

CORONARY ARTERY BYPASS GRAFTING IN PATIENTS WITH LOW EJECTION FRACTION: THE EFFECT OF INTRA-AORTIC BALLOON PUMP INSERTION ON EARLY OUTCOME

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ABSTRACT

BACKGROUND: Survival benefit with intra-aortic balloon pump (IABP) insertion for coronary artery bypass grafting (CABG) patients with left ventricular dysfunction is controversial. The aim of this study was to assess the early results of CABG that predict 30-day mortality and prolonged length of hospital stay (LOS) after isolated CABG and the role of IABP application as a main predictor in patients with an ejection fraction (EF) of 30% or less. **MATERIALS AND METHODS:** Eight hundred and thirty-three patients who underwent isolated CABG with $EF \leq 30\%$ were entered and compared with 10881 patients with $EF > 30\%$ as the control group. Demographic and clinical characteristics and postoperative complications were considered. Data were analyzed using the student's t-test and chi-square test for univariate analysis and the analysis of covariance and logistic regression for multivariate analysis. **RESULTS:** The thirty-day mortality rate (1.6% vs. 0.7%, $P < 0.001$), the mean of LOS ($P < 0.001$), and the mean of the length of ICU stay ($P < 0.001$) were significantly higher in the severe left ventricular dysfunction group than in the control group. In patients with severe left ventricular dysfunction, the use of intra-aortic balloon pump was related to the 30-day mortality rate ($P = 0.002$) and prolonged LOS ($P = 0.009$). Also, urinary tract infection, prolonged ventilation, and renal failure as postoperative complications were statistically more in the group with the application of IABP. **CONCLUSION:** Low ejection fraction can positively affect thirty-day mortality and prolonged LOS and ICU stay in patients who undergo CABG. In these patients, IABP insertion is a strong predictor for early complication and mortality.

Key words: Coronary artery bypass grafting, intra-aortic balloon pump, left ventricular dysfunction, outcome

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INTRODUCTION

Some randomized controlled trials showed a survival benefit with intra-aortic balloon pump (IABP) insertion for coronary artery bypass grafting (CABG) patients with low ejection

fraction (EF).^[1,2] Also, it has been clear that IABP is an effective means of supporting failing circulation in patients at high risk of cardiovascular events post-operatively.^[3] However, IABP is an intensive care-based treatment and is therefore costly. In addition, it can be accompanied by complications including limb ischemia, aortic or iliac dissection bleeding, infection, hemolysis, paraplegia, and stroke.^[4,5]

Any survival benefit after CABG in the face of severely depressed LV function is relatively known; however, determination of factors such as IABP, which affect this survival, is necessary. Furthermore, there has been no widespread recognition of the results of IABP procedure in these patients. We aimed to develop multivariable models of preoperative, operative, and postoperative risk factors that predict 30-day mortality and prolonged length of stay (LOS) in hospital after isolated CABG and also determine the effect of IABP support on these outcomes in patients with an ejection fraction of 30% or less.

MATERIALS AND METHODS

Demographic and clinical characteristics of 11714 patients undergoing isolated CABG (833 patients with LVEF \leq 30% as the study group and 10881 patients with EF > 30% as the control group) from 1 January 2002 to 1 January 2007 were collected and entered into a computerized database. All patients with the history of concomitant cardiac and non-cardiac operations were excluded.

Final determination of ejection fraction was based on angiographic reports. In this study, CAD was considered significant if

there was a 75% or greater stenosis in the cross-sectional diameter and 50% or greater stenosis in the luminal view.^[6] The following variables were collected for statistical analysis including the preoperative variables: 1) general characteristics: age, gender, and body mass index; 2) preoperative risk factors (total cholesterol \geq 5.0 mmol/l, HDL-cholesterol \leq 1.0 mmol/l in men, or \leq 1.1 mmol/l in women, triglyceride \geq 2.0 mmol/l),^[8] (first-degree relatives before the age of 55 in men and 65 years in women),^[9] (systolic blood pressure \geq 140 mmHg and/or diastolic \geq 90 mmHg and/or on anti-hypertensive treatment),^[10] n \geq 11.1 mmol/l or fasting plasma glucose \geq 7.0 mmol/l or 2-hp \geq 11.1 mmol/l renal failure (creatinine > 355 μ mol/l with a rise of > 44 units or urine output below 0.3 ml/kg for 24 h), cerebrovascular disease, peripheral vascular disease, and chronic lung disease; 3) preoperative cardiac status: recent myocardial infarction (an acute event with abnormal creatine phosphokinase and troponin levels), New York Heart Association (NYHA) score, arrhythmia, and previous CABG and PCI; and 4) preoperative homodynamic status: number of defective coronary vessels, left main disease \geq 50%, and LVEF. The operative data included type of surgery (elective or emergency), the number of distal anastomoses with vein grafts, the use of internal mammary artery (IMA) as grafts, and the use of IABP.

We considered four criteria for a complicated postoperative short-term outcome: 1) in-hospital postoperative complications including at least one of these: cardiac complications (heart block, cardiac arrest, tamponade, and atrial fibrillation) and non-cardiac complications (brain stroke, transient ischemic attack, renal

failure, urinary tract infection, pulmonary emboli, pneumonia, acute limb ischemia, multi-system failure, continuous coma \geq 24 hours, and prolonged ventilation \geq 10 hours); 2) prolonged LOS in ICU before and after surgery; 3) prolonged hospital stay before and after operation; and 4) 30-day mortality rate (sometimes termed operative mortality) defined as death within 30 days of operation.^[12]

Results were reported as mean \pm standard deviation (SD) for quantitative variables and percentages for categorical variables. The groups were compared using the student's t-test for continuous variables and the chi-square test or Fisher's exact test if required for categorical variables. The analysis of covariance (ANCOVA) was used as the multivariate analysis for the evaluation of differences in LOS between the study and the control groups in the presence of possible confounding factors. Predictors exhibiting a statistically significant relationship with 30-day mortality and prolonged LOS in the univariate analysis (*P* value equal or less than 0.15) were taken for a multivariate logistic regression analysis to investigate their independence. Odds ratios (OR) and 95% confidence intervals (CI) for OR were calculated. Model discrimination was measured using the c statistics, which is equal to the area under the ROC (Receiver Operating Characteristic) curve. Model calibration was estimated using the Hosmer-Lemeshow (HL) goodness-of-fit statistic (higher *P* values imply that the model fits the observed data better). The data analyzer was anonymous, and data collection and processing were approved by the institutional review board of our heart center. *P* values of 0.05 or less were considered statistically significant. All the

statistical analyses were performed using SPSS version 13 (SPSS Inc., Chicago, IL, USA) and SAS version 9.1 for Windows (SAS Institute Inc., Cary, NC, USA).

RESULTS

The two groups were similar with respect to mean age (*P* = 0.247) [Table 1]. There were no significant differences between the two groups in terms of family history of CAD and hypertension. Among the risk factors, hypercholesterolemia (*P* < 0.001) and obesity (*P* < 0.001) were more prevalent in the patients with EF > 30, whereas other risk factors were more frequent in the patients with severe left ventricular dysfunction. According to the medical management, within 24 hours preceding surgery, some drugs such as digitalis, diuretics, and ACE-inhibitors were administered more in low EF group prior to surgery, whereas nitrates and beta-blockers were used more in another group [Table 1]. There was a significant difference in the number of defective vessels between the two groups, so that three-vessel disease was found more common in patients with severe left ventricular dysfunction (*P* < 0.001). Both arterial and venous grafts were similar in the two groups [Table 2]. Emergency CABG was more frequent in the patients with severe left ventricular dysfunction (*P* = 0.005). Furthermore, IABP was significantly used more in patients with EF less than 30% (*P* < 0.001). According to the echocardiographic findings, no significant differences were found in the left atrial and left ventricular diameters between the two groups; however, except for tricuspid valve insufficiency that was more frequent in the group with higher EF, other valvular pathological changes were

Table 1: Preoperative characteristics in patients with EF* ≤ 30% and EF > 30% undergoing CABG†

Characteristics	Group with EF > 30 (n=10881)	Group with EF ≤ 30 (n= 833)	P value
Male gender	74.3	85.7	<0.001
Age (year)	58.52±9.62	58.12±9.33	0.247
Body mass index (kg/m ²)	27.18±3.97	26.53±3.71	<0.001
Obesity	21.7	16.0	<0.001
Current cigarette smoking	38.7	47.4	<0.001
Family history of CAD‡	35.7	33.8	0.280
Diabetes mellitus	31.3	34.8	0.035
Hypercholesterolemia	67.1	58.4	<0.001
Last creatinine (µmol/l)	1.16±0.29	1.24±0.32	<0.001
Renal failure	1.6	2.4	<0.001
Hypertension	52.7	50.4	0.211
Cerebrovascular disease	6.5	9.5	0.001
Peripheral vascular disease	1.7	2.7	0.049
Previous myocardial infarction	36.8	67.9	<0.001
Congestive heart failure	10.8	31.0	<0.001
NYHA§ score	2.00±0.77	2.50±0.94	<0.001
Arrhythmia	2.3	5.8	<0.001
Ejection fraction (%)	50.51±8.12	27.59±3.84	<0.001
Previous CABG	0.1	0.1	0.999
Previous PTCA¶	3.9	2.4	0.028
Previous stenting	1.0	0.4	0.064
Left main disease (>50%)	9.2	10.1	0.382
Single-vessel disease	5.0	3.2	
Two-vessel disease	21.7	17.3	<0.001
Three-vessel disease	73.3	79.5	
Medical management:			
Digitals	3.0	27.3	<0.001
Diuretics	6.9	21.8	<0.001
ACE inhibitors	39.5	61.0	<0.001
Beta blockers	86.0	76.7	<0.001
Anti-coagulants	20.9	22.6	0.237
Nitrates	85.2	80.0	0.001

Data are presented as percentages or mean ± SD, †Ejection fraction, ‡Coronary artery bypass grafting, §Coronary artery disease, ¶New York heart association, ¶Percutaneous trans coronary angioplasty

found higher in the group with lower EF [Table 3]. Rates of complete revascularization were similar between the group with lower EF and another group (84.4% vs. 85.7%, $P = 0.342$).

Clinical outcomes and postoperative complications are detailed in Table 4. Prolonged ventilation (>10 hours), cardiac arrest, heart

Table 2: Operative characteristics in patients with EF* ≤ 30% and EF > 30% undergoing CABG†

Characteristics	Group with EF > 30 (n=10881)	Group with EF ≤ 30 (n= 833)	P value
Emergency CABG	12.5	15.9	0.005
Minimally invasive CABG	2.3	1.6	0.180
Cardiopulmonary bypass	97.7	98.4	0.180
Intra-aortic balloon pump insertion	1.9	8.4	<0.001
Perfusion time (min)	70.33±23.88	77.04±26.57	<0.001
Cross-clamp time (min)	42.18±14.36	45.12±14.57	<0.001
Anastomoses with venous grafts	98.0	98.4	0.431
IMA‡ used as graft	98.6	98.2	0.343
Radial artery used as graft	89.6	88.0	0.151

Data are presented as percentages or mean ± SD, †Ejection fraction, ‡Coronary artery bypass grafting, §IMA, Intra mammary artery

Table 3: Echocardiographic findings in patients with EF* ≤ 30% and EF > 30% undergoing CABG†

Indices	Group with EF ≤ 30 (n= 833)	Group with EF > 30 (n= 10881)	P value
Left ventricle end systolic diameter (mm)	46.1±8.9	34.2±7.6	<0.001
Left ventricular end diastolic diameter (mm)	57.7±9.3	49.5±7.0	<0.001
Left atrial diameter (mm)	37.9±6.9	37.6±6.3	0.291
Wall motion abnormality	18.0	19.5	0.330
Left ventricular hypertrophy	7.9	10.3	0.027
Aorta stenosis	45.0	32.8	<0.001
Aorta insufficiency	48.7	37.6	<0.001
Mitral stenosis	45.0	32.8	<0.001
Mitral insufficiency	60.4	53.0	<0.001
Tricuspid stenosis	45.6	32.2	<0.001
Tricuspid insufficiency	49.9	61.7	<0.001

Data are presented as percentages or mean ± SD, †Ejection fraction, ‡Coronary artery bypass grafting

block, and renal failure were more prevalent in the severe left ventricular dysfunction group; however, there were no statistically significant differences between the two groups in terms of other postoperative complications. The thirty-day mortality rate ($P = 0.009$), length of stay

Table 4: Early postoperative outcomes in patients with EF* ≤ 30% and EF > 30% undergoing CABG†

Characteristics	Group with EF > 30 (n= 10881)	Group with EF ≤ 30 (n= 833)	P value
Re-intubation	1.1	1.6	0.213
Continuous coma	0.2	0.2	0.697
Prolonged ventilation (≥ 10 hours)	1.9	3.3	0.006
Cardiac arrest	0.6	2.4	<0.001
Heart block	0.4	1.3	0.001
Atrial fibrillation	5.9	6.4	0.559
Urinary tract infection	0.1	0.1	0.522
Renal failure	0.7	1.7	0.002
Brain stroke	0.3	0.7	0.119
Pneumonia	0.2	0.4	0.222
Pulmonary emboli	0.4	0.1	0.370
30 days mortality	0.7	1.6	0.009
Mean of LOS‡/day	7.62±4.63	8.84±7.49	<0.001
Mean of ICU stay/hour	40.30±36.11	50.96±48.29	<0.001
LOS > 12 days	7.1	11.5	<0.001
ICU§ stay > 72 hours	10.4	19.3	<0.001

Data are presented as percentages or mean ± SD, †Ejection fraction, ‡Coronary artery bypass grafting, §Length of stay in hospital, §Intensive care unit

in ICU ($P < 0.001$) and in hospital, before and after surgery, ($P < 0.001$) were also higher in the severe ventricular dysfunction group.

Covariance analysis also showed that the LOS was longer in lower EF group ($P < 0.001$). Furthermore, multivariate logistic regression analysis revealed that the early mortality rate was slightly higher in this group ($P = 0.075$).

Multivariate logistic regression analysis showed

Table 5: Factors influencing 30-day mortality in patients with EF* ≤ 30% undergoing CABG†

Variables	Univariate analysis				Multivariate analysis			
	Odds	95% confidence lower	Upper	P value	Odds	95% confidence lower	Upper	P value
Cigarette smoking	0.365	0.098	1.358	0.118	0.216	0.041	1.131	0.070
Cerebrovascular disease	2.925	0.788	10.858	0.118	6.949	1.395	34.629	0.018
Congestive heart failure	7.683	2.096	28.159	0.001	5.259	1.200	22.864	0.027
Arrhythmia	5.113	1.359	19.233	0.035	4.855	0.692	34.045	0.112
Left main disease	2.730	0.736	10.125	0.136	2.000	0.303	13.197	0.472
Peripheral vascular disease	7.980	1.641	38.808	0.038	18.875	2.482	143.523	0.004
IABP‡	19.561	6.213	61.590	<0.001	9.819	2.287	42.151	0.002
Perfusion time	1.017	1.002	1.033	0.029	1.011	0.991	1.031	0.291

*Ejection fraction, †Coronary artery bypass grafting, ‡Intra-Aortic Balloon Pump, Hosmer - Lemeshow goodness of fit test, $\chi^2=11.0745$, df= 8, $P=0.1975$ Area under the ROC curve, c=0.86737

that in patients with severe left ventricular dysfunction, the use of IABP ($P = 0.002$), congestive heart failure ($P = 0.027$), peripheral vascular disease ($P = 0.004$), and history of cerebrovascular disease ($P = 0.018$) were related to the 30-day mortality rate [Table 5]. In addition, prolonged length of stay in hospital in these patients was related to IABP ($P = 0.009$), hypertension ($P = 0.040$), and the increase of age ($P < 0.001$) [Table 6].

Early complications in patients with and without IABP application are summarized in Table 7. All studied complications were numerically more common in IABP application group; however, urinary tract infection, prolonged ventilation, renal failure, mortality, and prolonged LOS were statistically more frequent in this group.

DISCUSSION

The role of IABP application is well known as a death related risk factor in patients who undergo CABG.^[13] However, mortality, morbidity, and long-term prognosis of patients with low LVEF who underwent concomitant CABG and IABP were not as optimistic as those of patients with normal cardiac function and the assessment of outcome of these

Table 6: Factors influencing the prolonged length of stay in hospital in patients with EF* ≤ 30% undergoing CABG†

Variables	Univariate analysis				Multivariate analysis			
	Odds	95% confidence lower	Upper	P value	Odds	95% confidence lower	Upper	P value
Female gender	1.962	1.164	3.305	0.010	1.615	0.910	2.866	0.101
Diabetes mellitus	1.852	1.201	2.855	0.005	1.352	0.842	2.171	0.212
Hypertension	2.063	1.315	3.236	0.001	1.646	1.022	2.650	0.040
Congestive heart failure	1.491	0.959	2.320	0.075	1.368	0.855	2.189	0.191
Peripheral vascular disease	2.346	0.845	6.513	0.096	1.632	0.553	4.815	0.375
Emergency surgery	1.572	0.930	2.655	0.089	1.210	0.686	2.135	0.510
IABP‡	3.319	1.864	5.911	<0.001	2.462	1.246	4.868	0.009
Age	1.054	1.029	1.080	<0.001	1.049	1.022	1.077	<0.001
Perfusion time	1.012	1.005	1.020	0.001	1.007	0.999	1.016	0.081

*Ejection fraction, †Coronary artery bypass grafting, ‡Intra-Aortic Balloon Pump,

Hosmer - Lemeshow goodness of fit test, $\chi^2= 5.8230$, df= 8, $P=0.6670$, Area under the ROC curve, $c=0.71173$ **Table 7: In-hospital complications in groups with and without Intra-aortic balloon pump application among patients with EF* ≤ 30% undergoing CABG†**

Characteristics	No IABP group (n = 763)	IABP‡ group (n = 70)	P value
Prolonged ventilation (≥ 10 hours)	1.6	22.1	<0.001
Heart block	1.2	1.5	0.827
Atrial fibrillation	5.9	10.3	0.146
Urinary tract infection	0.1	1.5	0.016
Renal failure	1.5	5.9	0.009
Brain stroke	0.5	1.5	0.293
Pneumonia	0.3	1.5	0.128
30-day mortality	0.7	13.2	<0.001
LOS§ > 12 days	61.4	80.6	<0.001

*Ejection fraction, †Coronary artery bypass grafting,

‡Intra-Aortic Balloon Pump, §Length of stay in hospital

patients in variant population is necessary. In our study, however, perioperative mortality was 1.6% in patients with EF ≤ 30%, which was significantly higher than that in patients with greater EF, and this mortality was strongly influenced by IABP application. Similarly, in a study by Aksnes *et al.*, insertion of IABP was a strong predictor of death for patients in need of IABP support in the course of cardiac surgery.^[14] Arafa *et al.* found a mortality rate of 52.6% in patients undergoing cardiac operations who required the use of an IABP and confirmed that the early mortality rate in patients who received an IABP was high.^[15] Although the beneficial effects of IABP treatment in high-risk

patients who have coronary artery bypass grafting have been shown,^[16-18] determination of the main factors that can influence the IABP-associated mortality in low EF patients is recommended. In the present study, prolonged LOS was observed even more in patients with IABP application. It can be related to the higher occurrence of postoperative in-hospital complications, which need to be managed and removed before discharge in this group.

In the present study, no difference in 30-day mortality between the two genders was found. Similarly, in the Argenziano study, no relation was found between 30-day mortality and gender,^[19] whereas in the Wang studies, the female gender was a main predictor of mortality.^[14] Some of the suggested contributing factors in women are advanced age, advanced disease, comorbidities, and smaller body surface area.^[20] Also, in both Argenziano^[19] and our studies, advanced age was not a risk factor for mortality, but this relation was seen in other studies.^[20,21]

In our study, congestive heart failure was a strong risk factor for 30-day mortality in

patients with left ventricular dysfunction. In the Argenziano *et al.* study, mortality was significantly higher in patients with preoperative symptomatic heart failure.^[19] Patients with severe congestive heart failure have been previously shown to have four times the mortality rate after bypass compared to patients with better ventricular performance.^[22] Improvements in the ejection fraction may have a beneficial effect on survival, and this is likely to be greatest in patients with severe left ventricular dysfunction.^[23,24]

In our study, female gender was an important predictor for prolonged length of stay in hospital and this result was also found in the Borzak study.^[25] In several studies, female sex is reported to be an independent predictor of length of stay in hospital.^[26-28] It seems that the most common causes of prolonged length of stay in hospital in females are higher incidence of preoperative risk factors and postoperative complications of CABG in female than male.^[29] Therefore, it is important to control these risk factors in female patients before operation.

In the present study, only 8.4% of patients in the low ejection fraction group were on IABP. We believed that the surgeons have different indications about IABP insertion and it seems that the use of IABP is dependent on the surgeons' perception. Also, because of the shorter perfusion time and cross-clamp time in our research in comparison with other previous reports in Iran^[30] and other countries,^[31-33] our data about the frequency of IABP insertion could be lower than the other reports.

CONCLUSION

Low ejection fraction can positively affect

thirty-day mortality and prolonged LOS and ICU stay in patients who undergo CABG. One of the most important predictors of the 30-day mortality rate and prolonged LOS was IABP insertion. Furthermore, IABP application can increase early postoperative complications.

Although left ventricular dysfunction is itself an important risk factor in patients undergoing CABG, the early outcome of CABG in patients with left ventricular dysfunction is acceptable and the management of this factor will help to reduce the mortality and total length of stay in hospital.

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