickleborough 2000].

As emphasized by Kaul and colleagues, we think that myocardial protection is very important in patients with low LVEF. Multi-dose antegrade (and in some situations considered insufficient) application of both antegrade and retrograde cardioplegia (6.26%) techniques were used in all of our patients [Kaul 1996]. Cardiac transplantation is another treatment option in patients with severe impaired left ventricular function. Although it is an effective method, because of limitations in the number of donors it can be applied to, 10% of those in need and most of the patients die while waiting for transplantation.

We believe that patient selection is very important during the surgical planning in patients with impaired LVEF value. In this study, we found in-hospital mortality rates below 2% and a 2-year survival rate after surgery approximately 90%. All of the in-hospital mortality among our patients was due to left ventricular failure resulting in multi-organ failure. These rates are compatible with the results of other studies done in the past 10 years [Lslamoglu 2002; Topkara 2005; Hovnanian 2010].

In our clinic, 99.35% of the patients with LVEF value below 49% underwent CABG. CABG was applied to only a portion of patients with LVEF value below 20%. These patients are not included in this study.

Studies showed that preoperative risk factors should be identified affecting long-term survival rate, mortality, and morbidity [Evans 1986; Mickleborough 1995]. In our patients, we observed that if there were signs of acute liver failure, kidney failure, or congestive heart failure in patients with the LVEF value less than 30%, applying CABG after medical treatment of these problems would decrease mortality. We think it would be preferentially appropriate to apply the interventional cardiac procedures or medical treatment during acute myocardial infarction.

As a result, in patients with impaired left ventricular function, especially in patients with LVEF value below 35%, CABG is the best treatment option. In this patient group, CABG can be done safely and with low mortality and morbidity rates. The viable myocardium could be determined by PET imaging securely. For planning surgery in patients with LVEF value less than 30%, PET imaging for the determination of viable tissue may be helpful in surgical decisions.

Limitations of Our Study

Long-term follow-up is required to determine the effectiveness of PET for assessment of myocardial viability. In this study, short-term results are reported. Previous studies showed that revascularization of patients with viability results in an improvement of heart failure symptoms and exercise capacity [Marwick 1999]. Patients selected for CABG on the basis of PET viability studies may also have fewer perioperative complications [Haas 1997].

The current study evaluates the use of PET imaging in the decision-making process for poor left ventricular function before CABG and determines that postoperative patient survival improves with the cutoff point of 40% of scar tissue as an indication for CABG.

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