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Coronary Artery Bypass Grafting in Patients With Low Ejection Fraction

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- *Background*—Patients with low ejection fraction (EF) are at a higher risk for postoperative complications and mortality. Our objective was to assess the effect of low EF on clinical outcomes after coronary artery bypass grafting (CABG). *Methods and Results*—We analyzed 55,515 patients from New York State database who underwent CABG between 1997 and 1999. Patients were stratified into 1 of the 4 EF groups: Group I (EF≤20%), Group II (EF 21% to 30%),
- Group III (EF 31% to 40%), and Group IV (EF>40%). History of previous myocardial infarction, renal failure, and congestive heart failure were higher in patients with low EF (all P < 0.001). Group I experienced a higher incidence of postoperative respiratory failure (10.1% versus 2.9%), renal failure (2.5% versus 0.6%), and sepsis (2.5% versus 0.6%) compared with Group IV. In-hospital mortality was significantly higher in Group I (6.5% versus 1.4%; P < 0.001). Multivariate analysis showed hepatic failure [odds ratio (OR), 11.2], renal failure (OR, 4.1), previous myocardial infarction (OR, 3.4), reoperation (OR, 3.4), emergent procedures (OR, 3.2), female gender (OR, 1.7), congestive heart failure (OR, 1.6), and age (OR, 1.04) as independent predictors of in-hospital mortality in the low EF group. The discharges to home rate were significantly lower in Group I versus Group IV (73.1% and 87.7%, respectively; P < 0.001).
- *Conclusions*—Patients with low EF are sicker at baseline and have >4 times higher mortality than patients with high EF. However, outcomes are improving over time and are superior to historical data. Therefore, CABG remains a viable option in selected patients with low EF. (*Circulation.* 2005;112[suppl I]:I-344–I-350.)

Key Words: bypass ■ contractility ■ coronary disease ■ epidemiology ■ surgery

espite improvements in medical therapies and surgi-cal techniques, the management of patients with coronary artery disease (CAD) and low ejection fraction (EF) is still challenging. Current treatment options for this cohort include intensive medical therapy, surgical revascularization, ventricular remodeling, and heart transplantation. Medical treatment alone is problematic because of limited long-term survival.¹⁻⁵ Heart transplantation offers excellent results with a 65.6% 5-year survival rate; however, the scarcity of donor organs makes this option impractical for a majority of patients.⁶ Coronary artery bypass grafting (CABG) has shown to be superior to medical therapy alone for low EF patients, demonstrating significant clinical improvement and long-term survival.1-5 For this population, CABG is associated with higher postoperative morbidity and mortality compared with patients with normal left ventricular function.3,7 However, previous reports have been limited by inadequate sample sizes. This study reviews a large, mandatory statewide database to evaluate the risk factors and outcomes of CABG patients with poor left ventricular function.

Methods

Patient Population

The New York State cardiac surgery database, a mandatory registry for all adult patients who underwent cardiac surgery in the state of New York, was obtained for the years 1997 to 1999, which were the last years available for review at the time of this study. The data used for these analyses are collected as part of the New York State Department of Health Cardiac Surgery Reporting System, which is overseen by the New York State Department of Health Bureau of Hospital and Primary Care Services, Cardiac Services Program. We included 55,515 patients undergoing CABG who were discharged between January 1, 1997, and December 31, 1999, in the study and stratified them into 1 of the 4 EF groups: Group I (EF≤20%), Group II (EF 21% to 30%), Group III (EF 31% to 40%), and Group IV (EF>40%) (Figure 1). Only patients who underwent CABG as the sole procedure were included. Patients who underwent combined CABG and valvular or congenital heart procedures were excluded from the review.

Demographics and Risk Factors

Demographic and preoperative variables included age, gender, race, body mass index, Canadian Cardiovascular Society angina classification, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, renal failure on dialysis, hepatic failure, previous

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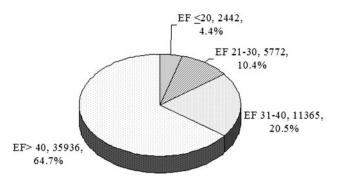


Figure 1. Number of patients undergoing CABG in New York State from 1997 to 1999.

myocardial infarction, smoking history, carotid disease, aortoiliac disease, and femoral-popliteal arterial disease, preoperative intraaortic balloon pump (IABP) use, coronary vessel disease distribution, and percutaneous transluminal coronary angioplasty history. The operative factors evaluated were priority of surgery (elective, urgent, or emergent), off-pump technique, minimally invasive approach, ischemic time, and cardiopulmonary bypass time. Postoperative outcome variables included incidence of stroke, sepsis or endocarditis, reoperation for bleeding, gastrointestinal bleeding, renal failure, respiratory failure, total hospital length of stay, in-hospital death, and early mortality (\leq 30 days). Discharge placement locations included home, acute care facilities, skilled nursing home, hospice, and other facilities.

Preoperative Assessment of EF

EF was measured using left ventricular angiography (76.2%), TEE including intraoperative (16.7%), echocardiogram (5.5%), radionuclide studies (1.0%), and other (0.1%). Remaining cases were unknown (0.5%) (Figure 2).

Statistical Analysis

Data were examined univariately by the ANOVA test for continuous variables, and the χ^2 analysis was used for discrete data. Variables with P < 0.25 were entered into a logistic regression analysis for multivariable analysis.^{8,9} This multiple regression analysis examined dichotomous outcomes, such as early mortality versus no early mortality, and their potential associated risk factors by using a linearized function of a set of covariates. The interpretation of a risk factor allowed into the final model with P < 0.05 is that it is an independent risk factors included in the event, over and above other potential risk factors included in the equation. Data were analyzed using SPSS 11.5 (SPSS).

Results

Baseline Characteristics

The preoperative characteristics of patients within the EF groups are represented in Table 1. In comparison with higher

EF groups, the frequency of men and minorities was significantly higher in Group I. Low EF patients had lower body mass index and higher incidence of COPD, dialysisdependent renal failure, renal insufficiency with high creatinine (>2.5 mg/dL), and peripheral vascular disease. In comparison with patients with high EF, a history of remote myocardial infarction and IABP use were also higher in patients with low EF. Both previous history of congestive heart failure (CHF) and presence of CHF at the time of admission were higher in the low EF groups. Each of the differences between the groups was found to be statistically significant (P<0.001). Coronary artery vessel disease distribution within the 2 groups showed that frequencies of severe left main trunk (LMT), proximal left anterior descending artery (LAD), mid/distal LAD, right coronary artery, or posterior descending artery and left circumflex artery stenoses were significantly higher in Group I ($P \le 0.001$) (Table 2).

Operative Details

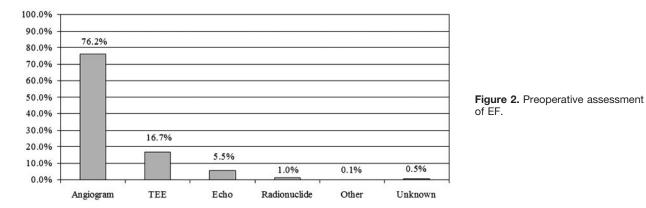
There was a higher frequency of urgent (65.4%, 63.8%, 61.4%, and 55.7% for Groups I, II, III, and IV, respectively), as well as emergent (11.7%, 8.6%, 6.3%, and 5.4% for Groups I, II, III, and IV, respectively) operations, and off-pump CABG technique was performed more often in patients in the low EF group (12.1%, 11.3%, 11.5%, and 10.7%, for Groups I, II, III, and IV, respectively). Those procedures performed using CPB showed cardiopulmonary bypass time to be significantly higher in Group I compared with the high EF groups (Table 3).

Postoperative Complications

The incidences of postoperative stroke, sepsis or endocarditis, deep sternal wound infection, bleeding requiring reoperation, gastrointestinal bleeding, renal failure, and respiratory failure were significantly higher in low EF patients. The requirement of IABP and left ventricular assist device during or after surgery were also significantly higher in patients with low EF (Table 4). Hospital length of stay was significantly longer for patients with low EF (15.9 \pm 17.9, 14.3 \pm 17.2, 12.0 \pm 12.6, and 10.0 \pm 10.6 for Groups I, II, III, and IV, respectively; *P*<0.001).

Discharge Status and Mortality

Discharge-to-home rate was significantly lower in patients with low EF (73.1%, 77.5%, 82.3%, and 87.7% for Groups I,



Variable	EF≤20%	EF 21% to 30%	EF 31% to 40%	EF>40%	P Value
Age (years)	$66.2 {\pm} 10.8$	66.9±10.5	66.7±10.6	$65.6{\pm}10.5$	< 0.001
Female gender	21.8%	25.9%	27.4%	30.1%	< 0.001
Race					
White	85.0%	87.7%	88.7%	90.3%	< 0.001
Black	7.6%	6.3%	5.5%	4.8%	< 0.001
Other	7.4%	6.0%	5.8%	4.9%	< 0.001
BMI (kg/m ²)	$27.0{\pm}5.0$	27.8±5.0	28.1 ± 5.1	$28.3{\pm}5.0$	< 0.001
Diabetes mellitus	40.7%	40.3%	34.0%	27.3%	< 0.001
Hypertension	69.4%	72.1%	72.5%	72.9%	0.002
COPD	21.6%	20.5%	16.7%	14.6%	< 0.001
Renal failure (Cr>2.5)	5.0%	4.3%	3.1%	1.4%	< 0.001
Renal failure on dialysis	2.2%	2.2%	1.4%	0.9%	< 0.001
Hepatic failure	0.4%	0.1%	0.1%	0.1%	< 0.001
Pre-op IABP	23.1%	12.0%	6.5%	3.6%	< 0.001
PTCA at admission	1.4%	1.5%	1.3%	1.3%	0.756
Prior PTCA	12.7%	12.1%	14.6%	15.3%	< 0.001
Smoking past 2 weeks	18.4%	17.3%	16.6%	15.3%	< 0.001
Smoking past year	9.5%	8.3%	7.3%	6.5%	< 0.001
CCS angina class					
I	6.5%	6.1%	6.5%	6.5%	0.755
II	5.0%	6.5%	7.7%	11.2%	< 0.001
III	31.7%	35.4%	39.3%	42.8%	< 0.001
IV	56.8%	52.0%	46.5%	39.5%	< 0.001
Previous MI					
<6 hours	2.8%	1.5%	1.0%	0.5%	< 0.001
6-23 hours	1.6%	1.5%	1.1%	0.6%	< 0.001
>24 hours	78.6%	77.7%	68.6%	43.7%	< 0.001
Previous heart operations					
1	6.9%	7.2%	6.7%	5.0%	< 0.001
2	0.7%	0.6%	0.5%	0.3%	< 0.001
≥3	0.0%	0.1%	<0.1%	<0.1%	0.002
CHF this admission	45.2%	29.3%	15.1%	6.3%	< 0.001
CHF before	23.8%	18.3%	10.1%	4.6%	< 0.001
Carotid disease	15.3%	15.3%	14.8%	14.1%	0.023
Aorta-iliac disease	7.8%	6.7%	5.8%	4.3%	< 0.001
Femoral-popliteal disease	15.6%	13.1%	10.2%	7.4%	< 0.001

TABLE 1. Baseline Characteristics of Patients Undergoing CABG

BMI indicates body mass index; COPD, chronic obstructive pulmonary disease; Cr, creatinine; PTCA, percutaneous transluminal coronary angioplasty; CCS, Canadian Cardiovascular Society angina classification; MI, myocardial infarction.

II, III, and IV, respectively; P < 0.001), whereas discharges to acute care facilities, skilled nursing homes, and other facilities were significantly higher (Table 5). Low-EF patients had significantly higher in-hospital mortality (6.5%, 4.1%, 2.7%, and 1.4% for Groups I, II, III, and IV, respectively; P < 0.001) after surgery (Figure 3).

Multivariate Analysis of Low-EF Subgroup

Significant independent predictors of in-hospital mortality in patients with $EF \le 20\%$ included older age, female gender, renal failure on dialysis, hepatic failure, CHF at admission, emergent operation, previous myocardial infarction <6 hours, and previous open heart operation (Table 6).

Discussion

Patients with CAD and advanced ventricular dysfunction have poor prognoses with medical treatment alone despite recent advances. The Coronary Artery Surgery Study (CASS) study demonstrated that only 38% of medically treated patients (EF <35%) were alive and free of moderate or severe limitations 5 years after the onset of treatment.¹ Surgical approaches to CAD patients with low EF include CABG, ventricular remodeling, and cardiac transplantation. Luciani et al¹⁰ reported an 82% 5-year actuarial posttransplant survival rate in patients with ischemic heart disease and a left ventricular EF <0.30. However, organ shortages remain a

Diseased Vessel	EF≤20%	EF 21% to 30%	EF 31% to 40%	EF>40%	P Value
LMT					
None	72.6%	75.8%	77.4%	75.2%	< 0.001
50–69%	7.5%	8.9%	9.0%	10.2%	< 0.001
70–89%	10.3%	8.0%	8.1%	9.4%	< 0.001
90–100%	9.6%	7.3%	5.5%	5.2%	< 0.001
Proximal LAD or major diagonal					
None	17.0%	18.3%	18.5%	21.0%	< 0.001
50-69%	3.6%	4.3%	4.9%	7.0%	< 0.001
70–100%	79.4%	77.4%	76.6%	72.0%	< 0.001
Mid- or distal-LAD or major diagona	l				
None	41.7%	44.1%	43.3%	46.4%	< 0.001
50-69%	3.4%	3.4%	4.0%	5.5%	< 0.001
70–100%	54.9%	52.5%	52.7%	48.1%	< 0.001
RCA or PDA					
None	8.8%	9.9%	11.8%	17.6%	< 0.001
50-69%	3.0%	4.2%	4.4%	6.5%	< 0.001
70–100%	88.2%	85.9%	83.8%	75.9%	< 0.001
LCX or larger marginal					
None	12.7%	13.6%	16.6%	22.9%	< 0.001
50-69%	3.7%	4.9%	5.1%	6.7%	< 0.001
70–100%	83.6%	81.5%	78.3%	70.4%	< 0.001

TABLE 2. Coronary Vessel Disease Distribution

LMT indicates left main trunk; LAD, left anterior descending; RCA, right coronary artery; PDA, posterior descending artery; LCX, left circumflex.

long-standing problem, and only a small proportion of CAD patients with low EF can benefit from cardiac transplantation.¹¹ Studies evaluating ventricular reconstruction are currently underway, and this option may become an attractive alternative treatment in the near future.^{12,13}

CABG in low-EF CAD patients has been reported to be superior to medical therapy by several authors. Alderman et al¹ showed that patients with an EF \leq 35% who were treated with medical management had a 43% 5-year survival rate compared with a 63% 5-year survival in the surgically treated patients. Passamani et al⁵ followed a group of CABG patients with an EF <50% for 7 years and showed that 84% of the surgically treated patients were alive at 7 years, whereas only 70% of medically treated patients were alive. Furthermore, in a study by Di Carli et al,⁴ there was a significant decrease in anginal symptoms after CABG treatment compared with medically treated patients in which no significant change was observed. Although CABG provides superior benefits in survival and quality of life over medical therapy, outcomes of low-EF patients after surgery have been shown to be considerably worse than high-EF patients.

This study has shown that low-EF patients had a higher incidence of preoperative comorbid conditions. Regardless, low EF has been shown previously to be an independent predictor of higher operative mortality.^{14,15} Similarly, in this review from the New York State database, the early mortality of patients with EF \leq 20% has been found to be >4 times higher than patients with EF>40% (4.6% versus 1.0%). However, the observed 4.6% early mortality rate is lower than those reported in many major studies of isolated CABG in patients with low EF. Di Carli et al⁴ reported 9.3% 30-day perioperative mortality in patients with EF <40%. Christakis

Variables	EF≤20%	EF 21% to 30%	EF 31% to 40%	EF>40%	P Value
Surgical priority					
Elective	22.9%	27.6%	32.3%	38.9%	< 0.001
Urgent	65.4%	63.8%	61.4%	55.7%	< 0.001
Emergent	11.7%	8.6%	6.3%	5.4%	< 0.001
Off-pump surgery	12.1%	11.3%	11.5%	10.7%	0.017
Ischemic time (min)	54.8±31.7	56.2±31.1	54.6±32.1	55.1 ± 30.8	0.017
CPB time (min)	88.7 ± 48.4	87.8±47.3	84.0 ± 46.9	83.4±45.1	< 0.001
Minimally invasive	2.5%	2.4%	2.9%	3.2%	0.002

TABLE 3. Operative Details

CPB indicates cardiopulmonary bypass.

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Complication	EF≤20%	EF 21% to 30%	EF 31% to 40%	EF>40%	P Value
No major complications	79.1%	84.5%	87.7%	91.0%	< 0.001
Stroke	2.8%	2.4%	2.4%	1.7%	< 0.001
Transmural MI	0.5%	0.4%	0.7%	0.8%	0.002
Nontransmural MI*	1.5%	0.7%	1.7%	1.2%	0.012
Deep sternal wound infection	1.4%	1.2%	1.1%	0.9%	0.010
Bleeding requiring reoperation	2.9%	2.4%	2.6%	2.0%	< 0.001
Sepsis or endocarditis	2.5%	1.4%	1.0%	0.6%	< 0.001
GI bleeding, perforation, or infarction	1.7%	1.4%	1.1%	0.7%	< 0.001
Renal failure (dialysis)	2.5%	1.5%	1.2%	0.6%	< 0.001
Respiratory failure	10.1%	7.0%	4.7%	2.9%	< 0.001
IABP insertion during or after surgery*	8.4%	5.3%	2.7%	1.6%	< 0.001
LVAD insertion during or after surgery*	0.7%	0.2%	0.0%	0.1%	< 0.001

TABLE 4.	Postoperative	Complications
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MI indicates myocardial infarction; GI, gastrointestinal; LVAD, left ventricular assist device.

*Data were only available for the year 1997.

et al⁷ demonstrated a 9.8% operative mortality rate in patients with EF <20%, and Carr et al¹⁶ have shown an 11% perioperative death rate in patients with EF between 10% and 20%. More recently, 4% in-hospital mortality rate has been reported in patients with EF <30% .¹⁷ These mortality rates decline over time, showing a clear improvement from the double-digit rates reported before 1990. We believe that improvements in cardiac anesthesia, surgical technique, extracorporeal perfusion, perioperative care, and postoperative management have contributed significantly to more encouraging outcomes.

In this review, 87.7% of patients with EF>40% were discharged to home, whereas only 73.1% of the EF \leq 20% group were successfully discharged to home. Discharge to acute care facilities and nursing homes was found to be higher for patients with low EF. The in-hospital mortality rate was 6.5% for patients with an EF \leq 20% and 1.4% for patients with an EF \geq 40%. The mean total hospital length of stay was 15.9 days for the low-EF patients (EF \leq 20%) compared with 10.0 days for the high-EF (EF>40%) group. Alderman et al¹ observed a mean duration of postoperative hospitalization of 12 days in patients with poor left ventricular function after surgery.

Case selection has been shown to be an important factor in achieving favorable outcomes after CABG in CAD patients

with low EF. Evaluation of myocardial viability has been performed as a preoperative workup in these patients. Di Carli et al⁴ showed that patients with EF <40% and viable myocardium evidenced by a positron emission tomographic (PET) mismatch, who were treated surgically, had a higher 4-year survival rate compared with those patients who received medical therapy alone (75% to 30%; P=0.007). In patients with EF <40% who did not have demonstrable viable myocardium by PET scan, a trend toward improvement in 4-year survival (100% versus 60%; P=0.085) was observed only in the subgroup of patients with severe angina. No survival advantage (63% versus 52%; P=0.462) was found in patients with minimal or absent anginal symptoms.⁴

Patients undergoing CABG with impaired left ventricular function constitute a distinctive group of patients, and factors that contribute to mortality rates may not be similar to the traditional risk factors for all of the patients undergoing CABG. Christakis et al⁷ found urgency of operation as the sole independent predictor of operative mortality in patients with EF <20% undergoing CABG. Islamoglu et al¹⁸ reported age >70 years as the only independent predictor of hospital mortality in patients undergoing CABG with EF <20%. Hausmann et al¹⁹ reported increased left ventricular end diastolic pressures, decreased cardiac index, and New York Heart Association (NYHA) Class IV as univariate predictors

TABLE 5.	Discharge	Status
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Variables	EF≤20%	EF 21% to 30%	EF 31% to 40%	EF>40%	P Value
Discharge status					
Home	73.1%	77.5%	82.3%	87.7%	< 0.001
Acute care facility	11.9%	10.6%	8.4%	6.0%	< 0.001
Nursing home	3.6%	2.3%	2.0%	1.3%	< 0.001
Hospice	0.0%	<0.1%	<0.1%	<0.1%	0.765
Other	4.9%	5.5%	4.6%	3.6%	< 0.001
In-hospital mortality	6.5%	4.1%	2.7%	1.4%	< 0.001
Early mortality	4.6%	2.8%	1.9%	1.0%	< 0.001

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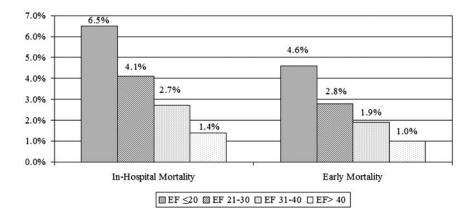


Figure 3. Mortality rates in patients undergoing CABG in New York State from 1997 to 1999.

of operative mortality for patients with EF 10% to 30%.19 Argenziano et al²⁰ found reoperative CABG and CHF as predictors of perioperative mortality in 897 patients with EF <36%. Previous reports have been limited because of relatively small sample sizes. This review, using multivariate logistic regression analysis, found increased age, female gender, hepatic failure, renal failure, presence of CHF, emergent procedure, myocardial infarction <6 hours before the operation, and previous open heart operation to be significant predictors of in-hospital mortality in patients with $EF \leq 20\%$. These findings suggest that preoperative hepatic insufficiency in patients with low EF should be managed before carrying on elective CABG surgery. Furthermore, alternative medical or intervention treatment options might be considered in low EF patients presenting with acute myocardial infarction.

In our review, respiratory failure, IABP insertion, renal failure, sepsis, and gastrointestinal complications were observed more often in the low-EF group. Bouchart et al¹⁵ also observed increased respiratory, renal, and cardiac complications in the low-EF group. Islamoglu et al¹⁸ showed age and NYHA class to predict an increased incidence of postoperative morbidities.

Limitations of this Study

To our knowledge, this review is the first large study to evaluate outcomes in patients with low EF undergoing CABG surgery. However, there are several limitations of this study. First, clinical outcomes are restricted to postoperative morbidity, in-hospital mortality, and discharge location, with data lacking beyond these end points. There is no information on late mortality, survival, or quality of life. Although the data are audited, the New York State Department of Health believes complications to be underreported. Furthermore, postoperative EFs are also not available in New York State Cardiac Surgery Data Registry. Therefore, it was not possible to calculate the left ventricular functional improvement attributed to coronary revascularization. However, previous studies yielded very encouraging trends for surgically treated patients. Bouchart et al¹⁵ and Mickleborough et al²¹ reported 70±4% and 72% 5-year survival rates, respectively. Isbir et al²² have demonstrated a 73% 4-year survival rate after CABG in patients with EF <30%. Significant improvements in EF have been observed by almost every researcher attempting to study this subject. In a study by Bouchart et al,¹⁵ EF improved from 22.2% to 33.5% (P<0.001), along with a drop in the mean end diastolic volume index (98 to 83 mL/m²) after surgery. Carr et al¹⁶ measured the EF at different time points postoperatively starting from 1 month to 11 years and found a significant improvement in the EF at all of the time points. Elefteriades et al²³ observed a 36% change from the baseline values of the EF from 24.6% to 33.2% postoperatively.

In conclusion, CABG can be safely performed in low-EF patients with minimal postoperative morbidity and mortality in addition to encouraging home discharge rates. Preoperative evaluation of myocardial viability in this group of patients using PET scanning or dobutamine echocardiography might

TABLE 6. Independent Predictors of In-Hospital Mortality in Patients With FF < 20%

WILLI EF <20%					
Risk Factor	Variable Estimate	SE	P Value	OR	95% CI
Age	0.039	0.009	< 0.001	1.040*	1.021-1.059
Female gender	0.546	0.185	0.003	1.726	1.201-2.482
Renal failure on dialysis	1.417	0.426	0.001	4.125	1.788–9.513
Hepatic failure	2.416	0.688	0.001	11.203	2.907–43.175
CHF, this admission	0.488	0.196	0.013	1.629	1.110-2.390
Emergent operation	1.165	0.341	0.001	3.207	1.645-6.251
Previous MI $<$ 6 hours	1.221	0.349	< 0.001	3.392	1.713–6.717
Reoperation	1.215	0.248	< 0.001	3.369	2.071-5.481

Hosmer-Lemeshow goodness-of-fit test: P=0.586; MI indicates myocardial infarction. *OR for every 1 year increase in age.

additionally improve outcomes of this surgical approach. Low-EF patients could greatly benefit with respect to increased postoperative EF, increased long-term survival, improvement in NYHA classification, and higher quality of life. Strong predictors of worse outcomes, including renal failure on dialysis, hepatic failure, CHF at admission, and advanced age might be considered in patient selection for surgical approach.

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